

CORRESPONDENCE

Covid-19 and Kidney Transplantation

TO THE EDITOR: Kidney-transplant recipients appear to be at particularly high risk for critical Covid-19 illness due to chronic immunosuppression and coexisting conditions.¹ At Montefiore Medical Center, we identified 36 consecutive adult kidney-transplant recipients who tested positive for Covid-19 between March 16 and April 1, 2020. A total of 26 recipients (72%) were male, and the median age was 60 years (range, 32 to 77). Fourteen recipients (39%) were black, and 15 recipients (42%) were Hispanic. Twenty-seven recipients (75%) had received a deceased-donor kidney; 34 recipients (94%) had hypertension, 25 (69%) had diabetes mellitus, 13 (36%) had a history of smoking tobacco or were current smokers, and 6 (17%) had heart disease. Thirty-five of the patients (97%) were receiving tacrolimus, 34 (94%) were receiving prednisone, and 31 (86%) were receiving mycophenolate mofetil or mycophenolic acid.

The most common initial symptom was fever (in 21 patients [58%]), and diarrhea was observed in 8 patients (22%). Eight patients who were in stable condition without major respiratory symptoms (22%) were monitored at home, and 28 patients (78%) were admitted to the hospital. Twenty-seven of the hospitalized patients (96%) had radiographic findings that were consistent with viral pneumonia, and 11 (39%) received mechanical ventilation. Six patients (21%) received renal replacement therapy. At a median follow-up of 21 days (range, 14 to 28), 10 of the 36 kidney-transplant recipients (28%) and 7 of the 11 patients who were intubated (64%) had died. Two of the 8 patients who were monitored as outpatients died at home; both were recent kidney-transplant recipients who had received antithymocyte globulin within the previous 5 weeks (see the Supplementary Appendix, available with the full text of this article at NEJM.org).

Table 1 summarizes the initial laboratory results in the 28 hospitalized patients. Twenty-two (79%) were lymphopenic, 12 (43%) had thrombocytopenia, 19 (68%) had low CD3 cell counts, 20

(71%) had low CD4 cell counts, and 8 (29%) had low CD8 cell counts. Inflammatory markers were measured, and 10 patients (36%) had ferritin levels higher than 900 ng per milliliter, 13 (46%) had C-reactive protein levels higher than 5 mg per deciliter, 12 (43%) had procalcitonin levels higher than 0.2 ng per milliliter, and 16 (57%) had D-dimer levels higher than 0.5 μ g per milliliter.

Although effective treatment of Covid-19 is currently unknown,² immunosuppressive management included withdrawal of an antimetabolite in 24 of 28 patients (86%). In addition, tacrolimus was withheld in 6 of the 28 severely ill patients (21%). Hydroxychloroquine was administered to 24 of these 28 patients (86%). Apixaban was administered to patients with D-dimer levels higher than 3.0 μ g per milliliter. Six severely ill patients received the CCR5 inhibitor leronlimab (PRO 140, CytoDyn) on a compassionate-use basis, and 2 received the interleukin-6 receptor antagonist tocilizumab. Interleukin-6 levels were very elevated (range, 83 to 8175 pg per milliliter) when leronlimab was initiated (on day 0) in the 5 patients with elevated interleukin-6 levels; these levels decreased markedly 3 days later (range, 37 to 2022 pg per milliliter) (see Table S2 in the Supplementary Appendix). However, only the 1 patient who had the lowest interleukin-6 level (at 83 pg per milliliter) remained in stable condition without intubation.

In conclusion, at our institution, kidney-transplant recipients with Covid-19 had less fever as an initial symptom,³ lower CD3, CD4, and CD8 cell counts,⁴ and more rapid clinical progression than persons with Covid-19 in the general population. The number of our patients with very low CD3, CD4, and CD8 cell counts indirectly supports the need to decrease doses of immunosuppressive agents in patients with Covid-19, especially in those who have recently received antithymocyte globulin, which decreases all T-cell subsets for many weeks. Our results show a very high early mortality among kidney-transplant recipients with Covid-19 — 28% at 3 weeks as compared with

Table 1. Clinical Features and Outcomes in the Kidney-Transplant Recipients.	
Variable	Value
Presenting symptom — no./total no. (%)	
Fever	21/36 (58)
Cough	19/36 (53)
Dyspnea	16/36 (44)
Myalgias	13/36 (36)
Diarrhea	8/36 (22)
Hospitalization — no./total no. (%)	
Chest radiographic findings consistent with viral pneumonia — no./total no. (%)	
Treatment — no./total no. (%)	
Withdrawal of antimetabolite	24/28 (86)
Withdrawal of tacrolimus	6/28 (21)
Hydroxychloroquine	24/28 (86)
Azithromycin	13/28 (46)
Leronlimab	6/28 (21)
Tocilizumab	2/28 (7)
High-dose glucocorticoids	2/28 (7)
Laboratory values	
White-cell count	
Median (range) — per mm ³	5300 (2100–14,700)
Patients with count <400 per mm ³ — no./total no. (%)	6/28 (21)
Lymphocyte count	
Median (range) — per mm ³	600 (100–1900)
Patients with count <1000 per mm ³ — no./total no. (%)	22/28 (79)
Platelet count	
Median (range) — per mm ³	146,000 (78,000–450,000)
Patients with count <150,000 per mm ³ — no./total no. (%)	12/28 (43)
CD3 cell count	
Median (range) — per mm ³	319 (34–1049)
Patients with count <706 per mm ³ — no./total no. (%)	19/28 (68)
CD4 cell count	
Median (range) — per mm ³	173 (6–507)
Patients with count <344 per mm ³ — no./total no. (%)	20/28 (71)
CD8 cell count	
Median (range) — per mm ³	132 (39–654)
Patients with count <104 per mm ³ — no./total no. (%)	8/28 (29)
Ferritin	
Median (range) — ng/ml	1230 (191–9259)
Patients with level >900 ng/ml — no./total no. (%)	10/28 (36)
D-dimer	
Median (range) — μg/ml	1.02 (0.32–5.19)
Patients with level >0.5 μg/ml — no./total no. (%)	16/28 (57)
Patients with level >3 μg/ml — no./total no. (%)	3/28 (11)

Table 1. (Continued)	
Variable	Value
C-reactive protein	
Median (range) — mg/dl	7.9 (0.5–48.7)
Patients with level >5 mg/dl — no./total no. (%)	13/28 (46)
Procalcitonin	
Median (range) — ng/ml	0.2 (0.1–5.1)
Patients with level >0.2 ng/ml — no./total no. (%)	12/28 (43)
Lactate dehydrogenase	
Median (range) — U/liter	336 (158–309)
Patients with level >1.5 times upper limit of normal range — no./total no. (%)	10/28 (36)
Creatine kinase	
Median (range) — U/liter	145 (48–815)
Patients with level >200 U/liter — no./total no. (%)	9/28 (32)
Outcomes at a median of 21 days (range, 14–28) — no./total no. (%)	
Death	10/36 (28)
Intubation	11/28 (39)
Death after intubation	7/11 (64)
Renal replacement therapy	6/28 (21)
Remained hospitalized	12/28 (43)
Discharged from hospital	10/28 (36)

the reported 1% to 5% mortality among patients with Covid-19 in the general population who have undergone testing in the United States and the reported 8 to 15% mortality among patients with Covid-19 who are older than 70 years of age.

Enver Akalin, M.D.
 Yorg Azzi, M.D.
 Rachel Bartash, M.D.
 Harish Seethamraju, M.D.
 Michael Parides, Ph.D.
 Vagish Hemmige, M.D.
 Michael Ross, M.D.
 Stefanie Forest, M.D., Ph.D.
 Yitz D. Goldstein, M.D.
 Maria Ajaimy, M.D.
 Luz Liriano-Ward, M.D.
 Cindy Pynadath, M.D.
 Pablo Loarte-Campos, M.D.
 Purna B. Nandigam, M.D.
 Jay Graham, M.D.
 Marie Le, M.D.

Juan Rocca, M.D.
 Milan Kinkhabwala, M.D.

Montefiore Medical Center
 Bronx, NY
 eakalin@montefiore.org

Drs. Akalin and Azzi contributed equally to this letter.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on April 24, 2020 at NEJM.org.

1. 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* 2020 April 9 (Epub ahead of print).
2. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020 April 13 (Epub ahead of print).
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
4. Diao B, Wang C, Tan Y, et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). *medRxiv*. February 20, 2020 (<https://www.medrxiv.org/content/10.1101/2020.02.18.20024364v1>).

DOI: 10.1056/NEJMc2011117

Correspondence Copyright © 2020 Massachusetts Medical Society.