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Impact of the COVID-19 pandemic on the kidney community: lessons learned and future directions

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has disproportionately affected patients with kidney disease, amplified profound disparities in marginalized populations and posed significant challenges in the management of patients with kidney disease, kidney research and trainee education. For patients, the increased infection risk and disease severity, often complicated by acute kidney injury, contributed to high mortality. Clinicians were faced with high clinical demands, resource shortages and novel ethical dilemmas in providing patient care. In this review, we address the impact of COVID-19 on the entire spectrum of kidney care, including acute kidney injury, chronic kidney disease, dialysis and transplantation, trainee education, disparities in health care, changes in health care policies, moral distress, and the patient perspective. Based on current evidence, we provide a framework for the management and support of patients with kidney disease, infection mitigation strategies, resource allocation and support systems for the nephrology workforce.

Introduction

The COVID-19 pandemic has impacted the kidney community at multiple levels. Acute kidney injury (AKI) is a common consequence of hospitalization with COVID-19 and portends high mortality¹. The rates of severe COVID-19 have been high in patients with chronic kidney disease (CKD) including dialysis patients and kidney transplant recipients¹⁻³. There have been dilemmas surrounding the delivery of safe clinical care, triaging provision of kidney replacement therapy (KRT), the safety of donors and recipients for kidney transplantation, managing COVID-19 in patients with kidney disease, modulating immunosuppression in immune-mediated kidney disease and transplant recipients, and best ways to protect patients and health care providers during the pandemic. Despite their high risk and increased mortality and concern that CKD may alter the safety profile of drugs, patients with kidney disease were excluded from therapeutic clinical trials of COVID-19 and a lack of pre-specified subgroup analyses resulted in the application of novel therapies to this population with low evidence. Nephrologists have faced multiple challenges in patient care including nursing shortages and supply chain issues. The pandemic has raised ethically challenging questions about the allocation of scant health care resources. There has been a significant impact on trainee education and on the emotional well-being of the nephrology workforce and patients. In this review, we discuss the challenges encountered in the care of patients across the spectrum of kidney disease during the pandemic, strategies that were adopted to address them, innovations in patient care delivery and advocacy efforts. We discuss the global inequities in provision of health care and highlight how the pandemic may exacerbate preexisting disparities in kidney disease. While some lessons learned by the kidney community during the pandemic have been heartening and stimulating innovation, others have been devastating with profound effects. These experiences by the kidney community shape preparedness efforts for future pandemics. From the lessons learned thus far, we provide a framework for management of patients with kidney disease for future pandemics.

Managing kidney disease in the times of COVID-19: Challenges and opportunities

Acute kidney injury incidence throughout the pandemic

Acute kidney injury (AKI) is common in patients diagnosed with COVID-19. AKI due to COVID-19 infection is multifactorial and includes direct invasion of the virus and indirect mechanisms through acute tubular necrosis, dysregulation of the immune system, hypercoagulopathy and collapsing glomerulopathy⁴. In the early stages of the pandemic, the reported incidence of AKI ranged from 0.5 to 42%^{1,5,6}, with a large percentage of these patients requiring dialysis. Charytan and colleagues explored the changing incidence of AKI in critically ill patients with COVID-19⁶ and found that, while the overall incidence of AKI was 29.3%, the rates of AKI and KRT declined over time in the pandemic, attributable to multiple factors including improved recognition and management, vaccine rollout and transmission of less virulent strains⁷. In Africa, AKI in COVID-19 patients occurred in 33.9% of 1102 patients in a study in two teaching hospitals in South Africa. About a quarter of patients with AKI required ICU management and 8.6% received KRT⁸. There were challenges in the management of COVID-19 associated AKI in low and low-middle income countries⁹.

APOL1 and risk for COVID-19 associated AKI

In April of 2020, initial case reports described collapsing glomerulopathy in the setting of COVID-19, and a case series published soon afterwards described 6 patients with collapsing glomerulopathy each with high-risk *APOL1* genotypes¹⁰. In the largest study to date, out of 240 native kidney biopsies in patients with COVID-19, 62 (26%) had evidence of collapsing glomerulopathy¹¹. *APOL1* genotyping studies have demonstrated that patients with high-risk alleles had significantly higher odds of AKI, and death compared to low-risk patients with 0 to 1 risk variants¹². Furthermore, in African Americans who tested positive for COVID-19, *APOL1* high-risk alleles were associated with greater odds of AKI and higher rates of persistent AKI and requirement of dialysis.

Possible reasons for the higher risk of adverse kidney outcomes in individuals carrying *APOL1* high-risk alleles include a heightened inflammatory response to COVID-19, leading to inflammatory kidney injury. Thus, the incidence and severity of AKI are likely increased in the presence of *APOL1* variants, with an increased requirement for chronic dialysis.

Long-term kidney complications after acute COVID-19

Hospitalized patients with COVID-19 had a higher incidence of AKI overall, and AKI stage when compared to patients with influenza¹³. In an observational study from the UK, 16% of AKI survivors, progressed to CKD at 90 days¹⁴. Similarly, about 20% of AKI patients requiring KRT had no recovery

at 3 months after discharge in a multicenter study from the U.S.¹⁵. A Veterans administration study on Long COVID reported a higher risk of CKD with COVID-19^{16,17}. Similarly, in a Chinese cohort study, a third of COVID-19 infected patients had reduced kidney function 6 months post-hospitalization¹⁶. Patients developing AKI during their COVID-19 disease course had no increased risk of CKD at 12 months follow up when compared to non-COVID-19 AKI cases¹⁸. Further studies are needed to evaluate risk factors for progression to CKD following COVID-19-associated AKI.

Patients with chronic kidney disease

The incidence of COVID-19 in CKD patients is difficult to establish due to under-reporting, under-diagnosis of CKD, and variations in access to SARS-CoV2 testing. A large nationally representative cohort from United Kingdom demonstrated a CKD incidence and prevalence ranging from 0.5% to 37% and, that CKD is associated with high co-morbidity burden and high one-year mortality¹⁹. CKD, including end-stage kidney disease (ESKD), is associated with increased risk of COVID-19 and subsequent adverse outcomes including hospitalization, respiratory failure, and mortality^{2,20-22}, with risk proportional to kidney dysfunction^{20,22}. There have been care delivery repercussions, including the postponement of kidney biopsies²³, delays in arteriovenous fistula surgery and salvage, and disruption in initiation of KRT²⁴. There was a notable decline in incident ESKD in the U.S. early in the pandemic, both due to increased mortality in patients with advanced CKD and compromised access preparation for KRT²⁵. Large-scale lockdowns resulted in interruption of routine healthcare, including access to dialysis leading to preventable deaths, especially in those parts of the world with already compromised access to dialysis while highlighting the advantages of telemedicine in CKD patients²⁶⁻²⁸.

There is a lack of guidelines related to the management of COVID-19 in patients with CKD. Dexamethasone was associated with both reduced requirement for KRT and lower mortality in all patients with severe COVID-19, however fewer than 10% of patients in this trial had eGFR less than 30 mL/min/1.73 m²²⁹. Remdesivir, a direct-acting antiviral, remains off-label in patients with an eGFR < 30 mL/min/1.73 m²³⁰. Several monoclonal antibody therapies have been afforded emergency use authorization but their net benefit in patients with CKD remains untested. Tocilizumab, a recombinant anti-IL-6 receptor antibody was granted emergency use authorization in patients with moderate-to-severe COVID-19³¹, and case reports demonstrate successful

114 deployment in patients with ESKD. Phase III trials evaluating vaccination benefit have however
115 afforded limited focus on specific subgroups such as patients with CKD³². Patients with CKD were
116 prioritized for vaccination and mounted a comparable seroconversion rate to the general
117 population (Table 1). However, patients who did not receive a third dose of the vaccine had a
118 significant decline in antibody titer after 3 to 6 months³³.

119 **Patients with immune-mediated kidney disease**

120 Managing patients with immune-mediated glomerular disease has presented unique challenges. At
121 the start of the pandemic, the primary concerns for patients receiving immunosuppression included
122 the assessment of the risk and severity of COVID-19, ways to mitigate infection risk, methods of
123 clinical and laboratory surveillance, strategies to treat active disease and evaluation of the need for
124 continued immunosuppressive therapy. After the vaccine rollout, questions were posed regarding
125 the immunogenicity and safety of the vaccine, measurement of vaccine efficacy and need for
126 modification of immunosuppressive therapy to improve vaccine response.

127 Although immunosuppressive therapy increases the risk of infection, there was no evidence to
128 support deviation in the standard of care treatment of active disease³⁴. COVID-19 in patients with
129 immune-mediated kidney disease conferred an increased risk of AKI and death³⁵. Additionally, case
130 reports of de novo immune-mediated kidney disease, including collapsing focal and segmental
131 glomerulosclerosis, vasculitis, IgA nephropathy have been described with COVID-19 infection.
132 Among the immunosuppressive medications commonly used in this cohort, rituximab and
133 prednisone dose ≥ 10 mg were associated with increased severity of COVID-19³⁶, while information
134 on other therapies such as cyclophosphamide has remained scarce.

135 Although patients were prioritized for vaccines, understanding of the safety and immunogenicity of
136 vaccines in this cohort was based only on observational studies. Studies in patients with rheumatic
137 diseases on immunosuppressive therapy have consistently shown impaired humoral response with
138 largely preserved cellular response (Table 1). Additionally, these studies have shown that prednisone
139 dose ≥ 10 mg, mycophenolate mofetil and rituximab were associated with impaired humoral
140 response and that the response in rituximab-treated patients was improved when B cells were
141 reconstituted or time elapsed from last rituximab administration was longer³⁷. Temporary cessation
142 of mycophenolate mofetil augmented humoral response in patients with rheumatic disease³⁸. In

143 non-responders, administration of a booster vaccine dose was shown to increase the response rate.
144 *De-novo* or relapsing autoimmunity triggered by COVID-19 vaccines remain a concern and isolated
145 reports of de-novo and relapsing minimal change disease, membranous nephropathy, IgA
146 nephropathy and ANCA vasculitis have been described³⁹. However, large series with increased
147 inflammatory disease incidences have not been described following COVID-19 vaccination.

148 In the absence of guidelines, caring during a pandemic requires personalizing immunosuppressive
149 therapy balancing the risk of infection and disease control, and recognizing that treatment of active
150 disease cannot be delayed. An important lesson learned is that the early establishment of global
151 collaborative registries is critical to assessing the severity and risk factors of infection and guiding
152 modulation of immunosuppressive therapy in this population.

153 **Patients on chronic dialysis**

154 Early data from Wuhan foreshadowed the major challenges other regions would have to tackle in
155 caring for patients on dialysis during the COVID-19 pandemic. Patients on dialysis were amongst
156 those at highest risk of death, not just due to propensity for serious illness but due to missed
157 treatments. These data generated a mandate for dialysis facilities to intensify infection prevention
158 protocols to reassure patients and staff, to ultimately prevent missed sessions and loss of workforce.
159 There was a strong recommendation for transition to home modalities⁴⁰.

160 But without additional resources to match the guidance, there was a constant shortage of personal
161 protective equipment (PPE)⁴¹, and SARS-CoV-2 tests. Data from universal screening of a single
162 dialysis unit in the U.K. showed that patients experienced a spike in infection after the health care
163 workers' spike, implying potential transmission⁴². Nonetheless, widespread in-facility transmission
164 was not reported. Lack of transportation, staff shortages and possibly personal fear or symptoms
165 may have contributed to missed treatments in up to half of the surveyed facilities in Africa, Latin
166 America, Middle East, South East Asia and South Asia⁴¹. Mortality among infected and hospitalized
167 patients receiving dialysis exceeded 50% in most regions of the world. The pivot to home modalities
168 was not feasible in many already strained environments. Thus, despite early and sensible guidance
169 on infection prevention and management—a majority of which still holds relevance in face of the
170 changing nature of the pandemic—there was a stark loss of life among patients receiving dialysis⁴³.
171 With improvement in testing capacity and identification of patients with no or minimal symptoms,

172 there has been improvement in crude mortality rates between the first and second wave of COVID-
173 19 ⁴⁴.

174 The success of vaccines has been accompanied by challenges. Among countries that procured
175 vaccine supply in late 2020 or early 2021, European countries prioritized vaccination for patients
176 receiving dialysis. In the U.S., there was no specific prioritization until March 2021, at which point
177 policy makers acknowledged that patients receiving dialysis were disproportionately from
178 underserved populations and at high risk for complications from COVID-19 illness leading to a
179 federal effort to offer vaccination in dialysis clinics. This vaccine allocation in dialysis clinics improved
180 vaccines access, especially for the Hispanic and black patients ⁴⁵. Compared with the general
181 population, a smaller proportion of patients on dialysis expressed vaccine hesitancy. Capitalizing on
182 central record keeping, the U.S. Centers for Disease Control and Prevention has created a real-time
183 dashboard tracking vaccination in dialysis facilities, indicating that more than 75% of patients on
184 dialysis have had at least two doses of COVID-19 vaccines.

185 Several lines of evidence suggest that immunogenicity of vaccination is lower among patients on
186 dialysis, compared with the general population (Table 1). Although the majority of patients
187 ‘seroconverted’ post-vaccination, the strength of the early antibody response to vaccination was
188 suboptimal. Furthermore, 20% lost a detectable antibody response within 6 months. Concordant to
189 data from hepatitis B vaccination, low circulating antibody titers were associated with a 10-fold
190 higher risk for infection among patients who had completed the initial vaccination series. Data from
191 a large not-for-profit dialysis center indicated efficacy against hospitalization or death of 81%, only
192 slightly lower than contemporaneous data for the general population noting vaccine effectiveness
193 around 86-87%. Vaccine immunogenicity by vaccine type has been studied closely, and concerns
194 raised regarding the lack of immunogenicity of Ad26.COV2.S, although clinical effectiveness of this
195 vaccine may be similar to the mRNA platform vaccines⁴⁶. Furthermore, there was no difference in
196 vaccine response by vaccine type among home dialysis versus in-center patients ⁴⁷.

197 Boosters (third doses for persons with mRNA platform vaccines) have seen lower uptake among
198 patients on dialysis in the US, with roughly 50% of patients reporting an additional dose thus far.
199 Again, there was a heterogeneous policy implementation, with countries in Europe implementing

earlier offers of third doses among patients on dialysis. Data from France and the U.S. on immunogenicity are encouraging, with strong responses reported even among older patient groups. In this landscape, given the uncertainty around persistent immunogenicity to COVID-19 vaccines and substantial risk for ‘breakthrough’ infection—a majority of which will have some clinical consequences for patients receiving dialysis, at the very least a need for isolation during incenter dialysis—it will be critical to continue to develop future protocols for prevention, detection, and early treatment of COVID-19.

Lessons for Policymakers

Policymakers have important lessons to learn from the COVID-19 pandemic that are specific to the dialysis population²⁷. Below, we outline key lessons learned from the US.

First, policymakers should strongly consider extending waivers to exempt providers from pre-existing value-based purchasing programs, including the Quality Incentive Program⁴⁸ and the End-stage Renal Disease Treatment Choices model⁴⁹. These programs have laudable goals but might pose a distraction for dialysis facilities that need to remain nimble during a public health emergency. To its credit, the Centers for Medicare and Medicaid Services (CMS) rapidly implemented waivers early in the pandemic, allowing facilities to focus on the emergency⁵⁰.

Second, we address the risk that in-center dialysis poses for patients, particularly with airborne diseases. Early in the pandemic, providers rightly recognized that facilities could quickly become hubs for widespread infection⁵¹. One welcome addition was the broad expansion of telehealth benefits⁵². However, the beginning of the COVID-19 pandemic was also fraught because of strapped supply chains that exacerbated the already limited supply of PPE. American Society of Nephrology (ASN), European Renal Association (ERA) and International Society of Nephrology (ISN) issued calls for governments around the world to prioritise PPE for dialysis personnel and increasing access to lifesaving dialysis. To prepare for the next pandemic, not only should policymakers stockpile more emergency medical equipment, they should also be more aggressive in distributing these supplies to providers of vulnerable populations, including dialysis facilities. A major concern is ongoing shortages in dialysis supplies, including dialysate.

227 Third, we must customize policies to address the specific needs of the dialysis population. For
228 instance, per CMS guidance, many hospitals deferred “nonessential” surgical procedures. However,
229 these deferrals may have inadvertently harmed incident ESKD patients who needed dialysis access
230 procedures ²⁵.

231 New therapeutics that can treat COVID-19 have shown incredible promise in reducing
232 hospitalizations and mortality^{53,54}. Dialysis facilities are unique in the healthcare industry because
233 patients must return to the facility regularly. In the future, dialysis facilities should be considered a
234 major site for the distribution of new therapeutics and vaccines.

235

236 **Kidney transplant recipients**

237 The pandemic has created significant challenges for kidney transplantation. Transplant candidates
238 and recipients, especially in the early post-transplant period, experienced significant excess
239 mortality related to COVID-19, with a disproportionate impact on racial minorities and
240 socioeconomically disadvantaged individuals^{55,56}. Both the innate and adaptive immune systems
241 seemed profoundly altered in the transplanted cohort, with significantly lower levels of anti-spike
242 antibodies up to two months following the onset of COVID-19 symptoms compared to patients on
243 dialysis ⁵⁷. The prime concerns centered around continuing kidney transplant surgeries, minimizing
244 the risk of infection and management of post-transplant immunosuppression. Globally, living and
245 deceased donor transplantation has been adversely impacted to various extents and at different
246 periods of time, due to efforts to conserve resources during a surge and concern for the risk of newly
247 immunocompromised individuals, particularly in periods of high community transmission given
248 their increased risk and poor outcomes ³. Mortality rate was 20 to 30% in kidney transplant
249 recipients, with reduction in mortality during the second wave ⁴⁴, . While there was a 16% global
250 decrease in transplant activity most notable in the first 3 months of the pandemic, there were
251 substantial differences in transplant activity between the countries⁵⁸. Whilst living donation came to
252 a near complete stop during the early pandemic, it has resumed since but does not appear to have
253 reached pre-pandemic levels ⁵⁹. Notably, deceased donor transplantation rates have continued to
254 increase in the U.S. allocation system despite a dramatic increase in organ discards reflecting
255 increased selectivity of organs and patients⁶⁰. There are notable differences in mortality rates of

waitlisted individuals compared to transplant recipients, with the United States reporting a higher mortality in waitlisted individuals, and Europe and United Kingdom reporting higher mortality in transplant recipients. The decision to continue transplant during a pandemic needs to be individualized for each country and should take into consideration the mortality risk of waitlisted individuals and transplant recipients and infection risk in the immediate post-transplant period. The pandemic has also impacted transplant activity due to concern for donor derived viral transmission. A systematic review of 69 transplants from 57 donors infected with SARS-CoV-2 demonstrated that non-lung transplantation was safe with a low risk of transmission ⁶¹.

Efforts to lower the risk of transmission along with overwhelmed healthcare systems created significant challenges in the care of these patients. Healthcare systems pivoted quickly to telehealth strategies and there was increased interest in the use of non-invasive biomarkers when performing kidney biopsies became a challenge⁶²⁻⁶⁴. While the value of monitoring strategies for allograft health remains uncertain, there does not appear to have been a dramatic uptick in acute rejection episodes⁶⁵.

The mainstay of treatment for COVID-19 in transplant recipients included reduction or cessation of antimetabolite therapy for 2 weeks or longer in addition to standard adjuvant therapies used in the general population⁶⁶. While this approach also contributed to early concerns about adverse allograft consequences, recent data suggests that brief cessation of therapy was not associated with the development of donor-specific antibodies (DSA). Additional concerns in the SARS-CoV-2 infected recipient include the abrupt increase in tacrolimus levels that has been observed at the time of presentation ⁶⁷. Immunosuppressed individuals also appear to have a prolonged high viral burden with persistent positive polymerase chain reaction (PCR) results which may have implications for when to allow patients with prior COVID-19 back in to the transplant clinic setting.

While immunosuppressed patients and those with kidney disease were excluded from the initial vaccine trials, significant real-world experience has been gained in these groups. Studies of immunogenicity after vaccination revealed poor humoral responses to 2 doses of both mRNA and viral vector vaccines ^{68,69}. Older age, impaired allograft function, use of triple maintenance immunosuppression, belatacept, steroids and anti-metabolite were associated with poor humoral response. Additionally, breakthrough infections were observed frequently in kidney transplant

285 recipients, even before the omicron surge. An enhanced humoral response was observed after a
286 third and fourth vaccine dose, use of heterologous vaccination and modulation of
287 immunosuppression⁷⁰⁻⁷².

288

289 **A Special Population: Kids, Kidneys and COVID-19**

290

291 **Outcomes in children with kidney disease and COVID-19**

292 Children and adolescents are a vulnerable group and subject to special considerations in health care,
293 research, and public policy. While the clinical impact of COVID-19 on pediatric patients has been less
294 profound than in adults so far, successive waves of the pandemic have led to more children being
295 directly impacted. There was an initial decrease in deceased and living donor kidney transplantation
296 in the US at the start of the pandemic, however rates of transplantation returned to pre-pandemic
297 levels by May 2020⁷³. Unlike in adults, children taking immunosuppression for kidney disease or
298 kidney transplant and children on dialysis have not had worse outcomes from COVID-19 infection
299 than the general pediatric population⁷⁴⁻⁷⁷. When sick enough to be admitted, however, 12-23% of
300 hospitalized children with COVID-19 developed AKI⁷⁸⁻⁸⁰ and AKI is more common in patients with
301 the multisystem inflammatory syndrome in children (MIS-C)⁷⁸. Consistent with other studies of AKI
302 in children, AKI was associated with increased levels of care, length of hospital stay, and worse
303 outcomes^{78,80-82}.

304

305 **Gaps in science and child health policy**

306 Gaps remain for the pediatric population compared to adults. Long-term COVID-19 outcomes will
307 be important to study, and we should be developing safe and effective strategies to incorporate
308 children in such studies. Research studying “long COVID” is lacking in children, despite evidence that
309 it is at least as common for children as adults⁸³. What’s more, while vaccination rates are much
310 lower for children than adults, we need to learn more about vaccination patterns and perceptions
311 among children with kidney disease and their caregivers⁸⁴. It will take years to understand the
312 impact of educational disruptions that affected children with CKD, who already have lower cognition
313 compared to the general population⁸⁵. Moreover, pediatric research addressing the impact of
314 pandemic disruptions on access to transplant, the early detection of kidney disease, and the impact

on family dynamics could aid in the development of more equitable and durable pediatric care delivery models and public policy.

Table 2 outlines the challenges and missed opportunities faced by the kidney community in managing patients during the pandemic.

Human consequences of the COVID-19 pandemic; psychosocial and ethical implications

The COVID-19 pandemic has necessitated a change in almost every aspect of kidney care. Healthcare resources shifted to prevent, detect and manage waves of COVID-19, leading to dramatic alterations in routine kidney care in many countries. This section highlights some of the changes instituted, and their impact on patients, caregivers and healthcare providers.

As the potential severity of COVID-19 disease became clear, international efforts were made to identify people at-risk. Many nations endorsed targeted public health measures to minimize both mortality and economic impact ^{86,87}. For example, in the U.K., a targeted national policy of “shielding” was implemented. Those considered most at-risk from COVID-19 were centrally identified using electronic records, and government letters were issued advising individuals to socially isolate themselves, restricting contact even within their household group, with the help of financial and logistical support. Many people with advanced kidney disease, kidney transplantation, and/or those requiring immunosuppressive treatment, were advised to shield ^{88,89}. Whilst these measures were broadly supported, the personal impact varied, with some feeling protected while others felt fearful and isolated ⁸⁹. In countries without such protective policies, public health messaging likely encouraged similar exposure-avoidant behaviors, particularly in at-risk groups ⁹⁰⁻⁹².

Additional strategies to minimize infection were implemented internationally, including reduced visitor access in hospitals ^{93,94} and dialysis units ⁹⁵. End-of-life care provision was dramatically altered due to the restrictions, with limitations of social contact and rituals before and after death ⁹⁶. Even with technological innovations to provide human connection, the impact of reduced physical contact between patients, caregivers and clinicians were significant. Some patients experienced loneliness and depressive symptoms, and caregivers described heightened anxiety and an increased

343 desire for information from healthcare professionals⁹⁷. Many patient and provider groups described
344 ethical compromise and psychological distress, as they felt unable to provide or receive care at pre-
345 pandemic levels^{98,99}.

346 Patient and provider groups have described adversity, fear, abandonment, hope and resilience¹⁰⁰⁻
347 ¹⁰³. A multinational mixed methods study of 251 kidney healthcare providers found nearly one-third
348 of respondents were at high risk of burnout and mental health distress during the pandemic, with
349 feelings of emotional exhaustion, depersonalization, and a reduced sense of personal
350 accomplishment¹⁰⁴.

351 Moral distress in healthcare during the COVID-19 pandemic has been extensively described and may
352 explain some of the negative psychological consequences illustrated above⁹⁹. Moral distress can
353 occur when an individual perceives they are unable to act according to their ethical values due to
354 external barriers¹⁰⁵. If individuals perceive their ethical duties are compromised in settings of severe
355 resource constraints, where institutional, health policy or financial barriers limit access to optimal
356 treatments that are clinically indicated, moral distress may occur^{106,107}. It occurs in both patients
357 and caregivers and has been described in relation to the intentional separation between loved ones
358 during end-of-life care and hospital visitation restrictions^{98,103}. The consequences of moral distress
359 include experiences of anger, guilt, depersonalization and, for healthcare professionals, a desire to
360 leave the workforce entirely¹⁰⁸. If persistent, moral distress can result in moral injury causing long-
361 term social and psychological trauma^{109,110}.

362 Children and young adults with kidney disease face unique and pervasive mental and behavioral
363 health challenges with higher rates of depression, anxiety, and neurocognitive disorders compared
364 to their peers⁸⁵. One survey reported that they felt they were missing out on work-related and
365 educational opportunities, missing family and friends, and compared to their peers, they lived with
366 more COVID-related restrictions⁸⁵. Health-related quality of life and physical activity decreased
367 significantly for both children and adolescents during the pandemic due to school closings, social
368 distancing, and home confinement¹¹¹. While these strategies are employed to reduce the viral
369 spread, their prolonged use requires assessment to mitigate the adverse psychological effects,
370 especially on vulnerable populations. Furthermore, parents and caregivers of children with kidney
371 disease experience significant psychosocial stressors that leave many families dysfunctional and

372 disempowered. During the pandemic, this often-unseen care burden has been experienced
373 disproportionately by families struggling with adverse social determinants of health and health
374 disparities. Caregivers of children with kidney disease reported feelings of stress, anxiety,
375 depression, and insomnia during the pandemic, mirroring findings in parents of children with other
376 chronic conditions^{112,113}. Children with medical complexity have lost access to therapies,
377 educational services, and peer interactions, all while parents and caregivers have taken on
378 additional responsibilities to navigate changes in employment and keeping their families healthy¹¹⁴.
379

380 **Health equity/global health perspective**

381 The COVID-19 pandemic with its rapid spread across the globe revealed that most health systems
382 were unprepared for or underestimated the challenge. Initially, the lack of readiness, and almost a
383 lack of belief that such a pandemic could occur in the current day and age, resulted in acute
384 shortages of many items needed for an effective response. Early on, the scarcity of PPE sometimes
385 resulted hoarding by countries and by individuals. This “catastrophic breakdown in global
386 cooperation”¹¹⁵ highlighted the need to develop global strategies to improve equity and access
387 equipment, treatment and vaccines to treat COVID-19 ^{115,116}. This lack of equity and empathy
388 persists, with booster doses of vaccines being administered to most adults and children in some
389 countries before adults at risk of poor outcomes even receive their first vaccine in others¹¹⁷.
390 Hoarding, pricing, protection of intellectual property and dissemination of misinformation regarding
391 vaccines have exacerbated inequities and contributed to deaths ¹¹⁸. These persistent and pervasive
392 inequities, which impact how individuals and nations have been (un)able to tackle the challenges
393 posed by the pandemic have coined a new term: “political determinants of health”¹¹⁹.

394 Political and social determinants of health exist within as well as between countries, and the same
395 populations who have experienced centuries of structural violence, e.g. African Americans and
396 indigenous populations, are those most vulnerable to COVID-19 and at most risk of poor outcomes
397 ¹²⁰⁻¹²⁶. People living with chronic diseases, and especially kidney disease, are at the highest risk¹²⁷.
398 These facts have finally raised global awareness that non-communicable diseases cannot continue
399 to be overlooked, including when looking beyond the pandemic^{128,129}. As the demand for hospital
400 beds and health care services outstripped availability at various stages, triage guidance had to be

urgently drawn up to allocate scarce intensive care unit beds, raising debates around which criteria would be morally acceptable^{130,131}. Rationing of healthcare services became a reality, faced by many for whom until now the concept had been merely theoretical¹³²⁻¹³⁵.

The nephrology community was rapidly drawn into the eye of the storm. The capacity to provide dialysis became strained in some settings, leading to complex triage algorithms and in some cases deaths even in high income countries (HICs) because of lack of access to dialysis^{135,136}. People living with kidney disease are often vulnerable at baseline, tending to have lower socio-economic status, belonging to minority populations and living with multiple co-morbidities¹³⁷.

The pandemic has had a significant global impact on health care delivery in general, with consequences being particularly evident in low and lower-middle income countries (LLMICs)⁴¹. There were gross inequities in the provision of dialysis services¹³⁸. Many guidelines were developed and disseminated for the management of patients with kidney disease, including those on dialysis, but most of these guidelines could not be adhered to because of the lack of resources in most LLMICs¹³⁹. Surveys conducted by the International Society of Nephrology (ISN) in partnership with the Dialysis Outcomes and Practice Patterns group aimed to understand how clinical practice was being impacted by the pandemic, and if and how people living with kidney disease were being prioritized across the globe^{41,140}. Challenges affecting both staff and patients were common in LLMICs. The patient level impact reported by survey respondents included challenges in accessing diagnostic testing, interruptions in hemodialysis delivery, restricted access to intensive care, mechanical ventilation, and in-hospital hemodialysis, affecting patients in LLMICS more frequently compared to upper middle-income countries (UMIC) and high-income countries (HIC). Staff in dialysis units in LLMICs had less access to COVID-19 testing, PPE (Fig 1) and training in infection control, and suffered a greater psychological impact⁴¹.

At the time of the survey, conducted during the first year of the pandemic, diagnostic tests for SARS-CoV-2 were unavailable or of limited availability with longer turnaround times for test results in the majority of low income (LIC) and lower-middle income (LMICs) countries⁴¹. Patients in LIC frequently had to pay out-of-pocket for diagnostic (PCR) testing. Due to multiple factors including lockdowns, curfews and delays awaiting COVID-19 test results, patients in LIC and LMIC missed dialysis with a greater frequency than pre-pandemic and these delays cost lives.

430 A subsequent survey focused on access to vaccination for people living with advanced kidney
431 disease. At least one COVID-19 vaccine was available in 97% of respondent countries. Over 90% of
432 the respondent countries reported prioritization of healthcare workers within the first two phases
433 of vaccine rollout, whereas patients living with stage 4/5 CKD, dialysis, or kidney transplants were
434 prioritized within the first two phases in 51%, 71%, and 62% of countries respectively. Overall, at
435 least 50% of patients receiving in-center hemodialysis, peritoneal dialysis or living with a kidney
436 transplant were reported to have completed vaccination in around half of respondent countries,
437 with the lowest rates reported in Africa and the highest rates in Western Europe. Vaccine hesitancy,
438 vaccine shortages and difficulties in mass distribution of vaccines were common and reported more
439 in LLMICs compared to HICs. Although the vaccination rate in the dialysis population may appear
440 relatively high in lower income settings, indicating that the vulnerability of this group has been
441 acknowledged globally, the global disparities echo the call by the World Health Organization for
442 more equitable access to vaccines, having set a global target of 40% of the population of every
443 country to have completed vaccination by the end of 2021 and 70% by mid-2022. Two major global
444 efforts, COVAX and ACT- Accelerator, where richer countries should contribute to supplying and
445 distributing vaccines to poorer countries, have been launched to facilitate global
446 vaccination^{115,116,141}. These schemes however, have not yet translated into action in terms of global
447 solidarity, although equity gaps may be beginning to narrow^{142,143}.

448 Children are an inherently vulnerable population which modern society has a duty to protect.
449 However, the unique social status of children places them at an equally unique risk of health
450 inequities. Current research and pharmaceutical development processes are designed to protect
451 children by studying drugs and diseases in adults first; however, the lack of timely available
452 interventions and immunizations for children including those with underlying chronic disease during
453 the pandemic has raised concern for age-based health inequity that should be reevaluated.
454 Protection of children is paramount; however, equipoise with timely availability of emerging
455 therapies and robust safety information are critical to this endeavor. At a national level, the
456 prevalence of childhood poverty, specifically its relationship to health and its disproportionality
457 across sociodemographic groups most at risk during the pandemic, highlights another important
458 pediatric kidney health risk¹¹⁴. Evidence of social deprivation along racial, ethnic, and class divisions

have been shown to have adverse consequences in both children and adults with kidney disease, but the specific effect of the pandemic on this population is yet to be studied^{144,145}.

The almost miraculous rapidity with which the scientific community tackled the COVID-19 problem has been a simultaneous triumph and a failure. The rapid development of tests, vaccines and therapeutics has been life-saving for many, but has left many behind. The early robust efforts to identify and publish potential management strategies led to great advances in clinical understanding and rapid knowledge sharing but also led to dissemination of pseudoscience and misinformation. This has severely impacted trust in health systems globally and has led to loss of life. The COVID-19 pandemic has revealed how necessary solidarity is at all levels, beginning with global governance and trickling down to the individual in the dialysis chair in a remote dialysis unit (Fig 2)^{118,146,147}. This requires attention being paid to justice and ethics at all levels. Global collaboration and cooperation are needed between countries, institutions, industry and academia. Collaborative focus on “building back better” is required such that health systems and societies emerge from the pandemic stronger, more resilient and fairer.

Trainee education

The surge of patients with COVID-19 also impacted nephrology training. Nephrology trainees have been at the front-line of care for COVID-19 patients, including in the intensive care units, dedicated COVID-19 wards, and the new era of telemedicine. While this comes with the possibility of reinvigorating interest in nephrology, it also comes with the threats of increased workload, stress, and burnout for our trainees.

Activities our nephrology trainees have typically relied on for education and career advancement have undergone significant adjustments in this era. Major conferences such as the ASN Kidney Week and the ERA meetings were held virtually with fewer opportunities for networking. Local conferences at one’s own institution were also shifted overnight to virtual formats, limiting in-person interaction with faculty, and requiring additional effort to stay engaged.

In the U.S., adult and pediatric fellows and recent graduates of nephrology training were surveyed by the ASN Workforce and Training Committee in August-September 2020 using our Annual Fellows’ Survey instrument¹⁴⁸. The impact of COVID-19 on fellows’ training experiences and wellbeing was

488 measured, yielding 425 respondents (42% response rate). The majority of current fellows (84%) felt
489 their education was maintained during the pandemic. Fellows needed to adapt to this new
490 landscape in real-time, with up to 91% reporting adoption of telemedicine and 76% remote
491 conferences. While their education was maintained overall, 42% of fellows reported a negative
492 impact of the pandemic on their overall quality of life, 33% reported a poorer work-life balance, and
493 15% scored as experiencing high distress measured using the Resident Well-Being Index. Similar
494 findings were seen for trainees in the U.K.¹⁴⁹, France and Belgium¹⁵⁰.

495 The pandemic has offered opportunities to better understand, develop, and train future
496 nephrologists. Training programs, such as those in Canada¹⁵¹, have have seized this opportunity to
497 develop personalized learning plans for postgraduate nephrology trainees. It remains to be seen
498 whether resilience of nephrology fellows will be maintained through this pandemic, and what
499 impact the pandemic will have for board certification, job prospects, and recruitment of the next
500 generation of nephrologists.

501

502 **A Patient's Voice on the COVID19 Pandemic**

503 Telehealth offered a safe way to continue medical care and conferred multiple advantages but
504 limitations exist and must be acknowledged and addressed. A scoping review identified technical
505 difficulties, digital literacy, lack of physical exam, privacy and confidentiality and loss of
506 interpersonal interaction as main barriers to telehealth (PMID: 35338610).

507 COVID-19 patient communication impacted the entire spectrum of patients with kidney disease
508 throughout the pandemic. Since the beginning of the COVID-19 pandemic, COVID-19 patient
509 communication with kidney disease patient communities has remained unclear. From a patient
510 perspective, the most impactful communications centered around use of personal protective
511 measures, risk and consequences of AKI, vaccine efficacy and update and guidance on use of COVID-
512 19 therapeutics. In the absence of direction, navigation was dependent upon the patient activation
513 skills of the individual. Town halls were conducted by the American Society of Transplantation and
514 webinars were facilitated by the American Society of Nephrology but these were accessed only by
515 patients who were part of professional patient advocacy groups.

516 Patient organizations such as the American Association of Kidney Patients, National Kidney
517 Foundation and Kidney Care UK and have attempted to address the gap in COVID-19 information.
518 While their efforts have been successful, they have reached only a small percentage of the CKD and
519 ESKD patients. A process is needed in which all patients hear directly from their care team about
520 the current guidance, and what actions they can take to avoid COVID-19.

521

522 **Future guidance**

523 The pandemic has highlighted the challenges posed by surges in hospital occupancy, forced the
524 digital transformation of many healthcare systems, underscored the need for authoritative and
525 consistent communication from local, state and federal governments and identified striking global
526 inequities in the care of patients with kidney disease. Additionally, the pandemic has highlighted the
527 importance of proactively addressing psychosocial and ethical issues to ensure patient, caregiver,
528 and clinician wellbeing. The strategies to address the challenges faced by the kidney community
529 during a pandemic is displayed in Fig 3. For obvious reasons, these strategies will differ between
530 low, lower-middle, upper-middle and high income countries and global collaboration and
531 cooperation is required at all levels to ensure equity in health care delivery for patients with kidney
532 disease.

533 **Conclusions**

534 The COVID-19 pandemic has been one of the worst infectious disease crisis in over a century and
535 given the increase in emerging diseases, pandemic threats may become a new normal. Our
536 experience within the nephrology community has been extremely challenging. Hospitalization
537 surges during the pandemic exposed fundamental weaknesses in all health care systems. While this
538 led to innovations in health care delivery and policy change, there remains an urgent need to invest
539 in resilient health care systems and develop transparent and fair triage guidelines for scarce
540 resources. The breakdown of global cooperation further exacerbated existing healthcare inequities.
541 The pandemic illustrated that building public trust in scientific recommendations is critical to
542 avoiding social and political divisions over following risk mitigation strategies. Moral distress has
543 increased and must be recognized and addressed. One in 10 people is living with kidney disease.

544 There is a need to include patients with kidney disease in clinical trials especially during pandemics
545 to accelerate access to potential therapeutics, and to invest in the establishment of global
546 collaborative disease registries to study risk factors and outcomes. Finally, we must be prepared to
547 run a leaner regulatory state during future public health emergencies. Strategic deregulation would
548 accelerate the development and distribution of new therapeutics.

549

550

551 **Key points**

1. Acute kidney injury is common in severe COVID-19 and associated with increased mortality
2. Patients with chronic kidney disease are at high risk for severe COVID-19 and severe outcomes, and should be prioritized for therapeutics including vaccines
3. Establishment of global collaborative registries is key to assessing the severity and risk factors of infection
4. Interruptions in routine care was common and highlighted the advantages of temporary implementation of telemedicine and home dialysis
5. There were gross inequities in access to COVID-19 testing, personal protective equipment, provision of dialysis services, COVID-19 vaccines and therapeutics rollout
6. To prepare for future pandemics, it is important to stock pile emergency medical equipment, invest in resilient health care systems, have global cooperation in providing care, explore and advance remote care globally, address moral distress to improve well-being of patients and care providers, build public trust in scientific recommendations and advocate for kidney patients to be included in clinical trials and global registries.

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Table 1: Important studies with a focus on vaccine response after one, two and more COVID-19 vaccine doses.

Author	Population	Primary objective	Vaccine doses	Main outcomes	Risk factors
Al Jurdi A et al. ¹⁵²	Transplant: 51	Anti-S levels/ Neutralizing antibody responses against variants of concerns	3	-Anti-S levels were higher for wild-type (WT) SARS-CoV-2 compared with the omicron variant, and similar between WT and the delta variant -The % of neutralization was lower for the omicron compared with the WT and delta variants	- Older age and steroid use: lower odds of developing neutralizing responses to WT and delta variant - Belatacept use: lower odds of developing neutralizing responses to the delta variant
Angel-Korman A et al. ¹⁵³	Dialysis: 409 COVID-19 naive controls: 148	Seroconversion rate; anti-S and neutralizing antibodies	2	Seroconversion -Anti-S: 89% (69.6 versus 196.5) Neutralizing antibodies: -77% (23.3 versus 222.7)* ¹	Dialysis: age, immunosuppression, low serum albumin, and low lymphocyte count, and time to sampling
Ashby DR et al. ¹⁵⁴	Dialysis: 1,323 COVID-19 cases	Effectiveness on the vaccine (hospitalization, death)	2	Outcome: 75% lower risk of admission 88% fewer deaths	No loss of protection in population over 65 years of age, increasing time since vaccination, and no difference between vaccine types
Benotmane I et al. ¹⁵⁵	Transplant: 77 patients	Response to 4 th dose	4	- Anti-S titers increased from 13 to 112.5 BAUs/ml - Neutralizing antibodies against the delta variant (increase from 16% to 66% after 4 th dose)	Patients with undetectable neutralizing antibodies after the 3 rd dose were less likely to have their neutralizing capacity increased after the 4 th dose
Bensouna I et al. ¹⁵⁶	Dialysis: 69	Effects of a 3 rd dose on antibody levels	3	-Anti-S: from 284 (IQR 83-1,190) increase to 7,554 (IQR 2,268-11,736) -1/3 seroconversion after 3 rd dose -1/12 "weak" responders remained below 50 AU/mL	Ratio increase of antibody titers after 3 rd dose (>43; 7.5-43; <7.5): - Low anti-S antibodies after 2 nd dose (94 versus 347 versus 1,718 AU/mL) - Interval between 2 nd and 3 rd doses (74 versus 73 versus 59 days)

					- Ratio of antibodies after 3 rd versus 2 nd dose (99.9 versus 23.0 versus 1.6)
Brunelli S et al. ⁴⁶	Dialysis: 2,572 (BNT162b2); 2,572 (Ad26.COV2.S)	SARS-CoV-2 infection within six months after vaccination	1+	- COVID-19: 75 versus 83 - Hospitalizations: 36 versus 44 - Deaths: 5 versus 3 - Seroconversion (Ad26.COV2.S): 59.4% (244 patients)	-
Charmetant X et al. ¹⁵⁷	Transplant: 873 (137 group "infected"; 736 group vaccinated)	Re-infection, infection after mRNA-1273	2 (3)	- COVID-19: No symptomatic re-infection (n=137), symptomatic COVID-19 in 20 out of 736 vaccinated	- Vaccinated and infected patients: 14% detectable anti-S antibodies, and no sample indicated neutralization - Non-responders received significantly higher doses of MMF - A third vaccine dose led to an increase in % with an antibody response and 41% developed neutralizing antibodies
Chavarot N et al. ¹⁵⁸	Transplant: 62 belatacept-treated patients	Seroconversion rate	3	- Seroconversion: 4 (6.4%) developed anti-S antibodies (with low antibody titers) - 5 patients with prior infection mounted a strong antibody response	-
Espi M et al. ¹⁵⁹	Dialysis: - 1,474 COVID-19 cases - 75 patients with a 3rd dose	Rate of infection in unvaccinated, partially and fully vaccinated patients	0-3	- Infection incidence (France): 1.98% (unvaccinated), 0.65% (1st dose), 0.25% (2nd dose) - Fatality rate: 11% (2 doses) - Patients with low/no humoral response after 2 doses experienced a significant increase in anti-S antibodies (10.5 versus 353.1 BAU/mL)	Response to a 3 rd dose more likely if presence of low titers of anti-S antibodies and spike-specific CD4+ T cell IGRA positive after 2 nd dose

Garcia P et al. ⁴⁷	Dialysis: - 2367 patients	Seroconversion rate	1-2	Fully vaccinated (day 14-28): - No response (mRNA-1273: 2.6%; BNT162b2: 4.3%; Ad26.COV2.S: 58.4%) Fully vaccinated (day 29-60): - No response (mRNA-1273: 2.0%; BNT162b2: 4.0%; Ad26.COV2.S: 33.3%)	- Patients receiving Ad26.COV2.S had a higher likelihood of no seroconversion/no detectable or diminished IgG response - Antibody positivity resulted in higher seroconversion rates, and better quantitative results
Masset C et al. ¹⁶⁰	Transplant: - 49 (non-responders after 3 vaccine doses)	Seroconversion rate	4	21 (42.8%) seroconverted after a 4 th dose; with a median titer of 82 BAU/mL (four of them had a titer considered as neutralizing)	- No statistical significance, but higher response rates when lower steroid usage, less frequent lymphopenia, longer time between 3 rd and 4 th dose and use of BNT162b2
Oliver MJ et al. ¹⁶¹	Dialysis: - 13,759 patients (2,403 unvaccinated)	SARS-CoV-2 infection, and severe outcomes (hospitalization, death)	1 or 2	1 dose: SARS-CoV-2 infection (HR 0.59); Severe outcomes (HR 0.54) 2 doses: SARS-CoV-2 infection (HR 0.31), Severe outcomes (HR 0.17)	No significant differences in vaccine effectiveness among age groups, dialysis modality, or vaccine type
Predecki M et al. ¹⁶²	Transplant: - 920 patients (previous infection in 152 (17%))	Seroconversion rate	2	- Seroconversion occurred in 269 (66%) receiving BNT162b2 (median antibody level 58 BAU/mL) - Seroconversion occurred in 156 (44%) receiving ChAdOx1-nCoV19 (median antibody level 7.1 BAU/mL) - Negative seroconversion in only 8/152 (5%) of patients with previous infection	- Tacrolimus monotherapy associated with seroconversion - Vaccination with BNT162b2 (as opposed to ChAdOx1-nCoV19) - Reduced likelihood if transplanted less than a year ago and with a diagnosis of diabetes
Reindl-Schwaighofer et al. ¹⁶³	Transplant: - 197 patients with no	Seroconversion rate	3	- 76 patients (39%) with seroconversion	- Patients not on triple-maintenance immunosuppression had

	response to 2 doses of mRNA vaccine			- 35% (mRNA vaccine) - 42% Ad26.COV2.S - Only 22% with functional neutralizing capacity	higher chance of seroconversion - Lower TTV level were associated with response - Longer time since last kidney transplant
Sanders JSF et al. ¹⁶⁴	- CKD stages 4/5: 162 - Dialysis: 159 - Transplant: 288 - Controls: 191	Seroconversion rate	2	- CKD stages 4/5: 100% (2405 BAU/mL) - Dialysis: 99.4% (PD 100%) (1650 BAU/mL) - Transplant: 56.9% (25 BAU/mL) - Controls: 100% (3186 BAU/mL)	- Transplant: higher age, lower lymphocyte count, lower eGFR, not using steroids, shorter time after transplantation, and the use of MMF/MPA
Sibbel S et al. ¹⁶⁵	Dialysis: 35206 patients (12169 BNT162b2, 23037 mRNA-1273) and matched unvaccinated controls (44377 and 64243)	Vaccine effectiveness	1-2	- BNT162b2 and mRNA-1273 (COVID-19 free survival after 1st dose, vs. unvaccinated): d1-21, d22-42, and d≥43 HR 0.83/0.96, 0.61/0.51 and 0.22/0.27 - BNT162b2 and mRNA-1273 (hospitalization vs. unvaccinated): 28.0%/37.2% vs. 43.4%/45.6% - BNT162b2 and mRNA-1273 (mortality vs. unvaccinated): 4.2%/5.6% vs. 12.1%/14.5%	-
Smith RM et al ¹⁶⁶	Dialysis: 260 Transplant: 209 Autoimmune disease: 223 Healthy controls: 144	Seroconversion rate	2	Seroconversion: -Dialysis: 96% -Transplant: 52% Autoimmune patients: 70% Healthy controls: 100%	Poor response predictors: Transplant: Triple immunosuppression; MMF Autoimmune patients: RTX within 12 months; immunosuppression with eGFR 15-29 ml/min/1.73 m ²
Stumpf J et al. ¹⁶⁷	Dialysis: 1135 (humoral)*, 119 (cellular) Transplant: 333 (humoral)*, 124 (cellular)	Seroconversion rate; cellular response	2	Seroconversion: -Dialysis: 1083 (95.3%) -Transplant: 140 (42%) Cellular response:	- Dialysis: time on dialysis, immunosuppression, vaccine type (mRNA-1273 > BNT162b2) - Transplant: age (per year), time (after transplantation), number

				- Dialysis: 93 (78.2%) - Transplant: 37 (29.8%)	of immunosuppressive drugs, vaccine type (mRNA-1273 > BNT162b2), immunosuppression: CNI, MMF/MPA, belatacept
Floyd L et al. ¹⁶⁸	ANCA-associated vasculitis: - 159 patients	Seroconversion rate	2	- 87 (55%) with detectable antibodies	- The use of rituximab was associated with poor humoral response and the absence of anti-S antibodies, especially in those treated within 6 months before the first vaccine dose - CD19 reconstitution associated with the likelihood. Of a positive humoral vaccine response
Predecki M et al. ¹⁶⁹	- Mixed cohort (AAV/anti-GBM, podocytopathy, membranous nephropathy, SLE, and others (n=4): 119 patients	Seroconversion rate; T cell response	2	- 54/91 (59.3%) with detectable antibodies - 42/50 (84%) had a detectable T cell response	- ChAdOx1-nCoV19 and increasing age associated with lower seroconversion rate (rituximab users) - B cell depletion at the time of vaccination associated with lower seroconversion rate - Age associated with absence of T cell response - The magnitude of response was lower in tacrolimus users
Yahav D et al. ¹⁷⁰	Transplant: 190 patients	Seroconversion rate; cellular response (in 53 patients)	3	- 133/190 (70%) seropositive, 70/190 (37%) after 2nd dose - T-cell response in 7/53 (13%)	Factors associated with seropositivity: - Higher antibody levels after the 2nd dose - Discontinuation of antimetabolite prior to vaccination

* 8 weeks after first vaccination (5 weeks after 2nd dose of BNT162b2, and 4 weeks after 2nd dose of mRNA-1273)

*1 Comparison of hemodialysis patients compared to COVID-19 naïve controls, and age was significantly different (71.9 years versus 48.5 years)

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Table 2: Challenges and missed opportunities in managing patients with kidney disease during the COVID-19 pandemic

Cohort type	Challenges	Solutions	Actions required
Acute kidney injury (AKI)	Increased demand for bedside dialysis and CRRT. Shortage of dialysis solutions and workforce	Organization of multidisciplinary crisis team to include nephrologists, nurses and hospital administrators. Taking inventory of all aspects of RRT Tracking daily need for RRT Modification of HD and CRRT protocols to meet increased demand Utility of acute PD Redeployment of faculty, trainees and nurses to meet needs	Develop a framework for addressing system capacity, challenges in communication and allocating resources founded on ethical principles Educate patients about AKI and risks

Chronic kidney disease (CKD)	Interruption of new consultations and follow up care Laboratory monitoring of CKD Limited pre-dialysis access care due to the pandemic Lack of data on therapeutics and vaccine response in the CKD population	Adoption of telemedicine for all except urgent cases requiring in-person evaluation Restrict laboratory tests to those with rapid turnaround for clinical care and using non-hospital-based labs for blood draw Home urine dipstick monitoring Include vascular access surgeries and PD catheter placement among essential procedures during a pandemic	Evaluate disparities in digital literacy and establish a protocol to include telemedicine navigators to facilitate telemedicine Advocacy for inclusion of CKD cohort in clinical trials of therapeutics and vaccines

End stage kidney disease (ESKD) patients on maintenance dialysis	Safe continuation of thrice weekly in-center dialysis Training for home dialysis modalities Longitudinal care for home dialysis patients Delay in dialysis access placement Delays in transplant evaluation and placement on wait list Lack of data on therapeutics and vaccine response in the CKD population	Protocol for symptom screening for infection and universal masking Cohorting infected patients in designated COVID units. Wider adoption of home dialysis modalities Conversion from in-person to televisit for in-center and home dialysis patients Inclusion of dialysis access as an essential procedure Reduction of dialysis sessions to twice a week Conversion to home dialysis	Universal viral testing for symptomatic in-center dialysis patients Stock-piling of emergency medical equipment and dialysis supplies Adoption of assisted peritoneal dialysis and home hemodialysis. Development of algorithms to accelerate evaluation and placement of medically stable on wait list Inclusion of ESKD patients in clinical trials of therapeutics and vaccines
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Kidney transplant recipients	Strategies to reduce risk of infection Continuation of evaluation for transplant candidacy Continuation of transplant surgeries Evaluating vaccine efficacy	Adoption of telemedicine and remote monitoring Suspension of live donation and decrease in DDKT Vaccine prioritization, booster doses, vaccination of household contacts	Leveraging health care technology to aid remote monitoring of vital signs and glucose Algorithm for individualized approach to continuing transplant surgery Strategies to enhance vaccine efficacy
Immune mediated kidney disease	Strategies to reduce risk of infection Identifying immunosuppressive classes associated with increased risk of infection	Adoption of telemedicine and remote monitoring Decrease in frequency of laboratory monitoring	Leveraging health care technology to aid remote monitoring of disease activity and adoption of urine dipstick monitoring Comparing utility of non-invasive disease

	Evaluating vaccine efficacy	Delaying use of biologics in stable patients Vaccine prioritization, booster doses, vaccination of household contacts	biomarkers and kidney biopsy for glomerular diseases Algorithms to personalize maintenance immunosuppressive therapy for relapsing diseases Strategies to enhance vaccine efficacy
Children living with kidney disease	Interruption of follow up care for CKD Continuation of transplant surgeries Lack of data on therapeutics and vaccine response in the CKD population	Adoption of telemedicine and remote monitoring Suspension of live donation	Wider adoption of home dialysis Strategies to address caregiver burden Inclusion of children in clinical trials and prioritization of high-risk groups for vaccines. Research to study the kidney health

	Psychologic impact of isolation and shielding Caregiver burden		and cardiovascular consequences of the pandemic Address pediatric health equity through research and public policy Ensuring resources to maintain critical services for children on dialysis Utilizing patient-reported outcomes along with relevant health measures
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