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Kidney Disease and Sars-coV-2 Infection
Challenges and Considerations for Nursing

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KEYWORDS
• Kidney disease • COVID-19 infection • Treatment challenges
• Infection control measures • Acute kidney injury • Kidney transplant
• Sars-coV-2 infection

KEY POINTS
• The COVID-19 pandemic has significantly affected the morbidity and mortality of patients with kidney disease worldwide.
• The challenges encountered during the COVID-19 pandemic have presented valuable lessons learned for future pandemics, other public health emergencies, and disasters.
• The COVID-19 pandemic has further exposed the need for more nurses to be knowledgeable about the care of kidney disease.
• Nursing leaders are needed to identify innovative methods for educating the nursing workforce that is specialized in nephrology care.

INTRODUCTION

The novel Coronavirus Disease (COVID-19) was declared a pandemic by the World Health Organization on March 11, 2020. A national emergency was declared in the United States concerning the COVID-19 outbreak on March 13, 2020. The COVID-19 pandemic has significantly affected the morbidity and mortality of patients with kidney disease across the spectrum of disease worldwide. Sars-coV-2 infection has been linked to the development of acute kidney injury (AKI) and worsening of underlying kidney function. The long-term sequelae of sars-coV-2 infection and kidney disease remain to be seen. Before the COVID-19 pandemic, approximately 15% of the population in the United States had kidney disease with 1 in 3 adults at risk for developing the disease. According to the National Kidney Foundation (2021), approximately 90% of individuals with kidney disease are unaware of their disease status. A lack of
awareness leads to poor health outcomes due to missed opportunities for treatment and preventative efforts. There is concern that there will be an increase in the number of individuals affected with kidney disease because of the long-term effects of sars-coV-2 infection.

The COVID-19 pandemic presented many challenges for nurses in the hospital and outpatient settings. Nurses in the hospital setting provided care to many individuals with kidney disease and sars-coV-2 infection. According to the United States Renal Data System (2021), out of 302,128 Medicare recipients with end-stage renal disease (ESRD) receiving dialysis treatments, 47,860 individuals were diagnosed with COVID-19 by the end of December 2020. The cumulative incidence of COVID-19 diagnosis during that same period was 15.8% with 14% in white individuals, 16.6% in black individuals, and 18.7% in individuals of other races/ethnicities. Almost 8% of Medicare recipients with chronic kidney disease (CKD) were diagnosed with COVID-19 by the end of 2020. More than 9% of Medicare recipients with a kidney transplant were diagnosed with COVID-19 by the end of December 2020. Among outpatient dialysis clinics more than 20% of patients had contracted sars-coV-2 infection by the end of 2020. Overall, the rates of hospitalization for Medicare recipients with CKD were 3 times higher than recipients without CKD. At the highest, the hospitalization rates for individuals with ESRD receiving dialysis ranged from 4 to 6 admissions per 1000. The hospitalization rate among individuals with kidney transplant ranged from 0.6 to 3.2 admissions per 1000. The significance of nursing’s interaction with individuals with kidney disease should not be underestimated. Nurses provided care to individuals infected with the sars-coV-2 infection and kidney disease across multiple settings. Each nursing encounter with individual patients and their families is an opportunity to increase awareness of disease status and to assist preventative efforts to reduce the prevalence of kidney disease and improve the overall population health.

Nurses who are knowledgeable regarding the care of individuals with kidney disease are vitally important to improving health outcomes. As seen during the COVID-19 pandemic, nurses are extremely important for the delivery of quality health care. A shortage of more than 900,000 nurses is anticipated by the year 2030. Nephrology nurses require specialized training, and the shortage of nephrology nurses trained to provide dialysis has been ongoing for more than a decade. The number of individuals receiving dialysis has been steadily rising for more than 20 years. Since 2009, there has been a 91% increase in the number of individuals that receive in-center hemodialysis. Because the number of individuals receiving dialysis increases, the need for nurses trained in dialysis also increases. The nursing shortage has been affecting nephrology nursing for many years. Since 2004, 5% to 7% of outpatient dialysis nursing positions have remained unfilled and does not account for variability in location, and inpatient or transplant clinic positions that are available. Nephrology nursing shortages have had a significant impact on the delivery of care to individuals with requiring dialysis treatments due to the sars-coV-2 infection. During the initial stages of the pandemic, the need for dialysis treatments in the hospital for individuals acutely ill with sars-coV-2 infection rapidly overwhelmed available resources including dialysis nurses, machines, and supplies for acute dialysis treatments and continuous renal replacement therapy (CRRT). Boyle and colleagues (2022) reported the number of bedside hemodialysis treatments tripled and patient days for continuous renal replacement (CRRT) doubled. Nurses and other clinic staff were at a heightened risk for contracting infection due to recurrent and prolonged exposure that led to staffing shortages due to illness. The ongoing shortage of trained dialysis nurses, the significant increase in the number of dialysis nurses needed to deliver the
overwhelming number of acute dialysis treatments and staff the outpatient dialysis clinics, and the significant number of dialysis nurses that contracted the sars-coV-2 infection created a scheduling nightmare that ultimately pushed dialysis nurses to the limit, requiring superpower strength for survival. The COVID-19 pandemic has further exposed the extensive need for more nurses to be knowledgeable about infectious disease and the care of kidney disease. It was evident that nurses require specialized training to administer dialysis.

Background

The COVID-19 pandemic has been linked to the development of AKI, collapsing glomerulopathy, acute tubular necrosis (ATN), progression of CKD, and higher rates of infection among patients with ESRD and kidney transplant. In the United States, AKI occurred more frequently in patients with underlying CKD (57%) before sars-co-V-2 infection than those without a history of CKD (28%).

The incidence of AKI related to sars-coV-2 infection was variable and was reported from 20% to 57% of hospitalized patients depending on the study.

Higher rates of AKI have been noted in the United States when compared with other countries and have been attributed to higher rates of comorbid diseases such as diabetes mellitus, CKD, and hypertension in the United States.

However, the presence of comorbid diseases alone does not account for all cases of AKI. Moledina and colleagues (2021) demonstrated that COVID-19 is highly associated with AKI even after adjustment for the presence of comorbid conditions, demographic data, current medications, and laboratory results (n = 2600 patients). Variable definitions of AKI have also been a contributing factor to the variability in reported incidence rates. In a retrospective observational study conducted by Chan and colleagues (2021), out of almost 4000 hospitalized patients with sars-coV-2 infection, 46% developed AKI with 19% requiring dialysis and 35% of patients did not regain kidney function at the time of discharge. AKI is an independent risk factor for mortality in COVID-19 patients. Poorer health outcomes and increased rates of mortality have been linked to sars-coV-2 infection among patients with AKI and/or kidney disease.

The exact pathophysiology of kidney failure in COVID-19 is unclear. Multiple mechanisms can contribute to the development of AKI related to sars-coV-2 infection. Immune system overaction, complement activation, release of cytokines, angiotensin II overactivation, and other inflammatory markers can lead to organ dysfunction, hypotension, acute heart failure, and cardiomyopathy due to cardiorenal syndrome. The development of a hypercoagulable state can also occur. Prerenal causes include azotemia related to intravascular volume depletion, and ATN due to hypotension, and shock. Sepsis can trigger multiple pathophysiologic mechanisms contributing to the development of AKI. The utilization of multiple commonly used medications such as antibiotics, nonsteroidal anti-inflammatory medications, antivirals, and others can cause acute interstitial nephritis. Endothelial dysfunction leads to the development of a hypercoagulable state, leading to ischemia and infarction within the kidneys, other organs, and the vasculature. Direct invasion of the kidney by the sars-coV-2 infection can lead to the development of several glomerulopathies.

Histologic findings of sars-coV-2 infection include ATN most commonly, glomerulosclerosis, myoglobin cast nephropathy, thrombotic microangiopathy, crescentic glomerulonephritis, and cortical necrosis. Initial postmortem autopsy results identified diffuse proximal tubular necrosis from ischemia or the presence of sars-coV-2 infection of the epithelial cells in the kidney. The study conducted by Hessler and colleagues (2021) evaluated kidney biopsies of living and deceased patients for the presence of viral protein by immunohistology, immunofluorescence, viral RNA by
in situ hybridization, or viral RNA polymerase chair reaction (PCR) testing and found that 43% of patients had sars-coV-2 infection present. Subsequent studies have detected sars-coV-2 RNA with viral replication occurring in the tubular epithelial cells of the kidneys in 73% of patients with sars-coV-2 infection and AKI.\textsuperscript{13} Urine testing for sars-coV-2 RNA has also been conducted and was present less frequently in the urine (8%) when compared with blood (21%) and stool (40%) when compared in a meta-analysis of 30 studies.\textsuperscript{9} Some theorize that the alteration or dysregulation of the immune system is related to uremic syndrome in patients with ESRD or due to the effects of immunosuppressive medications after transplantation and is attributed to the variability noted in susceptibility, course, and severity of illness, and subsequently outcomes.\textsuperscript{14,15}

The prevalence of sars-coV-2 infection among patients with CKD in the United States varies depending on the study with rates ranging from 3.5% to 48%.\textsuperscript{8} A large cohort study conducted by Pakhchanian and colleagues (2021) concluded that the presence of CKD is an independent risk factor for severe sars-coV-2 infection. A patient’s risk heightens with the presence of additional comorbid conditions. Patients with CKD stage 3 and sars-coV-2 infection have a higher risk for requiring renal replacement therapy.\textsuperscript{13} An observational, retrospective study (n = 3905) was conducted by Kharti and colleagues (2021) and evaluated the health outcomes of individuals with sars-coV-2 infection and CKD or ESRD, and without CKD. Mortality rates were higher for individuals with kidney disease. Early in the COVID-19 pandemic, the overall rate of mortality for individuals with CKD was 34% and 27% for individuals with ESRD requiring dialysis.\textsuperscript{7} The overall mortality for individuals without kidney disease was 24%.\textsuperscript{7} The highest rate of mortality was among individuals with sars-coV-2 infection and CKD.\textsuperscript{7}

Renal transplant patients have been one of the populations most vulnerable to sars-coV-2 infection. The number of kidney transplants performed from 2020 (n = 22,817) to 2021 (n = 24,670) increased 8.14%.\textsuperscript{16} In this pandemic era, management of induction and maintenance immunosuppression has been challenging to clinicians treating kidney transplant patients. COVID-19 has had a significant influence on wait-listed patients, elucidating the need to properly balance the risks and benefits of transplantation in the setting of an ongoing pandemic.

CHALLENGES ENCOUNTERED

There have been multiple challenges experienced during the COVID-19 pandemic with lessons learned for future pandemics, public health emergencies, or disasters. Unclear messaging regarding the COVID-19 from public health officials created challenges for health-care providers and patients resulting in the lack of preparedness and timely response due to the uncertainty of the virus. Diagnostic, treatment, logistical, and preventive challenges were identified during the delivery of care to patients with kidney disease during the COVID-19 pandemic. Gaps in planning efforts were identified that led to challenges affecting the availability of staff, infection control measures, and allocation of resources.

Clinical Presentation

Clinical presentation depends on organ involvement, severity of disease, and individual patient factors. The clinical presentation of sars-coV-2 infection in individuals with kidney disease presented unique challenges. The classic symptoms of sars-coV-2 infection reported from the general population included fever, cough, lack of taste, and/or smell. Early studies demonstrated that the clinical presentation of sars-coV-2
infection in patients with ESRD receiving dialysis was atypical and varied from the general population. Individuals with ESRD and the early stage of sars-coV-2 infection presented with symptoms commonly associated with uremia such as fatigue and anorexia making the diagnosis of COVID-19 challenging. Respiratory symptoms, fever, and lymphadenopathy were experienced less frequently among individuals with ESRD and sars-coV-2 infection. The lack of fever and cough in the ESRD population raised questions regarding the generalizability of the data from the general population. The atypical response may reflect an altered immune response and ability to mount the characteristic cytokine storm. Although the ESRD population often experiences less symptoms at the onset of the disease, the clinical course of the disease was frequently characterized by more severity of disease, higher rates of bilateral lung fields affected, complications such as shock, acute respiratory distress syndrome, myocardial infarction, arrhythmias, and death than the general population (14% vs 4%) demonstrating the need for an increased vigilance. It is imperative that nurses are aware of the potential atypical presentations of sars-coV-2 infection in individuals with kidney disease for an early identification and treatment.

Treatment Challenges

A patient with sars-coV-2 infection was at a 130% increased risk for the development of AKI during the pandemic compared with prepandemic. Treatment of AKI in hemodynamically unstable patients includes supportive therapy and the use of CRRT. Anger and colleagues (2021) studied the demand for CRRT equipment and supplies during the pandemic comparing pre-pandemic use from a manufacturer’s perspective. The use of CRRT increased 370% with a shortage of 1088 CRRT machines within the first 6 months of the pandemic. By the peak of the pandemic, the number of CRRT machines used increased by 279%. The demand for dialysis fluids also increased significantly causing an increased need for production and approval of an emergency use order, which permitted the use of fluids imported from other countries. Some hospitals were forced to produce their own fluids due to the shortage. To increase production at the manufacturing company, protocols to ensure the safety of the employees had to be developed. Manufacturing had to be increased and protocols reevaluated to streamline distribution. Training of the employees and troubleshooting services for the nurses had to be converted to a virtual environment, which increased staff training by 300%. Important lessons learned include continued maintenance of emergency preparedness plans is essential to ensure the continuity of operations; refurbished machines can be held in reserve to use if needed; inventory and patient census should be closely monitored; and an inventory management system to include tracking should be developed or improved.

Infection Control Measures

Controlling the spread of sars-coV-2 infection in the dialysis facilities presented a multitude of unique challenges further challenging current infection control measures. The primary focus of prior infection control efforts included suppressing the transmission of blood-borne infections. Transmission of a highly contagious airborne disease that caused a worldwide pandemic was not anticipated. Because the COVID-19 pandemic evolved, additional logistical challenges emerged. Individuals with ESRD and receiving hemodialysis as well as the clinic staff were unable to comply with the stay-at-home orders during the COVID-19 pandemic, which contributed to a higher risk for contracting the sars-coV-2 infection due to repeated and prolonged exposure. In some instances, the infection spread among the patients and the clinic’s staff causing clustering of cases. To reduce the cluster outbreaks and the rapid
respiratory transmission of the sars-coV-2 infection, dialysis facilities implemented universal respiratory precautions such as screening for symptoms and temperature screenings on entry into the facilities, masking during treatment, additional handwashing, and distancing to reduce the spread. The number of provider rounds conducted in person was limited and visits transitioned to a virtual telehealth format. The number of patients receiving treatment during a shift was also limited to assist with reducing exposure. Limiting the number of patients per shift may extend the number of hours that the nurses and clinic staff worked, which could lead to exhaustion and burnout.

Most dialysis units are designed with patients seated more than 6 feet apart, which has been a benefit for complying with the social distancing requirements. Depending on the method of transportation that the patient utilized, social distancing may have been difficult to maintain during transportation. Each dialysis clinic has at least one isolation room that may be available for isolating patients with suspected sars-coV-2 infection as needed. However, the need for isolation quickly exceeded the availability, leading to the need for designated COVID-19 units or shifts to be created. Logistical challenges were encountered with the creation of the designated COVID-19 units or shifts. Ideally, a dialysis clinic is close to a patient’s home. Transportation to the clinic is usually by the patient, family, friends, or a hired service. The parish or county that a patient resides in often offers public transportation services for medical visits. The location of the designated COVID-19 units presented unique transportation challenges especially if travel across parish lines was required and often created access barriers. Public transportation services for medical visits do not offer travel across parish lines.

Because COVID-19 testing efforts expanded, there were many patients that tested positive for sars-coV-2 infection but were asymptomatic, which created complex decisions about the most appropriate isolation method for these individuals. According to a study conducted by Kharti and colleagues (2021), approximately 32% of all COVID-19 cases in the outpatient dialysis clinics were asymptomatic. Prevalence rates were variable among units depending on the comorbid conditions, age, and other vulnerabilities of the population. Evidence is currently lacking regarding the asymptomatic transmission among vulnerable individuals. Additional questions surrounded when an individual could safely return to the dialysis clinic following recovery from sars-coV-2 infection and no longer transmit the virus to others in the clinic. Until formalized guidance was developed, decisions were determined on a case-by-case basis. Because the COVID-19 pandemic continued to unfold, The Centers for Disease Control (CDC) and Prevention (2021) developed recommendations that included 2 negative test results within a 24-hour period, the onset of symptoms was more than 14 days ago, and that the patient was afebrile for more than 72 hours. Another challenge encountered included patients that persistently tested positive but were asymptomatic. The CDC determined that patients who are asymptomatic could no longer transmit the virus after 10 days. For patients who are immunocompromised or have severe disease, the recommendation is 20 days before returning to the clinic. Additional research is needed to identify how long an asymptomatic patient receiving dialysis can transmit live virus after recovering from sars-coV-2 infection. Many argue that individuals with ESRD and receiving dialysis should be considered immunocompromised, which further complicates the decision of whether 10 or 20 days is most appropriate. Thus, more research is needed.

Supply Chain Problems

The COVID-19 pandemic caused immense disruption to the dialysis equipment supply chain. Similar to the limited number of ventilators during the initial surge of sars-
coV-2 cases, dialysis machines, other dialysis-related equipment, personnel, and personal protective gear were also in short supply. When the demand for treatment exceeds the supply of personnel and equipment necessary to administer dialysis, providers are called on for complex ethical decision-making. With the COVID-19 pandemic, patients with AKI requiring dialysis were admitted to the intensive care units overwhelming the current system and allocation of resources.\textsuperscript{18} The preparation for pandemics or other large-scale disasters should be part of disaster planning and include efforts addressing dialysis needs. Allocation of resources should include consideration of surge capacity, outpatient and inpatient dialysis needs for future pandemic and/or disaster needs. Distribution of resources should be adequate and ethical. The medical community has often placed the focus on optimizing the aggregate benefit. Carson and colleagues (2021) in Canada proposed an ethical framework for the allocation of dialysis services to reduce distress associated with decision-making and to optimize decision-making utilizing the framework. The ethical principles utilized to create this framework include maximizing benefits, equitable treatment of individuals, prioritizing the individuals who are more severe, and procedural justice.\textsuperscript{18}

**Vaccination**

Kidney disease also affects the effectiveness of vaccination. Several barriers have been identified. Initial drug trials often exclude individuals with kidney disease, thus there are limited data available regarding vaccine effectiveness. Because kidney function declines, an individual’s response to a vaccination is altered.\textsuperscript{19–24} Hepatitis B and Influenza A vaccines have been studied to identify alternative strategies for improving responsiveness to vaccines for individuals with kidney disease.\textsuperscript{19} The COVID-19 vaccinations developed also excluded individuals on dialysis, limiting the data available regarding humoral and cellular response among the dialysis population.\textsuperscript{19} Before the study conducted by Speer and colleagues\textsuperscript{19} (2021), varying results of seroconversion were noted in smaller studies. Methods to ensure success of vaccination for individuals with kidney disease and at a higher risk for contracting sars-coV-2 infection are crucial. Additionally, vaccination protocols may require different protocols depending on degree of kidney function. Speers and colleagues, (2021) conducted a prospective, single center study, which was one of the earliest studies evaluating the humoral response of individuals receiving dialysis after vaccination with the BioNTech 162b2 mRNA vaccine. Individuals receiving dialysis (n = 22) were compared with healthy individuals without CKD (n = 46). Antibody levels were measured before enrollment and following vaccinations. Antigen rapid tests for sars-coV-2 infection were performed before each dialysis treatment. Individuals that contracted the disease were excluded. IgG levels were also monitored. Due to the difference in age among the dialysis and control groups, a subanalysis was performed. Speers and colleagues (2021) identified that individuals on dialysis developed significantly less sars-coV-2 anti-S1 IgG antibodies following the first and second COVID-19 vaccination compared with the age-matched healthy individuals. The results obtained by Speers and colleagues (2021) were consistent with prior studies examining the immune response of individuals receiving the influenza A and Hepatitis B vaccines in the presence of kidney disease. Individuals receiving dialysis are a high-risk group for sars-coV-2 infection. The findings by Speer and colleagues\textsuperscript{19} (2021) indicate that the first COVID-19 vaccination dose may not provide adequate coverage. Additional research is needed to evaluate the response and effectiveness of vaccinations for individuals receiving dialysis.
NURSING IMPLICATIONS

The challenges encountered during the COVID-19 pandemic have presented valuable lessons learned for future pandemics, other public health emergencies, and disasters. Emergent disease such as COVID-19 created crisis in the health-care system and challenged existing roles. Organizational priorities and staff responsibilities shifted. Nursing leadership is critical during health-care challenges that cause widespread disruption to the delivery of health care. The COVID-19 pandemic has further exposed the extensive need for more nurses to be knowledgeable about the care of kidney disease and receive the specialized training required to administer dialysis effectively. The significant increase in the need for dialysis nursing services also reinforced the realization that the shortage of dialysis nurses needs to be addressed. The patient advocacy role of nephrology nurses is vital, allowing the nurse to assist patients in gaining a full understanding of their treatment plan and participate in decision-making. Incorporating education to increase patient awareness, methods for prevention and to reduce the progression of disease, the complications of CKD, dialysis modalities, and dialysis management into nursing education could increase interest in nephrology nursing and reduce the nursing shortages in nephrology.

Multiple areas for improvement at the institutional and systems level were unveiled. Planning efforts should include preparation for pandemics or other large-scale disasters. Targeted training, drills, and exercises should be executed to assist in preparedness for readiness to respond. Nursing’s involvement in improving health and health care for all patients at a policy level is but an extension of the advocacy work. Facility-level policies are needed to reduce the spread of an infectious disease in a congregate setting such as the dialysis facilities, universal infection control measures that address multiple routes of transmission, methods to isolate patients when test results are pending, infection control measures when delivering a dialysis treatment to a patient who is in isolation while protecting the nurse from exposure, and the increased use of personal protective equipment. Policies limiting access to health care related to medical transportation across parish/county lines during times of disaster or a pandemic need to be reevaluated and barriers eliminated. Policies at the system and facility levels to address the development of ethical, evidence-based methods for allocating resources during times when the need for resources significantly exceeds the supply. Allocation of resources should include consideration of surge capacity, outpatient and inpatient dialysis needs for future pandemic and/or disaster needs. Distribution of resources should be adequate, equitable as possible, and ethical.

The COVID-19 pandemic is occurring within a context of social and economic inequalities. Inequalities in COVID-19 infection and mortality rates are a result of inequalities in chronic diseases such as renal disease and are socially patterned and associated with the social determinants of health. Nurses can be strategic contributors to making substantive progress toward achieving health-care equity by taking on expanded roles, working in innovative ways, and partnering with communities and other sectors.

Nursing implications for research include that additional research is needed regarding the best methods for vaccination of individuals with kidney disease. The best methods for infection control in a congregate setting also require additional research.

SUMMARY

The COVID-19 pandemic disproportionately affected individuals with kidney disease causing significant morbidity and mortality worldwide. Sars-coV-2 infection has
been linked to the development of AKI and worsening of underlying kidney function. The long-term sequelae of sars-coV-2 infection and kidney disease remain to be seen. System, provider, and patient level challenges have been identified during the COVID-19 pandemic. Nurses are the largest group of health-care professionals in the United States and must be knowledgeable regarding the care of individuals with kidney disease. Nursing leaders are needed to identify innovative methods for educating the nursing workforce that is specialized in nephrology care, reduce the nephrology nursing shortage, to address the diagnostic, treatment, logistical, and preventive challenges identified, and to improve the delivery of nephrology health care.

**CLINICS CARE POINTS**

- Approximately 90% of individuals with kidney disease lack awareness of their disease status which contributes to poor health outcomes due to missed opportunities for treatment and prevention.
- Clinical Practice Guidelines for the care of individuals with kidney disease are available from the National Kidney Foundation KDOQI at https://kidney.org/professionals/guidelines and from Kidney Disease Improving Global Outcomes (KDIGO) at https://kdigo.org/guidelines/.

**DISCLOSURE**

The authors have nothing to disclose.

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