

DR MONICA FUNG (Orcid ID : 0000-0002-1725-5259)

DR TIMOTHY HENRICH (Orcid ID : 0000-0002-6684-0622)

Article type : Case Report

Title: Clinical Outcomes and Serologic Response in Solid Organ Transplant Recipients with COVID-19: A Case Series from the United States

Authors:

Monica Fung, MD, MPH,¹ Charles Y. Chiu, MD, PhD,^{1,2,3} Catherine DeVoe, MD,¹ Sarah B. Doernberg, MD, MAS,¹ Brian S. Schwartz, MD,¹ Charles Langelier, MD, PhD,^{1,4} Timothy J. Henrich, MD,^{1,5} Deborah Yokoe, MD,¹ John Davis, MD, PhD,¹ Steven R. Hays, MD,⁶ Sindhu Chandran, MD,⁷ Jasleen Kukreja, MD, MPH,⁸ Dianna Ng, MD,² John Prostko, MS,⁹ Russell Taylor, BS,⁹ Kevin Reyes, BS,² Emma Bainbridge, MD,¹ Allison Bond, MD,¹ Peter Chin-Hong, MD,¹ Jennifer M. Babik, MD, PhD¹

ORCID: Monica Fung (https://orcid.org/0000-0002-1725-5259)

Affiliations:

¹ Division of Infectious Disease, Department of Medicine, University of California San Francisco, San Francisco, USA

- ²Department of Laboratory Medicine, University of California, San Francisco, California, USA
- ³ UCSF-Abbott Viral Diagnostics and Discovery Center, San Francisco, California, USA
- ⁴ Chan Zuckerberg Biohub, San Francisco, USA
- ⁵ Division of Experimental Medicine, University of California San Francisco, San Francisco, U.S.A.

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 <u>Version of Record</u>. Please cite this article as <u>doi:</u> 10.1111/AJT.16079

⁶ Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, Department of Medicine, University of California San Francisco, San Francisco, USA

⁷ Division of Nephrology, Department of Medicine, University of California San Francisco, San Francisco, USA

⁸ Division of Adult Cardiothoracic Surgery, Department of Surgery, University of California San Francisco, USA

⁹ Abbott Laboratories, Inc., Abbott Park, Illinois, USA

Corresponding author:

Monica Fung monica.fung@ucsf.edu

Abbreviations:

Accepte

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2 COVID-19: Coronavirus disease 2019 SOT: solid organ transplant

ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic caused by SARS coronavirus 2 (SARS-CoV-2) has caused significant morbidity and mortality for patients and stressed healthcare systems worldwide. The clinical features, disease course, and serologic response of COVID-19 among immunosuppressed patients such as solid organ transplant (SOT) recipients, who are at presumed risk for more severe disease, are not well characterized. We describe our institutional experience with COVID-19 among ten SOT patients, including the clinical presentation, treatment modalities, and outcomes of seven renal transplant recipients, one liver transplant recipient, one heart transplant recipient, and one lung transplant recipient. In addition, we report the serologic response in SOT recipients, documenting a positive IgG response in all seven hospitalized patients. We also review the existing literature on COVID-19 in SOT recipients to consolidate the current knowledge on COVID-19 in the SOT population for the transplant community.

INTRODUCTION

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a global pandemic with over 3 million reported cases and over 200,000 deaths.^{1,2} Clinical coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 varies from asymptomatic infection to critical illness with acute respiratory distress syndrome.^{3,4} Clinical manifestations include fever, fatigue, myalgias, dry cough, dyspnea, anosmia, and dysgeusia.^{5,6}

Along with comorbidities such as hypertension, diabetes, cardiovascular disease, and chronic lung or kidney disease, malignancy is an identified risk factor for severe COVID-19 disease.^{4,7,8} However, the clinical presentation and disease course among other immunocompromised patients, including solid organ transplant (SOT) recipients, are not well characterized. Although SOT recipients with other respiratory virus infections often exhibit severe lower respiratory tract infection,⁹ the association between COVID-19 and intense cytokine release¹⁰ raises the possibility that immunosuppression may actually temper the exuberant inflammatory response in severe disease. Furthermore, despite interest in using SARS-CoV-2 serology to improve diagnosis and predict immunity, it is unknown whether SOT recipients will mount an antibody response against SARS-CoV-2.

This study aims to build our understanding of COVID-19 disease in the SOT population. We present the clinical features of COVID-19 in ten SOT recipients at our institution and describe the SARS-CoV2 serologic response in the seven hospitalized SOT recipients.

MATERIALS AND METHODS

Study Subjects and Setting

Adult SOT recipients (age ≥18 years) cared for at the University of California San Francisco (UCSF) diagnosed with COVID-19 by RNA testing were identified via comprehensive standard clinical reporting to the UCSF SOT Program from March 9, 2020 to April 28, 2020. This study was approved under UCSF IRB protocols #20-30629 and #10-02598. Data on demographics, medical history, clinical results, treatment, and outcomes were extracted from the electronic medical record.

During the study period, our institutional treatment approach was to enroll patients with COVID-19 lower respiratory tract infection into clinical trials, if possible. The main trial has been the National Institute of Allergy and Infectious Diseases Phase 2 adaptive, randomized, double-blind, placebocontrolled trial of the investigational antiviral drug remdesivir (NCT04280705). Patients not qualifying for the study with moderate-to-severe hypoxemia were considered for either compassionate use remdesivir, hydroxychloroquine, or convalescent plasma. All admitted COVID-19 patients were provided aggressive supportive care.

Laboratory testing

COVID-19 RNA testing of nasopharyngeal and pooled nasopharyngeal/oropharyngeal swab samples was performed using a real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) assay based on a U.S. CDC assay approved by FDA Emergency Use Authorization (EUA).¹¹

SARS-CoV-2 IgG serology was performed using an Abbott chemiluminescent microparticle immunoassay detecting IgG antibodies to the nucleocapsid protein of SARS-CoV-2 approved under FDA EUA¹² where a chemiluminescent reaction measured as relative light units is used to calculate an index value. At a predefined index value threshold of 1.4 for positivity, this assay performs with an analytical specificity of 99.5%. Compared to SARS-CoV-2 PCR, the assay has a positive percent

agreement of 91.2% and 100.0% at >7 days and ≥14 days from symptom onset, respectively and a negative percent agreement of 99.6%. Results of serologic testing were not reported clinically. Other laboratory and microbiology testing were conducted as part of standard medical care at the discretion of the clinical team.

CASE SERIES

We identified ten SOT recipients at our institution with COVID-19 infection (Table 1).

Demographics, Transplant Details, Co-morbidities

The median age was 56.5 years (range 42-80 years) and six were men. Three patients were African-American, two were Hispanic/Latino, two were Asian, one was Native Hawaiian/Pacific Islander, and one was white. There were seven kidney (Cases 1-6, 9), one lung (Case 7), one heart (Case 8), and one liver (Case 10) transplant recipient. The median time from transplant to presentation was 6.1 years: two patients (Cases 4 and 5) underwent transplant within six months prior to presentation; the others were between 1.1-14.2 years post-transplant. None experienced recent rejection and seven were on triple immunosuppression (Cases 2, 8, and 10 had weaned off steroids). No patients were taking an ACE inhibitor or angiotensin receptor blocker. All patients had underlying co-morbidities (most commonly hypertension, diabetes, and cardiovascular disease) and three were obese (body mass index≥30).

Clinical Presentation

No patient had recent travel, although three had known or possible contact with a COVID-19 case. The median duration of symptoms at presentation was 4.5 days (range 1-21 days). Of the seven hospitalized patients, all had objective fevers during admission, but only two had fever >38.0°C on presentation. Other common symptoms in these ten patients were subjective fever (N=8), cough (N=8), dyspnea (N=6), myalgias (N=5), fatigue (N=5). Less common symptoms were diarrhea (N=3) and anosmia/dysgeusia (N=2).

Laboratory Studies and Microbiology

Two patients had leukopenia and eight had lymphopenia, although five had baseline lymphopenia during the three months prior. Only one patient (Case 3) had a marginally elevated alanine

aminotransferase. Four patients (two of whom were kidney transplant recipients) had an elevated creatinine. Of the seven admitted patients, two had slightly elevated procalcitonin (0.30 and 0.31 µg/mL) and all had elevated C-reactive protein. Other laboratory values are reported in **Table 1**. No patient had a documented viral co-infection based on standard microbiology testing; Case 8 had a sputum culture positive for *Klebsiella* late in his admission, thought to represent a ventilator associated pneumonia.

COVID-19 RNA Testing

All patients had positive COVID-19 RNA testing on nasopharyngeal or pooled nasopharyngeal/oropharyngeal samples (**Figure 1**). One patient (Case 10) underwent asymptomatic screening at her assisted living facility where she was found to be positive; four days later she presented to the emergency department with dyspnea and hypoxia. All other patients were tested upon presentation to care with acute symptoms. Four patients underwent repeat testing (Cases 1, 3, 7, 8) as indicated in **Table 1**; two of the critically ill patients (Cases 1 and 7) had repeat positive tests out to days 39 and 33, respectively. Two patients (Cases 7 and 8) met our institutional criteria for discontinuation of isolation precautions (at least 14 days from symptom onset, at least 72 hours fever-free without anti-pyretic, and two consecutive negative COVID-19 swabs collected at least 24 hours apart) near the end of their hospitalization.

Imaging Findings

Chest X-ray (CXR) was performed in nine patients: five were abnormal, with three showing bilateral opacities and two showing unilateral opacities. Computer tomography (CT) of the chest was performed in three patients (Cases 1, 7, 8) and all showed bilateral ground-glass opacities and consolidations.

Complications and Therapies

Seven patients required hospitalization, six required supplemental oxygen, and three (Cases 1, 7, and 9) required ICU admission (between days 10-14 after symptom onset). All ICU patients developed acute respiratory distress syndrome requiring mechanical ventilation (at between days 16-19 after symptom onset) and shock requiring vasopressors. Five patients had acute kidney injury (one requiring renal replacement therapy) and two patients had a deep venous thrombosis. Cases 1 and 7 were enrolled in the randomized controlled trial of remdesivir versus placebo, Case 7 was also

subsequently treated with hydroxychloroquine in the setting of critical illness, and Case 8 was treated with hydroxychloroquine alone. Case 9 was treated at a referring hospital with hydroxychloroquine/azithromycin, lopinavir/ritonavir, methyprednisolone and tocilizumab; he was then treated with convalescent plasma at our institution. No other patients received antivirals, steroids, or biologics for COVID-19 (although Case 7 received stress dose steroids for shock). Six of the seven hospitalized patients received antibiotics, as did one outpatient. Immunosuppressive therapy was decreased in all but two patients when COVID-19 was diagnosed (**Table 1**).

Outcomes

The duration of follow-up ranged from four to 39 days (median 32 days). Five of the seven hospitalized patients were discharged (median length of stay 11 days, range 7-29) and the other two remain hospitalized. Two of the three patients requiring mechanical ventilation have been successfully extubated. No patient has died as of the time of this report.

SEROLOGIC ANALYSIS

SARS-CoV-2 IgG serology was performed on all seven of ten SOT recipients with COVID-19 who were hospitalized (Cases 1, 2, 3, 5, 7, 8 and 9) (**Figure 1, Supplement**). Patients were tested serially over 1-22 timepoints throughout the course of their illness, ranging from 4 to 38 days after symptom onset. All seven patients had a positive SARS-CoV-2 IgG serology result, with six seroconverting from negative to positive at timepoints ranging from day 6 (Case 8) to day 27 (Case 2) from symptom onset (median 15 days). The only patient who did not seroconvert was tested once on day 17 of illness (Case 9).

LITERATURE REVIEW

Existing literature on COVID-19 among SOT recipients is accumulating rapidly, and currently consists of case series and case reports. Among these, five studies from China, Spain, and the U.S. (New York City) included over ten patients each.^{13–17}

Focusing on these five large series, SOT recipients were older (median age 51-72 years) and predominantly male (59-80%). In the U.S. studies reporting race/ethnicity,^{16,17} significant proportions of patients were Hispanic (42%) or African American (22-39%). Comorbidities including hypertension, diabetes, cardiovascular disease, chronic kidney disease, and obesity were highly prevalent. Common presenting symptoms were fever (58-90%), dry cough (53-90%), and diarrhea (22-31%), with most patients exhibiting lymphopenia (67-80%) and elevated CRP (49-100%) on presentation. Rates of complications including intubation and ICU level of care were high is most reports, including up to 39% in a New York City report of 36 kidney transplant recipients.¹⁶ Mortality among SOT recipients ranged from 7-28%, with the largest study of 90 SOT recipients (kidney, lung, liver, heart, heart-kidney) from New York City reporting a mortality rate of 18%.¹⁷ Although treatment of COVID-19 among SOT recipients varied significantly by study, decreased immunosuppression was a mainstay of treatment. The majority of patients had antimetabolite therapy held (53-90%) and a smaller proportion had calcineurin inhibitor held or decreased (18-70%). Other therapies administered included hydroxychloroguine (4 of 5 studies, 86-91% of patients), tocilizumab (4 of 5 studies, 6-16% of patients), boosted protease inhibitors (1 of 5 studies, 50% of patients) and IVIG (3 of 5 studies, 3-70%).

Among the smaller case series and individual case reports, notable findings included SOT recipients with COVID-19 who were early in their post-transplant course and had favorable outcomes.^{18–20} Authors from Italy describe their experience with six liver transplant patients, among whom three were less than two years post-transplant and had mild disease whereas the three over 10 years from transplant died.²⁰ In addition to the significant variability in treatment, patients who received boosted protease inhibitors experienced significant drug-drug interactions and toxicity.²¹ While most cases of COVID-19 among SOT recipients were managed with immunosuppression reduction, there were several case reports describing patients where immunosuppression was maintained and patients recovered.^{22–24}

DISCUSSION

We report our institutional experience with ten SOT recipients with COVID-19, who demonstrated a wide spectrum of disease from mild infection successfully managed as an outpatient to severe

disease requiring mechanical ventilation. We also reviewed the existing literature on COVID-19 in SOT recipients and found significant variability in clinical features and management.

Considering our cases and those reported in the literature, it is notable that the symptoms, laboratory values, and imaging in SOT recipients were similar to those of immunocompetent patients.^{3–6} The majority of patients described here were African-American, Hispanic/Latino, or Native Hawaiian/Pacific Islander. While our observations are derived from a small cohort, the racial/ethnic distribution of SOT patients in additional, larger studies will be of interest given emerging data from the U.S. indicating that African-American race may predispose to severe COVID-19 disease.²⁵ Two of our SOT recipients, including one who was critically ill, were obese. This is slightly increased compared to the 11% prevalence of obesity among SOT recipients in Spain with COVID-19.¹³ Obesity is a recently described potentially risk factor for severe disease in COVID-19,^{26,27} and more research is needed to determine if this association is seen in SOT recipients as well.

It is notable that 30% of our patients required mechanical ventilation, which may indicate an increased risk of severe disease. However, despite being immunosuppressed with significant comorbidities associated with poor outcomes in COVID-19,^{3–6} there have been no deaths among SOT recipients with COVID-19 at our institution. This result, taken in the context of high mortality rates reported among larger case series of COVID-19 in SOT recipients from the epicenters of the pandemic, may suggest the potential contribution of healthcare resource availability on patient outcomes. Further research is needed to establish the true mortality rate in SOT recipients and the role of immunosuppressive therapy in disease modulation.

We also describe SARS-CoV-2 serology in SOT recipients. Despite poor performance of many infectious disease serologic tests in this population, we found that all seven patients assayed displayed an IgG serologic response, including a patient less than 6 months post-transplant. For three patients, seroconversion was documented, and occurred between days 6 and 27 after symptom onset. In the immunocompetent population, recent data suggest that most (78-100%) patients develop a detectable IgG response 10-21 days after symptom onset.^{28–31} A study from China reported a liver transplant patient diagnosed with COVID-19 in the immediate post-transplant period who had a "higher than baseline" COVID-19 IgG nine days after symptom onset, and a kidney transplant recipient with IgG production 59 days after symptom onset.¹⁸ Further investigation into the

dynamics of the SARS-CoV-2 serologic response is required in SOT recipients, but this early report suggests that SOT patients are able to mount an antibody response to SARS-CoV-2, which may have diagnostic and prognostic implications.

Our study has several limitations. First, this is a single center analysis of a limited number of patients and may not be generalizable to other centers with different patient populations or treatment approaches. Second, the duration of follow-up is limited for some cases, as it has been in many clinical COVID-19 studies given the need to rapidly share knowledge in this quickly evolving pandemic. Lastly and most importantly, the role of serologic testing as a diagnostic tool and measure of immunity among SOT and other populations is currently not well defined. There is a risk of false positives, particularly with IgM testing, and a lack of clear evidence on which antibodies are surrogates of protection or potent at neutralizing virus.³²

In summary, we report our experience with ten SOT patients with COVID-19 and found that, despite immunosuppression, their clinical features and serologic response seem to mirror immunocompetent patients. Notably, no SOT recipients at our institution have died despite existing literature documenting increased mortality in this population, emphasizing the importance of further studies to determine SOT subgroups who may have more favorable outcomes. Additional research is urgently needed to close the knowledge gap regarding COVID-19 among SOT recipients.

ACKNOWLEDGEMENTS / FUNDING

The authors would like to acknowledge Wei Gu, MD and Elaine Hsu of the UCSF Department of Pathology for biobanking and John Hackett of Abbott Biosciences for running serology testing.

Serologic testing and analysis were funded in part by NIH grant R01-HL105704 (CYC) from the National Heart, Blood, and Lung Institute, the Charles and Helen Schwab Foundation (CYC), and Abbott Laboratories. No funding was provided for clinical aspects of study (case and literature review).

DISCLOSURE

The authors of this manuscript have conflicts to disclose as described by the American Journal of Transplantation. CYC is the director of the UCSF-Abbott Viral Diagnostics and Discovery Center and receives research support in pathogen discovery from Abbott Laboratories, Inc. SD is a coinvestigator for the Adaptive COVID-19 Treatment Trial funded by the National Institute of Allergy and Infectious Diseases (NIAID). She also receives grant support from the NIAID unrelated to this study under Award Number UM1AI104681. She is a consultant for Genentech and Basilea Pharmaceutica, unrelated to this report. JP and RT are employees of Abbott Laboratories, Inc. The remaining authors (MF, CD, VSS, CL, TJH, DY, JD, SRH, SC, JK, DN, KR, EB, AB, PCH, and JB) have no conflicts of interest to disclose.

Data availability statement: The data that supports the findings of this study are available in the supplementary material of this article

FIGURE LEGENDS

Figure 1. SARS-COV-2 IgG serology and PCR results for all seven solid organ transplant recipients requiring hospitalization. IgG serology was conducted using Abbott chemiluminescent microparticle immunoassay detecting IgG antibodies to the SARS-CoV-2 nucleocapsid protein with index value of 1.4 (dotted line) set as positive threshold. PCR was conducted on nasopharyngeal and pooled nasopharyngeal/oropharyngeal swab samples.

REFERENCES

World Health Organization. WHO statement regarding cluster of pneumonia cases in Wuhan, China. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-ofpneumonia-cases-in-wuhan-china. Published 2019. Accessed August 4, 2020.

Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. February 2020. doi:10.1016/S1473-3099(20)30120-1

Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus

Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. February 2020. doi:10.1001/jama.2020.2648

- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3
- Guan W-J, Ni Z-Y, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. February 2020. doi:10.1056/NEJMoa2002032
- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. February 2020. doi:10.1001/jama.2020.1585
- Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol.* 2020;21(3):335-337. doi:10.1016/S1470-2045(20)30096-6
- Chow N, Fleming-Dutra K, Gierke R, et al. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(13):382-386. doi:10.15585/mmwr.mm6913e2
- 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). doi:10.1111/ctr.13511
- Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet (London, England)*. 2020;395(10229):1033-1034. doi:10.1016/S0140-6736(20)30628-0
- 11. Centers for Disease Control and Prevention (CDC). Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus.
- 12. Abbott Laboratories. SARS-CoV-2 IgG [package insert]. 2020.
- 13. Fernández-Ruiz M, Andrés A, Loinaz C, et al. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. *Am J Transplant*. 2020:0-3. doi:10.1111/ajt.15929
- Zhu L, Gong N, Liu B, et al. Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China. *Eur Urol*. 2020;83665283:1-7. doi:10.1016/j.eururo.2020.03.039
- 5. Columbia University Kidney Transplant Program. Early Description of Coronavirus 2019

Disease in Kidney Transplant Recipients in New York. *J Am Soc Nephrol*. 2020. doi:10.1681/ASN.2020030375

- Akalin E, Azzi Y, Bartash R, et al. Covid-19 and Kidney Transplantation. N Engl J Med. April 2020:NEJMc2011117. doi:10.1056/NEJMc2011117
- 17. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in Solid Organ Transplant Recipients: Initial Report from the US Epicenter. *Am J Transplant*. 2020:0-3. doi:10.1111/ajt.15941
- 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*. 2020. doi:10.1111/ajt.15928
- 19. Arpali E, Akyollu B, Yelken B, Tekin S, Turkmen A, Kocak B. Case Report: A Kidney Transplant Patient with Mild COVID-19. *Transpl Infect Dis*. 2020:0-1. doi:10.1111/tid.13296
- Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol.* 2020;1253(20):2019-2020. doi:10.1016/S2468-1253(20)30116-3
- Ning L, Liu L, Li W, et al. Novel Coronavirus (SARS-CoV-2) Infection in A Renal Transplant Recipient: Case Report. *Am J Transplant*. 2020:0-2. doi:10.1111/ajt.15897
- 22. Wang J, Li X, Cao G, Wu X, Wang Z, Yan T. COVID-19 in a Kidney Transplant Patient. *Eur Urol*. 2020:19-20. doi:10.1016/j.eururo.2020.03.036
- 23. Bussalino E, De Maria A, Russo R, Paoletti E. Immunosuppressive therapy maintenance in a kidney transplant recipient SARS-CoV-2 pneumonia: a case report. *Am J Transplant*. 2020:0-2. doi:10.1111/ajt.15920
- Seminari E, Colaneri M, Sambo M, et al. SARS Cov2 infection in a renal transplanted patients.
 A case report. *Am J Transplant*. 2020:0-1. doi:10.1111/ajt.15902
- 25. Garg S, Kim L, Whitaker M, et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(15). doi:10.15585/mmwr.mm6915e3
- Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis*. April 2020:1-29. doi:10.1093/cid/ciaa415
- 27. Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation.

Obesity (Silver Spring). 2020:0-1. doi:10.1002/oby.22831

- 28. Guo L, Ren L, Yang S, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). *Clin Infect Dis*. 2020:1-28. doi:10.1093/cid/ciaa310
 - To KK-W, Tsang OT-Y, Leung W-S, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020;3099(20):1-10. doi:10.1016/s1473-3099(20)30196-1
- 0. Zhao J, Yuan Q, Wang H, et al. Antibody Responses to SARS-CoV-2 in Patients of Novel Coronavirus Disease 2019. *SSRN Electron J*. 2020:1-22. doi:10.2139/ssrn.3546052
- Du Z, Zhu F, Guo F, Yang B, Wang T. Detection of antibodies against SARS-CoV-2 in patients with COVID-19. *J Med Virol*. 2020:0-2. doi:10.1002/jmv.25820
- 2. Infectious Diseases Society of America. *IDSA COVID-19 Antibody Testing Primer.*; 2020.

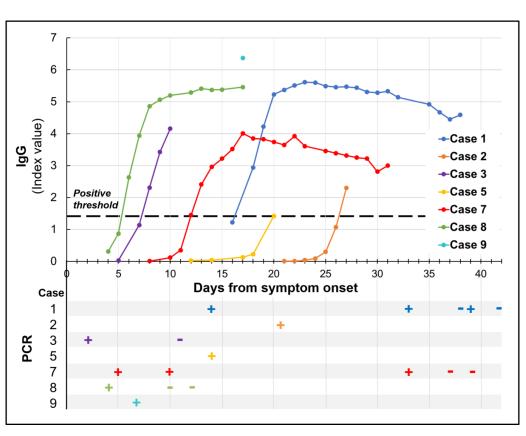
| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 | Case 10 |
|---------------------------|----------------------|--------------|---------------|-------------|-------------|---------------|----------------|--------------|---------------|--------------|
| Demographics | | | | | | | | | | |
| Age (y) | 47 | 73 | 77 | 61 | 71 | 52 | 50 | 42 | 44 | 80 |
| Gender | Male | Male | Male | Female | Female | Male | Female | Male | Male | Female |
| Race/Ethnicity | Black | Unknown | Black | Latino | Asian | Asian | Latino | NH/PI | Black | White |
| Transplant Details | | | | | | | | | | |
| Туре | Kidney (LRRT) Kidney | Kidney | Kidney | Kidney | Kidney | Kidney | Bilateral Lung | Heart | Kidney | Liver |
| | 7.4 | (LRRT) | (DDRT) | (DDRT) | (DDRT) | (LURT) | 4.8 | (OHT) | (DDRT) | (LDLT) |
| Yrs from transplant | No | 4.8 | 10.8 | 0.33 | 0.42 | 1.1 | No | 7.8 | 9.3 | 14.2 |
| Rejection last 3 mo | | No | No | No | No | No | | No | No | No |
| Co-morbidities | DM, HTN, | CAD, DM, | CAD, HFrEF, | DM, HLD | CAD, DM, | DM, HTN, | RA, DM, | CKD, HTN, | HTN, CKD | CAD, DM, |
| | CVD | HTN, HLD | sarcoidosis | | CVD | HLD, | hypothyroid | OSA, gout, | | HTN, CKD, |
| U | | | | | | hypothyroid | | hypothyroid | | asthma, |
| | | | | | | | | | | hypothyroid, |
| E | | | | | | | | | | dementia |
| BMI (kg/m ²) | 27.8 | 27.4 | 18.0 | 20.4 | 20.0 | 28.6 | 36.1 | 49.4 | 23.6 | 36.6 |
| Medications | | | | | | | | | | |
| ACE/ARB use | No | No | No | No | No | No | No | No | No | No |
| Immunosuppression | Tac 0.5mg bid, | Tac 1mg bid, | Tac 3mg bid, | Tac 1.5/2gm | Tac 0.5/1mg | Tac 1mg bid, | Tac 1.5mg | Tac 9mg bid, | Tac 6mg bid, | Tac 0.5mg |
| | MMF 1gm bid, | MMF 750mg | MMF 500mg | bid, MMF | bid, MMF | MMF 1gm | bid, MMF | MMF 250mg | MPS 540mg | bid, MMF |
| C | pred 5mg qd | bid | bid, pred 5mg | 500mg bid, | 500mg bid, | bid, pred 5mg | 360mg bid, | bid | bid, pred 5mg | 500mg bid |
| | | | qd | pred 5mg qd | pred 5mg qd | qd | pred 7.5 qd | | рр | |
| C | | | | (thymo | (thymo | | | | | |
| | | | | | | | | | | |

| Recent travel No | No | No | No | No | No | No | No | No | No |
|---------------------------------------|-------------|---------|------------|------------|----------------|-------------|------------|------------|------------|
| COVID contacts No | Maybe(SNF) | No | No | No | No | Yes(family) | No | No | Maybe(ALF) |
| Symptom duration(d) 14 | 21 | 2 | ω | 14 | З | 5 | 4 | 0 | - |
| Fever (subjective) Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No |
| Fever (°C, initial) 38.3 | 36.5 | 36.2 | n/a | 38.3 | 36.9 | 37.5 | 37.7 | 37.7 | 36.8 |
| Fever (°C, Tmax) 39.4 | 38.6 | 38.2 | n/a | 39.5 | n/a | 39.5 | 39.1 | 39.3 | n/a |
| Other symptoms Dry cough, | Dry cough, | Fatigue | Productive | Productive | Dry cough, | Dry cough, | Dry cough, | Dry cough, | Dyspnea |
| dyspnea, | dyspnea, | | cough | cough, | myalgia, | dyspnea, | dyspnea, | dyspnea, | |
| myalgia | myalgia, | | | fatigue, | fatigue, nasal | myalgia | myalgia, | diarrhea | |
| | chest pain, | | | anosmia, | congestion | | fatigue, | | |
| | fatigue, | | | dysgeusia | | | diarrhea | | |
| | diarrhea, | | | | | | | | |
| b. | anosmia, | | | | | | | | |
| | dysgeusia | | | | | | | | |
| Laboratory Findings ^a | | | | | | | | | |
| WBC count (x10 ⁹ /L) 5.8 | 3.6 | 5.6 | 5.3 | 2.8 | 4.0 | 4.9 | 4.6 | 4.3 | 4.9 |
| Lymphocyte (x10 ⁹ /L) 0.70 | 1.48 | 0.73 | 0.16 | 0.08 | 0.16 | 0.57 | 1.11 | 0.2 | 0.54 |
| Platelets (x10 ⁹ /L) 275 | 89 | 226 | 335 | 174 | 280 | 133 | 117 | 141 | 103 |
| Creatinine (mg/dL) 1.10 | 1.06 | 3.21 | 0.75 | 0.82 | 1.14 | 1.10 | 5.23 | 2.93 | 1.53 |
| AST/ALT (U/L) 15/10 | 43/37 | 52/58 | 21/16 | 23/20 | 16/17 | 14/16 | 24/16 | 19/15 | 21/14 |
| Troponin (µg/L) <0.02 | 0.03 | 0.14 | n/a | n/a | n/a | <0.02 | <0.02 | n/a | 0.02 |
| CRP (mg/L) 176.9 | 48.6 | 35.6 | n/a | 22.6 | n/a | 208.9 | 92.5 | 135 | n/a |
| LDH (U/L) 275 | n/a | 340 | n/a | n/a | 145 | 353 | 234 | n/a | 172 |
| Procalcitonin (μg/L) 0.11 | 0.03 | 0.31 | n/a | 0.07 | n/a | 0.05 | 0.30 | n/a | n/a |
| D-dimer (ng/mL) n/a | n/a | n/a | n/a | 1276 | n/a | 9725 | 408 | 543 | 1020 |

| COVID RNA | d14(+), d33(+), d21(+) | d21(+) | d2(+), | d4(+) | d14(+) | d3(+) | d5(+), d10(+), | d4(+), | d7(+) | d -4(+) |
|-----------------------------------|------------------------|--------|------------|-------|--------------|-------|----------------|---------------|-----------------|--------------|
| | d38(-), d39(+), | | d11(-) | | | | d33(+), | d10(-), | | |
| | d42(-) | | | | | | d37(-), | d11(-) | | |
| | neg | | | | | | d39(-) | | | |
| | neg | | | | | | neg | | | |
| Influenza/RSV PCR | neg | n/a | neg | n/a | n/a | n/a | neg | n/a | n/a | n/a |
| Extended viral panel ^b | neg | neg | n/a | n/a | neg | n/a | neg | neg | n/a | n/a |
| Sputum culture | | n/a | n/a | n/a | n/a | n/a | neg | n/a | Klebsiella | n/a |
| Blood cultures | | neg | neg | n/a | neg | n/a | | neg | neg | n/a |
| Imaging | | | | | | | | | | |
| Chest X-ray | Bilat nodular | Clear | Clear | n/a | Bilat patchy | Clear | Clear | Chronic bilat | Patchy | Left midlung |
| E | opacities | | | | opacities | | | opacities | infiltrate left | opacity |
| Chest CT | Bilat GGO, | n/a | n/a | n/a | n/a | n/a | Bilateral | Bilateral | n/a | n/a |
| | nodular | | | | | | GGO, | GGO, | | |
| | consolidation | | | | | | consolidation | consolidation | | |
| Complications | | | | | | | | | | |
| Hospital admission | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | No |
| ICU (time from sx, d) | Yes (14) | No | No | No | No | No | Yes (10) | No | Yes (11) | No |
| Other complications | ARDS, shock, | None | AKI | None | None | None | ARDS, | AKI | ARDS, | AKI |
| | AKI (resolved) | | (resolved) | | | | shock, DVT | (persistent) | shock, AKI | |
| Thorphice | | | | | | | | | | |
| Supplemental O ₂ (L) | Yes | No | No | No | Yes (2L) | No | Yes | Yes (3L) | Yes | Yes (2L) |
| Mech ventilation | Yes | No | No | No | No | No | Yes | No | Yes | No |
| Time from sx (d) | 16 | | | | | | 17 | | 19 | |
| Duration (d) | 11 | | | | | | 13 | | 8+ | |
| Required proning | | | | | | | Yes | | Yes | |

| | | Yes | | No | |
|---|---|--|--|--|---|
| Yes - tac Yes - MMF | IF No | Yes - MMF | Yes - MMF | Yes - tac, | No |
| decreased decreased | đ | held | held | MMF held | |
| | | | | | |
| None None | None | RCT, then | нса | HCQ/azithro, | None |
| | | НСQ | | LPV/r | |
| None None | None | CTX/azithro | CTX/doxy x | vanc/CTX/do | Cefuroxime/ |
| | | 6d, | 5d | xy 7d, | doxy x 7d |
| | | vanc/mero 5d | | vanc/mero 7d | |
| | | Stress dose | | Tocilizumab, | |
| None None | None | steroids | None | methylpred | None |
| | | (shock) | | | |
| | | 20 | | Yps | |
| No | | | | | |
| | No | Ŕ | No | Ģ | No |
| n/a n/a | Zo | ē | No | | No |
| n/a Yes | No n/a | Yes | n/a | 8 | No n/a |
| (LOS 10 | No n/a | No Yes | No n/a Yes | 88 | No n/a n/a |
| | | No S | No n/a Yes (LOS 16) | N N S | No n/a |
| No No | | No No S | No n/a Yes (LOS 16) No | 8 8 8 8 | No n/a n/a No |
| | | 39 NO NO S | No n/a Yes (LOS 16) No 27 | 21 N N N S | n/a n/a |
| No No 32 21 available during the hos | No n/a n/a No 37 italization. | 39 N N Yes | No n/a Yes (LOS 16) No 27 | ²² 8 8 8 | n/a No |
| No No 32 21 available during the hos and H3) and B, RSV A a | No n/a n/a No 37 sitalization. nd B, parainfluenza | Yes No No 39 | No n/a Yes (LOS 16) No 27 27 | and rhinovirus. | n/a No 4 |
| No No No 21 Available during the hos and H3) and B, RSV A a ssisted living facility; BM | No n/a n/a () No 37 italization. nd B, parainfluenza , body mass index; | Yes No No 39 CRP, C-reactive pr | No n/a Yes (LOS 16) No 27 27 27 27 us, adenovirus, | No No 21 21 and rhinovirus. | n/a No 4 |
| No No 32 21 available during the hos and H3) and B, RSV A a and H3) and B, RSV A a xsisted living facility; BM T: deceased donor rena XT: deceased donor rena | No n/a n/a 1) No 37 37 1d B, parainfluenza , body mass index; transplant; DM: dia pertension; LDH: la | Yes No No 39 CRP, C-reactive pro betes mellitus; GG0 | No n/a Yes (LOS 16) No 27 27 27 27 27 27 27 27 27 27 27 27 27 | No No No 21 21 and rhinovirus. axone; CVD: axone; HCQ: ir/ritonavir; LDLT | - |
| No No 32 21 available during the hos and H3) and B, RSV A a and H3) and B, RSV A facility; BM RT: deceased donor rena RT: deceased donor rena RT: deceased donor rena Invperlipidemia; HTN: hy unrelated renal transplit | No n/a n/a () No 37 37 italization. 37 oitalization. 37 italization. 37 italization. 4 pertenza ind B, parainfluenza transplant; DM: dia pertension; LDH: la | Yes No No 39 1-3, metapneumovi CRP, C-reactive pro CRP, C-reactive pro betes mellitus; GG0 betes mellitus; GG0 | No n/a Yes (LOS 16) No 27 27 us, adenovirus, us, adenovirus, itein; CTX: ceftri tein; CTX: ceftri tein; CTX: ceftri tein; CTX: ceftri tein; CTX: ceftri | No No No 21 21 and rhinovirus. axone; CVD: axone; CVD: pacities; HCQ: ir/ritonavir; LDLT matoid arthritis; | - |
| No No 32 21 available during the hos and H3) and B, RSV A a and H3) and B, RSV A a XT: deceased donor rena RT: deceased donor rena RT: hyperlipidemia; HTN: hy g unrelated renal transplation heart transplant; RCT: r | No n/a n/a (1) No 37 37 11 alization. 14 B, parainfluenza , body mass index; transplant; DM: dia pertension; LDH: la nnt; NH/PI: Native H | Yes No No 39 1-3, metapneumovi CRP, C-reactive pro betes mellitus; GG0 betes mellitus; GG0 triate dehydrogenas ctate dehydrogenas sawaiian or Pacific Is | No n/a Yes (LOS 16) No 27 27 27 27 27 27 27 27 27 27 27 27 27 | No No No 21 21 and rhinovirus. and rhinovirus. apacities; HCQ: ir/ritonavir; LDLT, ir/ritonavir; LDLT, matoid arthritis; | n/a No 4 Vo |
| No availa and F and F RT: de RT: de RT: de g unru g unru ; hear | No n/a Yes (LOS 10c No 21 able during the hosp 13) and B, RSV A ar 3d living facility; BMI 3ceased donor renal 3rdipidemia; HTN: hy elated renal transpla t transplant; RCT: ra | Outcomes No No No No No No No Discharged ICU Yes n/a n/a | No No n/a n/a Yes n/a n/a Yes Yes n/a No (LOS 10d) No No No 21 37 39 able during the hospitalization. No No No 13) and B, RSV A and B, parainfluenza 1-3, metapneumovia ad living facility; BMI, body mass index; CRP, C-reactive proceased donor renal transplant; DM: diabetes mellitus; GGC sceased donor renal transplant; DM: diabetes mellitus; GGC ad living facility; RCT: randomized controlled trial; SNF: skilled it transplant; RCT: randomized controlled trial; SNF: skilled it transplant; RCT: randomized controlled trial; SNF: skilled it | No No No n/a n/a Yes n/a Yes n/a No Yes (LOS 10d) No No Yes No No No No 21 37 39 27 able during the hospitalization. No No No 43) and B, RSV A and B, parainfluenza 1-3, metapneumovirus, adenovirus, adenovirus, adenovirus, is ceased donor renal transplant; DM: diabetes mellitus; GGO: ground-glass ceased donor renal transplant; DM: diabetes mellitus; GGO: ground-glass ceased donor renal transplant; DM: diabetes mellitus; GGO: ground-glass ceased donor renal transplant; NH/PI: Native Hawaiian or Pacific Islander; RA: rheu elated renal transplant; NH/PI: Native Hawaiian or Pacific Islander; RA: rheu transplant; RCT: randomized controlled trial; SNF: skilled nursing facility; L | No No No No No No Yes n/a No Yes (LOS 16) No No No 39 27 |

Acc



ajt_16079_f1.tif