Availability and prioritisation of COVID-19 vaccines among patients with advanced chronic kidney disease and kidney failure during the height of the pandemic: a global survey by the International Society of Nephrology

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ABSTRACT

Objective Patients with advanced chronic kidney disease (CKD) or kidney failure receiving replacement therapy (KFRT) are highly vulnerable to COVID-19 infection, morbidity and mortality. Vaccination is effective, but access differs around the world. We aimed to ascertain the availability, readiness and prioritisation of COVID-19 vaccines for this group of patients globally.

Setting and participants Collaborators from the International Society of Nephrology (ISN), Dialysis Outcomes and Practice Patterns Study and ISN-Global Kidney Health Atlas developed an online survey that was administered electronically to key nephrology leaders in 174 countries between 2 July and 4 August 2021.

Results Survey responses were received from 99 of 174 countries from all 10 ISN regions, among which 88/174 (50%) were complete. At least one vaccine was available in 96/99 (97%) countries. In 71% of the countries surveyed, patients on dialysis were prioritised for vaccination, followed by patients living with a kidney transplant (KT) (62%) and stage 4/5 CKD (51%). Healthcare workers were the most common high priority group for vaccination. At least 50% of patients receiving in-centre haemodialysis, peritoneal dialysis or KT were estimated to have completed vaccination at the time of the survey in 55%, 64% and 51% of countries, respectively. At least 50% of patients in all three patient groups had been vaccinated in >70% of high-income countries and in 100% of respondent countries in Western Europe. The most common barriers to vaccination of patients were vaccine hesitancy (74%), vaccine shortages (61%) and mass vaccine distribution challenges (48%). These were reported more in low-income and lower middle-income countries compared with high-income countries.

Conclusion Patients with advanced CKD or KFRT were prioritised in COVID-19 vaccination in most countries. Multiple barriers led to substantial variability in the successful achievement of COVID-19 vaccination across the world, with high-income countries achieving the most access and success.

STRENGTHS AND LIMITATIONS OF THIS STUDY

This is the first study to look at vaccination strategies among the very high-risk group with advanced kidney disease/failure across the globe.

Responses were received from 99 of 174 countries, representing all 10 International Society of Nephrology regions (including complete responses from 88 countries).

Nephrologist leaders answered the survey in their own country.

Reliance on single responses from each country may be a limitation.

A significant number of non-responses may underestimate the true disparities in access to vaccination in patients with advanced kidney disease.

INTRODUCTION

Since the beginning of the COVID-19 pandemic, healthcare systems have faced the challenge of optimally deploying resources to mitigate morbidity and mortality from COVID-19. Although it is clear that a highly effective and universally acceptable vaccination programme is a game changer, stark global inequities in access to the COVID-19 vaccine have remained. While the equitable distribution of COVID-19 vaccines has been a key global priority, it has also been vital within countries to prioritise groups at the highest risk of COVID-19 and its complications, to reduce harm, ensure distributive justice in access to vaccines and to control the outbreak.
People living with advanced chronic kidney disease (CKD) and kidney failure with replacement therapy (KFRT) are a highly vulnerable group because of a complex interplay of an altered immune response, multiple comorbidities and high risk of exposure, especially among those requiring frequent visits to healthcare institutions. Patients on dialysis are 5–16 times more likely to develop COVID-19 than the general population. Several serological studies before the advent of vaccination revealed a seroprevalence rate of 28%–36% among patients undergoing in-centre dialysis. Reported mortality rates among dialysis patients hospitalised with COVID-19 are >20%. Similarly, COVID-19 in kidney transplant (KT) recipients has been associated with high mortality and adverse graft outcomes. These two groups represent those at the highest risk of death from COVID-19.

Early evidence showed that COVID-19 vaccination is associated with good immunogenicity among patients on dialysis (seropositivity of up to 89% following two doses of SARS-CoV-2 messenger RNA (mRNA) vaccines). In KT recipients, SARS-CoV-2 vaccines were found to be safe, however, the immunological response after two doses is documented to be suboptimal, ranging from 3% to 50%. Thus, KT recipients appear to benefit from third and four booster vaccination. This evidence clearly justifies a prioritised and proactive vaccination strategy for individuals with KFRT. However, the achievement of equitable access to COVID-19 vaccines has been hindered by multiple factors such as availability, vaccine hesitancy and acceptability. Given the stark global inequities in access to vaccination against COVID-19 in general, and the heightened vulnerability of patients living with advanced CKD and with KFRT in particular, advocacy is urgently required to achieve equitable access to vaccination. The current status of access to vaccination among patients with CKD and KFRT globally is unknown. Thus, this survey was designed to assess the availability, readiness and prioritisation of COVID-19 vaccines for patients with advanced CKD and kidney failure globally. Also, the Global COVID-19 Vaccine Survey (GCVS) aimed to identify the major challenges encountered in delivering COVID-19 vaccines to patients with kidney diseases to inform future vaccine deployment strategies.

**METHODS**

**Study design and participants**

The GCVS was a multinational survey developed by the International Society of Nephrology (ISN) and the Dialysis Outcomes and Practice Patterns Study (DOPPS) to understand and better inform the kidney community about current international practices and challenges surrounding COVID-19 vaccination. The survey was administered electronically to key leaders in nephrology representing different countries who were knowledgeable about their country’s kidney care and COVID-19 vaccination status (eg, ISN representative in regional boards/workgroups, national society leadership, health policymakers). Leaders were identified using purposive sampling through the ISN-Global Kidney Health Atlas (GKHA) database, ISN-DOPPS COVID-19 survey database and/or with the help of the national society or the ISN’s 10 regional boards to maximise completeness of representation (Africa, Central and Eastern Europe, Latin America, Middle East, North America, North and East Asia, Oceania and South East Asia, newly independent states and Russia, South Asia and Western Europe). At least one stakeholder each was identified from 174 countries representing all ISN regions. As in most countries, one leader took the survey, individual country data were not reported to maintain the anonymity of the respondent.

Participants were sent an email that included a letter of invitation and a link to the survey’s online portal (an electronic questionnaire via SurveyMonkey https://www.surveymonkey.com/). The survey was conducted from the 2 July 2021 to the 4 August 2021. During this period, ISN regional leaders and country leadership were contacted via email and telephone to encourage the timely completion of the survey. Personalised email reminders were sent to each key representative who had not yet returned the survey at weekly intervals up to a maximum of three reminders.

**Development and validation of survey instrument**

The GCVS collected information about the availability, accessibility, affordability, dosing, challenges and prioritisation of COVID-19 vaccines in patients living with advanced kidney disease (dialysis and KT). A core group of regional experts from the ISN-GKHA provided feedback on the content validity and comprehensiveness of initial drafts, which were refined as required. The survey was piloted across the 14 Emerging Leaders Programme Cohort members of ISN representing 12 countries. The questionnaire format and the content were finalised based on the feedback obtained from the content experts and the pilot study (online supplemental file 1). Duplicate entries were not allowed.

**Data handling, analysis and reporting**

Data from all individual questionnaires were directly uploaded anonymously to SurveyMonkey, which was password protected. Data from individual questionnaires were extracted and checked for inconsistencies, duplications and formatting errors and merged into a single file to create a global database.
Each responding country was considered one unit and the results were stratified by 10 ISN regions and 4 income groups as classified by World Bank (low-income, lower middle-income, upper middle-income and high-income country). A descriptive statistical approach was used to summarise the responses based on the key questionnaire domains which were reported as counts and percentages or medians and IQRs, as appropriate. Free-text comments were incorporated into the narrative synthesis of the data. Results were stratified by ISN region to maximise utility for advocacy by regional boards and by country income status to emphasise trends in inequities.

Patient and public involvement

The development of this study’s research question was guided by an urgent need to prioritise vaccination for patients living with advanced kidney diseases and the need to generate data on inequities in access, to support advocacy efforts for vaccine equity among people living with advanced kidney diseases (being among the highest risk for poor outcomes). Patients were not involved in the design, recruitment and conduct of the study. The study participants were key leaders in nephrology who took the survey by invitation. The results of the study will be disseminated to all respondents, country nephrology societies and through the ISN to support advocacy needs.

RESULTS

Response rate

Overall, 117 responses were received from 99 countries across all 10 ISN regions, giving a country response rate of 99/174 (57%) (table 1). The response to the survey was incomplete in 11 and therefore, the complete response rate was 88/174 (50%). The response rate was similar across the different income groups (low income—54%, lower middle income—48%, upper middle income—62% and high income—62%).

Vaccine availability and prioritisation

Ninety-six of 99 (97%) respondent countries had at least one COVID-19 vaccine available at the time of the survey. Oxford-AstraZeneca vaccine was available in 69 countries across the 10 ISN regions, Pfizer-BioNTech in 54 countries across 9 ISN regions, Moderna in 33 countries across 8 ISN regions, Johnson & Johnson in 23 countries across 8 ISN regions, Sputnik V in 23 countries across 8 ISN regions and Coronavac in 23 countries across 7 ISN regions (online supplemental table 1).

Healthcare workers were the most common high-priority group for vaccination, being eligible within the first two phases of vaccine rollout in 91% of respondent countries. Patients living with stage 4/5 CKD, dialysis or KT were vaccinated during the first two phases in 51%,

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<th>Table 1 Country response rates to the global COVID-19 vaccine survey by ISN regions and World Bank income groups</th>
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<td><strong>Total no. of countries recognised by UN</strong></td>
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<td><strong>ISN regions</strong></td>
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<td>High</td>
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*The percentage was calculated as the total number of countries that responded (complete+incomplete responses) to the survey/total number of countries that received the survey.
†The percentage was calculated as the total number of countries that completed (total responded–incomplete responses) the survey/total number of countries that received the survey.

ISN, International Society of Nephrology; OSEA, Oceania and South East Asia.
71% and 62% of respondent countries, respectively (online supplemental table 2) (figure 1). Among the 85 countries in which the data on dialysis were available: in-centre haemodialysis (ICHD) was the most common modality (81/85, 95%) followed by peritoneal dialysis (PD) (67/85, 79%) and home haemodialysis (HHD) (36/85, 42%) (table 2). Among 67 respondent countries with >1 dialysis modality available, patients receiving ICHD were prioritised for vaccination over those receiving PD or HHD in 14 (21%) countries.

Distribution and administration of vaccines
COVID-19 vaccines were administered to patients with kidney diseases at special COVID-19 vaccination sites (59/85, 69%), at their routine hospital/clinics (38/85, 45%), at primary healthcare units (31/85, 36%) and at
ICHD units (27/85, 32%) across respondent countries (online supplemental figure 1). In countries where the vaccine was administered at ICHD units, it was most often administered by dialysis staff (16/27, 59%) and/or specially trained vaccination teams (15/27, 56%). In these units, vaccination was performed before HD (6/27, 22%), after HD (10/27, 37%), on non-dialysis days (5/27, 19%), or without specific timing relative to dialysis (6/27, 22%).

The proportion of patients vaccinated varied dramatically in different regions (figure 2). Overall, at least 50% of patients receiving ICHD, PD or KT were estimated to be fully vaccinated at the time of the survey in 55%, 64% and 51% of respondent countries, respectively.

Government information campaigns were the primary source of information on the importance of COVID-19 vaccination for the patients in the majority of respondent countries (49/81, 60%), followed by dialysis staff (24/81, 30%), social media (3/81, 4%), family and friends (3/81, 4%) and news media (1/81, 1%) (online supplemental figure 2).

Challenges encountered during the delivery of vaccines
The most common barriers to vaccination of patients (sometimes, frequently or always) reported by respondents were vaccine hesitancy (63/85, 74%), vaccine shortages (52/85, 61%) and vaccine mass distribution challenges (41/85, 48%), followed by lack of prioritisation of patients with kidney disease (32/85, 38%), and an insufficient number of vaccination centres (26/85, 31%). Less frequently observed barriers included lack of formal vaccination programmes (15/85, 18%), staff shortages (14/85, 16%) and high out-of-pocket costs (4/85, 5%) (figure 3A). Most of these challenges were reported in low-income and lower middle-income countries compared high-income countries except for the shortage of staff to administer vaccines (figure 3B). Vaccines were provided free of charge, sponsored by the government,
Figure 3  Challenges encountered in COVID-19 vaccine deployment to patients with advanced kidney disease stratified by (A) International Society of Nephrology (ISN) region and (B) country income categories. (A) The percentage frequencies are based on responses by countries to: ‘How frequently are the following major challenges encountered in delivering COVID-19 vaccines to patients with kidney disease in your country?’ (B) If the response to the question on a particular challenge was either always, often or sometimes it was considered a major challenge. *Total number of countries per ISN region/income group is indicated in parentheses. OSEA, Oceania and South East Asia.
in all countries except for one, where they were paid for by the patient’s insurance. Vaccine side effects were reported as never (25/85, 29%) or rarely (43/85, 51%) by most respondents.

DISCUSSION

In light of the rapidly changing situation of the COVID-19 pandemic and its consequences on health and other aspects of life (family, economic, social and political), an important strategy to control the pandemic is expansion of vaccination coverage. Individuals living with kidney failure or those with immunocompromised status following KT are at high risk for severe outcomes following a COVID-19 infection. This survey of nephrologists representing 88 countries across the globe showed that the vaccines were available in almost all countries surveyed by August 2021 (9 months after the initial widespread deployment of vaccines) and that, indeed, in most countries, healthcare workers and patients with kidney disease were prioritised for vaccination relatively early, either in the first or the second phase of the country’s vaccination programme (online supplemental table 2). This likely reflects the rapid understanding of the high risk of infection and higher morbidities and mortalities in this population and that major nephrology societies like the National Kidney Foundation, the European Renal Association and the ISN issued statements as early as December 2020 calling for priority vaccination of people living with kidney disease. In addition, many local nephrology associations also swiftly advocated that people living with kidney failure in their countries should be included on the vulnerable lists together with other chronic diseases like diabetes, urging their own governments to prioritise patients with kidney disease as a priority for vaccination. Although vaccines were available in almost all countries, the type of vaccines varied across countries (online supplemental table 1). Given that the data on the efficacy of the various vaccines have shown some variability, this factor has become increasingly relevant when considering the global population of patients with kidney failure. Ongoing vaccination/booster strategies should assess vaccine effectiveness, given the high vulnerability of this group. For example, the viral vector-based vaccines were found to be less immunogenic compared with the mRNA vaccines in patients with kidney failure. Given the ongoing global inequity in access to vaccines, these inequities are being further exacerbated by inequitable access to the more effective mRNA-based vaccines, which are expensive and more logistically complex to administer, and are disproportionately more available in higher income regions (online supplemental table 1). Likely, true equity for people living with advanced CKD and KFRT may only be achieved once vaccine equity is improved globally.

It was reassuring to find that by early August 2021, more than half the countries surveyed had a vaccination rate of >50% for people with advanced CKD or KFRT. However, this varied according to regions and country income categories, demonstrating existing inequities. The stark global inequities are highlighted by the fact that all respondents from Western Europe reported that over 50% of all patients with KFRT were vaccinated, whereas, in Africa and South East Asia, only a minority of respondents reported a >50% vaccination rate among patients with KFRT (figure 2). Interestingly, 30% of African respondents reported that >50% of patients with KFRT were vaccinated in their units. This may appear surprising at face value, given that data on vaccination worldwide at the time showed that most of the African countries were well below the 10% rate, with South Africa reporting the highest rate among these countries of 24.9%. This observation may suggest that patients living with KFRT in Africa (and possibly other vulnerable or high-risk groups) were given priority to vaccination, or had greater visibility having frequent contact with health centres for dialysis. Given that vaccination was not paid for out of pocket, it is less likely but not implausible that this relatively high proportion suggests more access to vaccination among more affluent patients who can pay for dialysis out of pocket (still required in many African and Asian countries) and may be stronger advocates for themselves.

Shortage of vaccines was given as a reason for the low rate of vaccination in some countries despite the vaccines being free and paid for by the government. This was likely due to the inability of these governments to secure sufficient vaccine stocks from the global vaccine market. The inequalities in vaccine availability and administration have been strongly highlighted by WHO and many other organisations. WHO had set a target that by the end of 2021, countries should have 40% of their populations vaccinated and 70% by mid-2022. Although the vaccinated population targets were not yet achieved at the time of the survey, according to the real-time global data on COVID-19 vaccination (ourworldindata.org), the survey data suggest that the CKD and KFRT group mainly had been vaccinated. WHO also emphasised the importance of supporting lower-resource countries and has coordinated strategies involving collaborations between higher-income countries and multiple parties through programmes like COVID-19 Vaccines Global Access and Access to COVID-19 Tools-Accelerator, in an attempt to ensure optimal utilisation of the vaccines produced and help to streamline the logistics involved in delivering a successful vaccination programme. The drive for the vaccines to be provided to low-income countries has become more complicated given the emergence of the Omicron variants. High-income countries were vaccinating younger children and are actively advocating a multiple booster doses, before people elsewhere had received a single dose. The early push for booster and child vaccines globally, therefore, further exacerbated the global inequity in access to vaccines.

Although it is tempting to solely attribute the global inequity in access to vaccines to the lack of distribution...
of vaccines by more high-income nations, other factors also play a role. Vaccine hesitancy among patients was cited as a barrier to vaccine delivery by all the respondents in North America and the Caribbean, Oceania and South-East Asia and Middle East regions, and the majority of other respondents in our survey. The provision of information on COVID-19 and vaccinations has been mainly led by individual governments. However, due to potential cultural barriers and the alternative but often more widespread and more influential negative messaging on social media, these government campaigns have been undermined. Public health messaging must become more effective to overcome vaccine misconceptions. The cause of vaccine hesitancy was not explored in this survey, but a major concern has been the potential side effects. Vaccine hesitancy were also found to be different for specific regions, for example, in the African countries, conspiracy theories are prevalent, with perceptions that vaccines are meant to make profits for pharmaceutical companies and individuals, vaccines are harmful and Africans are used to test safety for others. In high-income countries, the pattern of vaccine hesitancy is primarily seen in the ethnic minorities, including Indigenous peoples, who cite mistrust of the government as a reason for shunning vaccines. Much has been made of vaccine hesitancy, and that expired vaccine doses were being discarded in some low-income and middle-income countries to justify the global inequities described daily in the news. However, this should not be used as a justification to delay distribution or presume that vaccines will not be accepted. Social media impacts individual decision-making daily, and everyone everywhere should have an opportunity to accept vaccination. It is also up to individual health systems to train their staff how to communicate correctly when talking about vaccines so that trust can be built in order to reduce such hesitancy.

A further significant barrier to access to vaccination among patients with kidney failure is the lack of logistical capabilities of lower-resource countries to store and deliver the vaccines. This includes the distribution of mass vaccines as well as the lack of vaccine centres to provide the vaccines to the patients. Setting up specialised centres is of utmost importance as most respondents replied that vaccines were commonly administered at specialised COVID-19 vaccine centres. The delivery and storage of vaccines is an essential aspect of vaccine management. UNICEF has been aiding with this complex logistical challenge of delivering vaccines to these countries, which lack a sufficient and efficient cold chain infrastructure.

Understanding the practices behind the vaccination of patients with kidney disease is essential. Patients with kidney disease are more vulnerable than others because they mount lesser responses to vaccines and are at higher risk of severe COVID-19 infection. Patients with kidney disease are also different from each other. ICHD, which requires patients to leave the house and mix with other patients for long periods, puts patients at increased risk of contracting COVID-19 compared with home dialysis. Our data reflect the vaccination rates of other vulnerable groups as well. Meeting the needs of diverse subpopulations of patients requires insight and logistics.

A limitation of surveys like ours looking at vaccination rates and practices during the COVID-19 pandemic is that the situation changes rapidly. For example, we could not determine the rate of booster doses, which became a priority given the emergence of the Omicron variant. Survey responses also depended on individual respondents’ knowledge and experience and were subject to response biases, such as demand bias and social desirability bias. It is anticipated, however, that these potential biases were minimised through the targeted invitation of country leaders in nephrology who were familiar with the vaccination policies and practices within their individual countries. The significant number of non-responders is also a potentially important limitation. It may be that these countries may have performed less well in their national vaccination policies. Therefore, it is possible that our findings may be an underestimate of the true extent of disparity in COVID-19 vaccination in the world. Notwithstanding these limitations, the primary strength of this study is the broad global representation, relative consistency of responses within regions and the focus on a uniquely vulnerable, often unseen, patient population.

Worldwide access to COVID-19 vaccines is an important strategy to slow the pandemic, save lives and hasten the global economic recovery. Vaccinating the world’s population quickly is also vital to prevent future new variants from emerging. We have found that despite global inequities in access to vaccination, in all regions, patients with kidney disease appear to have been appropriately prioritised for available vaccines. This is laudable, especially in countries where supplies continue to be limited. Recognition of the vulnerability of patients with kidney disease is essential to reduce inequities they face at baseline because of their disease and the dictates of their treatment. However, more work is needed to improve access to vaccination globally for people living with kidney disease and to prepare better for future pandemics. People living with kidney disease will benefit from being vaccinated themselves and will benefit from those around them being vaccinated, which in turn will enhance their protection in the face of suboptimal immune responsiveness. Progress in global solidarity and collaboration will benefit everyone.
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