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COVID-19 in pediatric kidney transplantation: The Improving Renal Outcomes Collaborative

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Abbreviations: AKI, acute kidney injury; CAKUT, congenital anomalies of the kidney and urinary tract; COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile ranges; IRB, Institutional Review Board; IROC, improving renal outcomes collaborative; IVIG, intravenous immunoglobulin; KT, kidney transplant; REDCap, research electronic data capture; SARS-CoV-2, severe acute respiratory syndrome 2; SOT, solid organ transplant.

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There are limited data on the impact of COVID-19 in children with a kidney transplant (KT). We conducted a prospective cohort study through the Improving Renal Outcomes Collaborative (IROC) to collect clinical outcome data about COVID-19 in pediatric KT patients. Twenty-two IROC centers that care for 2732 patients submitted testing and outcomes data for 281 patients tested for SARS-CoV-2 by PCR. Testing indications included symptoms and/or potential exposures to COVID-19 (*N* = 134, 47.7%) and/or testing per hospital policy (*N* = 154, 54.8%). Overall, 24 (8.5%) patients tested positive, of which 15 (63%) were symptomatic. Of the COVID-19-positive patients, 16 were managed as outpatients, six received non-ICU inpatient care and two were admitted to the ICU. There were no episodes of respiratory failure, allograft loss, or death associated with COVID-19. To estimate incidence, subanalysis was performed for 13 centers that care for 1686 patients that submitted all negative and positive COVID-19 results. Of the 229 tested patients at these 13 centers, 10 (5 asymptomatic) patients tested positive, yielding an overall incidence of 0.6% and an incidence among tested patients of 4.4%. Pediatric KT patients in the United States had a low estimated incidence of COVID-19 disease and excellent short-term outcomes.

KEYWORDS
clinical research/practice, epidemiology, health services and outcomes research, infection and infectious agents, infectious disease, kidney transplantation/nephrology, pediatrics

1 | INTRODUCTION

Pediatric solid organ transplant (SOT) patients are considered to be at increased risk for infection and sequelae thereof.[1,2] With the emergence of the severe acute respiratory syndrome 2 (SARS-CoV-2, also called Coronavirus disease 2019, COVID-19) in December 2019 in Wuhan, Hubei Province, China[3] the pediatric transplant community faced unprecedented unknowns in providing care to the SOT population. Limited international data from early in the COVID-19 pandemic suggest that despite a predisposition toward infection, immunosuppressed children with SOT may be at relatively low risk for adverse patient and graft outcomes from COVID-19.[1,2,4,5] There are multiple published case reports and case series detailing clinical descriptions, treatments, and outcomes of COVID-19 in adult SOT patients.[6-8] However, there have been no cohort studies to document the incidence of COVID-19 in the pediatric SOT population and only limited data available regarding the subsequent risk for short-term harm to both the graft and patient.[9]

The Improving Renal Outcomes Collaborative (IROC) is a multicenter, network-based learning health system including 34 academic pediatric kidney transplant (KT) centers in the United States. The primary aim of IROC was to characterize clinical outcome data for pediatric KT patients, provide center- and network-level analytics, and inform center-based quality improvement initiatives to improve health, longevity and quality of life for pediatric KT patients and families.[10,11] The objectives of the current study were twofold: (1) rapidly implement a web-based registry across the IROC network to describe the incidence of COVID-19 in pediatric KT patients using our existing collaborative infrastructure, and (2) describe short-term allograft and patient outcomes for pediatric KT patients experiencing COVID-19.

2 | METHODS

2.1 | IROC registry

IROC was formed in 2016 with 15 founding centers. Since that time, 19 additional centers have joined the collaborative on a rolling basis. Currently, over 50% of all pediatric KTs in the United States are performed at IROC-participating centers. IROC centers complete structured training in quality improvement and maintain site-specific infrastructure to report patient-level clinical variables to the IROC registry. The parent IROC study was approved by the Institutional Review Board (IRB) at Cincinnati Children's Hospital Medical Center under a master reliance agreement that was approved by each participating center. This agreement allows Cincinnati Children's Medical Center to act as the IRB of record for the registry-specific data analyzed in this study. This COVID-19 study was approved by the Cincinnati Children's IRB.

Clinical data for pediatric KT patients at each of the IROC sites are routinely uploaded into a central IROC data registry. These patient-level data include demographics, clinical visit data, laboratory data,

medications, hospitalization-related data, biopsy data, and rejection events/outcomes. These elements are processed and disseminated to centers as statistical process control charts, population management measures, and previsit planning forms to support ongoing pediatric KT care, quality improvement activities at the institutional level, and for benchmarking across the network. Demographic data in the registry included patient age, sex, and race (although race data were incomplete for some patients). Available medical data included cause of end-stage kidney disease leading to transplant, date of KT (including prior if multiple transplants), donor type (living or deceased), current nonimmunosuppression medications (e.g., ACE-inhibitors), current immunosuppression drug regimen, and history of rejection episodes with grade of rejection stratified according to Banff criteria.[12,13] IROC-based research studies are permitted to use these registry data as covariates as in the current study.

2.2 | COVID-19 data collection tool

To collect specific information regarding COVID-19 testing, results, and clinical outcomes, a Research Electronic Data Capture (REDCap) data collection tool was created and distributed to IROC centers (Figure 1). REDCap is a secure, web-based software platform designed to support data capture for research studies.[14,15] Entry of COVID-19 testing information into the REDCap data collection tool was voluntary for IROC centers during the study period. Centers were encouraged to enter all patients tested rather than only those who tested positive. During the study period of April 6 to September 3, 2020, centers entered patient-level data into REDCap for COVID-19 testing results, indication(s) for testing, symptoms at the time testing (if applicable), known history of lung disease, and the provided treatment(s) for confirmed or suspected COVID-19. Indications for testing were not mutually exclusive, thus centers can report multiple indications for testing. Additional outcome questions included the highest level of care the patient required (e.g., outpatient, inpatient wards, intensive care) and endpoints for both the allograft and patient following COVID-19 disease, such as acute kidney injury (AKI), rejection, respiratory failure, and/or death.

2.3 | Data linkage

Each patient in the IROC registry is assigned both a unique center ID and patient ID. The center ID and IROC registry ID(s) were entered

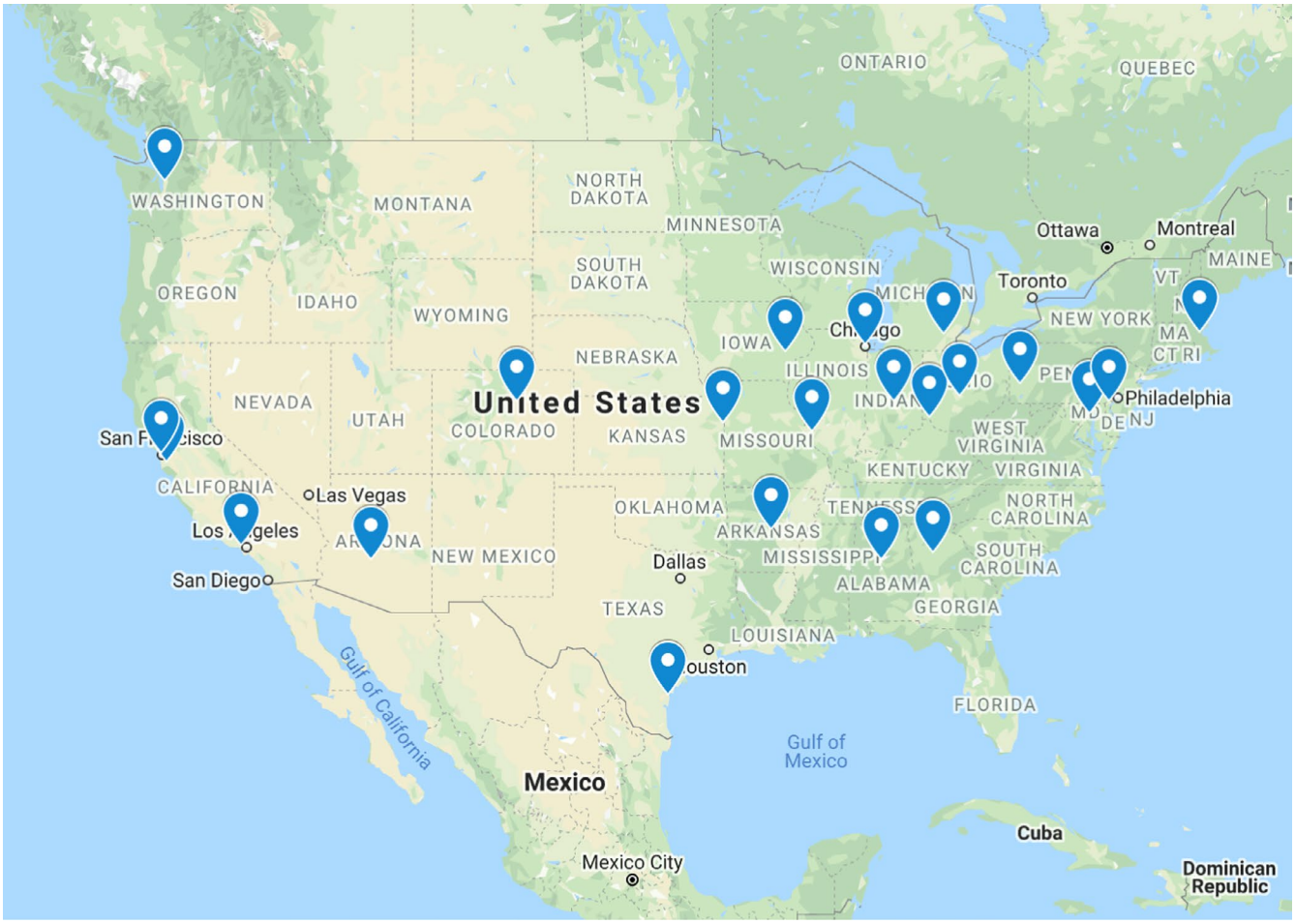

FIGURE 1 Map of IROC centers that participated in COVID-19 study

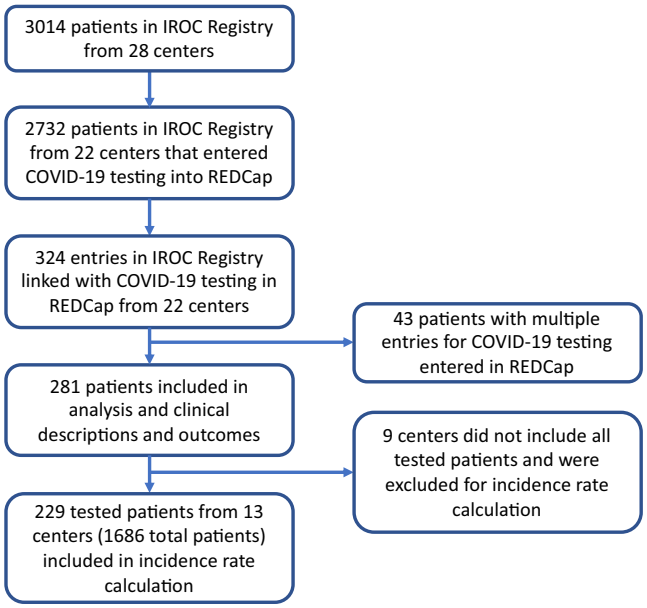

FIGURE 2 Flow diagram for patient enrollment

along with COVID-19 testing data in the REDCap data collection tool. Patient clinical data, including immunosuppressive and antihypertensive agent(s), were available from the IROC registry and linked to the COVID-19 testing data using patient-level, secure identifiers. Individual centers were contacted to provide follow-up for missing data, if available, on individual patients from either the IROC registry or the REDCap data collection tool.

2.4 | Statistical analysis

Linked data from the REDCap collection tool and IROC registry were analyzed to provide descriptive information on the patients entered in the database, including the number of patients tested, indication for testing, the incidence of COVID-19, and clinical outcomes. If a patient was tested and entered into REDCap tool multiple times, the individual was analyzed once. If subsequent testing revealed a positive test, or a test with symptoms was reported, those entries were prioritized. To estimate the incidence of COVID-19-positive testing using patients with a documented test result, we analyzed a subgroup of patients from centers that entered all COVID-19 testing data during the study period. Ages were calculated based on demographic data reported in the IROC registry relative to the date that testing data were entered into the REDCap database. Continuous variables were summarized using medians with interquartile ranges (IQR) and tested for differences between groups using Wilcoxon rank-sum test to accommodate the nonnormally distributed variables. Categorical variables were analyzed by Fisher's exact test due to the small number of patients with a positive test. $p < .05$ were considered significant results. Analyses were conducted using SAS version 9.4 (SAS Institute, Inc).

3 | RESULTS

3.1 | Indications for COVID-19 testing

Twenty-two IROC centers that collectively care for 2732 patients submitted COVID-19 testing data from 281 patients between April 6, 2020 and September 3, 2020 (see Figure 2). All centers reported using SARS-CoV-2 PCR for testing. Patient characteristics and demographics are detailed in Table 1 and COVID-19 testing indications and symptoms are detailed in Table 2. When evaluating testing indication for all tested patients, 105 (37.4%) displayed symptoms consistent with COVID-19, 24 (8.5%) had close contact with a confirmed case of COVID-19, and five (1.8%) had close contact with a person under investigation or displaying symptoms consistent with COVID-19. Most patients (55.9%) were tested per hospital policy, since many hospitals during this time required universal testing for all admitted patients, even without COVID-19 symptoms, as part of any admission or preprocedure anesthesia evaluation.

3.2 | Incidence of COVID-19

To estimate the incidence of a positive COVID-19 test in our cohort, we excluded any center that did not enter all their tested transplant patients during the study period. Thirteen IROC centers caring for a total of 1686 patients entered data on all tested patients (n = 229). The overall estimated incidence of COVID-19 at these centers was 0.6% (10/1686). The incidence of COVID-19 in tested patients at these centers was 4.4% (10/229). Five of the 10 positive patients (50%) from this subanalysis were asymptomatic.

3.3 | Characteristics of COVID-19-positive kidney transplant patients

Twenty-four patients (8.5%) tested positive for COVID-19 out of all those entered in the REDCap registry (n = 281). Treatment and outcomes data for the entire cohort are detailed in Table 3. The median (IQR) age for the positive patients was 18.6 years (14.3–20.6 years), and the range was 4.4–24 years, which was higher than the median age for negative patients of 14.3 (7.3–18.3). The COVID-19-positive patients had a median (IQR) time since transplant of 2.9 years (1.8–8.7) years. Twenty percent of our cohort were in their first year posttransplant (60/281), and three of those 60 (5%) patients tested positive for COVID-19. Over half of all positive patients were male (15/24, 62%). The top three primary kidney diseases reported were congenital anomalies of the kidney and urinary tract (CAKUT), glomerulonephritis, and nephrotic syndrome/FSGS.

When analyzing all positive patients, 15 of 24 (63%) had any symptoms associated with COVID-19, including cough (33.3%), fever (29.2%), vomiting (16.7%), diarrhea (12.5%), rhinorrhea (8.3%),

TABLE 1 Patient characteristics

	Positive test (*n* = 24)	Negative test (*n* = 257)	Total (*n* = 281)	*p*-value
Age (years) Median, IQR	18.6 (14.3, 20.6)	14.3 (7.3, 18.3)	14.7 (7.9, 18.7)	.004
Time from transplant (years) Median, IQR	2.9 (1.8, 8.7)	2.6 (1.0, 6.3)	2.7 (1.1, 6.5)	.28
Sex				1.00
Male	15 (62.7%)	156 (61%)	171 (60.9%)	
Female	9 (37.5%)	101 (39%)	110 (39.1%)	
Race				.64
White	10 (43.5%)	134 (54.3%)	144 (53.3%)	
Black	6 (26.1%)	35 (14.2%)	41 (15.2%)	
Asian	0	9 (3.6%)	9 (3.3%)	
Native Hawaiian/P.I.	0	7 (2.8%)	7 (2.6%)	
American Indian/A.N.	0	3 (1.2%)	3 (1.1%)	
More than one race	0	2 (0.8%)	2 (0.7)	
Not reported	7 (30.4%)	57 (23.1%)	64 (23.7%)	
Missing	1	10	11	
Primary diagnosis				.10
CAKUT	10 (41.7%)	115 (44.9%)	125 (44.6%)	
Glomerulonephritis	4 (16.7%)	29 (11.3%)	33 (11.8%)	
NS/FSGS	3 (12.5%)	14 (5.5%)	17 (6.1%)	
Ciliopathy	2 (8.3%)	5 (2.0%)	7 (2.5%)	
Infarct injury	1 (16.7%)	4 (1.6%)	5 (1.8%)	
PKD	0	8 (3.1%)	8 (2.9%)	
Other	4 (16.7%)	81 (31.6%)	85 (30.4%)	
Missing	0	1	1	
Donor type				.045
Living donor	4 (16.7%)	97 (37.9%)	101 (35.8%)	
Deceased donor	20 (83.3%)	159 (62.1%)	179 (64.2%)	
Medication regimen				
Calcineurin inhibitor	16 (66.7%)	152 (59.1%)	168 (59.8%)	.52
Antimetabolite	17 (70.8%)	158 (61.5%)	175 (62.3%)	.51
Steroid	11 (45.8%)	94 (36.6%)	105 (37.4%)	.38
Other IS	1 (4.2%)	22 (8.6%)	23 (8.2%)	.70
ACE-I/ARB	3 (12.5%)	18 (7.0%)	21 (7.5%)	.40
Treatment for rejection in prior 3 months				1.00
Yes	1 (4.2%)	17 (6.6%)	18 (6.4%)	
No	23 (95.8%)	240 (93.4%)	263 (93.6%)	
Hypertension				.20
Yes	15 (62.5%)	122 (47.5%)	137 (48.8%)	
No	9 (37.5%)	135 (52.5%)	144 (51.2%)	

Abbreviations: A.N., Alaskan Native; CAKUT, congenital anomolies of the kidney and urinary tract; FSGS, focal segmental glomerulosclerosis; NS, nephrotic syndrome; P.I., Pacific Islander; PKD, polycystic kidney disease.

and shortness of breath (8.3%). Fifteen of the 113 (13.3%) symptomatic patients tested positive compared to nine of the 168 (5.4%) asymptomatic patients testing positive (p = .03). Only one (4.2%) COVID-19-positive patient had a history of any lung disease (childhood asthma), and 15 (62.5%) had a diagnosis of hypertension, with 93% of those patients on antihypertensive medication.

TABLE 2 Clinical description for testing and symptoms

Indication for testing	Positive test (*n* = 24)	Negative test (*n* = 257)	Total (*n* = 281)	*p*-value
Symptoms consistent with COVID-19	14 (58.3%)[b]	91 (35.4%)	105 (37.4%)	.045
Close contact with a confirmed case	12 (50.0%)	12 (4.7%)	24 (8.5%)	<.001
Close contact with a person under investigation	1 (4.2%)	4 (1.6%)	5 (1.8%)	.36
Patient screened per hospital policy	6 (25.0%)	148 (57.6%)	154 (54.8%)	.002
Symptoms at time of testing				
Any symptom	15 (63%)[b]	98 (38%)	113 (40%)	.03
Cough	8 (33.3%)	42 (16.3%)	50 (17.8%)	.05
Fever	7 (29.2%)	69 (26.8%)	76 (27.0%)	.81
Vomiting	4 (16.7%)	17 (6.6%)	21 (7.5%)	.09
Diarrhea	3 (12.5%)	12 (4.7%)	15 (5.3%)	.13
Rhinorrhea	2 (8.3%)	17 (6.6%)	19 (6.8%)	.67
Shortness of breath	2 (8.3%)	7 (2.7%)	9 (3.2%)	.17
None	9 (37.5%)	159 (61.9%)	168 (59.8%)	.03
Other[a]	9 (37.5%)	35 (13.6%)	44 (15.7%)	.005

[a]Most common other symptoms included nonspecific symptoms such as headache (*n* = 6), congestion (*n* = 4), sore throat (*n* = 4), chest pain (*n* = 4), fatigue (*n* = 3).

[b]One patient only presented with vomiting, thus was not tested for symptoms consistent with COVID-19 but was found to be positive when tested.

3.4 | Treatment and outcomes in COVID-19-positive patients

Nineteen of the positive patients (79.2%) required supportive care only. Four (16.7%) had a reduction in their immunosuppression regimen, three of which were temporary reductions in mycophenolate mofetil dosing. Sixteen of the 24 positive patients (66.7%) were treated as outpatients, six (25%) were treated as inpatients in a non-ICU setting, and two (8.3%) required ICU admission. Upon further review with the submitting center, the first ICU patient was admitted per hospital policy in the early days of the pandemic out of an abundance of caution rather than the presence of critical illness. The second ICU patient was admitted with concern for shock that rapidly improved and was transferred to the inpatient wards within 48 h. This patient had concomitant pyelonephritis at the time of COVID-19 diagnosis. Of the six remaining hospitalized COVID-19 patients, one was asymptomatic and detected by hospital universal screening policy, the other five had symptoms requiring inpatient management.

Twenty of the patients (83.3%) had no transplant-related complications, two patients (8.3%) had AKI at the time of testing that resolved prior to discharge, one (4.2%) was diagnosed with T cell–mediated rejection at the time of COVID-19 diagnosis, and one (4.2%) was diagnosed with antibody-mediated rejection at the time of COVID-19 diagnosis. The cause of AKI in one patient was directly related to a supratherapeutic tacrolimus level that required holding the tacrolimus for 36 h. The second patient with AKI was admitted for a kidney biopsy secondary to elevated creatinine without apparent cause. The patient's biopsy did not show evidence of rejection and the creatinine normalized without specific intervention. This patient's COVID-19 test resulted positive after the procedure was completed.

The patient with T cell–mediated rejection had no COVID-19 symptoms but was screened per hospital policy prior to a diagnostic biopsy for elevated creatinine and presence of donor-specific antibodies (biopsy showed Banff 1A T cell–mediated rejection and no antibody-mediated rejection). The patient had no symptoms at the time of biopsy. The patient was treated with methylprednisolone and intravenous immunoglobulin (IVIG) for the rejection episode and donor-specific antibodies and subsequently developed fever and cough that required supplemental oxygen while admitted. Chest x-ray demonstrated patchy airspace densities with prominent central pulmonary vascularity and interstitial prominence. This patient received dexamethasone and over the subsequent week showed clinical improvement, becoming afebrile and weaning off oxygen. The patient was discharged home on maintenance immunosuppression and the creatinine returned to baseline.

The patient with antibody-mediated rejection had longstanding donor-specific antibodies, a history of antibody-mediated rejection, and a history of poor immunosuppression adherence. This patient was receiving IVIG for treatment of donor-specific antibodies and was tested for COVID-19 during an infusion visit. After monitoring for 20 days, this patient remained asymptomatic while the COVID-19

TABLE 3 Treatment and outcomes for COVID-19-positive patients

Treatment of patient	Positive test (n = 24)
Supportive care only	19 (79.2%)
Reduction of immunosuppression	4 (16.7%)
Highest level of care required	
Outpatient	16 (66.7%)
Inpatient, non-ICU	6 (25.0%)
ICU[a]	2 (8.3%)
Allograft outcome	
No graft-related complications	20 (83.3%)
Acute kidney injury	2 (8.3%)
T cell–mediated rejection	1 (4.2%)
Antibody-mediated rejection	1 (4.2%)
Graft loss	0
Patient outcome	
Self-limited disease	24 (100%)
ARF/SIRS/MODS	0
Death	0

Abbreviations: ARF, acute respiratory failure; MODS, multiple organ dysfunction syndrome; SIRS, systemic inflammatory response syndrome.

[a]Hospital policy patient to ICU (intensive care unit) for one of these patients.

test remained positive. A biopsy was done to follow-up treatment of donor-specific antibodies, which showed severe, active antibody-mediated rejection. This patient was treated with IV methylprednisolone, plasmapheresis, rituximab, bortezomib, and IVIG. Neither of the two patients who experienced rejection were on reduced immunosuppression due to their COVID diagnosis.

None of the patients who tested positive required dialysis or experienced graft failure, and none of them experienced respiratory failure, required intubation, or died.

4 | DISCUSSION

We report the largest cohort assembled to date of pediatric KT patients tested for COVID-19. Key findings include: (1) the overall estimated incidence of COVID-19 was 0.6% in 1686 patients from centers that submitted complete testing data, and the incidence among 229 tested patients at these centers was 4.4%; (2) 25% of COVID-19-positive cases were incidentally found when screening asymptomatic patients; (3) COVID-19 was not associated with graft loss, respiratory failure, or death. Of additional clinical interest, a minority of COVID-19-positive patients had reductions in immunosuppression as part of their treatment course, and patients who received treatment for acute rejection in the prior 3 months did not appear at increased the risk for COVID-19 in this cohort. Our observations extend the findings of smaller studies that SOT patients have a relatively low incidence of symptomatic COVID-19 and a low risk of short-term adverse outcomes. We also found that patients with a positive test tended to be older (median age 18.6 years compared to 14.3 years). While this study was not designed to report differences between the testing groups, this finding is consistent with the finding in the general population that the incidence of COVID-19 is higher in older children.[16]

Clinically, we were unable to identify any single symptom or set of symptoms in the transplant population that provides a heightened index of suspicion for COVID-19 compared to what is reported in the general population. Although cough was statistically more likely to be found in patients positive for COVID-19, this symptom is nonspecific to COVID-19. Unfortunately, the symptoms for mild COVID-19 infection mimic the most common routine viral infections of childhood. Centers did not submit alternative viral testing diagnoses for the majority of the symptomatic patients that tested negative for COVID-19, so we cannot present alternative diagnoses that mimic COVID-19. Consistent with the existing COVID-19 pediatric literature, we believe that one of the most helpful discriminating factors for COVID-19 diagnosis is an understanding of the patient's potential exposure history, as half of the COVID-19-positive patients in this cohort had a known exposure to an individual with COVID-19.

In the pediatric population, international data indicate that COVID-19-related outcomes are similar in immunosuppressed vs. nonimmunosuppressed children.[17-19] Marlais and colleagues reported an ongoing survey of children aged 0–19 with kidney disease and on immunosuppressive medication who were diagnosed with COVID-19.[18] They reported a mild clinical course in 18 children from 11 different countries. Similarly, D'Antiga et al. suggested that immunosuppressed patients were not at increased risk of severe pulmonary disease, and that children less than 12 years of age did not develop severe pneumonia regardless of their immune status.[19] This conclusion was derived from the observation that of 700 pediatric liver transplant patients cared for at Hospital Papa Giovanni XXIII in the epicenter of the Italian outbreak, only three tested positive and none developed severe respiratory illness. Our study confirms and strengthens this conclusion as among the 1686 children cared for at 13 IROC centers with complete data, only 10 tested positive and none experienced serious respiratory illness.

Our results are in contrast to studies in adults where COVID-19 is associated with poor patient and graft outcomes. A recent meta-analysis suggested a higher likelihood of severe COVID-19 in immunosuppressed and immunodeficient adults.[20] This is likely related to the finding of increasing COVID-19-related complications as age increases in the general population.[21,22] Furthermore, the adult population—in contrast to children—is more likely to have relevant comorbidities, such as diabetes mellitus and poorly controlled hypertension, that have been demonstrated as risk factors for more severe COVID-19.[21,23-25]

Similar to many other pediatric chronic conditions, pediatric kidney transplantation is a rare condition such that no single institution cares for enough patients to easily produce generalizable knowledge—a limitation that can be overcome with collaborative,

network-based learning health systems.[26] IROC has previously leveraged this pooled knowledge and expertise to standardize blood pressure measurement across diverse centers.[27] One of the most critical components to the current study was the availability of the existing IROC infrastructure to rapidly expand data capture with additional instruments during a global pandemic. Given that the majority of patient and population-specific information already existed within the IROC registry, we were able to leverage a simple, time-efficient data collection tool to capture COVID-19-specific information. The existing registry was supplemented with infrastructure for creation of virtual meetings early in the pandemic for both transplant teams and families of pediatric KT patients. At these meetings, centers with a high burden of COVID-19-positive cases shared their clinical experiences and outcomes with the rest of the network. The data capture tool within REDCap was emphasized on a recurring basis during these meetings to facilitate timely, accurate, and complete data entry across participating centers.

Despite the strengths of this large study describing the incidence and outcomes of COVID-19 among pediatric KT patients, our results should be interpreted in light of some limitations. First, the data collected from the REDCap collection tool were provided on a voluntary basis; thus, only submitted information was considered. For the purposes of reporting incidence data, we only included centers that confirmed all tested transplant patients were entered into the COVID-19 registry. However, for analysis of indications, symptoms, and outcomes of patients testing positive, we chose to include all reported patients from all centers. For this reason, positive cases may be overrepresented in Tables 1 and 2 and any associations should be interpreted with caution. We acknowledge that testing was not uniform across centers or for all patients. Thus, the incidence of COVID-19 may be underestimated if many asymptomatic patients in the community were not tested or if patients were tested outside of their center. This is particularly important as almost 40% of our cohort who tested positive had no symptoms of COVID-19. Additionally, the data collection tool was created early in the pandemic while clinical symptoms were still being described, so we did not collect data on loss of smell or taste as a symptom. This symptom has been added to our data collection tool and we hope to be able to describe this more specifically in future analyses. Finally, due to lack of complete race data available in the IROC registry, we could not study the impact of racial differences on COVID-19 testing or outcomes, which may affect the generalizability of our findings.

Overall, our findings demonstrate that immunosuppressed pediatric patients are at relatively low risk for severe pulmonary disease or death due to COVID-19. We will continue to collect COVID-19 testing data as this situation continues to rapidly change, particularly with reopening of schools across the United States in fall 2020 as well as with increasing case numbers across the United States. The pediatric KT population, like many other high-risk patient populations, are familiar with periods of social distancing and the need to mitigate risk of infectious exposure during periods of highest immunosuppression (e.g., immediately posttransplant or for treatment of acute rejection)—therefore the demographic findings and positive testing rates may change with heightened COVID-19 spread. Furthermore, the IROC learning health system infrastructure provides the opportunity to monitor patients over the coming months to years following patients with a history of COVID-19. Specifically, future questions of interest include long-term complications of prior COVID-19, assessing length of viral shedding in patients with multiple positive tests, and characterizing the development of humoral immunity.

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DISCLOSURE

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. G.B. – Consultant: Alnylam; P.B. – Advisory Boards: CareDX and Horizon Therapeutics USA, Inc.; L.D. – Consultant: Merck, Takeda; Grant support for contracted clinical research paid to institution: Astellas, Ansun, BioPharma, Merck, Takeda, Viracor; D.H. – Consultant: Hive Networks, Magnolia Innovation; President, Board of Directors: Improving Renal Outcomes Collaborative Inc. The other authors have no conflict of interests to disclose.

AUTHOR CONTRIBUTIONS

Varnell, Danziger-Isakov, Hooper, and Seifert conceptualized and designed the study. Varnell, Harshman, L. Smith, Liu, Danziger-Isakov, Hooper, and Seifert involved in analysis and interpretation of the data. Varnell and Harshman drafted the article. Varnell, Harshman, L. Smith, Liu, Chen, Al-Akash, Barletta, Belsha, Brakeman, Chaudhuri, Fadakar, Garro, Gluck, Goebel, Kershaw, Matossian, Nailescu, Patel, Pruette, Ranabothu, Rodig, J. Smith, VanSickle, Weng, Danziger-Isakov, Hooper, and Seifert involved in critical revision of the article for important intellectual content and approval of the article. Liu and Chen provided statistical expertise. Varnell, Harshman, L. Smith, Al-Akash, Barletta, Belsha, Brakeman, Chaudhuri, Fadakar, Garro, Gluck, Goebel, Kershaw, Matossian, Nailescu, Patel, Pruette, Ranabothu, Rodig, J. Smith, VanSickle, Weng, and Seifert involved in data collection and assembly. Hooper and Seifert are co-senior authors for this manuscript. Hooper is the principal investigator of IROC, responsible for the IROC registry and infrastructure to support the conduct of this study. Seifert is principal investigator of the COVID-19 registry and study itself.

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