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Antibody response to 2-dose SARS-CoV-2 mRNA vaccination in pediatric solid organ transplant recipients

While many adult solid organ transplant recipients (SOTRs) have impaired antibody response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination, pediatric SOTRs' response has not been assessed.[1,2] We report the immunogenicity and safety of BNT162b2 mRNA vaccination in pediatric SOTRs.

1 | METHODS

After approval by the Johns Hopkins University Institutional Review Board, pediatric (12–18 years) SOTRs were recruited April-August 2021 through clinic communications and social media for this prospective cohort. Samples were drawn before vaccination, two weeks after vaccine 1 (post-V1), and one month after vaccine 2 (post-V2) and were processed using the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay for antibodies against the spike protein receptor-binding domain.[3] A positive cutoff of ≥0.8 U/ml was used.[4]

All patients were included in the safety analysis ($N = 57$). After exclusion of patients with reported previous SARS-CoV-2 infection or history of a pre-vaccination positive antibody test ($n = 5$), antibody serologies from 52 patients were available for analysis. Of these 52 patients, 7 had only post-V1 serologies available, 15 had only post-V2 serologies available, and 30 had serologies for both post-V1 and post-V2. Fisher's exact test was used to compare patients who did and did not develop a positive antibody response post-V2 ($n = 45$). All analyses used Stata 15.1 (StataCorp).

2 | RESULTS

Fifty-seven pediatric SOTRs received the BNT162b2 vaccine. Median (range) age was 14 (12–18) years; 40% were male and 74% white. Patients were median 10 (IQR 5–13) years from transplant and liver transplant (44%) was most common. Reported main vaccine side effects included mild to moderate injection site pain (83.5%) and fatigue (39.5%). No patients developed allergic reactions or organ rejection.

Antibody titers were positive in 56.8% (21/37) of patients with post-V1 titers and 73.3% (33/45) with post-V2 titers. Median (IQR) antibody titers were 98.7 (12.9–158) U/ml and 1876 (178–2500) U/ml, respectively. Among patients with both serologies available ($n = 30$), 16.7% had negative titers after both, 33.3% had a negative titer that became positive, and 46.7% had positive titers after both. For those who had positive titers after both, antibody titer increased from the median (IQR) of 133 (78.7–207) U/ml post-V1 to 2500 (2500–2500) U/ml post-V2. One patient had a positive post-V1 titer that became negative post-V2.

Having received a transplant within the past 3 years ($p = .010$), multiple immunosuppressive agents ($p = .031$), and antimetabolite immunosuppression ($p = .020$) were associated with negative post-V2 response (Table 1).

Two patients tested positive for SARS-CoV-2 infection during the study period. The first experienced 7 days of mildly symptomatic infection not requiring hospitalization between their two vaccine doses without an available post-V1 serology. The second developed infection 46 days after both vaccine doses with negative antibody titers.

3 | DISCUSSION

In this observational cohort, 73.3% of pediatric SOTRs had a positive antibody response after receiving two doses of BNT162b2. Compared to adult SOTRs with reported seroconversation rates ranging from 5% to 58.8%,[5] these findings suggest that pediatric SOTRs may be able to mount more robust immune responses to SARS-CoV-2 vaccination. Similar to adult SOTRs, shorter time from transplantation, use of multiple immunosuppressive agents, and maintenance anti-metabolite immunosuppression were associated with a negative antibody response.[1,2] Importantly, no organ rejection or other unanticipated adverse events were reported.

While this is a small convenience sample, our preliminary data, which is the first on vaccine response in pediatric SOTRs in the United States, suggest that SARS-CoV-2 vaccination is immunogenic and safe. Given the recent Food and Drug Administration emergency authorization amendment for third vaccines in immunocompromised individuals, our data may provide further evidence for the potential need of additional vaccines for SOTRs. Larger studies will be needed on vaccination safety effectiveness in immunosuppressed children and interventions to optimize response.

KEYWORDS

clinical research/practice, health services and outcomes research, infection and infectious agents - viral, organ transplantation in general, pediatrics, vaccine

TABLE 1 Demographics and clinical characteristics of study participants who provided an antibody titer 1 month after vaccine 2, stratified by humoral response

n (%)	Positive response after vaccine 2 ($n = 33$)[a]	Negative response after vaccine 2 ($n = 12$)[a]	p-value[b]
Demographics			
Age group, years			1.0
12–15	28 (84.9)	11 (91.7)	
16+	5 (15.2)	1 (8.3)	
Sex, male	14 (42.4)	5 (41.7)	1.0
Race, white[c]	22 (71)	9 (90)	.4
Hispanic or Latino, yes[d]	2 (6.3)	0 (0)	1.0
Transplant characteristics			
Organ			.068
Liver	17 (51.5)	2 (16.7)	
Kidney	8 (24.2)	5 (41.7)	
Heart	8 (24.2)	4 (33.3)	
Liver-kidney	0 (0)	1 (8.3)	
Time since transplant, years			.024
<3	2 (6.1)	5 (41.7)	
3–11	18 (54.6)	4 (33.3)	
≥12	13 (39.4)	3 (25)	
<3 vs ≥3 Years since transplant			.010
Immunosuppression regimen			
Number of agents[e]			.013
0	1 (3.1)	1 (10)	
1	15 (46.9)	0 (0)	
2	10 (31.3)	4 (40)	
3+	6 (18.8)	5 (50)	
Single vs multiple agents (2+)[e]			.031
Agents used[f]			
Tacrolimus[g]	29 (87.9)	10 (90.9)	1.0
Anti-metabolite[h]	14 (42.4)	10 (83.3)	.020
Sirolimus[i]	6 (18.8)	1 (10)	1.0
Corticosteroids	5 (15.2)	5 (41.7)	.10
Cyclosporine	3 (9.1)	0 (0)	.6
Treated for rejection in past 6 months[j,k]	1 (3.3)	1 (10)	.4

[a]Table includes any patient in the study who had an antibody result available one month after their second vaccine, regardless of whether the patient was positive or negative after their first vaccine. Table does not include patients who reported a prior history of COVID, history of a pre-vaccination positive SARS-CoV-2 antibody test, or positive baseline serology in our study.

[b]All univariate statistical comparisons were performed using the Fisher's exact test.

[c]Four missing (2 positive, 2 negative).

[d]Three missing (1 positive, 2 negative).

[e]Three patients excluded because of incomplete data.

[f]Includes reported immunosuppression agents used at start of the study or at time of vaccine 1. Immunosuppression was not mutually exclusive, as some patients were on multiple agents. 0 patients were on everolimus or belatacept for their baseline immunosuppresion regimen prior to this study. 0 patients reported being on medications for other immune conditions including adalimumab, anakinra, baricitinib, belimumab, budesonide, certolizumab, cyclophosphamide, etanercept, hydroxychloroquine, infliximab, leflunomide, methotrexate, natalizumab, ocrelizumab, rituximab, sulfasalazine, tocilizumab, tofacitinib, and ustekinumab.

[g]One missing (negative).

[h]Includes myophenolate mofetil, mycophenolic acid, or azathioprine.

[i]Three missing (1 positive, 2 negative).

[j]Five missing (3 positive, 2 negative).

[k]No patients received rituximab, IVIG, plasma exchange, or thymoglobulin in the 6 months prior to this study.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. All authors contributed to drafting the work or revising it critically for important intellectual content and final approval of the version to be published. CQ and DM provided agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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