The pediatric solid organ transplant experience with COVID-19: An initial multi-center, multi-organ case series

Matthew B. Goss1 | N. Thao N. Galván2 | Wenly Ruan3 | Flor M. Munoz4 | Eileen D. Brewer5 | Christine A. O'Mahony2 | Ernestina Melicoff-Portillo6 | William J. Dreyer7 | Tamir A. Miloh8 | Francisco G. Cigarroa9 | Daniel Ranch10 | Dor Yoeli11 | Megan A. Adams11 | Sarah Koohmaralie12 | Diana M. Harter13 | Abbas Rana2 | Ronald T. Cotton2 | Beth Carter14 | Shreena Patel14 | Nicolas F. Moreno1 | Daniel H. Leung3 | John A. Goss2

1McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX, USA
2Division of Abdominal Transplantation, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, USA
3Department of Pediatrics, Gastroenterology, Hepatology, and Nutrition Section, Baylor College of Medicine, Houston, TX, USA
4Department of Pediatrics, Infectious Diseases Section, Baylor College of Medicine, Houston, TX, USA
5Renal Section, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA
6Pulmonary Section, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA
7Cardiology Section, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA
8Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA
9Division of Abdominal Transplantation, University Transplant Center, UT Health San Antonio, San Antonio, TX, USA
10Division of Nephrology, Department of Pediatrics, UT Health San Antonio, San Antonio, TX, USA
11Division of Transplant Surgery, Department of Surgery, University of Colorado Anschutz Medical Campus and Children's Hospital Colorado, Aurora, CO, USA
12Liver Transplantation Service, Texas Children's Hospital, Houston, TX, USA
13Transplant Services, Texas Children's Hospital, Houston, TX, USA
14Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Keck School of Medicine of USC, Los Angeles, CA, USA

Correspondence
Matthew B. Goss, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX, USA.
Email: matthew.b.goss@uth.tmc.edu

Abstract
The clinical course of COVID-19 in pediatric solid organ transplant recipients remains ambiguous. Though preliminary experiences with adult transplant recipients have been published, literature centered on the pediatric population is limited. We herein report a multi-center, multi-organ cohort analysis of COVID-19-positive transplant recipients ≤ 18 years at time of transplant. Data were collected via institutions’ respective electronic medical record systems. Local review boards approved this cross-institutional study. Among 5 transplant centers, 26 patients (62% male) were reviewed with a median age of 8 years. Six were heart recipients, 8 kidney, 10 liver, and 2 lung. Presenting symptoms included cough (n = 12 (46%)), fever (n = 9 (35%)), dry/sore throat (n = 3 (12%)), rhinorrhea (n = 3 (12%)), anosmia (n = 2 (8%)), chest,...

Abbreviations: AA, African American; ACR, acute cellular rejection; ATG, anti-thymocyte globulin; BMI, body mass index; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; CXR, chest X-ray; ECMO, extracorporeal membrane oxygenation; FDA, Food and Drug Administration; GBS, group B streptococcus; HCQ, hydroxychloroquine; Hct, hematocrit; Hgb, hemoglobin; HTN, hypertension; MMF, mycophenolate mofetil; NP, nasopharyngeal; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TAC, tacrolimus; USA, United States; UTI, urinary tract infection; WBC, white blood cell; Wnl, within normal limits.
pain (n = 2 (8%)), diarrhea (n = 2 (8%)), dyspnea (n = 1 (4%)), and headache (n = 1 (4%)). Six patients (23%) were asymptomatic. No patient required supplemental oxygen, intubation, or ECMO. Eight patients (31%) were hospitalized at time of diagnosis, 3 of whom were already admitted for unrelated problems. Post-transplant immunosuppression was reduced for only 2 patients (8%). All symptomatic patients recovered within 7 days. Our multi-institutional experience suggests the prognoses of pediatric transplant recipients infected with COVID-19 may mirror those of immunocompetent children, with infrequent hospitalization and minimal treatment, if any, required.

**KEYWORDS**
pediatric transplantation, viral infection

## 1 | INTRODUCTION

The COVID-19 pandemic caused by SARS-CoV-2 continues to evolve with surges in many states across the USA. While emphasis has been appropriately placed on social distancing, mask wearing, and hand hygiene, the population at large, including transplant patients, remains susceptible to infection. Many drugs that fight rejection and prolong life in organ recipients function through attenuated T-cell activation and proliferation, rendering patients more susceptible to viral infection. Thus, COVID-19 is postulated to cause disproportionate harm to transplant patients. There are currently no approved COVID-19 treatments, though the US FDA has granted emergency use authorizations for the antiviral remdesivir and the now-revoked antimalarials HCQ sulfate and chloroquine phosphate. As data on effective therapies for COVID-19 are limited, with management predominantly consisting of supportive care for patients not enrolled in clinical trials, insight into the clinical course of COVID-19 in transplant recipients is critical, particularly in children.

Many adult centers have suggested that transplant recipients are at particular risk for an arduous clinical course given their immunocompromised state, though highly associated comorbidities exist as confounders and appear to play a significant role in COVID-19 outcomes for the transplant subpopulation. In contrast, others have reported similar clinical manifestations and mortality in transplant recipients relative to the general population. It has also been suggested that immunosuppression may confer a clinical advantage by potentially mitigating immune-mediated lung injury and acute respiratory distress syndrome in late severe SARS-CoV-2 infection. This hypothesis may be more applicable to the pediatric population as children usually receive more immunosuppression per kilogram compared to adults.

As the transplant community seeks clarity regarding management and outcomes of recipients testing positive for COVID-19, experiences with adult patients currently comprise a vast majority of the literature. The few pediatric publications that do exist are limited to single case reports. In view of the age-dependent risk discrepancy observed in the general population, age may become an influential factor for treatment selection, modification of immunosuppression, and clinical prognosis upon post-transplant SARS-CoV-2 infection. Herein we report a multi-center, multi-organ cohort analysis focused on young transplant recipients and their clinical characteristics, management, and outcomes.

## 2 | MATERIALS AND METHODS

All solid organ transplant recipients ≤18 years at time of transplant with a positive test for COVID-19 between April 1, 2020, and July 20, 2020, from 5 centers (Texas Children’s Hospital, Children’s Hospital Los Angeles, Miami Transplant Institute, University of Colorado, and University of Texas Health Science Center at San Antonio) were included in this cohort analysis. COVID-19 positivity was determined via NP swab SARS-CoV-2 real-time RT-PCR (Hologic Aptima SARS-CoV-2 RT-PCR assay). IgM and IgG total SARS-CoV-2 antibodies were detected by the Ortho Clinical Diagnostics VITROS® Immunodiagnostics Products Anti-SARS-CoV-2 Test. Data were collected via institutions’ respective electronic medical record systems and were reviewed for patient characteristics, history of recent exposure, timing of presentation, symptomatology, laboratory values, immunosuppression management, antiviral treatment strategies, and clinical outcomes. Local review boards approved this cross-institutional study.

## 3 | RESULTS

During the COVID-19 pandemic between April 1, 2020, and July 20, 2020, 5 pediatric transplant centers in the USA identified 6 heart, 8 kidney, 10 liver, and 2 lung transplant recipients that were found to be COVID-19-positive post-transplant. Eight of 26 patients (31%) were hospitalized, 3 of whom were already admitted for unrelated problems. All patients with COVID-19 symptoms at the time of diagnosis recovered before manuscript submission, with full resolution
of symptoms within a median of 3 days. No patient experienced progressive deterioration or death.

### 3.1 | Demographics

Overall, patient demographics are summarized in Table 1. Sixteen of 26 patients (62%) were male. The median age of COVID-19-positive transplant recipients at time of transplant was 8 years (range 5 months–18 years). Nineteen of 26 (73%) were Hispanic, 5 (19%) were Caucasian, and 2 patients (8%) were AA. Seventeen of 26 patients (65%) were blood type O, while 8 (31%) were type A and 1 patient (4%) was of the AB blood group. BMI ranged between 17.4 and 38.8 kg/m² with 9 of 26 (35%) <20 kg/m², 11 (42%) between 20 and 30 kg/m², and 6 (23%) >30 kg/m². Eight of 26 patients (31%) had undergone kidney transplantation, 10 (38%) underwent liver transplantation, 6 (23%) were heart transplant recipients, and 2 (8%) were lung recipients. Twenty-five of 26 patients (96%) underwent transplantation with a deceased donor whole organ allograft, while a single affected kidney transplant recipient underwent living donor transplantation. The median time from transplant to initial positive COVID-19 test was 1246 days (range 12–6574 days). One patient (No. 8) tested COVID-19-positive during the index transplant hospitalization and developed cough. This 18-year-old patient had received induction immunosuppressive therapy with 3 daily doses of rabbit ATG. Thirteen of 26 patients (50%) were suspected to have had COVID-19 exposure from a family member, while 11 (42%) had community-acquired infection. Two patients (8%) were exposed by a healthcare provider.

### 3.2 | Presentation and clinical course

The 26 COVID-19-positive transplant recipients had variable clinical presentations (Table 1). The most common documented symptom was cough (n = 12 [46%]) followed by fever (n = 9 [35%]), dry/sore throat (n = 3 [12%]), rhinorrhea (n = 3 [12%]), anosmia (n = 2 [8%]), chest pain (n = 2 [8%]), diarrhea (n = 2 [8%]), and dyspnea and headache in 1 patient each (4%). Six patients (23%) did not have any symptoms (4 kidney, 1 liver, and 1 lung recipient).

Eight of the affected patients (31%) were hospitalized at the time of COVID-19 diagnosis; however, 3 patients (Nos. 3/7/8) were already admitted for unrelated problems. The remaining 5 patients (19%) were hospitalized for a median time of 3 days, with presenting symptoms including a combination of fever (n = 3), cough (n = 2), chest pain (n = 1), diarrhea (n = 1), and rhinorrhea (n = 1). Eight of 26 patients (31%) were evaluated by CXR or CT of the chest, and only patients 8 (kidney recipient) and 15 (liver recipient) had multifocal pulmonary infiltrates consistent with COVID-19. Six patients (23%) had a decreased WBC count (<4000 per µL of blood), and 4 (15%) had low Hgb (<13.5 g/dL for males, <12.0 g/dL for females) and Hct (<41% for males, <36% for females) (1 patient had both a decreased WBC count and low Hgb and Hct); however, none of the patients presented with laboratory evidence of hepatitis or other biochemical abnormalities. There were no observed or quantified differences in severity of clinical course or treatment dependent on blood type.

Twelve of 26 patients (46%) had inflammatory biomarkers measured. Of the 12, 7 (58%) had elevation of CRP (>1.0 mg/L) and/or ferritin (>300 ng/mL for males, >150 ng/mL for females). In addition, 5 patients (42%) had elevation of fibrinogen (>400 mg/dL) and/or D-dimer (>0.5 mg/L). A smaller subset of 4 patients (15%) had serum troponin levels measured, and all were Wnl (<0.4 ng/mL). Age among our pediatric cohort did not appear to influence clinical severity.

Follow-up COVID-19 NP swab testing was available in 10 of 26 patients (38%) with 5 of 10 testing negative (median time of 13 days after initial positive test) and the other 5 remaining positive (median time of 15 days after initial positive test). Only 1 patient (No. 18) was tested for the presence of SARS-CoV-2 antibodies, which detected IgG-specific antibodies, while IgM antibodies were negative indicating previous and not active infection.

### 3.3 | Treatment/immunosuppression

Of the 26 affected patients, none required supplemental oxygen or intubation (it should be noted that No. 3 is chronically ventilatory dependent—Table 1). One patient (No. 13) with paralysis and neurogenic bladder had a concomitant UTI with GBS, which was treated with 10 days of intravenous cefazolin. The majority of patients (25/26) received TAC-based immunosuppression; one received sirolimus. One liver transplant patient (No. 15), who presented with cough and patchy infiltrates on CXR, was hospitalized and had reduction in immunosuppression with oral sirolimus held and TAC decreased to trough level of 4-6 ng/mL from previous 6-8 ng/mL. Symptoms resolved in approximately 48 hours, and the patient was discharged home on pre-admission immunosuppression doses. One kidney transplant patient (No. 8), who contracted COVID-19 during the index transplant hospitalization and developed cough, had reduction in immunosuppression with MMF decreased to 270 mg/m²/dose from previous 360 mg/m²/dose and TAC decreased to trough level 8-10 ng/mL from previous 10-12 ng/mL. The cough resolved within 72 hours, but the patient remained hospitalized for other reasons. Seven days after reduction in immunosuppression, serum creatinine increased to 2 mg/dL and kidney transplant biopsy revealed moderate ACR, necessitating high-dose steroid therapy and an increase in maintenance immunosuppression. Immunosuppressive regimens were not adjusted in 24 of 26 COVID-19-positive post-transplant patients.

### 4 | DISCUSSION

As the morbidity and mortality associated with COVID-19 continue to impact the world, particularly in the USA, SARS-CoV-2 infection among solid organ transplant recipients is inevitable. Due to immunosuppressive treatment, elevated risk of co-infections...
TABLE 1  Demographics and clinical presentation of pediatric solid organ transplant recipients with SARS-CoV-2 infection

| Pt | Sex | Tx age (years) | Ethnicity | Blood type | BMI  | Organ | Donor type | Pertinent medical problems post-transplant |
|----|-----|----------------|-----------|------------|------|-------|------------|------------------------------------------|
| 1  | M   | 0.4            | Hispanic  | O+         | 20.2 | Heart | Deceased  | Shone's syndrome                          |
| 2  | M   | 4              | White     | O+         | 20.7 | Heart | Deceased  | Atherosclerotic disease, CVA, GERD, asthma |
| 3  | M   | 0.8            | Hispanic  | A+         | 21.8 | Heart | Deceased  | Cardiomyopathy, AKI, seizures             |
| 4  | M   | 0.5            | Hispanic  | O+         | 17.4 | Heart | Deceased  | Prematurity, chromosome 15q duplication, asthma |
| 5  | M   | 17             | White     | A+         | 25.1 | Heart | Deceased  | CVA, kidney disease                       |
| 6  | F   | 13             | Hispanic  | A+         | 30.7 | Heart | Deceased  | Restrictive cardiomyopathy, pulmonary HTN  |
| 7  | F   | 10             | Hispanic  | O+         | 33.1 | Kidney| Living    | Reflux nephropathy, DM, asthma, CVA, pancreatitis, migraines, hyponatremia |
| 8  | F   | 18             | Hispanic  | A+         | 22.2 | Kidney| Deceased  | Loss first transplant acute rejection, chronic peritoneal dialysis, ADHD, seizure disorder, bx reveals mod ACR |
| 9  | F   | 15             | Hispanic  | AB+        | 38.8 | Kidney| Deceased  | HTN, pulmonary edema, mild tricuspid and pulmonary regurgitation |
| 10 | M   | 17             | Hispanic  | A+         | 32.5 | Kidney| Deceased  | Sarcoidosis, UTIs                         |
| 11 | M   | 13             | AA        | O+         | 21.4 | Kidney| Deceased  | IgA nephropathy, HTN, DM, hypothyroidism  |
| 12 | M   | 12             | Hispanic  | O+         | 29.3 | Kidney| Deceased  | Cystic dysplasia, HTN                      |
| 13 | M   | 14             | AA        | O+         | 19.8 | Kidney| Deceased  | ACR/AMR, paralysis, neurogenic bladder     |
| 14 | M   | 6              | Hispanic  | O+         | 20.8 | Kidney| Deceased  | CMV, C diff, hepatoblastoma               |
| 15 | M   | 13             | Hispanic  | O+         | 33.3 | Liver | Deceased, Whole | Hepatic adenomatosis, insulin resistance |
| 16 | F   | 8              | White     | O−         | 25.5 | Liver | Deceased, Whole | Biliary atresia, failed Kasai |
| 17 | F   | 1.1            | White     | A+         | 24.4 | Liver | Deceased, Whole | Hepatoblastoma, HTN, CKD |
| 18 | F   | 0.6            | Hispanic  | O+         | 19.4 | Liver | Deceased, Whole | Failure to thrive |
| 19 | F   | 13             | Hispanic  | O+         | 33.5 | Liver | Deceased, Whole | Ellis-van Crevel syndrome, HTN, asthma, hypothyroidism |
| 20 | M   | 1.9            | White     | O+         | 19.1 | Liver | Deceased, Whole | Hepatoblastoma, adrenal insufficiency, RTA, chemo-induced anemia/thrombocytopenia |
| 21 | F   | 3              | Hispanic  | O+         | 17.7 | Liver | Deceased, Whole | None |
| 22 | M   | 1.8            | Hispanic  | A+         | 17.8 | Liver | Deceased, Whole | Seizure disorder, chronic lung disease, asthma, global development delay |
| 23 | F   | 4              | Hispanic  | O+         | 19.5 | Liver | Deceased, Whole | None |
| 24 | M   | 0.8            | Hispanic  | A+         | 18.8 | Liver | Deceased, Whole | Adrenal insufficiency, DM |
| 25 | M   | 8              | Hispanic  | O+         | 19.9 | Lung  | Deceased    | CF, chronic sinusitis, DIOS, osteoporosis |
| 26 | M   | 9              | Hispanic  | O−         | 23.5 | Lung  | Deceased    | Bone marrow tx, seizures, HTN, asthma |

| Time from Tx to Infection (days) | Presenting symptoms          | Exposure | Hospitalized | CXR/CT findings |
|---------------------------------|------------------------------|----------|--------------|-----------------|
| 6129                            | Anosmia                      | Family member | No        | N/O             |
| 1182                            | Cough, rhinorrhea            | Family member | No        | N/O             |
| 1874                            | Fever                        | Family member | Yes (trach care) | N/O             |
| 410                             | Fever                        | Family member | Yes        | Yes (normal)    |
| 1114                            | Cough, fever                 | Family member | No        | N/O             |
| 2879                            | Cough, dry throat            | Community-acquired | No    | N/O             |
| 4868                            | Anosmia, cough, fever, rhinorrhea | Community-acquired | Yes (migraine/hyponatremia) | N/O             |
| 12                              | Cough                        | Family member | Yes (post-transplant) | Yes (multifocal infiltrates) |
| 1256                            | Cough, fever                 | Hospital exposure | No        | Yes (normal)    |
| 436                             | None                         | Family member | No        | N/O             |

(Continues)
| Time from Tx to Infection (days) | Presenting symptoms | Exposure | Hospitalized | CXR/CT findings |
|---------------------------------|---------------------|----------|--------------|-----------------|
| 2677                            | Diarrhea            | Community-acquired | No          | Yes (normal)    |
| 2542                            | None                | Community-acquired | No          | N/O             |
| 1882                            | None                | Community-acquired | No          | N/O             |
| 119                             | None                | Home health RN     | No          | Yes (normal)    |
| 1236                            | Chest pain, cough   | Community-acquired | Yes         | Yes (multifocal infiltrates) |
| 784                             | Cough, dyspnea, sore throat | Community-acquired | No          | N/O             |
| 4444                            | Cough, diarrhea, fever | Family member | Yes         | Yes (normal)    |
| 1910                            | Fever               | Community-acquired | Yes         | N/O             |
| 958                             | Cough               | Family member     | No          | N/O             |
| 1138                            | Cough               | Family member     | No          | N/O             |
| 560                             | Fever               | Community-acquired | No          | N/O             |
| 814                             | Rhinorrhea          | Community-acquired | Yes         | N/O             |
| 1659                            | None                | Family member     | No          | N/O             |
| 6574                            | Chest pain, fever, headache | Family member | No          | N/O             |
| 3127                            | None                | Community-acquired | No          | Yes (normal)    |
| 933                             | Cough, sore throat  | Family member     | No          | N/O             |

**TABLE 1** (Continued)

| Basic labs          | Inflammation/ Hypercoagulable evaluation | New O₂ therapy | Maintenance immunosuppression | Immunosuppression change | COVID-19 therapy |
|---------------------|-----------------------------------------|----------------|-------------------------------|--------------------------|------------------|
| N/O                 | N/O                                     | No             | TAC, Rapa, Pred               | No                       | No               |
| Wnl                 | N/O                                     | No             | TAC, Rapa                     | No                       | No               |
| Wnl                 | N/O                                     | No             | TAC, MMF                      | No                       | No               |
| Wnl                 | Inc CRP, D-dimer                        | No             | TAC, MMF                      | No                       | No               |
| Dec WBC             | N/O                                     | No             | Rapa, Pred, cyclosporine      | No                       | No               |
| Wnl                 | N/O                                     | No             | TAC, azathioprine             | No                       | No               |
| Wnl                 | Inc CRP, fibrinogen, D-dimer            | No             | TAC, azathioprine             | No                       | No               |
| Dec WBC, Hgb, Hct   | Inc CRP, ferritin, fibrinogen, D-dimer  | No             | TAC, MMF, ATG                 | Yes (reduction)          | No               |
| Dec Hgb, Hct        | Inc CRP, fibrinogen, D-dimer            | No             | TAC, MMF                      | No                       | No               |
| Wnl                 | Wnl                                     | No             | TAC, Pred                     | No                       | No               |
| N/O                 | N/O                                     | No             | TAC, MMF, Pred                | No                       | No               |
| Dec WBC             | N/O                                     | No             | TAC, MMF                      | No                       | No               |
| Dec Hgb, Hct        | Inc ferritin                            | No             | TAC, MMF, Pred                | No                       | No               |
| N/O                 | N/O                                     | No             | TAC, MMF, Pred                | No                       | No               |
| Dec WBC             | Inc CRP, fibrinogen, D-dimer            | No             | TAC, Rapa                     | Yes (reduction)          | Azm              |
| Wnl                 | N/O                                     | No             | TAC                           | No                       | No               |
| Wnl                 | Wnl                                     | No             | TAC, MMF, Pred                | No                       | Azm, HCQ         |
| Wnl                 | Inc CRP                                 | No             | TAC, MMF                      | No                       | Azm              |
| Wnl                 | N/O                                     | No             | TAC                           | No                       | Azm              |
| Dec WBC             | N/O                                     | No             | TAC                           | No                       | No               |

(Continues)
GOSS et al. during the early post-transplant period,\textsuperscript{12} and highly associated comorbidities linked to poor outcomes,\textsuperscript{5,13,14} transplant recipients are expected to be particularly susceptible to infection and a severe clinical course in the event of SARS-CoV-2 exposure. Some transplant-specific studies report significant complications and mortality,\textsuperscript{2-4} while other analyses demonstrate similar symptomatology and mortality rates relative to the general population.\textsuperscript{6,7}

To date, the bulk of the literature examining COVID-19 following transplant is adult-focused, with pediatric reports limited to single patient experiences.\textsuperscript{9,10} Mirroring the majority experience of infected children in the general population\textsuperscript{15,16} and report of a single pediatric heart transplant recipient,\textsuperscript{9} our multi-center pediatric transplant cohort experienced mild symptoms or lack thereof. The underpinning of milder symptomatology in children remains obscure but is likely multifactorial. Suggested reasons include a maturing

| Basic labs | Inflammation/ Hypercoagulable evaluation | New O\textsubscript{2} therapy | Maintenance immunosuppression | Immunosuppression change | COVID-19 therapy |
|------------|-----------------------------------------|-------------------------------|-------------------------------|--------------------------|-----------------|
| Wnl        | N/O                                     | No                            | TAC                           | No                       | No              |
| Dec Hgb, Hct | Wnl                                    | No                            | TAC, Pred                     | No                       | No              |
| Wnl        | N/O                                     | No                            | TAC, Rapa, Pred               | No                       | No              |
| Dec WBC    | Wnl                                     | No                            | TAC, Pred                     | No                       | No              |
| Wnl        | Wnl                                     | No                            | TAC, MMF, Pred                | No                       | No              |
| Wnl        | N/O                                     | No                            | TAC, MMF, Pred                | No                       | No              |

| Bacterial co-infection | Antimicrobial agents | Disposition |
|------------------------|----------------------|-------------|
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | Levofloxacin, nitrofurantoin | Home        |
| No                     | Ceftriaxone          | Home        |
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | Azm, ceftriaxone     | Home        |
| No                     | No                   | Home        |
| No                     | Azm                  | Home        |
| No                     | Azm                  | Home        |
| No                     | Azm                  | Home        |
| No                     | No                   | Home        |
| No                     | No                   | Home        |
| No                     | Azm ppx              | Home        |
| No                     | None                 | Home        |

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AKI, acute kidney injury; AMR, antibody-mediated rejection; Azm, azithromycin; CF, cystic fibrosis; CKD, chronic kidney disease; CMV, cytomegalovirus; CVA, cerebrovascular accident; DIOS, distal intestinal obstructive syndrome; DM, diabetes mellitus; ESRD, end-stage renal disease; GERD, gastroesophageal reflux disease; N/O, not obtained; PIGN, post-infectious glomerulonephritis; Ppx, prophylaxis; Pred, prednisone; Rapa, rapamune/sirolimus; RN, registered nurse; RTA, renal tubular acidosis.
immune system primed to combat novel pathogens, decreased prevalence of comorbidities established as risk factors for severe disease, frequent infections with the common cold coronaviruses potentially providing protection, healthier respiratory tracts, and a difference in the distribution and functioning of viral receptors.

Though the virus manifested in various ways within our cohort, with cough being the most frequent presentation, complete resolution of symptoms occurred within a week for each patient. None of our liver recipients, nor other solid organs, experienced the described complication of COVID-19-induced hepatitis in an infant early after liver transplant\textsuperscript{10} nor multisystem inflammatory syndrome in children (MIS-C).\textsuperscript{17} As a hyperinflammatory response has been associated with complications and the multi-organ involvement with COVID-19,\textsuperscript{18} inflammatory biomarkers in chronically immunosuppressed patients are of particular interest. In our cohort, initial inflammatory biomarkers were not uniformly checked, though CRP, ferritin, fibrinogen, D-dimer, and troponin were measured in certain patients (Table 1). 58% of the measured cohort had elevation of CRP and/or ferritin, while 42% had elevation of fibrinogen and/or D-dimer. All troponin levels were Wnl. As our patients presented with mild symptoms and most recovered within days, and less than half had evaluation of serum inflammatory biomarkers, we are unable to determine the meaning and role of assessment of inflammatory biomarkers in pediatric transplant patients. More data, including serial monitoring as opposed to single measurements, are needed to assess potential predictive value.

Comorbidities associated with a severe COVID-19 clinical phenotype among adult transplant recipients, for example, HTN, obesity, and diabetes,\textsuperscript{14} are less prevalent in the pediatric population. This may explain in part our cohort’s mild symptoms at presentation and rapid recovery, without any patient requiring supplemental oxygen, intubation, or ECMO. That being said, 6 of our 26 patients (23%) were obese (BMI > 30 kg/m\textsuperscript{2}) but did not experience more severe manifestations. In addition, our cohort’s relatively small patient pool and ubiquitous mild symptomatology precluded firm conclusions with respect to the described disparities in clinical course severity dependent on blood type. Nonetheless, a majority of our cohort was type O (17/26 (65%)), for which a protective effect has been attributed given its unexplained link with a milder disease phenotype.\textsuperscript{19} It is also important to note that immunosuppression was reduced in only 2 of 26 patients (8%), with resolution of symptoms within 72 hours, suggesting that adjustment of maintenance immunosuppression may not be necessary. In fact, our experience suggests caution should be exercised when reducing immunosuppression, particularly if symptoms are mild, as renal allograft biopsy of patient No. 8 revealed moderate ACR after initially decreasing MMF and TAC.

We highlight the mild COVID-19 clinical course of 26 immunosuppressed pediatric transplant recipients across 5 institutions including California, Florida, and Texas, unfortunate COVID-19 hotspots in the USA. Our cohort suggests immunosuppression alterations may not be necessary for a complete and rapid recovery in the immediate post-infection period. Furthermore, minimal supportive therapy may be required, if symptoms remain mild. It will be critical to learn from and share our experience through the post-COVID-19 diagnosis and recovery period, with a focus on antibody kinetics and risk for re-infection, as we seek to understand the potential long-term effects of COVID-19 infection in immunosuppressed pediatric transplant patients.

ACKNOWLEDGMENTS

We would like to endorse the enthusiastic collaboration between pediatric transplant centers allowing our study. This manuscript is dedicated to COVID-19 victims, both living and deceased, and frontline medical professionals uniquely embodying public-spirited sacrifice and formidable resilience.

CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose as described by Pediatric Transplantation.

DATA AVAILABILITY STATEMENT

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

ORCID

Matthew B. Goss https://orcid.org/0000-0003-4663-0086
Ernestina Melicoff-Portillo https://orcid.org/0000-0001-5696-7112
Dor Yoeli https://orcid.org/0000-0002-5041-7782
Abbas Rana https://orcid.org/0000-0003-2979-0598
Nicolas F. Moreno https://orcid.org/0000-0001-8661-676X

REFERENCES

1. Khanna R, Smith C. Cellular immune therapy for viral infections in transplant patients. Indian J Med Res. 2013;138(5):796-807.
2. Alberici F, Delbarba E, Manenti C, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV-2 pneumonia. Kidney Int. 2020;97(6):1083-1088.
3. Fernández-Ruiz M, Andréis A, Loinaz C, et al. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. Am J Transplant. 2020;20(7):1849-1858.
4. Huang J, Zheng K, George J, et al. Fatal outcome in a liver transplant recipient with COVID-19. Am J Transplant. 2020;20(7):1907-1910.
5. Bhooi S, Rossi RE, Citterio D, et al. COVID-19 in long-term liver transplant patients: preliminary experiences from an Italian transplant centre in Lombardy. Lancet Gastroenterol Hepatol. 2020;5(6):532-533.
6. Travi G, Rosatti R, Merli M, et al. Clinical outcome in solid organ transplant recipients with COVID-19: a single-center experience. Am J Transplant. 2020;20(9):2628-2629.
7. Tschopp J, L'Huillier AG, Mombelli M, et al. First experience of SARS-CoV-2 infections in solid organ transplant recipients in the Swiss Transplant Cohort Study. Am J Transplant. 2020;20(10):2876-2882.
8. Zhong J, Tang J, Ye C, et al. The immunology of COVID-19: is immune modulation an option for treatment? Lancet Rheumatol. 2020;2(7):E428-E436.
9. Russell MR, Halnon NJ, Alejos JC, et al. COVID-19 in a pediatric heart transplant recipient: emergence of donor-specific antibodies. J Heart Lung Transplant. 2020;39(9):732-733.
10. Heinz N, Griesemar A, Kinney J, et al. A case of an infant with SARS-CoV-2 hepatitis early after liver transplantation. Pediatr Transplant. 2020;24(8):e13778.
11. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-848.
12. Snyder JJ, Israni AK, Peng Y, et al. Rates of first infection following kidney transplant in the United States. Kidney Int. 2009;75(3):317-326.
13. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. Am J Transplant. 2020;20(7):1919-1925.
14. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;323(20):2052-2059.
15. Tagarro A, Epalza C, Santos M, et al. Screening and severity of Coronavirus Disease 2019 (COVID-19) in children in Madrid, Spain. JAMA Pediatr. 2021;175(3):316-317.
16. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369:m1966.
17. Riollano-Cruz M, Akkoyun E, Briceno-Brito E, et al. Multisystem inflammatory syndrome in children (MIS-C) related to COVID-19: a New York City experience. J Med Virol. 2021;93(1):424-433.
18. Zaim S, Chong J, Sankaranarayanan V, et al. COVID-19 and multi-organ response. Curr Probl Cardiol. 2020;45(8):100618.
19. Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe COVID-19 with respiratory failure. N Engl J Med. 2020;383(16):1522-1534.

How to cite this article: Goss MB, Galván NTN, Ruan W, et al. The pediatric solid organ transplant experience with COVID-19: An initial multi-center, multi-organ case series. Pediatr. Transplant. 2021;25:e13868. https://doi.org/10.1111/petr.13868