Seroprevalence of antibody to S1 spike protein following vaccination against COVID-19 in patients receiving hemodialysis: a call to arms

To the editor: Adult patients with end-stage kidney disease on hemodialysis are at increased risk of coronavirus disease 2019 (COVID-19) infection and death.[1] This group is often multiracial, experiences from many comorbidities, and can be socioeconomically deprived, all factors strongly associated with COVID-19 mortality.[1] Vaccination is a priority for this at-risk group who are relatively immunosuppressed, and the effectiveness of vaccines has not been explicitly tested in patients with chronic kidney disease and on dialysis, meaning vaccine efficacy or immunogenicity is not well-understood.[2] To achieve maximum population coverage, in the United Kingdom, the second vaccine dose was delayed to 12 weeks. Retrospective review of the Oxford-AstraZeneca vaccine (AZD1222) trial data suggests that a single dose is efficacious and the delay may result in overall improved efficacy,[3] but prospective data and data on other vaccines are lacking. In health care workers, a single dose of the Pfizer-BioNTech vaccine (BNT162b2) elicited much stronger humoral and cellular responses in those with a previous natural infection.[4] Understanding the immune responses of patients receiving hemodialysis is vital to guide current and future vaccine dosing strategies in this vulnerable group.

Herein, we describe the antibody response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein 28 days after the first dose of either the BNT162b2 or AZD1222 vaccine in 94 patients receiving maintenance hemodialysis (full methods in Supplementary Appendix S1).

Mean time between vaccination and antibody testing was 27.8 ± 4.2 days. Clinical characteristics of the study population are shown in Table 1. Overall SARS-CoV-2 neutralizing antibodies against the receptor binding domain of the S1 spike protein were detectable in 75 patients (79.8%) and were not detectable in 19 patients (20.2%). Median antibody level was 2.4 [interquartile range, 8.8] relative light units. Patients with detectable antibodies were younger than patients without detectable antibodies (60.2 ± 11.6 years vs. 69.8 ± 11.8 years; $P = 0.002$). Patients who were immunosuppressed were less likely to have detectable antibodies than patients who were not immunosuppressed (50% vs. 83.3%; χ^2 [1, N = 94] = 6.2; $P = 0.013$). Patients previously infected with COVID-19 were more likely to have detectable antibodies than those with no history of COVID-19 infection (100% vs. 74.3%; χ^2 [1, N = 94] = 6.436; $P = 0.011$). There were no differences in detection of antibodies within the cohort between females and males (84.2% vs. 76,8%; χ^2 [1, N = 94] = 0.77; $P = 0.4$); the presence or absence of diabetes (86% vs. 74.5%; χ^2 [1, N = 94] = 1.9; $P = 0.17$); or race (Asian, 85.1%; White, 68.6%; Black, 90%; mixed, 100%; other, 100%; χ^2 [1, N = 94] = 4.7; $P = 0.32$). There were no differences between patients who received the Pfizer-BioNTech vaccine or the Oxford-AstraZeneca vaccine (81.8% vs. 70.6%; χ^2 [1, N = 94] = 1.089; $P = 0.3$) (Figure 1).

These findings are consistent with the findings in other populations,[5] but due to the small numbers in this study should be viewed as hypothesis-generating. Indeed, we publish these preliminary findings to highlight the urgent, international need for professional organizations, clinicians, charities, and stakeholder partners to work collaboratively to investigate the factors that influence the immune response following vaccination against COVID-19 in this patient group. There are a myriad of factors that may affect the ability of a patient receiving dialysis to successfully seroconvert following vaccination, and only through a joined-up, standardized approach will we be able to understand and mitigate these factors for dialysis populations around the world. For patients receiving hemodialysis, the United Kingdom has coordinated a multicenter study that will phenotype antibody

Table 1 | Baseline characteristics of hemodialysis patients

Clinical characteristics	Hemodialysis cohort (n = 94)
Age, mean $\pm$ SD, yr	62.1 ± 12.2
Female sex, n (%)	38 (40.4)
Race, n (%)	
Asian	47 (50)
White	35 (37.2)
Black	10 (10.6)
Mixed	1 (1.1)
Other	1 (1.1)
Diabetic, n (%)	43 (45.7)
Previous immunosuppression, n (%)	10 (10.6)
Previous COVID-19 infection, n (%)	20 (22.3)
Pfizer vaccine, n (%)	77 (82)
AstraZeneca vaccine, n (%)	17 (18)

COVID-19, coronavirus disease 2019.

Table 2 | Recommended reporting of clinical variables for future studies

Essential clinical characteristics
  Age
  Sex
  Race
  Previous COVID-19 infection (PCR-positive, or clear clinical features early in the pandemic when antigen testing was not widely available)
  Previous immunosuppression
  Diabetic status
  Type of vaccine
  Time *after* vaccination (recommended 28 days after vaccine doses)
Desired clinical characteristics
  Primary cause of kidney disease
  Prevaccination antibody status
  Medical comorbidities

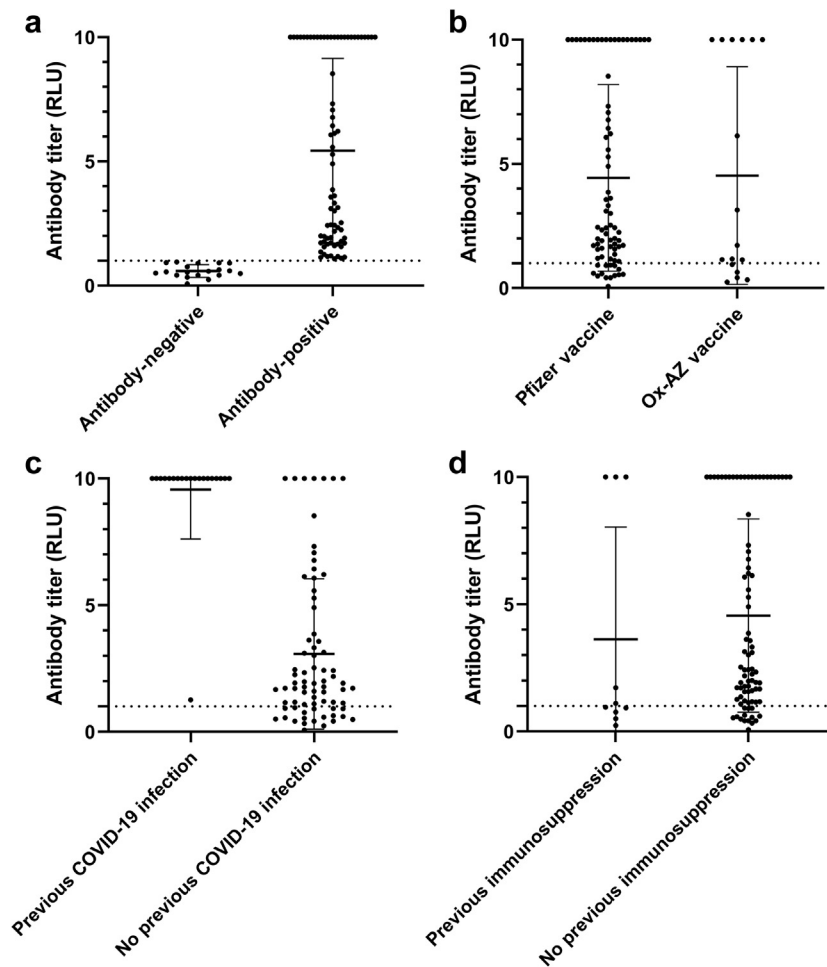COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction.

Figure 1 | Differences in antibody titers between groups. (a) Antibody-negative and antibody-positive patients. (b) Patients who received the Pfizer vaccine and those who received the Oxford-AstraZeneca (Ox-AZ) vaccine. (c) Patients with a previous history of coronavirus disease 2019 (COVID-19) infection and those without. (d) Patients with a previous history of immunosuppression and those without. RLU, relative light unit.

responses to vaccinations 28 days after the first and second doses of the vaccine with storage and centralized analysis at the Francis-Crick Institute (SP/VACCINE/2021). Centralized analysis using the same antibody assays is an essential component in the design of such studies, and we encourage international communities to conduct similar studies to allow contemporary study of seroconversion rates in response to the spectra of available vaccines, and differing vaccine deployment strategies in populations with different and unique characteristics. We encourage the standardized collection and reporting of clinical variables such that future data syntheses and meta-analyses are possible. Our recommendations for required and desired reporting of clinical measures are shown in Table 2.

The presence or absence of antibodies 28 days after the first vaccine dose in the data we present is not synonymous with protection or absence of protection from COVID-19. Rather, these data should be viewed as a call to arms to all who care for these patients to coordinate collection and standardized analysis of seroconversion following vaccination internationally to understand the immune response and how this relates to subsequent infection rates and outcomes for

these patients. These data are essential to inform current and future vaccination programs to protect patients receiving hemodialysis who have had to endure the worst of the pandemic.

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