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Riding the Waves: Infection by SARS-CoV-2 Variants in Solid Organ Transplant Recipients at Texas Children's Hospital

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Abstract

Background: Texas Children's Hospital is the largest pediatric solid organ transplant (SOT) program in the US, performing heart, kidney, liver, and lung transplants. Limited data exist about SARS-CoV-2 infection (COVID-19) in the pediatric SOT population. We evaluated the impact of different SARS-CoV-2 variants in a cohort of PCR positive SOT recipients.

Methods: SOT recipients with a positive SARS-CoV-2 PCR test from 3/1/2020 to 2/28/2022 were included in the cohort. The study period was divided into 3 eras based on the predominant circulating variant of SARS-CoV-2: 3/2020-6/2021 original/Alpha, 7/2021-11/2021 Delta, and 12/2021-2/2022 Omicron variants. Retrospective medical record review was performed; Chi-squared and Fischer exact test were used to compare groups.

Results: A total of 271 of 950 (29%) SOT recipients tested positive for SARS-CoV-2 during the study period. By organ, 87/270 (32%) heart, 57/212 (27%) kidney, 92/366 (25%) liver, and 25/83 (33%) lung recipients had COVID-19 infection. By era, there were 102 (38%) original /Alpha, 71 (26%) Delta, and 98 (36%) Omicron. The patients' median age was 12.72 years (IQR 6.6, 16.2) with a minority of recipients being female (42%). Common comorbidities included hypertension (50%), obesity (13%), diabetes (10%), and chronic kidney disease (10%); 35% had no comorbidities aside from chronic immunosuppression post-transplant (Table 1). Overall, 80% of recipients were symptomatic (Figure 2), and 56 (21%) required hospitalization. Hospitalization rates were highest (25%) during original/Alpha and Delta compared to 12% for Omicron (p=0.03) eras (Table 2). Need for respiratory support, ICU admission, and all-cause mortality did not vary by era (Table 2). Three SOT recipients (2 original/Alpha and 1 Delta) were diagnosed with multi-inflammatory syndrome in children (MIS-C).

Conclusions: Our study suggests that pediatric SOT recipients have a high risk for hospitalization and short-term complications with COVID-19; Omicron appears to cause less severe disease, including MIS-C. Additional studies are needed to understand long-term complications of COVID-19 in SOT recipients.

Background

- TCH is the largest pediatric solid organ transplant (SOT) program in the US, performing heart, kidney, liver, and lung transplants.
- We evaluated the impact of different SARS-CoV-2 variants in a cohort of PCR positive SOT recipients (SOTR).

Methods

- A retrospective review of electronic medical records of SARS-CoV-2 positive transplant patients seen at TCH from March 1, 2020 to February 28, 2022 was conducted to describe clinical manifestations, risk factors and short-term outcomes of each SARS-CoV-2 variant in SOTR
- The study period was divided into 3 eras based on the predominant circulating variant of SARS-CoV-2: 3/2020-6/2021 original/Alpha, 7/2021-11/2021 Delta, and 12/2021-2/2022 Omicron variants.
- Statistics: Demographic and clinical characteristics were compared using Chi-squared or Fisher exact tests for categorical data and Kruskal-Wallis test for continuous data. All analyses were completed using STATA.

Results

- There were 271 SARS-CoV-2 positive SOT recipients representing 29% of 950 SOT recipients followed at TCH. Of positive cases, 102 (38%) cases occurred during the original/Alpha variant, 71 (26%) during Delta variant, and 98 (36%) during Omicron period (Figure 1).

Results

Table 1: Patient Demographics

	SOT recipients with SARS-CoV-2 infection N=271	SOT recipients requiring hospitalization for SARS-CoV-2 infection N=56	SOT recipients not requiring hospitalization for SARS-CoV-2 infection N=215	P-value
Age [yr]				
Median, (IQR)	12.7 (6.6, 16.2)	13.4	12.4	0.49
Female	115 (42%)	24 (43%)	91 (42%)	>0.99
Ethnicity/ Race				0.12
Hispanic	117 (43%)	24 (43%)	93 (43%)	
Black	49 (18%)	15 (27%)	34 (16%)	
White	95 (35%)	17 (30%)	78 (36%)	
Other	10 (3%)	0	10 (5%)	
Organ				**<0.01**
Heart	87 (32%)	16 (29%)	71 (33%)	
Kidney	57 (21%)	26 (46%)	31 (14%)	
Liver	92 (34%)	7 (13%)	85 (40%)	
Lung	27 (9%)	5 (9%)	22 (10%)	
Multi/other	8 (3%)	2 (4%)	8 (3%)	
Time to infection from transplant				
Median [mo], (IQR)	41.9 (19.2, 91.6)	33.1 (13.1, 65.3)	44.3 (20.6, 92.7)	0.12
Induction/rejection therapy*				
ATG	21 (8%)	4 (9%)	17 (8%)	0.78
Basiliximab	5 (2%)	2 (4%)	3 (1%)	0.22
Rituximab	9 (3%)	2 (4%)	7 (3%)	0.67
Maintenance Immunosuppression				
Tacrolimus	253 (93%)	40 (85%)	213 (95%)	**0.02**
Mycophenolate	129 (47%)	30 (64%)	99 (44%)	**0.02**
Steroids	77 (28%)	18 (38%)	59 (26%)	0.11
Sirolimus	38 (14%)	8 (17%)	30 (13%)	0.49
Cyclosporine	9 (3%)	5 (11%)	4 (2%)	**<0.01**
Azathioprine	7 (3%)	2 (4%)	5 (2%)	0.35
Co-morbidities				
Obesity	35 (13%)	5 (9%)	30 (14%)	0.24
Diabetes	26 (10%)	6 (11%)	20 (9%)	0.43
Hypertension	136 (50%)	30 (54%)	106 (49%)	0.15
Heart disease	20 (7%)	4 (9%)	16 (7%)	0.76
Chronic lung disease	25 (9%)	7 (15%)	18 (8%)	0.17
Chronic kidney disease	27 (10%)	9 (19%)	17 (8%)	0.03
Tracheostomy	5 (2%)	2 (4%)	3 (1%)	0.22
None	95 (35%)	18 (32%)	77 (36%)	0.23
Vaccine prior to SARS-CoV-2 infection				
No doses				**0.09**
>= 1 dose	203 (75%)	47 (84%)	156 (73%)	
	68 (25%)	9 (16%)	59 (27%)	

*Within 6 months prior to SARS-CoV-2 diagnosis

Figure 1: Timeline of SARS-CoV-2 infection in SOT recipients at TCH, 3/1/20-2/28/22

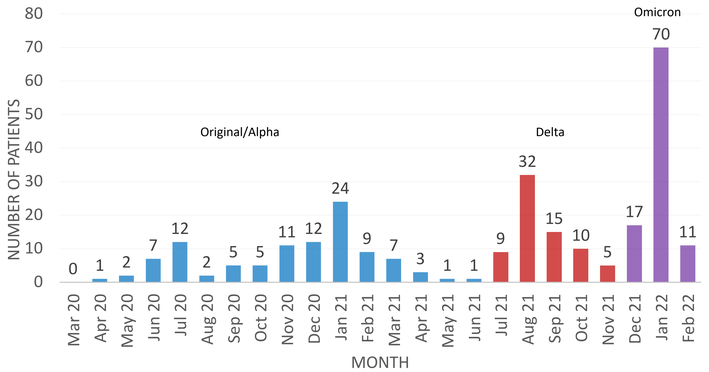
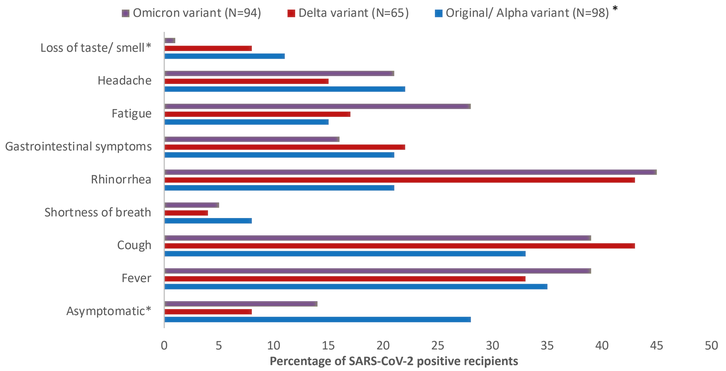


Figure 2 : Clinical Manifestations



*N for each era includes recipients for which symptom data was available

Table 2: Treatments and Outcomes

	Total N=271	Original/Alpha N=102	Delta N=71	Omicron N=98	p-value
Hospitalization for COVID-19	56 (21%)	26 (25%)	18 (25%)	12 (12%)	**0.03**
ICU admission	8 (3%)	3 (3%)	4 (7%)	1 (1%)	0.23
Oxygen therapy	9 (3%)	6 (6%)	2 (3%)	1 (1%)	0.18
Remdesivir treatment	18 (7%)	6 (6%)	6 (8%)	6 (6%)	0.79
Monoclonal antibody therapy	15 (6%)	1 (1%)	6 (8%)	8 (8%)	**0.02**
MIS-C	3 (1%)	2 (2%)	1 (1%)	0	0.48
All-cause mortality	5 (2%)	3 (3%)	2 (3%)	0	0.26

- Of the 18 patients who received remdesivir, two were prescribed a 3-day course and 16 were prescribed a 5-day course. Two children did not complete the intended 5-day course; one because of clinical improvement and the other due to elevated AST and ALT values that returned to normal after discontinuation of remdesivir.
- Fifteen recipients (6%) received monoclonal antibodies (1 during the original/Alpha variant era, 6 during Delta, and 8 during Omicron), 4 received convalescent plasma (2 during the original/Alpha variant era and 2 during Delta).

Table 3: Vaccine Status at First Time SARS-CoV-2 Infection^

Number of SARS-CoV-2 vaccine doses^^	Original/Alpha era N=695		Delta era N=661		Omicron era N=679	
	SARS-CoV-2 +	Total N	SARS-CoV-2 +	Total N	SARS-CoV-2 +	Total N
0 doses	102 (20%)	507	61 (17%)	369	39 (12%)	319
1 dose	0	26	1* (2%)	49***	5* (16%)	31**
2 doses	0	161	8 (6%)	131	18 (13%)	142
3 doses	0	1	3 (3%)	112	30 (16%)	185
4 doses	0	0	0	0	0	2

^ Population includes all SOT recipients followed at TCH during the study era who had no history of SARS-CoV-2 infection at the start of the study era and for whom vaccine records were available to review. ^^ By end of the SARS-CoV-2 era. * 1 subject received JJ vaccine. ** 2 subjects received JJ vaccine. *** 3 subjects received JJ vaccine.

- Vaccine status varied throughout cohort given timing of availability and emergency use authorizations for different age groups.
- Vaccine effectiveness for SARS-CoV-2 acquisition was calculated using one or more doses of vaccine. Vaccine effectiveness was 100% during the original/Alpha variant era, 76% during the Delta era, and 0% during the Omicron era.

Conclusions

- Pediatric SOT recipients with SARS-CoV-2 infection have a high risk for hospitalization and short-term complications, including MIS-C.
- Similar to the general population, Omicron appears to cause less severe disease in pediatric SOT recipients.
- Additional studies are needed to understand long-term complications of SARS-CoV-2 in SOT recipients.