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RESEARCH ARTICLE

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Assessment of clinical outcomes in renal transplant recipients with COVID-19

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Abstract

The coronavirus disease 2019 (COVID-19) has affected more than a hundred million individuals and caused more than three million deaths worldwide. Specific risk groups were defined for increased risk of mortality and morbidity in COVID-19, and renal transplant recipients are at a significantly increased risk regarding outcomes due to their immunosuppressed conditions. This study evaluated the general characteristics of kidney transplant recipients with COVID-19 infection. Among 1257 transplant cases, 56 had COVID-19 infection, and 23 (41%) were hospitalized during the 9-month study period. Among all COVID-19 cases, 58% were male with a mean age of 45.5 (±13.2, 19–71) years, and the most frequent comorbidities were hypertension (70.9%) and diabetes (23.6%). Hospitalized patients were older ($p = 0.03$) and had higher rates of hypertension ($p = 0.008$), diabetes ($p = 0.002$), and ischemic heart disease ($p = 0.03$). Therapeutic management included antimetabolite withdrawal and prednisolone increase in 71%, calcineurin inhibitor withdrawal in 8% and decrease in 58%, hydroxychloroquine in 17%, tocilizumab in 3%, and antivirals in 67% of patients. Acute kidney injury and respiratory failure developed in 34% and 85%, respectively. The mortality rate was 23%. These results emphasized that the COVID-19 infection in renal transplant recipients significantly increases the risk of morbidity and mortality. Therefore, these patients should be intervened earlier and monitored closely to prevent poor outcomes.

KEYWORDS

COVID-19, mortality, patient outcomes, renal transplant, transplant recipients

1 | INTRODUCTION

The world had witnessed a major health crisis caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the last year. Following the first case report in Wuhan city of Hubei District of China, in December 2019, the World Health Organization declared a pandemic in March 2020 due to the widespread outbreak and severe mortality rates worldwide. Since then, the number of confirmed cases of coronavirus disease 2019 (COVID-19) has increased to 128 million, and the total number of casualties has reached almost 3 million by the end of March 2021.[1] Turkey has the eighth highest number of confirmed cases, approximately 3.5 million as of April 2021.[2] Considering these strikingly high numbers, identification of high-risk groups and implementing intense prevention and treatment strategies became a topic with significant importance. Specialized populations like older ages, pregnant women, and patients with chronic diseases or multiple comorbidities were initially defined as the high-risk groups.[3,4]

Inclusion of renal transplant recipients among the high-risk groups is an intuitive approach concerning immunosuppression or multiple comorbid situations that these patients might have. Moreover, COVID-19 itself poses a significant risk on the kidneys by

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causing cytokine storm, hypoxia, or rhabdomyolysis, which all may trigger a kidney injury even without transplantation.[5] Nevertheless, there is still uncertainty about the effects of COVID-19 on patient outcomes in renal transplant recipients. In a study from Italy, they reported that more than 75% of 20 renal transplant recipients with COVID-19 pneumonia had rapid progression with 25% mortality during a follow-up of 7 days.[6] Another study from New York showed a mortality rate of 21% among hospitalized renal transplant recipients.[7] The primarily suspected mechanism of poor outcomes is immunosuppression; nevertheless, several studies reported that immunocompromised status is not a risk factor for COVID per se.[8] According to these, immunosuppression could protect the patients against severe immunologic response, viral replication, and cytokine storm. Moreover, data accumulated on the outcomes of COVID-19 in renal transplant recipients is not sufficient to make neater conclusions on the topic.[9] On this background, this study aimed to contribute to the available evidence by evaluating the general characteristics and disease outcomes of renal transplant recipients diagnosed with COVID-19.

2 | METHODS

This study was conducted at the Organ Transplantation Department of the Acibadem International Hospital in Istanbul, Turkey. Our transplantation center maintains a follow-up of more than 1200 renal transplant recipients, and all patients in our database were evaluated regarding the diagnosis of COVID-19 for this study. The study protocol was approved by the Ethical Committee of Acibadem University on April 7, 2021 with approval number 2021-07/30.

The confirmed diagnosis of COVID-19 was based on positive polymerase chain reaction analyses. Once the patient was diagnosed positive, clinical presentation, laboratory assessments, immunosuppression, and treatment strategies were recorded for analyses.

2.1 | Statistical analyses

Descriptive statistics of continuous variables were presented with mean and standard deviation. Categorical variables were presented using frequency and percent. The comparisons of continuous and categorical variables between independent study groups were made with the Mann–Whitney *U* test and the χ^2 test, respectively. A type-I error level of 5% was considered as the upper limit of statistical significance. All analyses were done in SPSS 23 software (IBM Inc).

3 | RESULTS

Among 1257 kidney transplant recipients in our center, 56 were identified as COVID-19 positive, 23 (41%) were hospitalized due to COVID-19 during the 9-month study period. Of the 56 patients, 58% were male ($n = 33$) with a mean age of 45.5 (±13.2, 19–71) years.

TABLE 1 Descriptive characteristics

Age (year)	45.5 ± 13.2
Gender, *n* (%)	
Female	23 (42)
Male	33 (58)
Comorbidities, *n* (%)	
HT	39 (70.9)
DM	13 (23.6)
Obesity	12 (21.8)
IHD	10 (18.2)
HT + DM	7 (12.5)
HT + IHD	4 (7)
HT + DM + IHD	4 (7)
Epilepsy	1 (1.7)
SSC	1 (1.7)
AS	1 (1.7)
MS	1 (1.7)
Hospitalization, *n* (%)	23 (41.07)
Therapeutic management, *n* (%)	
Antimetabolite withdrawal and prednisolone increase	40 (71.4)
Calcineurin inhibitor withdrawal	5 (8.9)
Calcineurin inhibitor dosage decrease	33 (58.9)
Hydroxychloroquine	10 (17.8)
Tocilizumab	2 (3.5)
Favipiravir	38 (67.8)
Remdesivir	3 (5.3)

Abbreviations: AS, Ankylosing spondylitis; DM, diabetes mellitus; HT, hypertension; IHD, ischemic heart disease; MS, multiple sclerosis; SSC, squamous cell carcinoma of the skin.

Prevalent comorbidities included hypertension (70.9%, $n = 39$), diabetes (23.6%, $n = 13$), obesity (21.8%, $n = 12$), ischemic heart disease (18.2%, $n = 10$), hypertension + diabetes (12.5%, $n = 7$), hypertension + ischemic heart disease (7%, $n = 4$), hypertension + diabetes + ischemic heart disease (7%, $n = 4$), epilepsy (1.7%, $n = 1$), squamous cell carcinoma of the skin (1.7%, $n = 1$), ankylosing spondylitis (1.7%, $n = 1$), multiple sclerosis (1.7%, $n = 1$), and hyperlipidemia (1.7%, $n = 1$; Table 1).

Among 23 hospitalized kidney transplant recipients with a mean age of 50.3 (±13.3) years, 78% ($n = 18$) were male, while 33 non-hospitalized ones with a mean age of 42.3 (±12.4) years included 15 male patients. Hospitalized patients were older ($p = 0.03$) and male dominance was significant ($p = 0.07$). Compared to nonhospitalized patients prevalent comorbidities, including hypertension (90%, $n = 20$; $p = 0.008$), diabetes (45%, $n = 10$; $p = 0.002$), and ischemic heart disease (31%, $n = 7$; $p = 0.03$) were determined to be higher in hospitalized ones (Table 2).

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TABLE 2 Descriptive characteristics of hospitalized and nonhospitalized patients

	Hospitalized patients (n = 23)	Nonhospitalized patients (n = 33)
Gender, *n* (%)		
Female	5 (22)	18 (55)
Male	18 (78)	15 (45)
Age (year)	50.3 (±13.3)	42.3 (±12.4)
Comorbidities, *n* (%)		
HT	21 (90)	19 (57.5)
DM	10 (45)	3 (9)
Obesity	6 (26)	12 (18)
IHD	7 (31)	3 (9)
Posttransplant time to diagnosis of COVID-19 (month)	56	44
Common symptoms, *n* (%)		
Respiratory symptoms	23 (100)	27 (82)
Mialgia	15 (65)	12 (36)
Diarrhea	2 (9)	2 (6)
Fever	16 (69)	11 (33)
Ageusia and anosmia	1 (4.3)	1 (3)
AKI, *n* (%)	14 (60)	5 (15)
Exitus, *n* (%)	11 (47)	2 (6)

Abbreviations: AKI, acute kidney injury; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; HT, hypertension; IHD, ischemic heart disease.

Therapeutic management included antimetabolite withdrawal and prednisolone increase in 40 (71%), calcineurin inhibitor withdrawal in 5 (8.9%), decrease in 33 (58.9%), hydroxychloroquine in 10 (17.8%), tocilizumab in 2 (3.5%), and favipiravir in 38 (67.8%) patients; 3 (5.3%) of these patients who had favipiravir also had remdesivir.

During a median follow-up period of 89 days (interquartile range: 10–304 days), 14 of these patients were admitted to the intensive care unit. Acute kidney injury (AKI) occurred in 34% (n = 19) cases, with respiratory failure requiring intubation in 85% (n = 12), and the mortality rate was 23% (n = 13). The patients who died with a mean age of 54.4 (±12.6) were older (p = 0.13).

4 | DISCUSSION

This study evaluated renal transplant recipients' general characteristics with COVID-19 and compared the hospitalized and nonhospitalized patients as a surrogate marker of advanced disease to evaluate the factors possibly associated with poor prognosis. As an overall interpretation of our findings, the prevalence of COVID-19 among our patients was about 4.5%. Increased age and comorbidities like cardiovascular events and diabetes were associated with advanced disease, and AKI and respiratory failure emerged as significant risk factors that increased mortality. The overall mortality rate was 23% among COVID-19 cases.

The results of this study were generally in accordance with the previous reports. In one of those, Alberici et al.[6] reported their experience and short-term outcomes on 20 kidney transplant recipients with COVID-19 pneumonia. The mortality rate was 25%, and the worsening of the respiratory functions despite aggressive immunosuppression and antiviral therapy as in our study was noted for the mortality. In another report by Akalin et al.,[10] 36 kidney transplant recipients who tested positive for COVID-19 were evaluated, and the mortality rate was reported as 28%, which was also similar to our results. Another study by Rahimzadeh et al.[9] reported slightly higher mortality rates, 33%, among their case series of six renal transplant recipients with COVID-19 infection. The authors underlined the development of AKI for poor prognosis in these patients. Some other studies reported significantly higher mortality rates. Abolghasemi et al.[11] reported a mortality rate of 41.6% in their case series which is, including 24 renal transplant recipients with COVID-19. When the ultimate endpoint was considered, the mortality in this patient group, basal characteristics, and treatment strategies play a significant role in the outcomes. We found that increased age, cardiovascular comorbidities, and diabetes are critical basal characteristics associated with poor prognosis. A similar high-risk pattern is also observed in the general population, and older age, hypertension, chronic respiratory disorders, and cardiovascular diseases were reported as significant risk factors. Nevertheless, particularly the increased age among kidney transplant recipients should not be confused with its definition in the general population. The mean age of patients who died in our study was approximately 55 years, which is considered low-risk in the general population. Thus, a proactive approach should be taken in this patient group, which may include early initiation of therapy or hospital admission for more intense follow-up and treatment to prevent further complications.

The AKI was developed in 34% (n = 19) of our cases. Reduced renal perfusion, multiorgan failure, and cytokine storm are the causes of AKI in COVID-19 patients. The accumulated evidence on the progression of AKI showed that angiotensin-converting enzyme 2 (ACE2) is responsible for virus entrance and increases susceptibility to infection in target cells, mainly the brush border of proximal tubular cells and the podocytes.[12] Moreover, studies showed that the kidney is a specific target of COVID-19 infection.[13] However, low AKI rates, such as 3%–9%, were reported among COVID-19 patients in the general population.[14] The significantly higher rates among kidney transplant recipients with COVID-19 should signal physicians that these patients are at a very high risk of developing AKI, which may proceed to death. In our study, graft failure occurred in two of these patients who developed AKI. One of these patients died and the other one returned to hemodialysis. Of 11 (57%) patients who developed AKI needed mechanical ventilation and 12 (63%) of our

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patients who developed AKI died. Several previous studies also reported the high AKI rates among COVID-19 patients with renal transplants. In one of those, Banerjee et al.[15] reported an AKI rate of 57%, which is also higher than our results. In another study by Nair et al.,[16] 50% of renal transplant recipients with COVID-19 infection were reported to develop AKI, which is also higher than our results. A total of 26 (46%) of 56 patients had respiratory symptoms but 12 of these patients needed mechanical ventilation. All of the patients who needed mechanical ventilation died. We can also report that AKI and requiring mechanical ventilation are associated with higher mortality. As these figures suggest, these patients should be closely monitored for the development of AKI, which is closely associated with poor prognosis.

The general treatment strategy in our study was accordant with the literature data. Accordingly, we stopped the antimetabolites, increased steroids, administered antivirals, hydroxychloroquine, and tocilizumab in suitable cases. In our study, therapeutic management included antimetabolite withdrawal and prednisolone increase in 40 (71%), calcineurin inhibitor withdrawal in 5 (8.9%), decrease in 33 (58.9%), hydroxychloroquine in 10 (17.8%), tocilizumab in 2 (3.5%), and favipiravir in 38 (67.8%) patients; 3 (5.3%) of these patients who had favipiravir also had remdesivir.

It is known that inflammatory cytokines induce the rapid progression of COVID-19 pneumonia. Therefore, glucocorticoids are seen to be a therapeutic agent for these patients. A study by Wu et al.[17] showed that treatment with methylprednisolone decreased the fatality risk of COVID-19 patients. But in another study, a meta-analysis of 21 350 patients with COVID-19, it is reported that mortality was greater among patients who were receiving corticosteroids than those there were not.[18] On the contrary, Fernández-Cruz et al.[19] reported that the mortality rate was lower in patients with ARDS or hyperinflammatory syndrome who were treated with methylprednisolone. Conversely, a study from Wuhan by Yuan et al.[20] demonstrated that patients with nonsevere COVID-19, who were treated with corticosteroids were associated with a higher risk of progression of the disease and prolonged hospital stay. All of our renal transplant recipients were receiving glucocorticoids and 40 (71%) patients' glucocorticoid dosages were increased during therapy.

Hydroxychloroquine is also proposed to control the cytokine storm in COVID-19 patients.[21] Inhibition of phospholipase A2, inhibition of toll-like receptor signals, T- and B-cell receptors, and decreasing interleukin (IL)-1 and IL-6 are some of its effects to decrease the inflammatory response.[22] Gautret et al.[23] reported that hydroxychloroquine treatment is significantly associated with viral load reduction in COVID-19 patients. Meo et al.[24] also reviewed in vitro and in vivo studies, clinical trials, and consensus reports that were conducted to evaluate the antiviral activities of chloroquine and hydroxychloroquine and, they reported that these drugs are effective in the treatment of COVID-19. A total of 10 (17.8%) of our patients received hydroxychloroquine and we also saw that it was effective to decrease the inflammatory response.

Immunosuppression seems to be effective for protecting the lungs from cytokine storms by reducing the inflammatory response.[25] But it is known that the mortality rate is higher in patients who are receiving immunosuppressive drugs. So calcineurin inhibitor and antimetabolite withdrawal or dose decreasing are recommended for COVID-19 patients.

Favipiravir is a RNA polymerase inhibitör and it blocks viral RNA synthesis. It is shown that favipiravir reduces viral load and provides an improvement in clinical and radiological outcomes of COVID-19 patients.[26] In another study that compared the effectiveness of favipiravir and lopinavir/ritonavir on disease progression and viral clearance, it was reported that favipiravir was more effective than the others.[27] A total of 38 (67.8%) patients received favipiravir. Favipiravir was effective in 35 of these patients, but three of the patients also received remdesivir because of the progression of the disease.

Remdesivir is a phosphoramidite prodrug of adenosine C-nucleoside and it has been found to inhibit the replication of SARS-CoV-2 in human lung cells.[28] A trial of intravenous remdesivir in COVID-19 patients documented faster recovery time (11 vs. 15 days) and reduced mortality by 14 days.[29] In another study, Wang et al.[30] reported that patients who received remdesivir had a shorter recovery time compared to those who received placebo. In our study, three (5.3%) of the patients received remdesivir after favipiravir because of the inadequate recovery with favipiravir and after remdesivir administration, they had faster recovery.

The treatment approaches were similar in previous studies, including stopping the immunosuppressive treatment and using steroids for antirejection and administering antivirals to stimulate the specific antiviral immune response.[31] However, there is no single or standard treatment for all, and a therapeutic approach should be tailored to specific clinical conditions of the patients.[32]

This study is not without limitations. First, the median follow-up was relatively short and limited to report the long-term outcomes of COVID-19 in renal transplant recipients. Second, the sample size was limited to conduct multivariable analyses for identifying the independent prognostic factors in this clinical entity. Third, the changes in the genomic pattern of the SARS-CoV-2 were not considered during assessments, but the clinical outcomes might be affected by the new mutated virus strains. However, we believe that these limitations do not deescalate the value of our results. To the best of our knowledge, the number of patients included in our study is one of the highest reported in a study in the literature. Moreover, a similar approach administered to this high number of patients made our results more robust on this topic.

5 | CONCLUSION

To conclude, COVID-19 infection in renal transplant recipients significantly increases the risk of poor outcomes. Early hospitalization, close monitoring, and aggressive treatments may be employed to prevent excess mortality and morbidity in these patients. Since AKI and respiratory failure emerge as the precipitators of mortality, further clinical interventions should be evaluated for their long-term efficacy.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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REFERENCES

1. World Health Organization WHO Coronavirus (COVID-19) Dashboard. 2021. https://covid19.who.int/. Accessed August 13, 2021.
2. Johns Hopkins University COVID-19 Dashboard. 2021. https://coronavirus.jhu.edu/map.html. Accessed August 13, 2021.
3. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis*. 2020;94:91-95.
4. Qiao J. What are the risks of COVID-19 infection in pregnant women? *Lancet*. 2020;395(10226):760-762.
5. Aleebrahim-Dehkordi E, Reyhanian A, Saberianpour S, Hasanpour-Dehkordi A. Acute kidney injury in COVID-19; a review on current knowledge. *J Nephropathol*. 2020;9(4):e31.
6. 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;97(6):1083-1088.
7. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*. 2020;323(20):2052-2059. https://doi.org/10.1001/jama.2020.6775
8. Vishnevetsky A, Levy M. Rethinking high-risk groups in COVID-19. *Mult Scler Relat Disord*. 2020;42:102139.
9. Rahimzadeh H, Keykhaei M, Razeghi E, Zivari E, Mansouri ES. COVID-19 progression in kidney transplant recipients: a single-center case series. *CEN Case Rep*. 2021;10:1-6.
10. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382(25):2475-2477.
11. Abolghasemi S, Mardani M, Sali S, Honarvar N, Baziboroun M. COVID-19 and kidney transplant recipients. *Transpl Infect Dis*. 2020;22, 13413(6):e13413.
12. Ye M, Wysocki J, William J, Soler MJ, Cokic I, Batlle D. Glomerular localization and expression of angiotensin-converting enzyme 2 and angiotensin-converting enzyme: implications for albuminuria in diabetes. *J Am Soc Nephrol*. 2006;17(11):3067-3075.
13. Diao B, Feng Z, Wang C, et al. Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. *Nat Commun*. 2021;12(1):2506. https://doi.org/10.1038/s41467-021-22781-1
14. Cheng Y, Luo R, Wang K, et al. Kidney impairment is associated with in-hospital death of COVID-19 patients. *Kidney Int*. 2020;97(5):829-838. https://doi.org/10.1101/1016/j.kint.2020.03.005
15. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. *Kidney Int*. 2020;97(6):1076-1082.
16. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant*. 2020;20(7):1819-1825.
17. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med*. 2020, 180, 934-943. https://doi.org/10.1001/jamainternmed.2020.0994
18. Cano EJ, Fuentes XF, Campioli CC, et al. Impact of corticosteroids in COVID-19 outcomes: systematic review and meta-analysis. *Chest*. 2020;159(3):P1019-P1040. https://doi.org/10.1016/j.chest.2020.10.054
19. Fernández-Cruz A, Ruiz-Antorán B, Muñoz-Gómez A, et al. Impact of glucocorticoid treatment in SARS-CoV-2 infection mortality: a retrospective controlled cohort study. *Antimicrob Agents Chemother*. 2020;64:e01168-20. https://doi.org/10.1128/AAC.01168-20
20. Yuan M, Xu X, Xia D, et al. Effects of corticosteroid treatment for non-severe COVID-19 pneumonia: a propensity score-based analysis. *Shock*. 2020, 54, 638-643. https://doi.org/10.1097/SHK.0000000000001574
21. Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin Infect Dis*. 2020, 71, 732-739. https://doi.org/10.1093/cid/ciaa237
22. Löffler BM, Hesse B, Bohn E, et al. Effects of antimalarial drugs on phospholipase A and lysophospholipase activities in plasma membrane, mitochondrial, microsomal and cytosolic subcellular fractions of rat liver. *Biochim Biophys Acta*. 1985;835:448-455. https://doi.org/10.1016/0005-2760(85)90114-6
23. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020;56(1):105949. https://doi.org/10.1016/j.ijantimicag.2020.105949
24. Meo SA, Klonoff DC, Akram J. Efficacy of chloroquine and hydroxychloroquine in the treatment of COVID-19. *Eur Rev Med Pharmacol Sci*. 2020;24(8):4539-4547. https://doi.org/10.26355/eurrev.2020.0421038
25. Fishman JA, Grossi PA. Novel coronavirus-19 (COVID-19) in the immunocompromised transplant recipient: #Flatteningthecurve. *Am J Transplant*. 2020, 20, 1765-1767. https://doi.org/10.1111/ajt.15890
26. Chen C, Zhang Y, Huang J, Yin P, Cheng Z, Wu J. Favipiravir versus arbidol for COVID-19: a randomized clinical trial. *medRxiv*. 2020. https://doi.org/10.1101/2020.03.17.20037432
27. Cai Q, Yang M, Liu D, et al. Experimental treatment with favipiravir for COVID-19: an open-label control study. *Engineering*. 2020;6:1192-1198. https://10.1016/jeng.2020.03.007
28. Pruijssers AJ, George AS, Schäfer A, et al. Remdesivir inhibits SARS-CoV-2 in human lung cells and chimeric SARS-CoV expressing the SARS-CoV-2 RNA polymerase in mice. *Cell Rep*. 2020;32(3):107940. https://doi.org/10.1016/j.celrep.2020.107940
29. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 final report. *N Engl J Med. 2020*, 383(19):1813-1826. https://doi.org/10.1056/NEJMoa2007764
30. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2020;395(10236):1569-1578. (published correction appears in Lancet. 2020 May 30;395(10238):1694). https://doi.org/10.1016/S0140-6736(20)31022-9
31. Gandolfini I, Delsante M, Fiaccadori E, et al. COVID-19 in kidney transplant recipients. *Am J Transplant*. 2020;20(7):1941-1943.
32. Machado DJB, Ianhez LE. COVID-19 pneumonia in kidney transplant recipients—where we are? *Transpl Infect Dis*. 2020;22, 13306(5):e13306.

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