COVID-19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS AT THE EPICENTER OF PANDEMIC

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ABSTRACT

We aimed to investigate the prevalence and clinical outcomes of COVID-19 in kidney transplant recipients in the Bronx, New York, one of the epicenters of the pandemic. Between March 16 and June 2, 2020, 132 kidney transplant recipients tested positive by SARS-CoV-2 RT-PCR. From May 3 to July 29, 2020, 912 kidney transplant recipients were screened for SARS-CoV-2 IgG antibodies during routine clinic visits, of which 152 (16.6%) tested positive. Fifty-five of the 152 patients had previously tested positive by RT-PCR, while the remaining 97 did not have significant symptoms and had not been previously tested by RT-PCR. The prevalence of SARS-CoV-2 infection was 23.4% in the 975 patients tested by either RT-PCR or SARS-CoV-2 IgG. Older patients and patients with higher serum creatinine levels were more likely diagnosed by RT-PCR compared to SARS-CoV-2 IgG. Sixty-nine RT-PCR positive patients were screened for SARS-CoV-2 IgG antibodies at a median of 44 days post-diagnosis (IQR 31-58) and 80% were positive. Overall mortality was 20.5% but significantly higher in the 111 patients who required hospitalization (37.8%). Twenty-three % of the hospitalized patients required renal replacement therapy and 6.3% lost their allografts. In multivariable analysis, older age, receipt of deceased-donor transplantation, lack of influenza vaccination in the previous year and higher serum interleukine-6 levels were associated with mortality. In conclusion, 42% of kidney transplant patients with COVID-19 were diagnosed on antibody testing without significant clinical symptoms and 80% of patients with positive RT-PCR developed SARS-CoV-2 IgG. Mortality was high among patients requiring hospitalization.

Key words: COVID-19, kidney transplantation, mortality, SARS-CoV-2 IgG antibody
ABBREVIATIONS

COVID-19: Coronavirus 2019 Infectious Disease

ESRD: End-Stage Renal Disease

RT-PCR: Reverse transcription polymerase chain reaction

IQR: Interquartile range

CI: Confidence interval

BMI: Body mass index

IL-6: Interleukine-6

Pro-BNP: Pro-NT Brain Natriuretic Peptide
Introduction

Following the first case of coronavirus infectious disease 2019 (COVID-19) in the USA in January 2020, New York quickly became the epicenter of the pandemic in March and April 2020. Initial results from 3 centers in New York reported a high mortality rate of 20%-39% in hospitalized patients \(^1\)-\(^3\). Kidney transplant recipients are expected to be at an increased risk of complications from COVID-19 not only due to their chronic immunosuppression but also frequently associated comorbidities including older age, hypertension, diabetes mellitus, chronic kidney disease and cardiovascular disease. We previously reported 28% mortality at 3 weeks follow-up in a cohort of 36 kidney transplant recipients with COVID-19\(^4\). Other kidney transplant centers in New York have reported similar mortality rates of 13% to 30%\(^5\)-\(^8\) as did an international multicenter registry, including our center and 12 others in the USA, Italy and Spain, with an initial mortality of 32% in kidney transplant recipients\(^9\). Another multicenter cohort study of 482 solid organ transplant recipients (318 kidney or kidney/pancreas) from more than 50 transplant centers in the USA reported 20.5% mortality\(^10\). In addition to transplant recipients, patients with end-stage renal disease (ESRD) also appear to be at increased risk of severe COVID-19 illness. Early reports from European centers showed a mortality rate of 20% to 30% among patients receiving chronic dialysis who were hospitalized for COVID-19\(^\text{11-13}\). The mortality rate in 114 ESRD patients admitted to our center was 28%\(^14\) and 31% at another New York center\(^15\).

Based on these early studies, there has been concern that kidney transplantation may be an independent risk factor for mortality compared to both the general population and ESRD patients, prompting questions regarding the safety of transplantation during the pandemic. However, the mortality of COVID-19 in renal transplant patients is difficult to determine without understanding the actual prevalence of SARS-CoV-2 infection, which has been hampered due limited PCR testing early in the pandemic and lack of widespread SARS-CoV-2 antibody testing in this population. Further, given their immunosuppression, it is unknown if kidney transplant recipients mount an antibody response to SARS-CoV-2 similar to general population and therefore, diagnosis of SARS-CoV-2 using antibody testing may be underreported among transplant recipients.
Accurate serologic tests for IgG antibodies to SARS-CoV-2 are imperative to better understand the immune response in the setting of SARS-CoV-2 infection. Zhao et al. found that RNA detectability by PCR decreased overtime to 45.5% by 15-39 days after onset while the presence of IgG increased to nearly 80% by days 15-39 days, concluding there may be improved diagnostic sensitivity when combining RNA and antibody detection. RT-PCR for diagnosis of SARS-CoV-2 infection has been associated with a high rate of false negative results. Recent reports have shown that utilizing SARS-CoV-2 IgG and IgM antibodies can help diagnose patients who present with COVID-like symptoms despite negative RT-PCR swabs. Furthermore, screening for antibody testing in the general population has determined that SARS-CoV-2 infections are 6 to 24 times more prevalent than initially thought. Notably, seropositivity in patients receiving hemodialysis has been reported as high as 36.2%. Data regarding the use of serologic testing for SARS-CoV-2 diagnosis in kidney transplant recipients is lacking. Moreover, differences in the clinical presentation and course of disease among kidney transplant recipients may differ between those diagnosed by serology rather than by RT-PCR, though this has not yet been evaluated.

Therefore, the objectives of our study were: 1) to determine the seroprevalence of SARS-CoV-2 IgG in our kidney transplant population, 2) to compare clinical and demographic features of patients diagnosed by SARS-CoV-2 IgG to those diagnosed by RT-PCR, 3) to identify the antibody response rate in kidney transplant recipients with confirmed SARS-CoV-2 on RT-PCR, and 4) to determine predictors of mortality including inflammatory markers, blood and HLA types.

RESULTS

COVID-19 DIAGNOSIS BY RT-PCR AND SARS-COV-2 IgG

Figure 1 summarizes the study design involving the 1,475 adult kidney transplant patients currently followed by our center. Between March 16 and June 2, 2020, 132 patients tested positive for SARS-CoV-2 by RT-PCR. Between May 3 and July 29, 2020, 912 patients were screened for SARS-CoV-2 IgG antibodies and 152 (16.6%) tested positive. Fifty-five of the 152 patients had confirmed COVID-19 by previously performed RT-PCR. The remaining 97 COVID-19 IgG positive patients did not have significant symptoms, did not seek medical
attention and were not tested for SARS-CoV-2 by RT-PCR. The prevalence of SARS-CoV-2 infection was 23.4% in the 975 patients tested by either RT-PCR or SARS-CoV-2 IgG.

Of the 132 patients with a positive SARS-CoV-2 RT-PCR, 21 were followed as outpatients with close monitoring of their symptoms by the transplant center. The remaining 111 patients were hospitalized, 79 at Montefiore Medical Center and 32 at outside facilities. Figure 2 shows the number of cases of SARS-CoV-2 RT-PCR positivity over the first 14 weeks of the pandemic. Our first confirmed case of COVID-19 was diagnosed on March 16, 2020 which corresponds to start date of Week 1. RT-PCR positive cases peaked at Week 4 and started to decline thereafter.

Table 1 summarizes the demographics and clinical presentation of the 229 patients with COVID-19 and compares those diagnosed by RT-PCR to those diagnosed by SARS-CoV-2 antibodies. Sixty-two% of the patients were male, 55% Hispanic, 32% African American and the median age was 59 (IQR, 49-68). Seventy-three% were deceased-donor recipients and diagnosis of COVID-19 occurred at a median of 58.2 months IQR (25.4-127.6) after transplantation. Only 9% and 7% underwent kidney transplantation within the preceding 12 and 6 months, respectively. Most patients were on triple immunosuppression with tacrolimus (97%), mycophenolate mofetil/mycophenolic acid (87%) and prednisone (95%). Patients had multiple additional medical comorbidities; 98% hypertension, 61% diabetes mellitus, 22% heart disease, and 36% history of smoking. Median body mass index (BMI) was 28.5 (IQR, 24.2-32.6).

Patients diagnosed by RT-PCR tend to be older (median age 62.5 vs 57 years old, p < 0.0024) and were more likely to have received a deceased-donor kidney transplant (77% vs 66%, p = 0.039). These patients were also more likely to be diabetic (68% vs 53%, p = 0.019), have diabetic nephropathy as cause of renal failure (55% vs 35%, p = 0.027), and had a higher baseline creatinine (median 1.4 vs 1.2 mg/dL, p = 0.039) compared to patients diagnosed by a positive SARS-CoV-2 IgG only. In the multivariate analysis, the odds of being diagnosed by RT-PCR compared to SARS-CoV-2 IgG were estimated to increase by 21% for every 5-year increase in age [OR 1.2, 95% CI 1.09-1.35, p<0.001] and by 7% for every 0.1 unit increase in baseline creatinine level [OR 1.07, 95% CI 1.02-1.12, p= 0.0082].
Thirty-five of the 97 patients (36.1%) diagnosed by SARS-CoV-2 IgG did not recall having any symptoms suggestive of COVID-19 during the peak of the pandemic and the remaining patients had mild symptoms that did not require medical evaluation. Patients who were diagnosed by positive RT-PCR were more likely to have fever (61% vs 30%), dyspnea (60% vs 28%), cough (62.5% vs 23%) and diarrhea (28% vs. 15%) compared to those diagnosed with SARS-CoV-2 IgG. Interestingly, anosmia was more common in those diagnosed with antibody testing (14.8%).

A total of 69 RT-PCR positive patients were tested for SARS-CoV-2 IgG antibodies during routine follow-up. Fifty-five (80%) patients were positive for SARS-CoV-2 IgG antibodies, measured at a median of 44 days after initial diagnosis (IQR 31-58). Only 7 of the 55 IgG positive patients were re-tested at a later date and their antibodies remained positive. Fourteen patients (20%) with confirmed positive SARS-CoV-2 RT-PCR were negative for SARS-CoV-2 antibodies. Four of these patients were re-tested within a month after the initial test and their IgG remained negative.

Of the 97 patients who were diagnosed with SARS-CoV-2 IgG only, 11 were retested 1 to 2 months after the initial test. Nine patients showed sustained IgG positivity while 2 tested negative. Thirty patients underwent repeat RT-PCR testing 14-90 days after their initial positive RT-PCR and 5 patients (16.7%) showed sustained positivity. Of the 25 patients with a repeat negative RT-PCR test, 16 were re-tested a third time and 8 patients a fourth time and all tests remained negative, except for one patient.

**MORTALITY**

The 229 COVID-19 patients were followed for a median of 140 days (IQR, 86-164). Forty-seven patients (20.5%) died at a median 10 days (IQR, 6-16) after diagnosis. Patient sex, race, time after transplantation, immunosuppressive medications, body mass index, history of smoking, angiotensin converting enzyme inhibitor or receptor blocker use, and statin use were not associated with mortality. Risk factors associated with mortality included older age (70 vs 58 years old, p < 0.001), receiving a deceased-donor renal transplant (89% vs 69%, p = 0.0058), having diabetic nephropathy as cause of renal disease (70% vs 40%, p = 0.0065), diabetes mellitus (77% vs 58%, p=0.016), not receiving influenza vaccination the previous year (76% vs 93%, p
higher baseline serum creatinine levels (1.5 vs 1.3 mg/dL, \(p = 0.032\)) in the univariate analysis. In multivariate analysis, age, type of transplant and receiving influenza vaccination were statistically significant. The odds of mortality were estimated to increase by 48% for every 5-year increase in age with an estimated 95% CI [OR, 1.48, 1.22-1.79, \(p < 0.001\)]. Deceased-donor recipients had an estimated OR of 1.22 of mortality compared to living-donor recipients with 95% CI [1.067-1.74, \(p= 0.015\]), and those who did not receive influenza vaccine previous year had an estimated OR of 1.13 of mortality compared to those who received the vaccine with 95% CI [1.040-1.43, \(p < 0.001\)].

There was no statistically significant association between blood group type and mortality. In terms of HLA typing, there was no association between any HLA type and mortality. The smallest adjusted \(p\)-value for the 75 alleles assessed was 0.973

**CLINICAL FEATURES AND INFLAMMATORY MARKERS OF HOSPITALIZED PATIENTS**

Among the 111 patients who required hospitalization, mortality was 37.8%. Of those, 79 patients were admitted to Montefiore Medical Center and had detailed monitoring of inflammatory markers and T cell subtypes. Supplemental Table 1 represents the demographic data of those 79 patients as well as demographic data for the subgroup of patients who survived the hospital admission (n=51) and those who died (n=28). There was no difference between survivors and non-survivors in terms of demographics, however non-survivors tend to have a higher BMI (30.4 vs 26.7, \(p = 0.057\)) and had a lower oxygen saturation on room air on presentation (93% vs 96%, \(p = 0.037\)).

On admission, 67 patients (85%) were lymphopenic, 54 (68%) had a low CD3 cell count, 52 (66%) had a low CD4 cell count and 22 (28%) had a low CD8 cell count. C- Reactive Protein level was > 10 mg/dL in 38 patients (48%), procalcitonin level > 0.2 ng/mL in 41 patients (52%), ferritin > 900 ng/mL in 50 patients (63%) and 66 patients (84%) had a D-Dimer > 0.5 µg/mL while 20 (25%) had a level > 3 µg/mL. Thirty-two patients (41%) had serum interleukine-6 (IL-6) levels > 60 pg/mL. Fifty-three (67%) patients had lactic dehydrogenase levels > 1.5 times upper range of normal, 19 (24.1%) had a creatine kinase level > 200 U/L, 49 (62%) had a fibrinogen level > 500 mg/dL, and 43 (54.4%) had Pro-NP Brain Natriuretic Peptide (Pro-BNP) level > 900
pg/mL. The details of admission laboratory values and inflammatory markers are presented in the Table 2. When comparing survivors and non-survivors, initial IL-6 levels (47 vs 101 pg/mL, p = 0.036) and initial Pro-BNP levels (1278 vs 2380, p = 0.031) were significantly higher in non-survivors. There were no other statistically significant differences in admission laboratory values or inflammatory markers between the two groups.

Inflammatory markers were checked frequently during patients’ hospitalizations at our institution. When peak laboratory values and inflammatory markers were compared (Table 3), non-survivors had lower median lymphocyte counts (300 vs 500 cells/µL, p = 0.021) and platelet counts (135 vs 170 k/µL, p = 0.045), and higher median C-Reactive Protein (22.8 vs 14.3 mg/dL, p = 0.0032), procalcitonin (1.9 vs 0.3 ng/mL, p = 0.006), lactic dehydrogenase (612 vs 389, p = 0.0017), creatine kinase (194 vs 106 U/L, p = 0.022) and IL-6 levels (182 vs 48 pg/mL, p = 0.0004). In the multivariate analysis, every 10 unit increase in serum IL-6 levels was associated with a 3.6% increase in the odds of death [OR 1.036, 95% CI 1.008-1.065, p=0.01].

The clinical outcomes of both survivors and non-survivors are summarized in Table 4. Twenty-eight patients (35%) required intubation and mechanical ventilation and an additional 7 patients decided not to be resuscitated/intubated. Acute renal failure requiring renal replacement therapy occurred in 18 patients (23%) and 5 patients (6.3%) lost their allografts. Ten (13%) patients developed new thromboembolic events and 3 patients (4%) suffered from cerebrovascular accidents. In terms of secondary infections, 7 patients developed bacteremia, 9 developed urinary tract infections and 4 had concurrent bacterial pneumonias. In terms of opportunistic infections, 12 patients developed low grade cytomegalovirus viremia, with viral loads between 50-559 copies, likely reflecting reactivation in the setting of acute illness and decreased lymphocyte numbers and function. Four patients developed fungal infections.

**TREATMENT**

Treatment modalities are summarized in Table 5. Seventy-four patients (93.7%) had their anti-metabolite withdrawn at time of diagnosis and calcineurin inhibitors were withdrawn in 11 patients (13.9%) mostly after clinical deterioration (7.8% of survivors and 25% of non survivors). Sixty-five patients (82.3%) were treated with antibiotics (ceftriaxone with doxycycline or azithromycin) for prevention of secondary
infections. Initially all the patients were started on hydroxychloroquine, however after the first 59 patients, this practice was discontinued at our institution due to lack of efficacy. Eighty six percent of non-survivors were treated with hydroxychloroquine while 69% of survivors received this agent (p=0.067). Anti-cytokine agents were used in patients with moderate to severe clinical pictures; 35 received increased doses of corticosteroids (44%), 11 tocilizumab (14%), and 6 leronlimab (7.6%), an experimental CCR-5 inhibitor. Seven patients received convalescent plasma (13.7%), 3 of whom survived. An anti-interleukin 1 agent, intravenous immunoglobulins and a tyrosine kinase inhibitor were each used in only one patient. Eight patients were enrolled in clinical trials: six in a remdesivir trial and two in a sarilumab trial. Forty-four patients (55.7%) received anticoagulation treatment with apixaban and/or heparin for prevention or treatment.

**DISCUSSION**

Our study represents the largest number of kidney transplant patients tested for SARS-CoV-2 IgG antibodies reported to date in a predominantly Hispanic and African American population. Seropositivity was 16.6% in our cohort of renal transplant recipients. The prevalence of SARS-CoV-2 infection was 23.4% among 975 patients who underwent testing by either RT-PCR and/or SARS-CoV-2 IgG. Forty-two% of SARS-CoV-2 diagnoses were made by antibody testing and one third of those patients were asymptomatic while the rest did not have severe enough symptoms to warrant medical attention. These patients were younger, less likely to be diabetic and had a better renal allograft function compared to those diagnosed with positive RT-PCR.

Our in-house SARS-CoV-2 IgG assay is performed on the Abbott Architect I instrument. The manufacturers reported sensitivity by day 14 after symptoms in RT-PCR positive patients is 100% (96.8% when five specimens from one immunocompromised patient included). The specificity was 99.6% from >1,000 specimens presumed to be SARS-CoV-2 negative, including pre-COVID 19 samples as well as specimens collected in 2020 from subjects who were exhibiting signs of respiratory illness but were negative for SARS-CoV-2 by PCR. Bryan et al. also evaluated the Abbott SARS-CoV-2 assay and found similar performance specifications with a specificity of 99.9% from 1,020 pre-COVID 19 serum specimens and a sensitivity of 100% 17 days after symptom onset. On internal validation of the assay, our laboratory found a specificity of 100%
for pre-COVID 19 specimens, PCR negative patient samples, and remnant samples from patients who tested positive for other coronavirus strains on respiratory panels from January or February 2020.

Whether measured antibodies are protective against reinfection and if so, for what duration remains unknown. In addition to antibodies, CD4 and CD8 responses to the virus are also potentially important in assessing immunity. Using HLA class I and II predicted peptide ‘megapools’, circulating SARS-CoV-2-specific CD8+ and CD4+ T cells were identified in ~70% and 100% of COVID-19 convalescent patients, respectively. Interestingly, the authors detected SARS-CoV-2-reactive CD4+ T cells in ~40-60% of unexposed individuals, suggesting cross-reactive T cell recognition between circulating ‘common cold’ coronaviruses and SARS-CoV-2. Although, antibody titers might decrease overtime, memory T and B cells may allow for enhanced antibody response upon re-exposure to the virus. In a study by Long et al, asymptomatic cases, defined as those with positive RT-PCR but no symptoms suggestive of COVID-19, were hospitalized for observation. These patients developed SARS-CoV-2 IgG at 4 weeks post diagnosis at rate of 81%, however, in the convalescent phase (8 weeks post-discharge) only 60% were still positive for antibodies. Interestingly, symptomatic patients had a higher positivity rate of antibodies in the convalescent phase than in acute phase (87.1% vs 83.8%)23. In our cohort, 80% of patients with positive RT-PCR tested positive for SARS-CoV-2 IgG antibodies. Only 7 of these patients were retested at a later date but all remained positive. Several of the 20% of patients who did not mount an antibody response were also retested later and remained negative. Seroprevalence in our patient population was lower than that reported by the New York City Department of Health, which reported 26% antibody positivity (33% in Bronx) among 1.8 million people who were tested (https://www1.nyc.gov/site/doh/covid/covid-19-data-testing.page).

In our cohort of kidney transplant recipients, overall mortality was 20.5% and in-hospital mortality was 37.8%. Our inpatient mortality rate is similar to that reported in hospitalized patients in New York during the peak of the pandemic 1-3 as well as in ESRD patients 11,13,15 and in some reports of kidney transplant recipients5,9. Our results should be evaluated in the context of our patient population in the Bronx, the majority of which are Hispanic or African American, have lower income, and live in more densely populated
areas. Compared to other New York City boroughs, the Bronx have been shown to have higher hospitalization and death rates from COVID-19. Other factors associated with higher mortality include older age, diabetes mellitus, obesity, frailty, chronic heart and lung disease, and longer dialysis vintage. In terms of laboratory values, lymphopenia and higher levels of CRP, ferritin, procalcitonin, IL-6, D-dimer and lactate dehydrogenase have been reported to be predictors of mortality. In our whole cohort, older age, receipt of deceased-donor renal transplant and not receiving flu vaccination was associated with an increased risk of mortality. The findings regarding flu vaccination are particularly interesting given a recent analysis of immunization records of individuals receiving non-COVID-19 vaccinations. This study found a decreased rate of COVID-19 infection in the population receiving non-COVID-19 vaccinations. These results might suggest the importance of annual influenza vaccination but further studies are needed.

Our hospitalized patients were lymphopenic, had low CD3/CD4/CD8 cell counts and high levels of C-Reactive protein, procalcitonin, ferritin, D-Dimer and IL-6. Elevated IL-6 levels on admission were associated with an increased risk of mortality indicating the importance of monitoring IL-6 levels in hospitalized patients. Early observational cohort studies of tocilizumab, a monoclonal antibody that blocks the IL-6 receptor, found that patients receiving tocilizumab had reduced mortality compared to standard of care, though larger randomized trials have failed to show a benefit with IL-6 therapy.

Among genetic factors that may influence the susceptibility to and clinical outcome of SARS-CoV-2 infection, HLA genes are attractive candidates due to their high diversity and key role in shaping the adaptive immune responses against viruses. Currently there are limited reports of HLA gene variation in COVID-19 patients. Nguyen et al. analyzed the binding affinity of SARS-CoV-2 derived peptides to HLA class I alleles. This model predicted that some peptide-HLA complexes may be shared across different SARS viruses. B*46:01 allele was found to bind the lowest number of peptides derived from SARS proteins, suggesting that this allele may be associated with a weaker immune response to SARS viruses. In our study, we did not identify any HLA alleles that were associated with COVID-19 related death. Large scale studies are warranted to analyze the full impact of HLA gene diversity on the immune responses to SARS CoV-2.
Our study has multiple strengths. It is the first study screening for SARS-CoV-2 IgG antibodies in a large cohort of renal transplant recipients to determine the seroprevalence of SARS-CoV-2 in this population. It is also the largest single center study documenting antibody response in kidney transplant patients with COVID-19 along with detailed analysis of predictors of mortality including inflammatory markers and HLA types. A limitation of our study is that only a minority of our cohort underwent repeat antibody testing and as such, we are unable to assess the durability of these antibodies in this patient population. Additionally, only qualitative IgG testing was performed and quantitative values may have provided further information. We also did not check for SARS-CoV-2 IgM antibodies.

In summary, a significant number of kidney transplant recipients (42%) were identified to be SARS-CoV-2 IgG positive without significant symptoms or testing for SARS-CoV-2 by RT-PCR. Among those with confirmed diagnosis of COVID-19 by RT-PCR, the majority (80%) developed an antibody response. Older age, receipt of deceased-donor transplantation and lack of flu vaccination were associated with mortality. Increased IL-6 levels were the most predictive inflammatory biomarker for mortality in hospitalized patients.

MATERIAL AND METHODS

COVID-19 diagnosis and study design

This was a prospective cohort study of two groups of kidney transplant recipients, which is summarized in Figure 1. The first group was kidney transplant patients who presented to healthcare facilities with COVID-like symptoms and tested positive for SARS-CoV-2 by RT-PCR (nasopharyngeal/oral swab). The second group was asymptomatic kidney transplant recipients who were screened as part of routine care for SARS-CoV-2 IgG antibodies during routine post-transplant clinic visits. Patient demographics and clinical information were obtained through routine patient care and chart review. Patients who were hospitalized at Montefiore Medical Center underwent frequent monitoring of inflammatory markers including CRP, ferritin, procalcitonin, IL-6, D-dimer, and T cell subtypes (CD3, CD4 and CD8) as part of our programmatic treatment protocol. The study was approved by Albert Einstein Medical College IRB.
COVID-19 RT-PCR and SARS-CoV-2 IgG antibody methods

Nasopharyngeal and/or oropharyngeal swabs were collected in 3mL viral transport media and RNA extraction followed by real-time RT PCR was performed using one of three commercial methods at our institution. IgG antibody testing was performed using the Abbott SARS-CoV-2 IgG antibody test on the Abbott Architect Immunoassay Analyzer. Testing was performed on serum samples following manufacturer’s instructions. The assay is a chemiluminescent microparticle immunoassay intended for the qualitative detection of IgG antibodies to SARS-CoV-2.

HLA typing

HLA genes were typed by low resolution DNA methods using sequence specific oligonucleotide probes (SSOP) and sequence specific primers (SSP). Typing results of HLA-A, B, DRB1 and DQB1 loci were available in 220 patients who tested positive by SARS-CoV-2 RT PCR and/or IgG antibody tests.

Statistical analysis

The characteristics of the sample were described using frequencies and relative frequencies for categorical variables and by the median and interquartile range for continuous variables. Significance tests of associations between categorical variables and outcome was based on chi-squared tests, or Fisher Exact Tests. Significance tests comparing outcomes for continuous variables were based on Wilcoxon rank-sum tests. No adjustments were made for the multiplicity of comparisons performed, and the nominal p-values are therefore primarily descriptive. Multivariable logistic regression models were used to test whether significant univariate effects (at p< 0.010) remained significant after adjustment for other significant variables. The associations between the independent variables in these models and outcome were quantified using odds ratios and their respective 95% confidence intervals. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute). A total of 75 alleles were assessed to determine whether expression was associated with increased risk of mortality. The association between expression and mortality was assessed by the chi-squared test, or Fisher’s exact test. The procedure of Benjamini and Hochberg was used to control the False Discovery Rate of claiming significance to be at most 20%.
DISCLOSURE

The authors do not have any financial disclosure for the manuscript.

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| Table 1 – Clinical characteristics of the patients comparing by type of COVID-19 diagnosis and mortality |
|--------------------------------------------------|--|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
| | | Total patients N = 229 | COVID RT-PCR positive N = 132 | SARS-CoV-2 IgG Antibody positive N = 97 | p-value | Survivors N = 182 | Non survivors N = 47 | p-value |
| **Sex** | | | | | | | | |
| Male,% | 141 (62%) | 82 (62%) | 59 (61%) | 0.84 | 113 (62%) | 28 (60%) | 0.75 |
| Female,% | 88 (38%) | 50 (38%) | 38 (39%) | | 69 (38%) | 19 (40%) | |
| **Age, median [IQR]** | 59 [49-68] | 62.5 [51-71] | 57 [46-65] | 0.0024 | 58 [46-66] | 70 [58-74] | < 0.001 |
| **Race** | | | | 0.87 | 74 (56%) | 51 (53%) | 0.53 |
| Hispanic | 125 (55%) | 74 (56%) | 51 (53%) | | 74 (56%) | 51 (53%) | |
| African American | 74 (32%) | 41 (31%) | 33 (34%) | | 41 (31%) | 33 (34%) | |
| Other | 30 (13%) | 17 (13%) | 13 (13%) | | 17 (13%) | 13 (13%) | |
| **Type of transplant** | | | | 0.039 | 124 (69%) | 41 (89%) | 0.0058 |
| Deceased donor | 165 (73%) | 101 (77%) | 64 (66%) | | 124 (69%) | 41 (89%) | |
| Living donor | 61 (27%) | 28 (21%) | 33 (34%) | | 56 (31%) | 5 (11%) | |
| **Time after transplantation, median [IQR] months** | 58.2 [25.4-127.6] | 60.8 [20-128.5] | 57.7 [28.7-124.6] | 0.9 | 57.7 [27.3-123.7] | 65.2 [16.3-134.1] | 0.82 |
| Transplant < 6 months | 13 (7%) | 9 (9%) | 4 (4%) | 0.49 | 10 (6%) | 3 (6%) | 0.21 |
| Transplant < 12 months | 18 (9%) | 11 (11%) | 7 (8%) | 0.97 | 13 (7%) | 5 (11%) | 0.43 |
| **Etiology of End-stage Renal Disease** | | | | | | | | |
| Diabetes mellitus | 106 (47%) | 72 (55%) | 34 (35%) | 0.005 | 73 (40%) | 33 (70%) | 0.0065 |
| Hypertension | 49 (22%) | 21 (16%) | 28 (29%) | | 45 (25%) | 4 (9%) | |
| Glomerulonephritis | 52 (23%) | 23 (18%) | 29 (30%) | | 44 (24%) | 8 (17%) | |
| Polycystic kidney disease | 9 (4%) | 2 (2%) | 7 (5%) | | 8 (4%) | 1 (2%) | |
| Others | 12 (5%) | 8 (6%) | 4 (4%) | | 11 (6%) | 1 (2%) | |
| **Body Mass Index (kg/m2) median [IQR]** | 28.5 [24.2-32.6] | 28.7 [23.7-32.5] | 28.1 [24.7-32.6] | 0.76 | 28.3 [24.2-32.3] | 29.1 [23.7-34.3] | 0.66 |
| History of smoking | 81 (36%) | 48 (37%) | 33 (34%) | 0.68 | 64 (35%) | 17 (36%) | 0.92 |
| Influenza vaccination | 193 (89%) | 102 (86%) | 91 (94%) | 0.055 | 162 (93%) | 31 (66%) | 0.0015 |
| **Comorbidities** | | | | | | | | |
| Hypertension | 224 (98%) | 128 (98%) | 96 (99%) | 0.47 | 178 (98%) | 46 (98%) | 0.83 |
| Diabetes mellitus | 140 (61%) | 89 (68%) | 51 (53%) | 0.019 | 104 (58%) | 36 (77%) | 0.016 |
|                  | Heart disease |  | Lung disease |  | Cancer |  | Angiotensin converting enzyme inhibitor or angiotensin receptor blocker use |  | Statin use |  | Baseline serum creatinine, mg/dL median [IQR] |  | Blood type |  |
|------------------|--------------|---|--------------|---|--------|---|--------------------------------|---|------------|---|--------------------------------|---|----------|---|
|                  | 49 (22%)     | 28 (21%) | 21 (22%)     | 0.96 | 38 (21%) | 11 (23%) | 0.72                        |   |            |   | 16 (7%) | 11 (8%) | 5 (5%) | 0.34 | 10 (6%) | 6 (13%) | 0.083                   |   | 23 (10%) | 12 (9%) | 11 (11%) | 0.59 | 18 (10%) | 5 (11%) | 0.89                   |   |           |   |   |   | 60 (26%) | 33 (25%) | 27 (28%) | 0.65 | 47 (26%) | 13 (28%) | 0.81                   |   | 143 (63%) | 84 (64%) | 59 (61%) | 0.61 | 113 (62%) | 30 (64%) | 0.86                   |   |           |   | 1.4 [1.0-1.7] | 1.4 [1.1-1.8] | 1.2 [1.0-1.5] | 0.0048 | 1.3 [1.0-1.6] | 1.5 [1.2-1.8] | 0.032                   |   |           |   | 84 (38%) | 47 (37%) | 37 (39%) | 0.73 | 64 (36%) | 20 (43%) | 0.68                   |   | 44 (20%) | 28 (22%) | 16 (17%) |   | 35 (20%) | 9 (19%)   |   | 6 (3%) | 4 (3%) | 2 (2%) |   | 4 (2%) | 2 (4%)   |   | 90 (40%) | 49 (38%) | 41 (43%) |   | 74 (42%) | 16 (34%) |   |
## Table 2- Laboratory values and inflammatory markers on admission of the patients admitted to Montefiore Medical Center

| Laboratory values and inflammatory markers on admission | Total patients N = 79 | Survivors N = 51 | Non survivors N = 28 | p-value |
|--------------------------------------------------------|------------------------|------------------|----------------------|---------|
| Hemoglobin, median [IQR] g/dL                          | 12.1 [10.6-13.2]       | 12.2 [10.6-13.3] | 11.8 [11.1-13]       | 0.94    |
| WBC, median [IQR] k/uL                                 | 6.2 [4.4-8.0]          | 5.8 [4.1-7.7]    | 6.4 [5.4-8.1]        | 0.23    |
| WBC count < 4 k/uL                                     | 12 (15%)               | 11 (22%)         | 1 (4%)               |         |
| Lymphocytes, median [IQR] k/uL                          | 0.6 [0.4-0.8]          | 0.6 [0.4-0.8]    | 0.7 [0.4-0.8]        | 0.96    |
| Lymphocyte count < 1 k/uL                              | 67 (85%)               | 42 (82%)         | 25 (89%)             |         |
| Platelets, median [IQR] k/uL                           | 178 [132-240]          | 189 [132-241]    | 162 [118.5-205.5]    | 0.22    |
| Platelets count < 150 k/uL                             | 30 (38%)               | 18 (35%)         | 12 (43%)             |         |
| CD3 cell count, median [IQR] cells/uL                   | 319 [205-552]          | 390 [226.5-574]  | 243 [158-529]        | 0.12    |
| CD3 count < 706 cells/uL                               | 54 (68%)               | 33 (65%)         | 21 (75%)             |         |
| CD4 cell count, median [IQR] cells/uL                   | 147 [88-304]           | 178 [117-305]    | 120 [74-252]         | 0.085   |
| CD4 count < 706 cells/uL                               | 52 (66%)               | 31 (61%)         | 21 (75%)             |         |
| CD8 cell count, median [IQR] cells/uL                   | 126 [83-272]           | 147 [87.5-263]   | 123 [71-272]         | 0.4     |
| CD8 count < 104 cells/uL                               | 22 (28%)               | 13 (26%)         | 9 (32%)              |         |
| C-Reactive Protein, median [IQR] mg/dL                  | 9.9 [4.9-16.2]         | 7.2 [4.6-14.8]   | 11.3 [5.7-18.1]      | 0.25    |
| C-Reactive Protein > 10 mg/dL                          | 38 (48%)               | 23 (45%)         | 15 (54%)             |         |
| Procalcitonin, median [IQR] ng/mL                       | 0.3 [0.1-1.7]          | 0.2 [0.1-1.6]    | 0.4 [0.2-2.9]        | 0.065   |
| Procalcitonin > 0.2 ng/mL                              | 41 (52%)               | 22 (43%)         | 19 (68%)             |         |
| Ferritin, median [IQR] ng/mL                           | 1345 [681-2397]        | 1516 [713-3179]  | 1029 [629-1939]      | 0.16    |
| Ferritin > 900 ng/mL                                   | 50 (63%)               | 35 (69%)         | 15 (54%)             |         |
| D-Dimer, median [IQR] ug/mL                            | 1.7 [0.8-3.3]          | 1.8 [0.7-3.5]    | 1.7 [1.1-2.2]        | 0.99    |
| D-Dimer > 0.5 ug/mL                                    | 66 (84%)               | 42 (82%)         | 24 (86%)             |         |
| D-Dimer > 3 ug/mL                                      | 20 (25%)               | 15 (29%)         | 5 (18%)              |         |
| Interleukine-6, median [IQR] pg/mL                      | 54 [25-154]            | 47 [26-98]       | 101 [22-335]         | 0.036   |
| Interleukine-6 > 60 pg/mL                              | 32 (41%)               | 15 (29%)         | 17 (61%)             |         |
| Lactic Dehydrogenase, median [IQR] U/L                 | 356 [274-414]          | 350 [271-406]    | 364 [286.5-433]      | 0.42    |
| Lactic Dehydrogenase > 1.5 times upper range of normal | 53 (67%)               | 33 (65%)         | 20 (71%)             |         |
| Creatine Kinase, median [IQR] U/L                       | 103 [56-204]           | 91 [55-143]      | 140 [68-362]         | 0.095   |
| Creatine Kinase > 200 U/L                              | 19 (24%)               | 8 (16%)          | 11 (39%)             |         |
| Fibronogen, median [IQR] mg/dL                          | 605.5 [504.5-728.5]    | 606 [511-754]    | 605 [459-666]        | 0.46    |
| Fibrinogen > 500 mg/dL                                 | 49 (62%)               | 33 (65%)         | 16 (57%)             |         |
| Pro-NT Brain Natriuretic Peptide, median [IQR] pg/mL    | 1785 [740-4987]        | 1278 [450-3234]  | 2380 [1152-9342]     | 0.031   |
| Pro-NT Brain Natriuretic Peptide > 900 pg/ml, %        | 43 (54%)               | 24 (47%)         | 29 (68%)             |         |
| Serum creatinine, median [IQR] mg/dL                    | 2.2 [1.5-3.0]          | 1.9 [1.3-3.0]    | 2.3 [1.7-2.9]        | 0.33    |
Table 3: Peak values of laboratory values and inflammatory markers of the patients during hospitalization

| Peak laboratory values and inflammatory markers | Total patients N = 79 | Survivors N = 51 | Non survivors N = 28 | p-value |
|------------------------------------------------|-----------------------|------------------|----------------------|---------|
| Lowest Hemoglobin, median [IQR] g/dL           | 10.2 [8.2-11.9]       | 9.9 [8.2-11.8]   | 10.9 [7.9-11.9]      | 0.19    |
| Lowest White Blood Cell, median [IQR] k/uL     | 4.7 [3.6-6.2]         | 4.6 [3.0-5.9]    | 5.8 [4.1-6.4]        | 0.052   |
| Lowest Lymphocytes, median [IQR] k/uL          | 0.4 [0.3-0.6]         | 0.5 [0.3-0.6]    | 0.3 [0.2-0.4]        | 0.021   |
| Lowest Platelets, median [IQR] k/uL            | 154 [111-214]         | 170 [124-222]    | 135 [102-170]        | 0.045   |
| Highest C-Reactive Protein, median [IQR] mg/dL | 16.2 [10.2-27.8]      | 14.3 [5.9-25.6]  | 22.8 [17.4-31.9]     | 0.0032  |
| Highest Procalcitonin, median [IQR] ng/mL      | 0.6 [0.1-2.7]         | 0.3 [0.1-1.7]    | 1.9 [0.4-3.9]        | 0.006   |
| Highest Ferritin, median [IQR] ng/mL           | 1908 [936-4489]       | 2079 [1057-4489] | 1568 [675.5-5493]    | 0.59    |
| Highest D-Dimer, median [IQR] ug/mL            | 3.5 [1.4-8.7]         | 3.3 [1.0-5.2]    | 4.4 [2.3-16.2]       | 0.06    |
| Highest Interleukine-6, median [IQR] pg/mL     | 64 [32-208]           | 48 [28-98]       | 182 [83-498]         | 0.0004  |
| Highest Lactic Dehydrogenase, median [IQR] U/L | 448 [337-683]         | 389 [303-578]    | 612 [446-868]        | 0.0017  |
| Highest Creatine Kinase, median [IQR] U/L      | 138 [69-318]          | 105.5 [64.5-182.5]| 194 [107-481]        | 0.022   |
Table 4- Clinical outcomes of the hospitalized patients

| Clinical Outcomes                                | Total patients N = 79 | Survivors N = 51 | Non survivors N = 28 | p-value  |
|--------------------------------------------------|-----------------------|------------------|----------------------|----------|
| Intubation                                       | 28 (35%)              | 5 (10%)          | 23 (82%)             | < 0.001  |
| Acute kidney injury requiring renal replacement   | 18 (23%)              | 9 (18%)          | 9 (32%)              | 0.15     |
| therapy                                         |                       |                  |                      |          |
| Bacteremia                                       | 7 (9%)                | 4 (8%)           | 3 (6%)               | 0.67     |
| Urinary tract infection                          | 9 (11%)               | 5 (10%)          | 4 (14%)              | 0.55     |
| Bacterial pneumonia                              | 4 (5%)                | 0 (0%)           | 4 (14%)              | 0.014    |
| Fungal infection                                 | 4 (5%)                | 1 (2%)           | 3 (11%)              | 0.12     |
| Cytomegalovirus viremia                          | 12 (15%)              | 8 (16%)          | 4 (14%)              | 0.87     |
| Deep Venous Thrombosis                           | 10 (13%)              | 6 (12%)          | 4 (14%)              | 0.75     |
| Cerebrovascular accident                         | 3 (4%)                | 1 (2%)           | 2 (7%)               | 0.29     |
Table 5- Therapeutics of patients hospitalized at Montefiore Health System

| Treatment                  | Total patients N = 79 | Survivors N= 51 | Non survivors N = 28 |
|----------------------------|-----------------------|-----------------|-----------------------|
| Anti-metabolite withdrawal | 74 (94%)              | 48 (94%)        | 26 (93%)              |
| CNI withdrawal             | 11 (14%)              | 4 (8%)          | 7 (25%)               |
| Antibiotics                | 65 (82%)              | 38 (75%)        | 27 (96%)              |
| Hydroxychloroquine         | 59 (75%)              | 35 (69%)        | 24 (86%)              |
| Remdesivir*                | 6 (8%)                | 5 (10%)         | 1 (4%)                |
| High dose corticosteroids  | 35 (44%)              | 14 (28%)        | 21 (75%)              |
| Tocilizumab                | 11 (14%)              | 5 (10%)         | 6 (21%)               |
| Sarilumab*                 | 2 (3%)                | 0 (0%)          | 2 (7%)                |
| Leronlimab                 | 6 (8%)                | 3 (6%)          | 3 (11%)               |
| Convalescent plasma        | 7 (9%)                | 3 (6%)          | 4 (14%)               |
| Intravenous Ig             | 1 (1%)                | 0 (0%)          | 1 (4%)                |
| Anakira                    | 1 (1%)                | 0 (0%)          | 1 (4%)                |
| Anticoagulation            | 44 (56%)              | 26 (51%)        | 18 (64%)              |

*Patients enrolled in randomized clinical trial and it is unknown which are arm patients were randomized.
Figure 1 – Study Design

1,475 adult kidney transplant recipients followed at Montefiore Transplant Center

- 132 patients tested positive for COVID-19 with RT-PCR
  - 21 followed as outpatient
  - 111 hospitalized
  - 79 admitted to Montefiore Medical Center
  - 32 admitted to an outside hospital

912 screened for SARS-CoV-2 IgG antibody

- 69 had a prior COVID-19 diagnosis with RT-PCR positive
  - 55 tested POSITIVE (80%)
    - 7 were re-tested and remained POSITIVE
  - 14 tested NEGATIVE (20%)

- 746 tested NEGATIVE

- 97 tested POSITIVE
  - 11 patients were re-tested
    - 9 remained POSITIVE
    - 2 became NEGATIVE

- 4 were re-tested and remained NEGATIVE
Figure 2- Weekly number of kidney transplant patients diagnosed by COVID-19 RT-PCR starting March 16, 2020
|                       | Total patients N = 79 | Survivors N = 51 | Non survivors N = 28 | p-value |
|-----------------------|-----------------------|------------------|-----------------------|---------|
| **Sex**               |                       |                  |                       |         |
| Male, %               | 50 (63%)              | 36 (71%)         | 14 (50%)              | 0.069   |
| Female, %             | 29 (37%)              | 15 (29%)         | 14 (50%)              |         |
| **Age, median [IQR]** | 61 [51-67]            | 61 [48-67]       | 63.5 [56-71.5]        | 0.073   |
| **Race**              |                       |                  |                       |         |
| Hispanic              | 43 (54%)              | 27 (53%)         | 16 (57%)              | 0.26    |
| African American      | 27 (34%)              | 20 (39%)         | 7 (25%)               |         |
| Other                 | 9 (11%)               | 4 (8%)           | 5 (18%)               |         |
| **Type of transplant**|                       |                  |                       |         |
| Deceased donor        | 61 (77%)              | 38 (75%)         | 23 (82%)              | 0.44    |
| Living donor          | 18 (23%)              | 13 (26%)         | 5 (18%)               |         |
| **Time after**        |                       |                  |                       |         |
| **transplantation, median [IQR] months** | 58.2 [25.4-127.6] | 57.7 [27.3-123.7] | 65.2 [16.3-134.1] | 0.22    |
| Transplant < 6 months | 6 (8%)                | 5 (10%)          | 1 (4%)                | 0.32    |
| Transplant < 12 months| 9 (11%)               | 8 (16%)          | 1 (4%)                | 0.22    |
| **Immunosuppressive regimen** |                  |                  |                       |         |
| Calcineurin inhibitors | 74 (71/3) (94%)       | 49 (48/1) (96%)  | 25 (23/2) (89%)       | 0.34    |
| (Tacrolimus/Cylosporin)|                      |                  |                       |         |
| MMF/MPA               | 70 (89%)              | 45 (88%)         | 25 (89%)              | 0.89    |
| Corticosteroid        | 75(95%)               | 50 (98%)         | 25 (89%)              | 0.12    |
| Sirolimus             | 7 (3%)                | 5 (4%)           | 2 (3%)                | 0.28    |
| **Etiology of ESRD**  |                       |                  |                       |         |
| Diabetes mellitus     | 42 (53%)              | 25 (49%)         | 17 (61%)              | 0.66    |
| Hypertension          | 13 (17%)              | 10 (20%)         | 3 (11%)               |         |
| Glomerulonephritis    | 15 (19%)              | 9 (18%)          | 6 (21%)               |         |
| Polycystic kidney disease | 3 (4%)            | 2 (4%)           | 1 (4%)                |         |
| Others                | 6 (8%)                | 5 (10%)          | 1 (4%)                |         |
| **Body Mass Index (kg/m2) median [IQR]** | 28.1 [23.7-32.3] | 26.7 [23.1-31.4] | 30.4 [25.7-34.7] | 0.057   |
| **History of smoking**| 28 (35%)              | 18 (35%)         | 10 (36%)              | 0.97    |
| **Influenza vaccination** | 59 (83%)          | 43 (88%)         | 16 (73%)              | 0.12    |
| **Comorbidities**     |                       |                  |                       |         |
| Condition                                      | Group 1 | Group 2 | Group 3 | p-value  |
|-----------------------------------------------|---------|---------|---------|----------|
| Hypertension                                  | 77 (98%) | 49 (96%) | 28 (100%) | 0.54     |
| Diabetes mellitus                             | 53 (67%) | 32 (63%) | 21 (75%) | 0.27     |
| Heart disease                                 | 15 (19%) | 10 (20%) | 5 (18%)  | 0.85     |
| Lung disease                                  | 9 (11%)  | 4 (8%)   | 5 (18%)  | 0.18     |
| Cancer                                        | 9 (11%)  | 5 (10%)  | 4 (14%)  | 0.55     |
| **Blood type**                                |         |         |         |          |
| A                                             | 28 (36%) | 15 (30%) | 13 (46%) |          |
| B                                             | 16 (21%) | 13 (26%) | 3 (11%)  | 0.19     |
| AB                                            | 3 (4%)   | 1 (2%)   | 2 (7%)   |          |
| O                                             | 31 (40%) | 21 (42%) | 10 (36%) |          |
| **Angiotensin converting enzyme inhibitor or angiotensin receptor blocker prior to admission** | | | | |
| 19 (24%)                                      | 12 (24%) | 7 (25%)  | 0.88     |
| **Statin prior to admission**                 | 49 (62%) | 31 (61%) | 18 (64%) | 0.76     |
| **Baseline creatinine, median [IQR]**         | 1.4 [1.2-2.0] | 1.4 [1.1-2.0] | 1.5 [1.2-2.0] | 0.86     |
| **Symptoms on admission**                     |         |         |         |          |
| Fever                                         | 46 (58%) | 31 (61%) | 15 (54%) | 0.53     |
| Dyspnea                                       | 46 (58%) | 26 (51%) | 20 (71%) | 0.078    |
| Myalgias                                      | 32 (41%) | 17 (33%) | 15 (54%) | 0.08     |
| Cough                                         | 46 (58%) | 31 (61%) | 15 (54%) | 0.53     |
| Diarrhea                                      | 28 (35%) | 18 (35%) | 10 (36%) | 0.97     |
| **Pulse oximetry on admission (%)**           | 95 [92-98] | 96 [94-98] | 93 [89-96.5] | 0.037    |
| **Temperature on admission (F)**              | 99 [98.3-100.5] | 99 [98.4-100.1] | 99.1 [98.3-100.9] | 0.87     |