Received: 24 June 2020 | Revised: 7 July 2020 | Accepted: 9 July 2020

DOI: 10.1111/tid.13416

ORIGINAL ARTICLE

WILEY

Kidney transplantation during coronavirus 2019 pandemic at a large hospital in Miami

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Abstract

Background: Coronavirus 2019 (COVID-19) pandemic has resulted in more than 350 000 deaths worldwide. The number of kidney transplants has declined during the pandemic. We describe our deceased donor kidney transplantation (DDKT) experience during the pandemic.

Methods: A retrospective study was conducted to evaluate the safety of DDKT during the COVID-19 pandemic. Multiple preventive measures were implemented. Adult patients that underwent DDKT from 3/1/20 to 4/30/20 were included. COVID-19 clinical manifestations from donors and recipients, and post-transplant outcomes (COVID-19 infections, readmissions, allograft rejection, and mortality) were obtained. The kidney transplant (KT) recipients were followed until 5/31/20.

Results: Seventy-six patients received kidneys from 57 donors. Fever, dyspnea, and cough were reported in 1, 2, and 1 donor, respectively. Thirty-eight (66.6%) donors were tested for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) prior to donation (mainly by nasopharyngeal or bronchoalveolar lavage polymerase chain reaction [PCR]) and 36 (47.3%) KT recipients were tested at the time of DDKT by nasopharyngeal PCR; all of these were negative. Our recipients were followed for a median of 63 (range: 33-91) days. A total of 42 (55.3%) recipients were tested post-transplant for SARS-CoV2 by nasopharyngeal PCR including 12 patients that became symptomatic; all tests were negative except for one that was inconclusive, but it was repeated and came back negative. Forty (52.6%) KT recipients were readmitted, and 7 (9.2%) had biopsy-proven rejection during the follow-up. None of the KT recipients transplanted during this period died.

Conclusions: Our cohort demonstrated that DDKT can be safely performed during the COVID-19 pandemic when preventive measures are implemented.

KEYWORDS

COVID-19, kidney transplant, PCR, safety, SARS-CoV2

1 | INTRODUCTION

In December 2019, several clusters of a severe acute respiratory illness were described in Wuhan, China.[1,2] These were the first cases of what was to later become the Coronavirus 2019 (COVID-19) pandemic. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2), a novel beta-coronavirus, was identified as the causative agent.[1,2] While initial spread was limited to China, the first international case was confirmed in Thailand on January 13, 2020.[1] By January 30, 2020, the World Health Organization declared that the outbreak was a public health emergency of international concern.[3]

As of June 1, 2020, the COVID-19 pandemic has been responsible for 6,206,773 cases and 372,752 deaths worldwide, in 188 countries and regions.[4] The United States (US) has borne the brunt of the pandemic, with nearly 29% and 28% of all worldwide cases and deaths, respectively. In the state of Florida, most of the cases have occurred in South Florida. The Counties of Miami-Dade, Broward, and Palm Beach alone have accounted for 55% of all cases and deaths of the Sunshine State.[5]

Solid organ transplant (SOT) recipients face significant risk from respiratory viral infections as they tend to be more severe in the immunocompromised host. For example, influenza in SOT recipients is associated with pneumonia in 14%-49% of patients[6,7] and is commonly associated with subsequent viral, bacterial, and fungal pneumonia, with a co-infection rate of 7%-29%.[8,9]

Kidney transplantation is a vital intervention for patients with end-stage renal disease (ESRD). Kidney transplantation significantly improves survival as it was demonstrated in a study that showed that the mortality rate was 48%-82% lower among kidney transplant (KT) recipients compared with people who remained on long-term dialysis.[10] The risk of hospitalization from infection is also lower in KT recipients.[11] In addition, kidney transplantation is associated with significant improvements in patient satisfaction and quality of life.[12,13] However, KT recipients are at a higher risk of complications from COVID-19 due to their degree of immunosuppression and comorbidities.[14,15] An observational study of 36 COVID-19-positive KT recipients showed 78% of patients requiring admission and 30% requiring intubation with a 28% mortality at 3 weeks.[14] Another study from Italy revealed a rapid clinical and radiographic deterioration with 25% mortality after a median period of 15 days from symptom onset among KT recipients.[15]

In this report, we describe our experience in conducting kidney transplants during the COVID-19 pandemic at a single, large transplant center located in the State of Florida.

2 | PATIENTS AND METHODS

2.1 | Study design

This is a single-center retrospective study conducted at Jackson Memorial-Miami Transplant Institute, a 1558-licensed bed tertiary care teaching hospital in Miami, Florida. The study was approved by the Institutional Review Board of the University of Miami. The main objective of this study was to evaluate the safety of deceased donor kidney transplantation (DDKT) during the COVID-19 pandemic. All the adult patients that underwent DDKT from 3/1/20 to 4/30/20 were included in the study and were followed until 5/31/20.

2.2 | Induction immunosuppression

The standard induction regimen in our institution is methylprednisolone 500 mg IV daily and anti-thymocyte globulin (ATG) 1 mg/Kg IV daily (three doses each), and basiliximab 20 mg IV (on post-operative days 0 and 3 or 4).

2.3 | COVID-19 preventive measures

Since late January 2020, when the first case of COVID-19 was reported in the United States, our hospital has implemented several preventive measures to prepare for the upcoming crisis.

- Screening and appropriate triage of patients under investigation for COVID-19.
- Scale up local testing capacity, especially in-house testing to meet the demands due to the increasing number of COVID-19 cases.
- Screening for potential symptoms of COVID-19 in every patient admitted for transplant.
- Monitoring all SOT recipients with a very low threshold to test (and re-test whenever necessary) for SARS-CoV2 with a nasopharyngeal swab PCR test.
- Education of transplant candidates and recipients on the importance of maintaining social distancing, using adequate personal protection, reducing in-person visits if feasible, utilizing telemedicine applications for routine care visits if feasible and reducing the number of non-essential laboratory visits.
- A separate location was opened in the transplant clinic to test symptomatic transplant patients to avoid transmission to other patients.
- The use of surgical mask in all the medical campus facilities was made mandatory for all the healthcare workers and employees.
- The entrance of non-employees to our hospital was restricted.
- The living kidney donor and kidney/pancreas programs were placed on hold.
- High-risk population: patients over the age of 75 years, patients between 70 and 75 years old with significant comorbidities, patients with HIV and sensitized patients (unless crossmatch was negative and no human leukocyte antigen (HLA)-donor-specific antibodies were noted on Luminex®) were placed on hold.
- Preemptive transplantation was also placed on hold unless the patients were very close to require dialysis (Glomerular filtration rate under 15 mL/min).
- At the beginning of 4/2020, additional measures were implemented in our DDKT program: All donors must test negative for

SARS-CoV2 and not reside in COVID-19 hot spots, and recipients must test negative for SARS-CoV2 upon admission for transplant.

2.4 | Donors' demographics, clinical manifestations, and SARS-CoV2 testing

DonorNet® was reviewed to obtain the donors' information. We obtained epidemiological and travel history within 1 month prior to donation. We investigated if donors had fever, cough, and dyspnea before hospital admission by reviewing the medical-social questionnaire obtained from donors' relatives. We assessed the donors' Chest X-rays (CXR) to evaluate for the presence of opacities or infiltrates. Findings suggestive of atelectasis, pleural effusion, and pulmonary edema were not included. In addition, we evaluated if the donors were tested for SARS-CoV2. The sample sources were documented for those who were screened for SARS-CoV2. Please note that donors were not always tested for SARS-CoV2. Testing for SARS-CoV2 was decided by the Organ Procurement Organizations based on testing availability, donor history, and suspicion for COVID-19. GeneFinder™ COVID-19 Plus Real*Amp* Kit (running time: 1 hour) by ELITechGroup was used to test the local donors.[16] The information of the SARS-CoV2 polymerase chain reaction (PCR) platforms used to test the imported donors was not available.

2.5 | Recipients' demographics, clinical manifestations, and SARS-CoV2 testing at the time of transplantation

The medical charts were reviewed to obtain demographics (age, gender, ethnicity, and Florida County of residence), to evaluate if they had symptoms of COVID-19 or abnormal CXR at the time of transplantation. Findings suggestive of atelectasis, pleural effusion, and pulmonary edema were not included, same as donors. We investigated for the following symptoms: cough, dyspnea, fevers, chills, chest pain, fatigue, headaches, body aches, rhinorrhea, sore throat, conjunctivitis, anosmia, dysgeusia, altered mental status, nausea/vomiting, abdominal pain, and diarrhea. We also evaluated if they were tested for SARS-CoV2 at the time of transplantation. GeneFinder™ COVID-19 Plus Real*Amp* Kit, Xpert® Xpress SARS-CoV2 (running time: 4 hours) by Cepheid and QI-Astat-Dx Respiratory SARS-CoV2 Panel (running time: 8 hours) by Qiagen were available in our hospital to test the KT recipients during the study period. The tests were chosen at the discretion of the ordering providers. The clinical performance of these three PCR platforms is excellent.[16-18]

2.6 | Outpatient visits during post-transplant follow-up

The total number of outpatient visits from discharge to end of follow-up (5/31/20) was obtained to get a sense of how frequently patients were leaving home and getting potentially exposed to COVID-19 in case they were not following the recommended preventive measures (eg, wearing mask and maintaining social distance). The outpatient visits include appointments with medical providers, appointments for laboratories and imaging studies, outpatient procedures, and emergency department (ED) visits. The telemedicine appointments via ZOOM® went live on 3/30/20 and were also obtained. The charts were reviewed to determine if any of the KT recipients claimed exposure to COVID-19.

2.7 | Post-transplant outcomes

We evaluated if any of the KT recipients developed COVID-19 during the follow-up period by reviewing their charts to determine if they developed symptoms of COVID-19, tested positive or were diagnosed with COVID-19 at an outside facility. We investigated for readmissions, biopsy-proven rejection, and mortality by the end of the follow-up period. The reasons for readmissions and the treatments used for allograft rejection were also obtained. We also assessed if patients who were readmitted were more likely to be tested for SARS-CoV2 compared with those who were not readmitted.

2.8 | Statistical analyses

Chi-square test was used to assess bivariate associations between categorical variables; Median was used to assess continuous variables, based on normality of the distributions. A p value $< .05$ was considered significant.

3 | RESULTS

3.1 | General

Seventy-six patients received kidney allografts from 57 donors from 3/1/20 to 4/30/20. Forty patients were transplanted in 3/2020 and 36 in 4/2020. The donors and KT recipients were analyzed.

3.2 | Donors' demographics, clinical manifestations, and SARS-CoV2 testing

Twenty-five (43.9%) donors were from Florida. The other donors were from Pennsylvania (11 donors), California (4), Georgia (3), New Jersey, Missouri, Delaware and Puerto Rico (2 each), Nebraska, Illinois, Washington, Michigan, Connecticut, and Nevada (1 donor each). None of the donors had traveled within 1 month prior donation. Fever, dyspnea, and cough were reported in 1, 2, and 1 donor, respectively (Table 1). CXR opacities or infiltrates were noted in 15 (26.3%) donors (Table 1). Thirty-eight (66.6%) donors were tested for SARS-CoV2 by PCR from different sources (mainly from

TABLE 1 Demographics and clinical manifestations of the donors

Variables	N° 57 (%)
Demographics	
Local donors (Florida)	25 (43.9)
Travels[a]	0
Symptoms	
Fever[b]	1 (1.8)
Dyspnea[b]	2 (3.5)
Cough[b]	2 (3.5)
CXR opacities or infiltrates	15 (26.3)[c]

Abbreviation: CXR, Chest-X-ray.

[a]Not specified in 25 donors.

[b]Fever, dyspnea, and cough were unclear in 9, 13, and 12 donors, respectively.

[c]Bilateral opacities (6 donors), unilateral opacities (4), bilateral infiltrates (2), and unilateral infiltrates (3 donors).

nasopharynx and bronchoalveolar lavage) (Table 2). All the donor SARS-CoV2 testing came back negative.

3.3 | Recipients' demographics, clinical manifestations, and SARS-CoV2 testing at the time of transplantation

A total of 76 patients underwent DDKT between March 1, 2020 and April 30, 2020. The median age of the recipients was 54.5 (range: 22-70) years. The majority of the KT recipients were Male (56 [73.7%]), Hispanic (42 [55.3%]), and resided in Miami-Dade County (53 [69.7%]). Only one patient was symptomatic at the time of transplantation. She had cough from a resolving cold. Her CXR was normal, and she was not tested for SARS-CoV2 at the time of transplant. Eight (10.5%) patients had opacities noted on CXR at the time of transplant (Table 3). A total of 36 (47.3%) KT recipients were tested for SARS-CoV2 at the time of transplantation by nasopharyngeal PCR; all of these were negative (Table 3). The median length of hospital stay was 6.1 (range: 3.2-20.8) days.

TABLE 2 SARS-CoV2 testing of the donors

SARS-CoV2 testing[a]	Donors N° 57 (%)
Nasopharyngeal PCR	14 (24.6)
Bronchioalveolar lavage PCR	14 (24.6)
Bronchioalveolar lavage and plasma PCR	2 (3.5)
Bronchioalveolar lavage PCR and unclear source	2 (3.5)
Nasopharyngeal PCR	2 (3.5)
Nasopharyngeal and plasma PCR	1 (1.8)
Nasopharyngeal and bronchioalveolar lavage PCR	1 (1.8)
Nasopharyngeal, right and left kidney biopsy PCR	1 (1.8)
Kidney biopsy PCR	1 (1.8)

Abbreviations: PCR, polymerase chain reaction; SARS-CoV2, Severe Acute Respiratory Syndrome Coronavirus 2.

[a]All tests were negative.

3.4 | Outpatient visits during post-transplant follow-up

All the KT recipients visited the medical center during the follow-up period (from hospital discharge to 5/31/20), 75 (98.7%) patients for outpatient follow-up visits (median: 3 [range: 1-9] visits), 76 (100%) for laboratory appointments (median: 11 [range: 3-19] appointments), 45 (59.2%) for imaging studies appointments (median: 2 [1-4] appointments), and 16 (21.1%) for procedures (median: 1 [1-3] procedures). Thirteen (17.1%) patients went to the Emergency Department for non-COVID-19 reasons (10 patients once and three patients twice). Sixteen (21.1%) KT recipients had telemedicine visits (15 patients once one patient twice). None of the KT recipients claimed exposure to COVID-19 during the follow-up period.

3.5 | Post-transplant outcomes

Our KT recipients were followed for a median of 63 (range: 33-91) days. None of our KT recipients developed COVID-19 infection during the follow-up period. A total of 42 (55.3%) recipients were tested for SARS-CoV2 by a nasopharyngeal PCR including 12 patients that became symptomatic (nausea/vomiting [4 patients], fevers, chills, dyspnea, fatigue, and diarrhea [3 each], abdominal pain (2), and headaches and body aches [1 patient each]). Of the 42 patients that were tested, 23 (54.8%) were tested once, 12 (28.6%) twice, 4 (9.5%) four times, and 3 (7.1%) six times. All tests came back negative except for one that was inconclusive, but it was repeated and came back negative. Forty (52.6%) KT recipients were readmitted to the hospital during the follow-up period. There were a total of 55 readmissions (Table 4). Seven (9.2%) KT patients had biopsy-proven rejection during the follow-up. The kidney biopsies revealed borderline changes "suspicious" for acute T cell–mediated rejection (5 patients), acute T cell–mediated rejection IA-IIA (1 patient), and acute and chronic T cell–mediated rejection IA (1 patient). The rejection was treated with steroids in seven patients, ATG in two patients, and intravenous immunoglobulin in three patients. Patients who were readmitted were more likely to be tested for SARS-CoV2 compared with patients who were not readmitted [33/40 (82.5%) vs. 9/27 (33.3%), $P = <.001$]. None of the KT recipients transplanted during the study period died by the end of the follow-up.

4 | DISCUSSION

Our DDKT program, which performed the largest number of KT during 2019 in the United States,[19] has remained fully active during the COVID-19 pandemic. A review of United Network for Organ Sharing

TABLE 3 Demographics, radiographic findings, and SARS-CoV2 testing of kidney transplant recipients at the time of transplant

Variables	N° 76 (%)
Gender (male)	56 (73.7)
Ethnicity	
Hispanic	42 (55.3)
African American	27 (35.5)
Others[a]	7 (9.2)
County of residence	
Miami-Dade	53 (69.7)
Broward	12 (15.8)
Palm beach	7(9.2)
Others[b]	4 (5.3)
CXR opacities or infiltrates[c]	8 (10.5)[d]
SARS-CoV2 Testing by nasopharyngeal PCR	36 (47.3)[e]

Abbreviations: CXR, Chest-X-ray; PCR, polymerase chain reaction; SARS-CoV2, Severe Acute Respiratory Syndrome Coronavirus 2.

[a]Caucasian (6 patients) and Asians (1).

[b]St. Lucie, Orange, Monroe, and Collier Counties (1 patient each).

[c]CXR not done in 6 recipients.

[d]Bilateral opacities and unilateral opacities (4 patients each).

[e]All tests were negative.

TABLE 4 Readmissions during the follow-up period

Causes of readmissions	55 (%)
Worsening creatinine (other than rejection)	8 (14.5)
Allograft rejection	6 (10.9)
Hematologic	7 (12.7)[a]
Infections	7 (12.7)[b]
Deep vein thrombosis or arteriovenous fistula thrombosis	3 (5.5)
Perinephric collection	4 (7.3)
Hyperkalemia	3 (5.5)
Odynophagia or dysphagia	3 (5.5)
Leukocytosis	2 (3.6)
Gastrointestinal bleeding	2 (3.6)
Others	10 (18.1)[c]

[a]Symptomatic anemia (6 patients) and hemolysis (1 patient).

[b]*Clostridioides difficile* (2 patients), and urinary tract infection, surgical wound infection, epididymitis, *Staphylococcus epidermidis* bacteremia, and donor culture positive for *Rhizopus* (1 patient each).

[c]Small bowel obstruction, bradycardia, chest pain, diabetic ketoacidosis, dizziness, diarrhea, abdominal pain, acidosis, dyspnea, and carvedilol overdose (1 patient each).

(UNOS) data showed the significant impact of COVID-19 pandemic on kidney transplantation in the United States. The total number of kidney transplants decreased from approximately 475-525 transplants a week prior to the pandemic to a nadir of 213 transplants in a week at the height of the pandemic, with living donor transplants decreasing to near zero numbers.[20] The mortality benefit afforded by transplantation and the sheer volume of patients on the waiting list make it imperative to avoid suspension of transplantation programs across the country whenever possible. As of June 2020, there were over 101,000 patients on the kidney transplant waitlist. In 2019, 3,923 patients died while waiting for a kidney transplant.[20] In addition, kidney transplantation could theoretically reduce risk of COVID-19 exposure as SARS-CoV-2 transmission has been reported in dialysis units.[21]

In this retrospective, single-center cohort study, we described our DDKT experience during the pandemic. Infection preventive measures, which were highlighted in the Patient and Methods section, were implemented from the beginning of the COVID-19 pandemic. Note, that our COVID-19 policies are updated as needed after multidisciplinary discussions with transplant nephrologists, surgeons, infectious diseases and infection control specialists and pharmacists.

In a COVID-19/SOT protocol from Baylor College of Medicine, transplant candidates must have had a negative SARS-CoV2 nasopharyngeal swab and normal chest computed tomography (CT) for COVID-19 to proceed to transplant.[22] The need for chest CT in asymptomatic patients admitted for SOT should be carefully evaluated as it has low specificity for COVID-19.[23]

Our cohort included 76 patients that safely underwent DDKT in March-April 2020 in spite of the COVID-19 pandemic. More than 40% of our donors were from Florida and by March 31st and April 30th (study end date for donation), there were 6338 and 33 690 confirmed cases in Florida, respectively.[24,25] None of our KT recipients were diagnosed with COVID-19 during a median follow-up time of approximately 2 months even though the majority (70%) resided in Miami-Dade County (most affected Florida County by COVID-19), and they had to leave home on multiple occasions for follow-up visits, laboratory appointments, etc By the end of the study follow-up (May 31st), there were 56 163 confirmed cases in Florida including 18 000 in Miami-Dade County.[26] These numbers would have been considerably higher if more people would have been tested. Around half of our KT recipients were readmitted during the follow-up period but none of them were admitted specifically to rule out COVID-19. Interestingly, the KT recipients who were readmitted were more likely to be tested for SARS-CoV2 than patients who were not readmitted. In addition, there were more patients tested for SARS-CoV2 than symptomatic patients. Therefore, it seemed that many asymptomatic KT recipients were screened for SARS-CoV2 during the follow-up period at the discretion of clinicians.

Blood transfusion transmission and donor-derived COVID-19 have not been reported but they could theoretically occur as viral RNA has been detected in serum in patients with severe COVID-19.[27,28] SARS-CoV2 has also been isolated in urine[29] but transmission through kidney transplantation has not been proved. SARS-CoV2 was not detected among our donors. However, one third of them were not tested. Performing plasma and urine SARS-CoV2 PCR could be considered among KT recipients when there is concern for donor-derived COVID-19 or when donors are from COVID-19 hot

spots, but it should be investigated. In-hospital COVID-19 transmission has been reported. In a single-center study from Wuhan, 41% patients were thought to have acquired COVID-19 in the hospital.[30] We believe that the in-hospital exposure probability in our center is low given all the preventive measures that were enforced. In-hospital COVID-19 transmission can be easily prevented through basic infection control measures such as wearing surgical masks and performing hand and environmental hygiene.[31] Our study demonstrates that a DDKT program can remain active during the COVID-19 pandemic as long as the COVID-19 preventive measures are followed strictly, and the hospital is not at the maximum capacity.

This study has several limitations. First, it is a retrospective study. Therefore, we could have missed clinical data, such as symptoms of COVID-19 among our KT recipients. Second, our sample size was relatively small, and the study follow-up time was not too long. The number of COVID-19 cases increased in Florida in June 2020 so we could have identified COVID-19 cases among our patients if they would have been followed longer. Lastly, this study includes all testing performed at our center and potentially excludes positive tests performed at other facilities. In conclusion, our cohort demonstrated that DDKT can be safely performed during the COVID-19 pandemic when preventive measures are implemented and followed. Larger studies with a longer follow-up are needed to confirm our encouraging results.

AUTHORS' CONTRIBUTIONS

A. Chandorkar. involved in study design, data analysis/interpretation, drafting article, critical revision of article. A.Coro. involved in data analysis/interpretation and critical revision of article. YN involved in data analysis/interpretation and critical revision of article. S.A involved in data analysis/interpretation and critical revision of article. LMA involved in data analysis/interpretation and critical revision of article. GG involved in data analysis/interpretation and critical revision of article. ADM involved in data analysis/interpretation and critical revision of article. LAM involved in data analysis/interpretation and critical revision of article. MIM involved in data analysis/interpretation and critical revision of article. JFC involved in data analysis/interpretation and critical revision of article. RV involved in data analysis/interpretation and critical revision of article. JS involved in study design, data analysis/interpretation, drafting article, and critical revision of article.

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How to cite this article: Chandorkar A, Coro A, Natori Y, et al. Kidney transplantation during coronavirus 2019 pandemic at a large hospital in Miami. *Transpl Infect Dis*. 2020;22:e13416. https://doi.org/10.1111/tid.13416