COVID-19 Infection after SARS-CoV-2 Vaccination in Solid Organ Transplant Recipients

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ABSTRACT

Background:
Solid organ transplant recipients (SOTR) have lower humoral responses following SARS-CoV-2 vaccination. Whether this equates to reduced vaccine effectiveness in SOTR or impacts disease severity is not yet known. We used the IDSA Emerging Infections Network (EIN) to identify SARS-CoV-2 cases in vaccinated SOTR. We describe their clinical characteristics and outcomes.

Methods:
On 4/7/21, we requested case reports via the EIN listserv of COVID-19 infection following SARS-CoV-2 vaccination in immunocompromised individuals. Case reports were collected until June 7th. Online data collection included patient demographics, dates of SARS-CoV-2 vaccine administration and clinical data related to COVID-19 infection. We performed a descriptive analysis of these patient factors and compared differences between early onset (< / = 21 days after completing vaccine series) and late onset infection (> 21 days after completing vaccine series).

Results:
As of 6/7/21, 34 cases of COVID-19 infection after vaccination in SOTR were submitted. Most cases (79%) occurred in individuals who were fully vaccinated. Only 3 cases (8.5%) occurred in SOTR within their first year after transplantation. Clinical characteristics are listed in Table 1. The vaccine administration date was known for 26 SOTR among whom symptoms occurred a median of 26.5 days (IQR 21.75 days, range 5-79 days) after completing the COVID-19 vaccine series. Twenty-three SOTR (68%) required hospitalization of which 12 had critical illness. Outcome data was available for 29 individuals of whom 20 (69%) demonstrated improvement. When comparing SOTR with early versus late onset COVID-19 infection in relation to vaccination timing, there were no differences in disease severity (80% vs 75% with severe or critical disease, p=NS) or outcome (30% vs 31% died or deteriorating, p=NS).Table 1: Characteristics of Solid Organ Transplant Recipients with COVID-19 Infection Following SARS-CoV-2 Vaccination

Conclusion:
SARS-CoV-2 infections after vaccination are occurring in SOTR, including cases of critical illness, suggesting reduced vaccine effectiveness within this vulnerable population. We did not appreciate any correlation between time from vaccination and COVID-19 disease severity or outcome. Further studies evaluating the true incidence of and risk factors for breakthrough infections among vaccinated SOTR are needed.

BACKGROUND

- Solid organ transplant recipients (SOTR) have diminished humoral immune responses to COVID-19 vaccines and have higher rates of vaccine breakthrough infections compared to the general population.
- There is limited data on the characteristics of COVID-19 vaccine breakthrough infections in SOTR.

METHODS

- Between 4/7/21 and 6/21/21 we requested case reports via the Emerging Infections Network (EIN) listserv of SARS-CoV-2 infection following COVID-19 vaccination in SOTR.
- Online data collection included patient demographics, dates of COVID-19 vaccine administration and clinical data related to COVID-19.
- Patients were considered fully vaccinated 14 days after completing COVID-19 vaccine series.
- We performed a descriptive analysis of patient factors and evaluated variables associated with critical disease or need for hospitalization using chi-square or Fisher's exact testing. Two-sided p-values <0.05 were considered statistically significant.

RESULTS

- 66 cases of SARS-CoV-2 infection after vaccination in SOTR were collected.
- Nearly two-thirds of cases (43/66, 65.2%) occurred in fully vaccinated SOTR with symptoms developing at a median of 34 days from last vaccination.
- Monoclonal antibodies were administered to 53.5% (15/28) of SOTR with mild disease; remdesivir was administered to 61.9% (13/21) of SOTR with severe disease and 29.4% (5/17) with critical disease.
- There were no differences in hospitalization (60.5% vs. 55.6%, p=0.72) or critical disease (20.9% vs. 33.3% p=0.30) among those who were fully vs. partially vaccinated.
- There were no differences in hospitalization or critical disease among SOTR who received BNT162b2 or mRNA-1273
- Maintenance immunosuppressive therapy at the time of SARS-CoV-2 infection did not impact the frequency of critical disease or need for hospitalization.
- Mortality among fully vaccinated SOTR with COVID-19 vaccine breakthrough infection was 7%.

Table 1: Patient demographics and clinical characteristics

Gender	Number (%)
Male	37 (56.1%)
Female	28 (42.4%)
Unknown	1
Age	
18-44	7 (10.6%)
45-64	28 (42.4%)
65-74	24 (36.4%)
75-84	7 (10.6%)
Organ Transplanted	
Lung	14 (21.2%)
Heart	10 (15.2%)
Kidney	30 (45.5%)
Liver	5 (7.6%)
Dual†	7 (10.6%)
Time from Organ Transplant	
<1 year	9 (13.6%)
1-2 years	9 (13.6%)
2-5 years	20 (30.3%)
>5 years	24 (36.4%)
Unknown	4 (6.1%)
Vaccine Administered	
BNT162b2 (Pfizer)	49 (74.2%)
mRNA-1273 (Moderna)	14 (21.2%)
Ad26.COV2.S (Johnson & Johnson)	1 (1.5%)
Unknown	1 (1.5%)
Symptom Onset‡	
After 1st vaccine dose	9 (13.6%)
After completing vaccine series	
<14 days after completing all recommended doses	9 (13.6%)
14 or more days after completing all recommended doses	43 (65.1%)
Maintenance Immunosuppression	
Calcineurin inhibitor + Mycophenolate	17 (25.8%)
Steroids + Calcineurin inhibitor + Mycophenolate or Azathioprine	38 (57.6%)
Other	10 (9.1%)

†5 kidney/pancreas, 2 liver/kidney

‡ Date of vaccine administration not known for 5 individuals, 2 fully vaccinated individuals were asymptomatic

Table 2: Outcomes of COVID-19 following SARS-CoV-2 vaccination in solid organ transplant recipients

Disease Severity	**Number (%)**
Mild	28 (42.4%)
Severe	21 (31.8%)
Critical†	17 (25.8%)
Outcomes	
Recovered/Improving	45 (68.2%)
Deteriorating/Sequelae	11 (16.7%)
Died	6 (9.1%)
Unchanged	2 (3%)
Unknown	2 (3%)

† 10 patients with critical illness required mechanical ventilation

Table 3: Outcomes of COVID-19 after vaccination in fully vs. partially vaccinated solid organ transplant recipients †

	Fully vaccinated¶ N=43 (%)	**Partially vaccinated N=18 (%)**	**P-value**
Hospitalized	26 (60.5%)	10 (55.6%)	p = 0.72
Not Hospitalized	17 (39.5%)	8 (44.4%)	
Critical Disease	9 (20.9%)	6 (33.3%)	p = 0.30
Not Critical Disease	34 (79.1%)	12 (66.7%)	
Recovered/Improving	29 (70.7%)	13 (72.2%)	p = 0.90
Not improving‡	12 (29.3%)	5 (27.8%)	

† Date of vaccine administration was not known for 5 cases. These cases were excluded from the analysis.

‡ Not improving includes the following complications: Died, deteriorating, sequelae, unchanged clinical status.

¶ Final outcome was not reported for 2 patients who were fully vaccinated.

LIMITATIONS

- Sampling bias.
- Data collection was not complete for all cases.
- Serological data was only available for a subset of cases but only at the time of or after PCR confirmation of SARS-CoV-2 infection.
- We did not capture viral sequencing data.

CONCLUSIONS

- Fully vaccinated SOTR remain at risk for severe and critical COVID-19.
- The mortality among SOTR with COVID-19 vaccine breakthrough infection is 7% which is higher than the mortality from COVID-19 vaccine breakthrough infection in the general population (2%).
- Further studies are needed to determine long-term effectiveness of COVID-19 vaccination in SOTR, impact of viral variants on outcomes of vaccinated SOTR, and whether additional vaccine doses of mRNA vaccine will provide enhanced protection.

Select References

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