DR KRISTEN M JOHNSON (Orcid ID : 0000-0002-4105-1811)

DR JULIE J BELFER (Orcid ID : 0000-0002-9189-0752)

Article type : Review of Therapeutics

# Managing COVID-19 in Renal Transplant Recipients: A Review of Recent Literature and Case Supporting Corticosteroid-sparing Immunosuppression

Kristen M. Johnson, Department of Pharmacy Services, Mercy Health Saint Mary's, Grand Rapids, MI, USA

Julie J. Belfer, Department of Pharmacy Services, Mercy Health Saint Mary's, Grand Rapids, MI, USA

Gina R. Peterson, Kidney Transplant Center, Mercy Health Saint Mary's, Grand Rapids, MI, USA

Mark R. Boelkins, Kidney Transplant Center, Mercy Health Saint Mary's, Grand Rapids, MI, USA

Lisa E. Dumkow, Department of Pharmacy Services, Mercy Health Saint Mary's, Grand Rapids, MI, USA

Corresponding Author: Kristen M. Johnson, Department of Pharmacy Services, Mercy Health Saint Mary's, Grand Rapids, MI, USA

kristen.johnson001@mercyhealth.com

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/PHAR.2410

Conflict of interest: The authors declare no conflicts of interest.

Keywords: COVID-19, immunosuppression, SARS-CoV-2, coronavirus, renal transplant, corticosteroid

Abstract: Novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome virus (SARS-CoV-2) has become a global healthcare crisis. The Centers for Disease Control and Prevention (CDC) lists immunocompromised patients, including those requiring immunosuppression following renal transplantation, as high-risk for severe disease from SARS-CoV-2. Treatment for other viral infections in renal transplant recipients often includes a reduction in immunosuppression, however, there are no current guidelines recommending the optimal approach to managing immunosuppression in the patients who are infected with SARS-CoV-2. It is currently recommended to avoid corticosteroids in the treatment of SARS-CoV-2 outside of critically ill patients. Recently published cases describing the inpatient care of COVID-19 in renal transplant recipients differ widely in disease severity, time from transplantation, baseline immunosuppressive therapy, and the modifications made to immunosuppression during COVID-19 treatment. The purpose of this review is to summarize and compare inpatient immunosuppressant management strategies of recently published reports in the renal transplant population infected with SARS-CoV-2 and to discuss the limitations of corticosteroids in managing immunosuppression in this patient population.

## Introduction

Novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome virus (SARS-CoV-2), was first identified in Wuhan, China in December 2019.[1] Since that time the disease has spread globally at an alarming rate, with the World Health Organization declaring the outbreak a pandemic and major threat to international public health in March of 2020. In the United States, the first case of COVID-19 was identified in January 2020; the spread of the virus since that time has been exponential with the number of cases in the U.S surpassing that of all other countries.[2] Person-

to-person spread of SARS-CoV-2 is highly efficient via close contact and respiratory droplets, with an incubation period that can extend from 2 to 14 days. Respiratory symptoms, which can range from mild to critically ill requiring mechanical ventilation, are the most common clinical feature of COVID-19, however, patients who are immunocompromised may present atypically.[3,4]

The Centers for Disease Control and Prevention (CDC) lists immunocompromised patients, including those requiring immunosuppressive therapy following organ transplantation, as high-risk for severe disease from SARS-CoV-2.[5] Unlike some other RNA viruses, such as influenza or RSV, no prophylactic agents, treatments, or vaccinations are approved for SARS-CoV-2.[6] At this time, supportive care is paramount to combating this virus in solid organ transplant recipients. Very little data are currently available regarding the optimal medical management of renal transplant patients testing positive for SARS-CoV-2, including strategies for reducing or modifying immunosuppression.[4,7-17] Corticosteroids are a cornerstone of many immunosuppressive regimens, however, their use in SARS-CoV-2 is controversial.[18-22] The purpose of this review is to summarize and compare inpatient immunosuppressant management strategies of recently published reports in the renal transplant population infected with SARS-CoV-2 and discuss the limitations of corticosteroids in managing immunosuppression.

**Methods**

A literature review was performed using PubMed and Science Direct to identify relevant English-language articles published through April 15, 2020. Search terms included *coronavirus*, *severe acute respiratory syndrome coronavirus 2*, *SARS-CoV-2*, *SARS-CoV*, *COVID-19, COVID, renal transplantation,* and *kidney transplantation.* The search resulted in 12 total articles reporting on patients who received inpatient treatment for SARS-CoV-2. Due to the lack of randomized controlled trials, the authors included case reports and case series. The authors independently reviewed the titles and abstracts for inclusion.

**Review of Published Literature In Renal Transplant Recipients**

While no controlled trials currently exist, there are currently 40 published cases demonstrating strategies for inpatient management of SARS-CoV-2 in renal transplant recipients (Table 1). The majority of patients were male, deceased-donor recipients, with an average age of 55 years and receiving maintenance immunosuppression that included tacrolimus with mycophenolate and prednisone. Recipients described were between 1 month and 22 years post-transplant with the majority of patients presenting with severe respiratory symptoms requiring oxygen. Immunosuppressant management in 30 cases consisted of complete cessation of calcineurin inhibitor and antiproliferative therapy with reliance on corticosteroid monotherapy, typically with IV methylprednisolone.[4,7-17] Only three patients were managed without making any change in baseline immunosuppressive regimen and one of these patients was receiving a steroid-sparing regimen at baseline. Of the three cases, none progressed to mechanical ventilation and all had a shorter duration of symptoms than average, lasting approximately two weeks or less.[7,10] Only one other case reported a steroid-sparing regimen at baseline; this patient's immunosuppression was managed with cessation of antiproliferative therapy and dose-reduction in tacrolimus, however, methylprednisolone 40 mg daily was also added for the duration of hospitalization. The patient fully recovered after 61 days of reported symptoms.[13]

Investigational agents targeting SARS-CoV-2 were administered to 34 of 40 cases, with 12 different strategies trialed among patients. Additionally, broad-spectrum antibiotic therapy was administered to 34 patients. The average duration of symptoms from those who reported was 21 days, with 18%

of patients progressing to respiratory failure requiring mechanical ventilation.[4,7-17] Eight patients who had presented with severe or critical oxygen needs had expired by the time of case publication; all eight patients had immunosuppressant therapy converted to corticosteroid monotherapy while hospitalized.[8,11,15,16]

## Discussion

Outside of supportive care, the optimal management of SARS-CoV-2 has not yet been established. This is especially true in solid organ transplant recipients where adjustments to immunosuppressive medications must be considered while balancing the potential for acute rejection and co-infection with bacterial or opportunistic pathogens. We have summarized recently published cases describing different immunosuppressant management strategies for renal transplant recipients with SARS-CoV-2. While there are many differences in the details presented in these cases, the majority of patients received corticosteroid monotherapy for maintaining immunosuppression while all but two of the remaining cases also received a corticosteroid in combination with other agents.

### *A Case Supporting Corticosteroid-sparing Immunosuppression Modifications*

We present the case and outcomes of a renal transplant recipient with SAR-CoV-2 treated within our hospital whose immunosuppressive therapy was managed with only modest reduction in calcineurin inhibitor target trough concentration and antiproliferative dose reduction. A 57 year-old African American male with a history of a deceased donor kidney transplant (DDKT) 8-months prior, contacted the renal transplant team with complaints of poor oral intake, reported fever of 38.2°C, abdominal bloating and back pain for the past 3 days, therefore, he was advised to go to the emergency department. He presented the following day with complaints of low-grade fever, chills,

decreased oral intake and ongoing abdominal discomfort. In accordance with CDC recommendations and state and local health officials, the patient was considered low risk and did not meet criteria to be a person under investigation or for COVID-19 testing at that time. During his visit an abdominal x-ray showed no acute abdominal findings and chest x-ray showed findings of congestive heart failure or positive fluid balance and left perihilar and basilar airspace opacity questionably due to pulmonary edema or superimposed pneumonia. Physical exam revealed body temperature of 37.2°C, blood pressure of 101/53 mmg/Hg, pulse of 79 beats per minute, respiratory rate of 18 breaths per minute and oxygen saturation of 93% on room air. His serum creatinine (Scr) had increased to 3.2 mg/dL from 2.0 mg/dL six days prior and white blood cell (WBC) count was 1.5 x $10^3$/µL with absolute neutrophil count (ANC) of 0.7 x $10^3$/µL. The patient improved with supportive care and was discharged with recommendations to follow-up with the renal transplant office.

On day 8 of illness, the renal transplant team was contacted again with reported ongoing concerns of poor oral intake, the patient presented to the clinic the same day for further evaluation. Symptoms included general malaise, fatigue, chills, myalgias, anorexia with poor oral intake, dyspnea while lying on the left side, diarrhea, abdominal bloating and decreased urine output. Upon arrival, the patient's physical exam revealed a blood pressure of 84/52 mmHg and pulse of 60 beats per minute, dry mucous membranes, erythematous injected conjunctiva, bilateral pulmonary crackles and poor capillary refill. Significant laboratory values included a further elevated Scr, 3.4 mg/dL, and continued neutropenia, ANC 1.2 x $10^3$/µL, and leukopenia, WBC 2.1 x $10^3$/µL. Following the results of a chest CT without contrast showing patchy ground glass opacities throughout both lungs, the patient was directly admitted to the hospital with differential diagnosis including dehydration, tacrolimus toxicity, renal transplant rejection, cytomegalovirus (CMV), COVID-19, influenza, and community acquired pneumonia.

End stage renal disease attributed to diabetic nephropathy and prior nephrotic syndrome led to DDKT (kidney donor profile index (KDPI) 66%, recipient calculated panel reactive antibodies (cPRA) 0%, estimated post transplant survival (EPTS) score 79%, cytomegalovirus donor positive/recipient negative). In the three months prior to admission, BK virus PCR and CMV PCR were negative, and Luminex was negative for donor specific antibodies. The patient had previously completed six months of CMV prophylaxis with valganciclovir. Immunosuppression at the time of presentation included tacrolimus extended-release (Envarsus XR®) 7 mg daily boosted with ketoconazole 100 mg daily and mycophenolic acid (MPA) 540 mg BID.

Upon hospitalization, the patient's immunosuppression regimen was continued with the exception of MPA being reduced to 360 mg BID. Cefepime and azithromycin were initiated and the infectious disease service was consulted. COVID-19 (polymerase chain reaction (PCR) test performed by NxGen MDx Lab), respiratory viral panel, blood cultures, CMV PCR, interleukin-6 level, and tacrolimus levels were obtained.

On day 9 of illness (hospitalization day 2), the patient required 3 liters of oxygen via nasal cannula, was afebrile and continued to deny cough or other respiratory symptoms. Infectious disease obtained a sputum culture, legionella urinary antigen, and invasive fungal workup (fungal beta-d-glucan, aspergillus galactomannan antigen, histoplasma antigen, fungal antibodies). Serum creatinine remained elevated at 3.0 mg/dL and sodium bicarbonate infusion was maintained for metabolic acidosis.

On day 10 of illness (hospital day 3), COVID-19 PCR was confirmed positive and infectious disease initiated hydroxychloroquine 400 mg twice daily for one day followed by 200 mg daily for 4 days.

Baseline QTc was obtained (436 ms) due to concern for QTc prolongation with the combination of hydroxychloroquine, tacrolimus and azithromycin. Patient continued to be neutropenic. MPA was further reduced to 360 mg AM and 180mg PM. Tacrolimus dose was maintained as levels were therapeutic (Table 1). Serum creatinine and metabolic acidosis improved allowing for transition to oral sodium bicarbonate.

Bacterial, CMV and fungal work-up were non-significant, the patient completed a seven-day course of cefepime and azithromycin. IL-6 level was 5 pg/mL, indicating that the patient was unlikely to benefit from administration of an IL-6 inhibitor. Despite the patient reporting feeling improved, he remained on 3-4 liters of oxygen. On day 17 of illness (hospital day 10), pulmonology was consulted due to the ongoing oxygen needs and recommended the patient be discharged home on oxygen allowing time for recovery from the acute lung injury. On day 19 of illness, MPA was further reduced to 180 mg BID due to continued low lymphocyte count and tacrolimus was reduced to 5 mg daily due to a supratherapeutic level. The patient was readied for discharge on day 23 of illness with a plan for sub-acute rehab to continue recovery on supplemental oxygen (4 liters).

*Rationale for Corticosteroid-sparing Regimens*

We have described the case of a renal transplant recipient who was successfully treated for COVID-19 with supportive care along with steroid-sparing immunosuppression regimen changes which included dose-reduced antiproliferative therapy and modest decrease in tacrolimus target trough level. Different from most of the previously described cases, our patient was not receiving a corticosteroid-containing maintenance immunosuppressive regimen prior to admission, which is typical for the majority of the patients who are transplanted and managed within our institution. There are several reasons that we chose to make only modest maintenance immunosuppressant modifications for our patient and to not rely on corticosteroid therapy to maintain immunosuppression. First, the data regarding outcomes following corticosteroid

administration in COVID-19 are mixed. The World Health Organization, CDC, Infectious Diseases Society of America, and Society of Critical Care Medicine currently recommend against the routine use of corticosteroids for managing respiratory distress in patients with SARS-CoV-2 unless they are indicated for another reason (ex. asthma), the patient is experiencing refractory septic shock, or for acute respiratory distress syndrome (ARDS).[18-23] It is also thought that corticosteroids may inhibit immune response, reduce pathogen clearance, and increase viral shedding if administered early during the clinical course of SARS-CoV-2 or with mild disease.[22-24] Finally, currently published cases of SARS-CoV-2 in renal transplant recipients have demonstrated variable results in progression of respiratory disease and survival when substituting higher doses of corticosteroids for complete cessation of maintenance calcineurin inhibitor and antiproliferative therapy.[4,7-17] Huang and colleagues noted that out of two transplant cases managed with this strategy, one renal transplant and the other a bone marrow transplant recipient, that both patients developed nosocomial bacterial infections. The authors cited that the use of corticosteroids to maintain immunosuppression in these patients likely increased the risk for these infections and warrants caution with the use of corticosteroids in maintaining immunosuppression for transplant patients with SARS-CoV-2.[8] Because of these risks coupled with our patient's 0% cPRA prior to transplant indicating that the patient was not highly sensitized to HLA antigens, we felt that he could be managed safely with modest reductions in immunosuppression without substituting corticosteroids.

As with a significant portion of patients presenting with SARS-CoV-2, our patient's lymphocyte count at presentation was below normal range.[25,26] Our patient's neutrophils were also below normal range at the time of admission, which is uncommon in most cases, however, likely the results of his baseline immunosuppressive regimen being steroid-sparing.[25] Due to the potential risks of corticosteroids and because our patient presented with only moderate respiratory symptoms we chose to focus on reducing antiproliferative therapy as our main strategy for reducing immunosuppression as well as maintaining pre-hospitalization tacrolimus dose and making a modest reduction in goal trough from 6-8 ng/mL to 4-6 ng/mL. Following these changes, the patient's

neutrophil count gradually increased, however, his lymphocyte count remained low. Further reduction in antiproliferative therapy was made in order to try to target lymphocyte improvement. Ultimately, the patient experienced a long clinical course, similar to many of the previously published cases in renal transplant recipients, and was able to be successfully readied for discharge and rehabilitated with continued supplemental oxygen.

*Limitations and Need for Future Study*

There are several limitations to making comparisons, generalizations, or drawing conclusions from the currently reported cases of renal transplant patients treated for SARS-CoV-2. The currently published cases present a large variation in transplant and clinical characteristics as well as SARS-CoV-2 and immunosuppressant management.[4,7-17] Time from transplantation differed greatly between patients which could indicate that immunosuppressive intensity at baseline also varied widely amongst the different cases. Unfortunately, most of the currently published cases do not describe medication doses or target tacrolimus trough concentrations in detail to allow for comparison. Additionally, very limited data regarding patient transplant matching characteristics and risk factors for poor prognosis have been presented, making it difficult to assess baseline immunosuppressive therapy, appropriateness of modifications, and risk for poor outcomes. Limited to no detail is given in some cases for important clinical variables such as oxygen requirements, which also makes comparing clinical courses difficult. Finally, the majority of patients received at least one investigational agent targeting SARS-CoV-2 as well as different empiric antibiotic therapies targeting a wide range of pathogens, including our patient who received a 5-day course of hydroxychloroquine plus 7-days of antibacterial therapy. While the efficacy of these investigational agents is unknown and there is thought to be low likelihood of bacterial co-infection, these treatments may confound generalizability of the data.[27] Furthermore, some investigational agents may have influenced the changes made to immunosuppression. For example, in some cases where lopinavir/ritonavir was administered, the calcineurin inhibitor may have been purposefully targeted for substitution due to CYP3A4 and p-glycoprotein drug-drug interactions.[8,11]

## Conclusion

It is difficult to compare and draw conclusions regarding optimal immunosuppressant management in renal transplant recipients treated for SARS-CoV-2 from the limited data presented in currently published cases along with significant confounding variables. The majority of cases have relied on corticosteroid monotherapy for maintaining immunosuppression while treating SARS-CoV-2 in renal transplant recipients; however, the routine use of corticosteroids to treat patients with SARS-CoV-2 is not recommended. Renal transplant recipients with moderate oxygen requirements may be able to be successfully managed with steroid-sparing modifications to immunosuppression including modest reduction calcineurin inhibitor trough concentrations and antiproliferative dosing. Further data are needed to determine optimal immunosuppressant management in this patient population, including if a corticosteroid-sparing strategy is viable in patients who present with severe clinical disease such as those requiring ventilator support or for those who are on steroid-containing regimens at baseline.

**References**


1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. JAMA. Published online February 24, 2020. doi:10.1001/jama.2020.2648
2. Centers for Disease Control and Prevention. First travel-related case of 2019 novel coronavirus detected in the United States. Published on January 21, 2020. https://www.cdc.gov/media/releases/2020/p0121-novel-coronavirus-travel-case.html)
3. Centers of Disease Control and Prevention. Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings. Updated April 1, 2020. https://www.cdc.gov/coronavirus/2019-ncov/infection-control/controlrecommendations.html
4. Guillen E, Pineiro GJ, Revuelta I, et al. Case report of COVID-19 in a kidney transplant recipient: does immunosuppression alter the clinical presentation? Am J Transplant. Published online March 20, 2020. https://doi.org/10.1111/ajt.15874
5. Centers for Disease Control and Prevention. Groups at higher risk for severe illness. Published April 2, 2020. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/groups-at-higher-risk.html
6. Manuel O, Estabrook M. RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13511. doi: 10.1111/ctr.13511
7. Zhang H, Chen Y, Yuan Q, et al. Identification of kidney transplant recipients with Coronavirus Disease 2019. Eur Urol. Published online April 2, 2020. doi:10.1016/j.eururo.2020.03.030
8. Huang J, Lin H, Wu Y, et al. COVID-19 in post-transplantation patients - report of two cases. Am J Transplant. 2020. Published online April 3, 2020. doi:10.1111/ajt.15896
9. Chen S, Yin Q, Shi H, et al. A familial cluster, including a kidney transplant recipient, of Coronavirus Disease 2019 (COVID-19) in Wuhan, China. Am J Transplant. Published online April 3, 2020. doi:10.1111/ajt.15903

10. Seminari E, Colaneri M, Sambo M, et al. SARS CoV2 infection in a renal transplanted patient. A case report. Am J Transplant. Published online April 3, 2020. doi:10.1111/ajt.15902
11. Gandolfini I, Delsante M, Fiaccadori E, et al. COVID-19 in kidney transplant recipients. Am J Transplant. Published online March 31, 2020. doi:10.1111/ajt.15891
12. Zhu L, Xu X, Ma K, et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. Am J Transplant. Published online March 17, 2020. doi:10.1111/ajt.15869
13. Zhong Z, Zhang Q, Xia H, et al. Clinical characteristics and immunosuppressants management of coronavirus disease 2019 in solid organ transplant recipients. Am J Transplant. Published online April 13, 2020. doi:10.1111/ajt.15928
14. Marx D, Moulin B, Fafi-Kremer S, et al. First case of COVID-19 in a kidney transplant recipient treated with belatacept. Am J Transplant. Published online April 13, 2020. doi:10.1111/ajt.15919
15. Banerjee D, Popoola J, Shah S, et al. COVID-19 infection in kidney transplant recipients. Kidney Int. Published online April 9, 2020. doi.org/10.1016/j.kint.2020.03.018
16. Alberici F, Delbarba E, Manenti C, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. Kidney Int. Published online April 9, 2020. doi.org/10.1016/j.kint.2020.04.002
17. Ning L, Liu L, Li W, et al. Novel coronavirus (SARS-CoV-2) infection in a renal transplant recipient: case report. Am J Transplant. Published online April 10, 2020. doi:10.1111/ajt.15897
18. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance. Published March 13, 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected

19. Centers for Disease Control. Healthcare professionals: Frequently asked questions and answers. Published March 30, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html
20. Alhazzani W, Møller MH, Arabi YM, et al. Surviving sepsis campaign: Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Crit Care Med. Published online March 27, 2020. doi:10.1097/CCM.0000000000004363
21. Bhimraj A, Morgan R, Hirsch Shumaker A, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. Published online April 11, 2020. https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
22. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. Published online March 13, 2020. doi:10.1001/jamainternmed.2020.0994
23. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-CoV lung injury. Lancet. 2020;395(10223):473-5. doi:10.1016/S0140-6736(20)30317-2
24. Farkas J. Internet Book of Critical Care. From EMCrit Project website. Accessed 2020 Apr 7. https://emcrit.org/ibcc/COVID19/
25. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early Clinical and CT manifestations of Coronavirus Disease 2019 (COVID-19) pneumonia. Am J Roentgenol. Published online March 17, 2020. doi:10.2214/AJR.20.22961
26. Xu YH, Dong JH, An WM, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. J Infect. 2020;80(4):394-400. doi:10.1016/j.jinf.2020.02.017
27. Kim D, Quinn J, Pinsky B, et al. Rates of Co-infection Between SARS-CoV-2 and Other Respiratory Pathogens. JAMA. Published online April 15, 2020. doi:10.1001/jama.2020.6266

| | Age (yr) | Sex | Time from RTx (yr) | Type of RTx | Baseline IS | Change to IS | COVID severity | COVID Treatment | Antibacterial Treatment | Time from sx onset to hosp (days) | Time from sx onset to recovery (days) | Clinical outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alberici F, et al[16] | 70 | F | 17 | unknown | CNI/mTORi | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Recovery |
| | 47 | F | 9 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | critical | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 71 | M | 13 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Expired |
| | 57 | M | 2 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | critical | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Expired |
| | 51 | M | 23 | unknown | MMF, CNI | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Recovery |
| | 46 | M | 2 | unknown | MMF, CNI | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Recovery |
| | 59 | M | 5 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | critical | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Expired |
| | 70 | F | 6 | unknown | CNI, pred | Cessation of all, MP 16mg QD | critical | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Expired |
| | 60 | M | 8 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | mild | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 73 | M | 6 | unknown | MMF, CNI, pred | Cessation of all, MP 16 mgQD | severe | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 59 | M | 10 | unknown | MMF, pred | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 63 | M | 15 | unknown | MMF, CNI | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Expired |
| | 49 | M | 2 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir, tocilizumab | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 60 | F | 2 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | severe | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 57 | M | 10 | unknown | MMF, CNI | Cessation of all, MP 16mg QD | mild | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 54 | M | 17 | unknown | CNI, pred | Cessation of all, MP 16mg QD | severe | HCQ, darunavir + ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 60 | M | 13 | unknown | CNI | Cessation, MP 16mg QD | mild | HCQ, lopinavir/ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 50 | M | 9 | unknown | MMF, CNI, pred | Cessation of all, MP 16mg QD | mild | HCQ, darunavir + ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 69 | M | 22 | unknown | CNI, pred | Cessation of all, MP 16mg QD | mild | HCQ, darunavir + ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| | 44 | M | 14 | unknown | CNI, mTORi | Cessation of all, MP 16mg QD | mild | HCQ, darunavir + ritonavir | Yes, not specified | unknown | unknown | Inpatient at time of publication |
| Ning L, et al[17] | 29 | M | 1 | LR | MMF, cyclosporine, MP | None | mild | Lopinavir/ritonavir + IVIG | Moxifloxacin | 2 | 15 | Recovery |
| Guillen E, et al[4] | 50 | M | 4 | DD | Tac, everolimus, pred | Cessation of Tac and everolimus | critical | Lopinavir/ritonavir + HCQ + Interferon beta | Ceftaroline and Meropenem | 6 | > 18 | Remained intubated at time of publication submission |
| Zhu L, et al[12] | 52 | M | 12 | LR | Tac, MMF, pred | Cessation of Tac & MMF | mild | Interferon alfa + IVIG | Biapenem | 7 | 21 days | Recovery |
| Chen S, et al[9] | 49 | M | 6 | DD | Tac, MMF, pred | Cessation of Tac & MFF, Pred changed to MP 20-40 mg daily followed by taper | moderate | Umifenovir + ribavirin + IVIG | Moxifloxacin | 15 | 22 days | Recovery |
| Huang J, et al[8] | 58 | M | 12 | unknown | MMF, pred | Cessation of MMF & Pred; MP 80 mg daily | severe | Lopinavir/ritonavir | No | 4 | 40 days | Expired |
| Zhang H, et al[7] | 38 | M | 0.25 | DD | Tac, MMF, steroid | Cessation of MMF and reduced tac | unknown | Oseltamivir or arbidol | No | 15 | 17 days | Recovery |
| | 64 | M | 3 | DD | MMF, rapamycin, steroid | Cessation of MMF, discontinuation of steroids following MP burst for suspected rejection | unknown | Oseltamivir or arbidol + IVIG | Cefixime | 4 | 32 days | Recovery requiring supplemental oxygen - remained hospitalized at time of publication |
| | 37 | F | .42 | DD | Tac, MMF, steroid | Cessation of MMF, tacro held and restarted at reduced dose | unknown | Oseltamivir or arbidol + IVIG | Cefixime | 1 | 12 days | Recovery - remained hospitalized at time of publication |
| | 47 | M | 1 | DD | Tac, MMF, | Cessation of all | unknown | Oseltamivir or arbidol | No | 4 | 19 | Recovery - remained |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | steroid | | | | | | | hospitalized at time of publication |
| | 38 | M | 2 | DD | Tac, MMF, steroid | None | unknown | Oseltamivir or arbidol | No | 8 | 8 | Recovery |
| Gandolfini I, et al[11] | 75 | M | 10 | DD | Tac, MMF, steroid | Cessation of tac and MMF | severe | HCQ + lopinavir/ ritonavir | Yes | 3 | 8 | Expired |
| | 52 | F | 0.67 | DD | Tac, MMF, steroid | Cessation of tac and MMF | severe | HCQ + darunavir/ cobicistat | Yes | 1 | 9 | Recovery requiring supplemental oxygen at time of publication |
| Marx D, et al[14] | 58 | M | 2 | Unknown | Belatacept, MMF, pred | Hold of next scheduled belatacept, cessation of MMF low-dose,CSA started prior to hospital discharge | mild | None | Yes, not specified | 6 | 24 | Recovery |
| Banerjee D, et al[15] | 67 | F | 1 | DD | Tac, MMF, pred | Cessation of MMF | critical | none | Yes, not specified | unknown | 12 | Expired |
| | 54 | F | 0.25 | DD | Tac, MMF, pred | Cessation of tac and MMF | critical | Oseltamivir | Yes, not specified | unknown | unknown | Still intubated at time of publication |
| | 65 | M | 1 | DD | Tac, MMF, pred | Cessation of MMF | moderate | unknown | unknown | unknown | unknown | Requiring supplemental oxygen - remained hospitalized at time of publication |
| | 69 | F | 0.08 | DD | Tac, MMF, pred | Cessation of MMF | moderate | none | Doxycycline, piperacillin-tazobactam | unknown | unknown | Required supplemental oxygen - remained hospitalized at time of publication |
| | 45 | M | 3 | unknown | Tac, azathioprine, pred | Cessation of azathioprine, reduced tac, increase pred | moderate | unknown | unknown | unknown | unknown | Requiring supplemental oxygen - remained hospitalized at time of publication |
| Seminari E, et al[10] | 50 | M | 4 | unknown | Tac, MMF | None | mild | None | Ceftriaxone | 9 | 13 days | Recovery |
| Zhong Z, et al[13] | 48 | M | 17 | LR | Tac, MMF | Cessation of MMF, lower trough concentration of tac, MP 40mg daily | unknown | Oseltamivir, abidol, interferon alpha, IVIG | Moxifloxacin | 10 | 61 | Recovery |
| Johnson K, et al** | 57 | M | 0.67 | DD | Tac, MMF | Reduced dose MMF and lower trough concentration of tac | moderate | HCQ | Cefepime and azithromycin | 8 | 23 | Recovery requiring supplemental oxygen at discharge |

**COVID severity: mild – room air, moderate – supplemental oxygen, severe – non-invasive ventilation, critical – mechanical ventilation**

**Abbreviations: IS – immunosuppression, DD – deceased donor, LR – living related, Tac – tacrolimus, MMF – mycophenolate, MP – methylprednisolone IV, HCQ – hydroxychloroquine, IVIG – intravenous immunoglobulin, CNI - calcineurin inhibitors, mTORi - mTOR inhibitors, ** - case within this publication**

Table 1. Published cases on COVID-19 in hospitalized renal transplant recipients

| Day of Illness | Scr (mg/dL) | WBC ($10^3$/µL) | Lymphocytes ($10^3$/µL) | ANC ($10^3$/µL) | QTC (ms) | Oxygen (L) | Oxygen sat (%) | Tacro Level (ng/mL) |
|---|---|---|---|---|---|---|---|---|
| **4** | 3.2 | 1.5 | 0.3 | | | | | |
| **8** | 3.4 | 2.1 | | 1.2 | 423 | 4 | 96 | |
| **9** | 3 | 2.2 | 0.3 | 1.4 | | 4 | 91-96 | 6.1 |
| **10** | 2.4 | 2.2 | 0.3 | 1.4 | 407 | 3 | 91 | 5 |
| **11** | 2.1 | 2.2 | 0.2 | 1.4 | 436 | 2 | 92-94 | 5.5 |
| **12** | 1.8 | | 0.3 | | 429 | 3 | 91-93 | 5.3 |
| **13** | 1.7 | 2.7 | 0.2 | 2.0 | 439 | 2 | 93-95 | |
| **14** | 1.8 | 3.0 | 0.3 | 2.3 | 424 | 3 | 91-92 | |
| **15** | 1.9 | 4.6 | 0.4 | 3.6 | 438 | 4 | 85-91 | 5.3 |
| **16** | 2.0 | 4.6 | 0.4 | 3.5 | 443 | 3 | 93-99 | |
| **17** | 1.9 | 5.7 | 0.4 | 4.3 | | 5 | 90-92 | 7.6 |
| **18** | 1.9 | 7.6 | 0.4 | 5.9 | | 5 | 87-96 | |
| **19** | 1.9 | 6.9 | 0.3 | 5.3 | | 4 | 90-98 | 4.4 |
| **20** | 1.7 | 6.4 | 0.8 | 5.1 | | 4 | 90-98 | |
| **21** | 1.8 | 7.2 | 0.1 | 5.8 | | 5 | 82-100 | |
| **22** | 1.8 | 8.1 | 0.5 | 6..3 | 427 | 5 | 87-96 | 7.4 |

Table 2. Pertinent laboratory values over course of SARS-CoV-2 illness in a renal transplant recipient

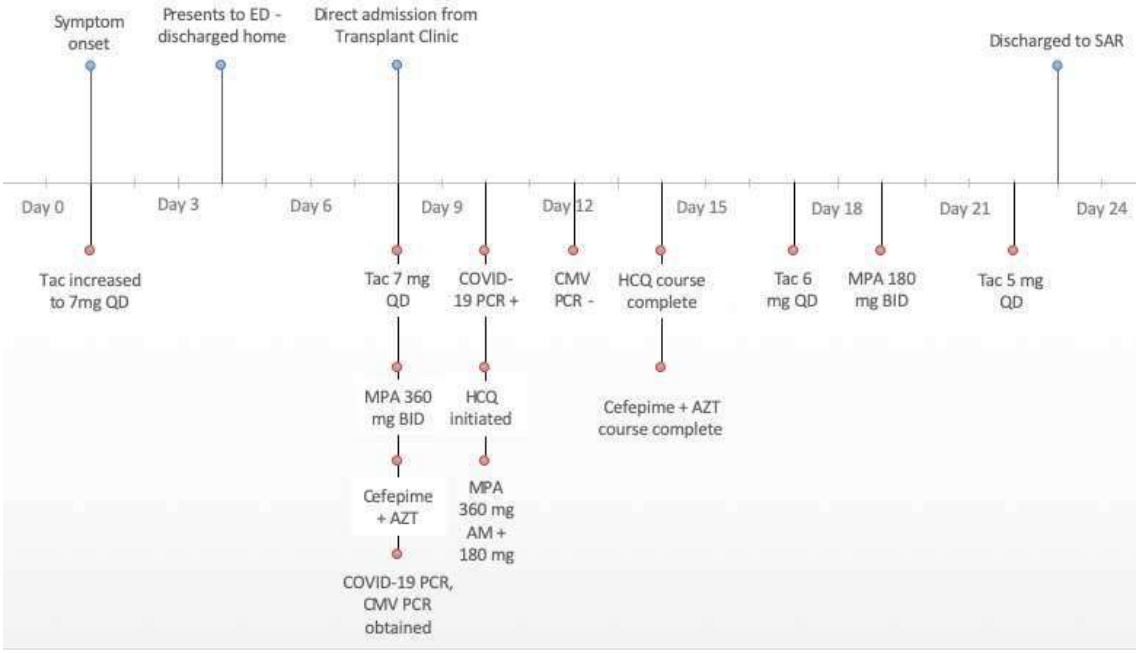


Figure 1. Course of SARS-CoV-2 illness in a renal transplant recipient. Tac - tacrolimus, MPA - mycophenolic acid, AZT - azithromycin, CMV - cytomegalovirus, HCQ – hydroxychloroquine, SAR - subacute rehabilitation