Breakthrough COVID-19 Infections After mRNA Vaccination in Solid Organ Transplant Recipients in Miami, Florida

Shweta Anjan, MD,[1,2] Yoichiro Natori, MD,[1,2] Anmary A. Fernandez Betances, MD,[1] Matthew S. Agritelley, BA,[1] Adela Mattiazzi, MD,[2] Leopoldo Arosemena, MD,[2] David M. Andrews, MD,[3] Jacques Simkins, MD,[1,2] Giselle Guerra, MD,[2] and Lilian M. Abbo, MD[1,2]

Administration of coronavirus disease 2019 (COVID-19) vaccines is critical to ending the pandemic. The available mRNA vaccines are 94%–95% effective in preventing COVID-19 in the general population. Vaccine-induced antibody responses are reported to be lower in solid organ transplant recipients (SOTRs) compared with the general population; 17% after the first dose and 54% after the second dose, with poor response, are generally associated with the use of antimetabolite agents.[1] In the United States, approximately 101 million persons are fully vaccinated with vaccine breakthrough infections reported in 10 262 (breakthrough rate 0.01%)[2] as of April 30, 2021. Data on postvaccine infections in SOTRs are limited.

We reported the largest series of vaccine breakthrough COVID-19 infections in SOTRs in the United States (the study approved by the University of Miami Institutional Review Board). Twenty-six patients were diagnosed with COVID-19 infection by nasopharyngeal polymerase chain reaction, after receiving 1 (n = 3, 12%) or both (n=23, 89%) doses of BNT162b2 (Pfizer-BioNTech) vaccine. They had no prior COVID-19 infection. The mean age at the time of vaccination was 58 y (32–81); 54% were males and 72% were of Hispanic ethnicity. Eleven patients (42.3%) reported exposure to unvaccinated family members with COVID-19. The median time from transplant to the vaccine (first dose) was 31 mo (range, 0.7–272), with 4 (15.3%) within 6 mo of transplant, and from vaccine to diagnosis was 34 d (range, 4–96). Antibody testing targeting the spike protein was performed via the VITROS test to measure immunoglobulin G and total antibodies (Table 1). All patients were symptomatic. Thirteen patients (50%) required hospital admission and were treated with remdesivir (92.3%, n = 12), high-dose steroids (84.6%, n = 11), and therapeutic plasma exchange (23%, n = 3; only for refractory cases in cytokine storm). Twelve patients (46%) were managed outpatient with early administration of monoclonal antibodies (MABs; casirivimab/imdevimab); all recovered with no progression of the disease. Two (16.6%) were admitted within 28 d of receiving MABs for non–COVID-19 issues. At a median follow-up of 28.5 d (range, 2–75), 5 (19.2%) had severe COVID-19 and 2 (7.6%) patients died. None of them developed rejection or graft loss.

As of April 30, 2021, 2957 SOTRs have been vaccinated at our center, with 26 cases of vaccine breakthrough infection (breakthrough rate 0.87%), which is higher than that reported in the general population. Our findings confirmed that severe COVID-19 and mortality can occur from vaccine breakthrough infections in SOTRs.[3,4] Data show transplant patients developed cellular and humoral responses despite immunosuppression, suggesting that vaccinated SOTRs may benefit from the vaccine even in the absence of antibody response.[5]

In conclusion, SOTRs remain at risk of severe COVID-19 even after the vaccination. Vaccinating SOTRs and ring vaccination of close contacts may provide better protection to immunocompromised patients. Transplant centers should continue to reinforce social distancing, mask use, and handwashing in fully vaccinated SOTR, even though mask mandates are relaxed nationally. Multicenter studies assessing cellular and humoral immunogenicity data, role of booster doses, use of MABs as prophylaxis in adjunct to vaccines, and genomic sequencing to identify variants causing vaccine breakthrough infections are needed.

Received 15 June 2021. Revision received 11 July 2021.

Accepted 12 July 2021.

[1] Department of Medicine, Division of Infectious Disease, University of Miami Miller School of Medicine Miami, FL.

[2] Miami Transplant Institute, Miami, FL.

[3] Department of Pathology, Jackson Health System, Miami, FL.

The authors declare no funding or conflicts of interest.

S.A., Y.N., and L.A. performed data collection and analysis. All authors were responsible for the study design, data interpretation, editing, and writing the article.

S.A. and Y.N. are cofirst authors.

Correspondence: Lilian M. Abbo, Department of Medicine, Division of Infectious Disease, University of Miami Miller School of Medicine and Jackson Health System, 1611 NW 12th Ave, Miami, FL 33136. (labbo@med.miami.edu).

ISSN: 0041-1337/21/10510-e139

DOI: 10.1097/TP.0000000000003902

REFERENCES

1. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA.* 2021;325:2204–2206.
2. CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC—United States, January 1–April 30, 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70:792–793.
3. Tau N, Yahav D, Schneider S, et al. Severe consequences of COVID-19 infection among vaccinated kidney transplant recipients. *Am J Transplant*. 2021;21:2910–2912.

<zdoi;10.1097/TP.0000000000003902>

TABLE 1.

Patient characteristics and outcomes

Patient	Age/sex	Type of organ transplant	Maintenance IS at the time of vaccine	Symptoms	Chest X-ray	Time from vaccine to COVID-19 diagnosis (d)	Antibody testing[a] (total; IgG)	Hospitalized for COVID-19/level of care	Treatment	Change in IS[b]	Severity of COVID-19	Outcome
1	74/F	Liver and kidney	TAC, MMF, Pred	Fatigue, nausea, vomiting, dyspnea	Bilateral interstitial opacities	6	Nonreactive	Yes/ICU	Remdesivir, TPE, solumedrol IV	MMF withheld	Severe	Death
2	61/F	Kidney	TAC, MMF, Pred	Dyspnea, nasal congestion, diarrhea	Bilateral interstitial opacities	26	—	Yes/ward	Remdesivir, Dexa	MMF withheld	Moderate	Alive
3[c]	41/M	Kidney	Everolimus, MMF, Bela, Pred	Fever, cough, dyspnea	Left-sided opacities	18	Nonreactive	Yes/ICU	Remdesivir, TPE, solumedrol IV	MMF, Bela withheld	Severe	Alive
4	56/F	Kidney	TAC, MMF	Fever, cough, myalgia	Normal	7	Nonreactive	No	None	MMF withheld	Mild	Alive
5	49/M	Kidney	TAC, MMF	Cough, myalgia, headache	Normal	9	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
6	46/M	Kidney	TAC, MMF	Fatigue, diarrhea, hematuria	Bilateral interstitial opacities	33	Nonreactive	No	Casirivimab/imdevimab	MMF dose decreased by 50%	Mild	Alive
7	81/F	Kidney	TAC, MMF	Fever	Left sided consolidation	50	Total: 15.5; IgG: nonreactive	Yes/ward	Remdesivir	MMF withheld	Moderate	Alive
8	46/M	Kidney	TAC, MMF, Pred	Fever, chills, fatigue, nausea, diarrhea	Bilateral opacities	6	Nonreactive	Yes/ICU	Remdesivir, Dexa, TPE	MMF withheld	Severe	Inpatient
9	47/F	Kidney-pancreas	TAC, MMF, Pred	Fever, fatigue, headache, cough	Normal	37	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
10	63/F	Kidney	TAC, MMF	Cough, dysuria, flank pain	Normal	15	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
11	58/M	Kidney	TAC, MMF, Pred	Cough, nasal congestion, fatigue	Normal	41	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
12[c]	47/F	Liver	TAC, MMF, Pred	Cough, fatigue	Normal	11	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
13	65/M	Liver	Sirolimus, MMF	Cough, dyspnea, diarrhea, nasal congestion, fatigue	Bilateral opacities	73	Total: 36.10; IgG: nonreactive	Yes/ward	Remdesivir, Dexa	MMF dose decreased by 50%	Moderate	Alive
14	62/F	Kidney-pancreas	TAC, MMF	Fever, fatigue, dyspnea	Right sided opacities	50	Nonreactive	Yes/ward	Remdesivir, Dexa	MMF withheld	Moderate	Alive
15[c]	56/M	Kidney	TAC, MMF, Pred	Cough, fatigue, arthralgia, fever, dyspnea	Bilateral opacities	4	Total: 18.8; IgG: 2.68	Yes/ICU	Remdesivir, Dexa	MMF withheld	Severe	Death
16	70/F	Lung	TAC, Pred, MMF	Nausea, diarrhea, chest pain	Right-sided opacities	23	Nonreactive	Yes/ward	Remdesivir, Dexa	MMF withheld	Moderate	Alive
17	62/M	Kidney	TAC, MMF	Dyspnea	Bilateral opacities	85	Total: 4.94; IgG: 3.85	Yes/ward	Remdesivir, Dexa	MMF withheld	Moderate	Alive
18	73/M	Kidney	Pred, MMF, Bela	Fever, cough, dyspnea	Bilateral interstitial opacities	96	Nonreactive	No	Casirivimab/imdevimab	MMF withheld	Mild	Alive
19	73/M	Heart	Cyclosporine, MMF, Pred	Cough	Normal	74	Total: 51.6; IgG: 2.54	Yes/ICU	None	MMF withheld	Moderate	Alive

(*Continued next page*)

TABLE 1. (Continued)

Patient characteristics and outcomes

Patient	Age/sex	Type of organ transplant	Maintenance IS at the time of vaccine	Symptoms	Chest X-ray	Time from vaccine to COVID-19 diagnosis (d)	Antibody testing[a] (total; IgG)	Hospitalized for COVID-19/level of care	Treatment	Change in IS[b]	Severity of COVID-19	Outcome
20	71/M	Kidney	Pred, Bela	Fatigue, cough, dyspnea, dysgeusia	Diffuse interstitial and alveolar opacities	68	Nonreactive	Yes/ICU	Remdesivir, Dexa	Bela withheld	Severe	Inpatient
21	52/F	Kidney	MMF, TAC	Cough, sore throat	Normal	31	Total: 29.70; IgG: 9.82	Outpatient	Casirivimab/imdevimab	None	Mild	Alive
22	80/M	Heart	MMF, TAC	Fever, chills, headache	Normal	61	Total: 71.9; IgG: 1.37	Outpatient	Casirivimab/imdevimab	None	Mild	Alive
23	47/F	Kidney	TAC, MMF, Pred	Fever, cough, myalgia	Normal	34	Nonreactive	Outpatient	Casirivimab/imdevimab	MMF withheld	Mild	Alive
24	37/M	Kidney-pancreas	TAC, MMF Azathioprine	Cough, nausea, vomiting	Normal	19	Total: 49.2; IgG: 16.2	Outpatient	Casirivimab/imdevimab	Azathioprine withheld	Mild	Alive
25	32/M	Kidney	TAC, MMF, Pred	Fever, chills, fatigue, dyspnea	Left-sided infiltrate	37	Nonreactive	Outpatient	Casirivimab/imdevimab	None	Mild	Alive
26	53/F	Kidney	TAC, MMF, Pred	Cough, dyspnea, diarrhea	Bilateral opacities	91	Nonreactive	Yes/ward	Remdesivir, Dexa	MMF withheld	Moderate	Inpatient

[a]Test developed by Ortho Clinical Diagnostics measured total and IgG antibodies, expressed in signal/cutoff ratio (lower limit of positivity: 1.0).
[b]Withheld until resolution of symptoms in each patient.
[c]Received only the first dose of the vaccine.
Bela, belatacept; COVID-19, coronavirus disease 2019; Dexa, dexamethasone; ICU, intensive care unit; IgG, immunoglobulin G; IS, immunosuppression; IV, intravenous; MMF, mycophenolate mofetil; Pred, prednisone; TAC, tacrolimus; TPE, therapeutic plasma exchange.

4. Ali NM, Alnazari N, Mehta SA, et al. Development of COVID-19 infection in transplant recipients after SARS-CoV-2 vaccination. *Transplantation*. 2021;105:e104–e106.
5. Thieme CJ, Anft M, Paniskaki K, et al. The magnitude and functionality of SARS-CoV-2 reactive cellular and humoral immunity in transplant population is similar to the general population despite immunosuppression. *Transplantation*. [Epub ahead of print. March 18, 2021]. doi:10.1097/TP.0000000000003755