Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Supplementary Material

Supplementary File (PDF)

Figure S1; Tables S1-S2.

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Clinically Significant COVID-19 Following SARS-CoV-2 Vaccination in Kidney Transplant Recipients

To the Editor:

Vaccination against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) represents an important path toward ending the COVID-19 (coronavirus disease 2019) pandemic and alleviating the severity of COVID-19 in most patient populations.[1-3] Solid organ transplant recipients are a vulnerable population with significant COVID-19–associated morbidity and mortality.[4,5] Initial reports indicate an impaired anti–SARS-CoV-2 antibody response among transplant recipients following mRNA vaccination, likely because of maintenance immunosuppression.[6-9] Whether kidney transplant recipients have low levels of virus-neutralizing antibody not detected by these assays or protective anti–SARS-CoV-2 T-cell immunity is currently unknown, and the critical question is whether the impaired antibody response corresponds to disease susceptibility. Here, we document 13 cases of COVD-19 in vaccinated kidney transplant recipients. The Columbia University Institutional Review Board approved this study

Table 1. Population Summary: SARS-CoV-2 Infection Following Vaccination

Case	Age, Sex	Time Post KTx	Blood Group	DM & HTN	BMI, kg/m²	Scr, mg/dL	IS	Symptoms; Hospitalization Requirement	Vaccine Type	Anti-Spike Protein IgG[c]	COVID-19 Dx[c]
1[a]	50 y, F	6.5 y	A	Both	29.3	1.33	Tac/MPA	Fever, cough; not hospitalized	Pfizer-BioNTech; series complete	Negative at 32 d	46 d
2[a]	68 y, M	4 y	O	Both	20.7	2.21	Tac/MPA	Cough, fatigue/malaise; hospitalized	Pfizer-BioNTech; series complete	–	35 d
3[a]	65 y, M	17 y	O	HTN	30	1.4	SRL/MPA	Cough, headache, fatigue/malaise; not hospitalized	Pfizer-BioNTech; series complete	Negative at 27 d	35 d
4[a]	29 y, F	6 y	A	HTN	36.4	1.86	Tac/MPA	Cough, dyspnea, GI, myalgia/arthralgia, fatigue/malaise; not hospitalized	Moderna; series complete	–	23 d
5[a]	51 y, M	6.5 y	B	Both	35.2	2.44	Tac/MPA/Pred	Fever, myalgia/arthralgia, fatigue/malaise; hospitalized	Moderna; series complete	Negative at 23 d	21 d
6[a]	53 y, F	1.5 y	A	HTN	35.5	0.72	Tac/MPA	Cough, headache, GI, myalgia/arthralgia, fatigue/malaise; not hospitalized	Pfizer-BioNTech; series complete	–	18 d
7[a]	60 y, M	18 y	O	None	26.3	1	Tac/MPA/Pred	None; not hospitalized	Pfizer-BioNTech; series complete	Positive at 38 d[b]	17 d
8	74 y, F	1 y	O	Both	23.4	1.01	Tac/MPA/Pred	None; not hospitalized	Pfizer-BioNTech; series complete	–	12 d
9	42 y, F	3 y	AB	None	35	1.63	Tac/MPA/Pred	Cough; not hospitalized	Pfizer-BioNTech; 1 dose	–	29 d
10	55 y, F	2.5 y	A	Both	35.9	1.35	Tac/AZA	Fever, dyspnea, GI, fatigue/malaise; not hospitalized	Pfizer-BioNTech; 1 dose	–	18 d
11	64 y, F	3 y	O	HTN	28.6	0.87	Tac/MPA	Fever, GI, myalgia/arthralgia; not hospitalized	Pfizer-BioNTech; 1 dose	–	8 d
12	65 y, F	13 y	A	DM	23	1.34	CsA/MPA	Dyspnea, GI, myalgia/arthralgia, fatigue/malaise; hospitalized	Pfizer-BioNTech; 1 dose	–	6 d
13	62 y, M	0.5 y	A	Both	30.7	2.22	CsA/MPA/IVIG	Headache, GI, fatigue/malaise; not hospitalized	Janssen/J&J; series complete	–	1 d

Abbreviations: AZA, azathioprine; BMI, body mass index; CsA, cyclosporine; DM, diabetes; Dx, diagnosis; HTN, hypertension; IS, immunosuppression; IVIG, intravenous Immunoglobulin; KTx, kidney transplant; MPA, mycophenolate; Pred, prednisone; Scr, serum creatinine; SRL, sirolimus; Tac, tacrolimus.
[a]Meets US Centers for Disease Control and Prevention criteria for breakthrough COVID-19.
[b]Tested after found to be SARS-CoV-2 polymerase chain reaction positive.
[c]Days indicate time since vaccination (counted from date of first vaccination for patients who only received 1 dose and from date of second vaccination for those who completed the 2-dose series).

with a complete waiver of informed consent before its conduct.

Between January 12 and April 22, 2021, there were 904 kidney and pancreas transplant recipients at our transplant center who received a COVID-19 vaccine with emergency use authorization in the United States: Pfizer-BioNTech (n = 658), Moderna (n = 229), and Janssen/Johnson & Johnson (n = 17). As of April 22, 13 (1.4%) developed PCR-positive SARS-CoV-2 infection after vaccination, of which 7 cases (0.8% of all vaccinated recipients) met the CDC definition of a breakthrough infection with a positive PCR test from a respiratory specimen collected ≥14 days after completing the primary vaccination series.[10] Twelve cases were clinically significant and 1 was identified on routine surveillance in an asymptomatic patient. Eight patients had completed a 2-dose mRNA vaccine series and 1 received Janssen/J&J, while 4 had received only 1 dose of vaccine (Pfizer-BioNTech) at the time of infection (Table 1).

As summarized in Table 1, patients infected with SARS-CoV-2 after partial vaccination did so 6 to 29 days after initial vaccination, whereas those who had completed the vaccine series developed infection 1 to 46 days after vaccination. Time after transplantation ranged from 1 to 18 years. Seven patients had diabetes and all but 1 had hypertension. Only 1 patient each was not taking a calcineurin inhibitor or mycophenolate. Presenting symptoms were typical: 8 patients (62%) reported fatigue/malaise; 6 (46%), GI symptoms; 5 (38%), cough; 4 (31%), fever; 3 (23%), dyspnea; and 3 (23%), headache. Three patients had a negative anti–SARS-CoV-2-S IgG test. One patient with detectable anti–SARS-CoV-2-S IgG was asymptomatic (testing was performed after COVID-19 diagnosis).

While 10 cases were successfully managed as outpatients, 3 (0.3% of all vaccinated patients) needed hospitalization. One patient required a 4-day hospitalization to manage dyspnea and hypoxia (requiring 2-L nasal

cannula). Another presented to the hospital 6 days after the first vaccine dose with weakness and GI symptoms and had a >30-day hospitalization to manage acute pancreatitis and hypoxic respiratory failure, both attributed to COVID-19, requiring a non-rebreather mask for 3 days and ICU care for 4 days. The final hospitalized patient presented with hypotension and a fall deemed related to concomitant urinary tract infection and COVID-19. The patient developed severe COVID-19, including septic shock, acute kidney injury, and hypoxic respiratory failure requiring mechanical ventilation, before dying 5 days after admission.

Initial SARS-CoV-2 vaccine trials demonstrated great efficacy in preventing severe COVID-19, with a 0.04% to 0.08% incidence after completion of the primary vaccination series.[1-3] Our data indicate a 0.8% incidence of breakthrough COVID-19 and 1.4% overall incidence of COVID-19 following any vaccination in a short follow-up period. Unlike the breakthrough cases observed in general population trials, our cases include patients who developed severe COVID-19 requiring hospitalization and mechanical ventilation. These cases suggest reduced SARS-CoV-2 vaccine efficacy in this vulnerable patient population, likely stemming from the use of maintenance immunosuppression. Our cases are too few to draw any conclusions about patient characteristics contributing to the likelihood of COVID-19 following vaccination. The potential for severe COVID-19 despite vaccination is a concern among transplant recipients, and these cases supplement recent reports that most transplant recipients do not develop a measurable antibody response to standard anti-SARS-CoV-2 mRNA vaccination schedules, although immunogenicity is higher once both doses are administered.[6-9] It is important to recognize that the efficacy of vaccination without the presence of detectable antibodies is presently unclear, as is the degree of protection afforded by the presence of a detectable anti–spike antibody response. Results from this single-center summary must be considered in relation to changes in SARS-CoV-2 infections, in the context of community disease transmission and vaccination rates. For example, high vaccination rates in the community may benefit transplant recipients by reducing the likelihood of disease exposure and infection even if the vaccines do not confer a robust protective response to the immunosuppressed recipient. Patients should be educated on the importance of vaccination but also on the need to remain vigilant and exercise caution and diligence with public health measures of mask wearing, social distancing, and hand washing even after vaccination.[11] Additionally, clinicians should include COVID-19 in the list of differential diagnoses for symptomatic transplant recipients even after COVID-19 vaccination. These findings underscore the urgent need to implement trials for the development of alternate effective vaccine dosing schedules for these patients.

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