

## LETTER TO THE EDITOR

# Severe consequences of COVID-19 infection among vaccinated kidney transplant recipients

## To the Editor:

As the COVID-19 pandemic has reached its second year, the global worldwide vaccination effort is underway, placing the elderly and higher risk people in higher priority of receiving immunization. These high-risk people include, among others, kidney transplant recipients (KTR), who are known to be vulnerable to higher infection rate and mortality of COVID-19.<sup>1</sup> A study by Rozen-Zvi et al<sup>2</sup> has shown that over 60% of KTR do not develop appropriate levels of anti-SARS-CoV-2 antibodies, with similar findings seen in liver, heart, and lung transplant recipients,<sup>3-5</sup> but it is yet unknown whether these results translate to lower protective effect of the SARS-CoV-2 vaccines.

Our KTR follow-up clinical includes 2350 recipients, the majority of whom have been vaccinated with at least one dose of the Pfizer-BioNTech SARS-CoV-2 vaccine (BNT162b2). We have identified 25 KTRs who received at least one vaccine dose and tested positive for SARS-CoV-2 using polymerase chain reaction, at least 14 days after the first dose. Data collection for these patients was approved by our institutional review board, and informed consent was waived. Patient characteristics are detailed in Table 1. Most were male (18/25); median time from transplantation was 4 years (range 0.4–20.8 years). None of the included KTRs had an event of organ rejection within the 12 months prior to vaccination. Eighteen (72%) KTRs who tested positive for SARS-CoV-2 received two vaccine doses prior to infection, 14 of them after over 14 days following the second vaccine dose (median 38, range 4–85 days). Ten KTRs who received two vaccine doses (10/18; 56%) required hospitalization, of whom nine with severe or critical COVID-19 (according to the disease severity classification defined by the World Health Organization), and four required invasive ventilation and later died in hospital. None required renal replacement therapy (RRT) during hospitalization. All hospitalized patients had their antimetabolite discontinued and steroid doses raised; three also had their tacrolimus dosage reduced. Of seven KTRs (28%) who tested positive following one vaccine dose, three (43%) were hospitalized, required mechanical ventilation, and died during hospitalization.

In summary, our report describes 25 KTRs who had breakthrough COVID-19 infection after receiving one or two doses of mRNA-based SARS-CoV-2 vaccine. Overall, 12 patients were hospitalized with severe-critical disease; seven KTRs died in hospital, and four of them were fully vaccinated with two vaccine doses. Our

findings, alongside other data showing lack of appropriate postvaccinated antibody development in KTRs<sup>2</sup> and higher morbidity and mortality from COVID-19 in this population,<sup>1</sup> reinforce the necessity to continue monitoring of KTRs even after receiving vaccination. Moreover, these patients will likely require to continue with social distancing and wearing protective masks for prolonged periods, until the COVID-19 pandemic subsides. Meanwhile, we suggest vaccinating any possible household contacts. Furthermore, as our population received only a single type of vaccine, other studies are required to assess efficacy of other vaccines in this population, including those employing other technologies (e.g., viral vector). Additional booster doses should be considered, either universal or serology-based.

## KEYWORDS

health services and outcomes research, immunosuppressant, infection and infectious agents - viral, infectious disease

## DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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TABLE 1 Patient characteristics

No. vaccine doses	Gender	Age	Time from transplant (month)	Comorbidities	Source of COVID-19 infection	Viremia <sup>a</sup>	BMI (kg/m <sup>2</sup> )	Time from last vaccine dose to positive SARS-CoV-2 test (days)	Maintenance therapy	Hospitalization status	COVID-19 disease severity <sup>c</sup>	COVID-19 therapy	Outcome
1	F	55	83		Unknown	None	22.5	7	Tac, P	Outpatient	NS	None	Discharged
1	F	58	38		Family contact <sup>b</sup>	None	19.1	14	Tac, P	Outpatient	NS	None	Discharged
1	M	55	58		Unknown	BK	28.3	14	E, P	Inpatient	Critical	Rem, dexta	Died
1	M	60	48		Unknown	None	32.6	18	Tac, MMF, P	Outpatient	NS	None	Discharged
1	M	51	5	DM, IHD	Unknown	None	30.6	21	Tac, MMF, P	Inpatient	Critical	Rem, dexta, conv	Died
1	M	57	49	DM	Unknown	None	24	22	Tac, MMF, P	Outpatient	NS	None	Discharged
1	F	42	64	HTN	Unknown	None	22.4	24	Tac, MMF, P	Inpatient	Critical	Dexta, conv	Died
2	M	51	23	DM, HTN, IHD	Unknown	BK	24.8	4	Tac, MMF, P	Inpatient	Mild	Bamlanivimab	Discharged
2	M	35	27	HTN	Unknown	None	22.8	9	Tac, MMF, P	Inpatient	Severe	None	Discharged
2	M	34	13		Unknown	None	27.1	12	Tac, MMF, P	Outpatient	Mild	None	Discharged
2	M	34	16	HTM	Unknown	None	26	12	Tac, MMF, P	Outpatient	Mild	None	Discharged with elevated creatinine
2	M	62	246	DM, HTN	Unknown	None	29.7	25	S, MMF, P	Inpatient	Critical	Rem, dexta, conv	Died
2	M	64	25	DM, IHD, HF	Unknown	None	30	33	Tac, MMF, P	Inpatient	Severe	Rem, dexta, conv	Discharged
2	M	49	7	DM, HTN, IHD, HF	Family contact <sup>b</sup>	None	24.6	35	Tac, MMF, P	Inpatient	Severe	Dexta, conv	Discharged
2	M	65	41	DM, HTN, IHD	Public contact <sup>b</sup>	None	30.4	36	Tac, MMF, P	Inpatient	Critical	Rem, dexta	Died
2	F	26	154		Family contact <sup>b</sup>	None	13.8	38	Tac, MMF, P	Outpatient	NS	None	Discharged
2	F	40	237		Family contact <sup>b</sup>	None	20.8	43	Tac, P	Outpatient	NS	None	Discharged
2	M	77	9	DM, HTN, IHD	Unknown	None	28.6	46	Tac, MMF, P	Inpatient	Severe	Dexta	Discharged
2	M	78	59		Unknown	None	23.8	52	Tac, MMF, P	Outpatient	Mild	Dexta	Discharged
2	M	72	94	IHD	Unknown	None	25.8	53	Tac, P	Inpatient	Critical	Rem, dexta, conv	Died
2	M	68	23	DM, HTN, IHD, HF	Public contact <sup>b</sup>	None	27.5	53	Tac, MMF, P	Outpatient	NS	None	Discharged
2	M	57	121		Unknown	None	23.5	54	Tac, MMF, P	Outpatient	NS	None	Discharged
2	F	63	69		Unknown	None	30.4	73	Tac, MMF, P	Inpatient	Severe	NS	Still hospitalized
2	M	26	250		Unknown	None	24.8	85	Tac, MMF, P	Outpatient	NS	None	Discharged
2	F	70	45	DM, HTN, IHD, HF	Unknown	None	37.1	NS	Tac, MMF, P	Inpatient	Critical	Rem, conv	Died

Abbreviations: BMI, body mass index; Conv, convalescent plasma; Dexta, dexamethasone; DM, diabetes mellitus; E, everolimus; F, female; HF, heart failure; HTN, hypertension; IHD, ischemic heart disease; M, male; MMF, mycophenolic acid; NS, no specified; P, prednisone; Rem, remdesivir; S, sirolimus; Tac, tacrolimus.

<sup>a</sup> BK virus viremia was defined as viral load of  $\geq 10\,000$  copies/ml in the last 12 months. All patients were negative for CMV viremia in the 12 months prior to vaccination.

<sup>b</sup> Contact with a COVID-19 PCR proven person.

<sup>c</sup> According to the World Health Organization (WHO) scale World Health Organization (WHO) guidelines. COVID-19 Clinical management: living guidance (<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>).

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