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Original Article

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COVID-19 in Kidney Transplant Recipients: A Single-Center Experience

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ABSTRACT

Objective: The body of literature regarding coronavirus disease 2019 infection in kidney transplant recipients is growing every day but is mostly comprised of case reports, small case series, and small cohorts. The aim of the current study was to describe our experiences with coronavirus disease 2019-positive kidney transplant recipients to reduce the difficulties that these patients face with coronavirus disease 2019.

Methods: This retrospective cohort study included 54 kidney transplant recipients diagnosed with coronavirus disease 2019, between April 1, 2020, and February 1, 2021, from our Kidney Transplant Center. The participants were followed up for a period of at least 30 days or until death.

Results: Of the 54 patients, 36 (66.66%) were followed up as outpatients and 18 (33.33%) were hospitalized, of which 13 (24.07%) were followed up in the service and 5 (9.26%) needed intensive care. All 5 patients (9.26%) in need of intensive care died and the remaining 49 (90.74%) recovered from coronavirus disease 2019 infection. None of the patients developed graft loss during follow-up.

Conclusion: The results indicated that the neutrophil-to-lymphocyte ratio and lactate dehydrogenase-to-lymphocyte ratio can be used to support the diagnosis and determine prognosis in kidney transplant recipients with suspected coronavirus disease 2019. In both the group comparisons and univariate logistic regression analyses, smoking was seen to be a significant risk factor for the development of pneumonia and mortality due to coronavirus disease 2019. Therefore, all patients must be strongly reminded and encouraged to stop smoking.

Keywords: COVID-19, SARS-CoV-2, pneumonia, infection, kidney transplant

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INTRODUCTION

The Center for Disease Control and Prevention has designated kidney transplant (KTx) recipients as a high-risk group for severe coronavirus disease 2019 (COVID-19).[1] Emerging research suggests that transplanted patients have a 10-fold greater likelihood of early case fatality than the general population,[2,3] due to their immunocompromised status, which impairs their immune response to infections, and the almost ubiquitous occurrence of comorbidities.[4-6]

Fever, respiratory symptoms, contact history, characteristic chest radiography, and biochemical results are used to diagnose COVID-19.[7,8] Coronavirus disease 2019 is confirmed by positive reverse transcription-polymerase chain reaction (RT-PCR) results in oral and nasopharyngeal swabs.[9] Coronavirus disease 2019 is associated with lymphopenia, elevated inflammatory markers, prothrombin time, lactate dehydrogenase (LDH), and creatine phosphokinase. In COVID-19 patients, acute kidney damage is linked to an elevated

risk of morbidity and mortality.[7,8] The most common symptom of the illness is pneumonia, which is marked by infiltrates in the lungs. Cytokine storms can also induce organ failure, which can lead to death.[10,11]

The risk, presentation, and consequences of COVID-19 in KTx patients are yet unknown. The collection of knowledge about COVID-19 infection in KTx recipients is increasing all the time, but it comprises primarily case reports, short case series, and small cohorts. When COVID-19 is detected in a KTx patient, it is important to treat the infection as well as regulate the immunosuppression and provide supportive care. Patients with COVID-19 have their own treatment regimens developed by local transplant facilities; however, there is no consensus on this problem to date.[10] The aim of this study was to investigate the clinical and laboratory parameters for severe COVID-19 infection in KTx patients to be able to reduce the difficulties that KTx recipients face with this disease.

METHODS

Study Population and Design

The Non-invasive Clinical Research Ethics Committee at Pamukkale University Faculty of Medicine granted the study approval (Decision No: 2021/04, dated: February 16, 2021). The study included KTx recipients followed up by our transplant center, who were diagnosed with COVID-19 infection, between April 1, 2020, and February 1, 2021. Patients were excluded from the study if they did not have typical findings (n = 1) and/or who were <18 years of age and/or were lost to follow-up after diagnosis of COVID-19 (n = 3). The remaining 54 KTx recipients diagnosed as COVID-19 positive were followed up for a period of at least 30 days or until death. Of the patients, 14 were transplanted from cadavers and 40 were from living donors. The living donors comprised 12 spouses, 11 mothers, 10 fathers, 3 brothers, 2 sisters, 1 son, and 1 paternal grandmother.

MAIN POINTS

- It should be considered that kidney transplant (KTx) recipients have a higher risk of morbidity and mortality compared to the normal population.
- Especially patients with elevated creatinine, blood urea nitrogen, lactate dehydrogenase, and neutrophil-to-lymphocyte ratio have high morbidity and mortality rates. Therefore, these patients should be followed more closely.
- In this study, 5 out of 6 patients using mammalian target of rapamycin (mTOR) developed pneumonia due to coronavirus disease 2019 (COVID-19) and 2 of them are dead. Consequently, a more thorough assessment of KTx recipients employing mTOR is recommended.
- The donor types of 14 patients with COVID-19 were cadavers. Coronavirus disease 2019 caused pneumonia in 11 of the 14 patients, with 3 of them dying. For this reason, it is important to remember that cadaveric kidney transplant recipients may have a worse outcome if they contract COVID-19.
- The history of smoking and amount of smoking pack-years directly increase the risk of developing pneumonia due to COVID-19 and the risk of mortality. As a result, all patients should be reminded and encouraged to quit smoking.

The diagnosis of COVID-19 infection in the patients was made with the positivity of the combined nasal and oropharyngeal swab samples taken for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ribonucleic acid (RNA) with RT-PCR test and/or thorax computed tomography (CT) results, which contained typical findings for COVID-19. The grouping of patients diagnosed with COVID-19 was made according to national guidelines: patients with symptoms such as fever, muscle/joint pain, cough, sore throat, without respiratory distress (respiratory rate < 24, SpO_2 > 93% in room air) and normal chest x-ray and/or thorax CT were accepted as without pneumonia (uncomplicated patient) (n = 32), and patients with symptoms such as fever, muscle/joint pain, cough, sore throat, with respiratory rate ≥24/min, SpO_2 level ≤93% in room air, and findings of pneumonia on chest x-ray and/or thorax CT were included in the pneumonia group (n = 22).[12]

Data Collection

From computerized medical records and telephone calls with patients, demographic and clinical data, comorbidities, laboratory and radiographic results, data on antiviral and anti-cytokine treatments, and immunosuppressive management were retrieved. Samples taken at the time of diagnosis were used for biochemical tests.

Adjustment of Immunosuppressive Regimen and Antiviral Therapy

Immunosuppression and antiviral treatment were managed according to a conventional regimen. Favipiravir was given to all of the patients (1600 mg BID for the first day, and then 600 mg BID for 4 days, orally). In the presence of a confirmed or suspected invasive bacterial infection, antibiotic therapy was delivered depending on the infection specialist's judgment.

In all of the cases, antimetabolites (mycophenolate derivatives and azathioprine) were stopped. Early on, steroid doses were increased to a stress level, then reduced to a maintenance level. The levels of calcineurin and mammalian target of rapamycin (mTOR) were not modified, and medication levels were tested twice a week to maintain stability.

Anticoagulation, Antiaggregant, and Oxygen Treatment

Unless there were contraindications, all of the hospitalized patients received low-molecular-weight heparin. The doses were adjusted based on the patients' risk of bleeding and coagulation. Outpatients were advised to take low-dose acetylsalicylic (81 or 100 mg) for 3 months if there were no contraindications. With a nasal cannula, oxygen was administered to patients with an oxygen saturation ≤93% or a mask with a reservoir if the nasal cannula was not sufficient. After non-invasive

ventilation, if respiratory failure persisted despite these therapies, mechanical ventilation was used.

Compliance with Ethical Standards

To the best of our knowledge, all of the study procedures involving human subjects were conducted in line with institutional and/or national ethical standards, the 1964 Helsinki Declaration and its subsequent revisions, or comparable ethical standards. The study was started after the approval of the Non-invasive Clinical Research Ethics Committee. Each individual participant in the study gave their informed consent.

Statistical Analysis

All of the statistical analyses were performed using IBM Statistical Package for Social Sciences Statistics for Windows 25.0 (IBM SPSS Statistics, Armonk, NY, USA). Continuous variables were expressed as the mean ± standard deviation (SD), and categorical variables were expressed as the number (n) and percentage (%). The Shapiro–Wilk test was used to determine the conformity of the data to normal distribution. For the comparisons of independent groups, the independent samples *t*-test was applied when parametric test assumptions were provided; otherwise, the Mann–Whitney *U* test was used. Univariate logistic regression analysis models determined which variables affected the presence of pneumonia and mortality. Differences between categorical variables were analyzed with chi-square analysis. $P < .05$ was accepted as statistically significant.

RESULTS

Demographic and Clinical Characteristics

A retrospective review was made of 54 patients (18 female, 33.33%) over a follow-up period of 30 days after being diagnosed with COVID-19. Of these, 32 patients (59.26%) survived the disease without pneumonia (uncomplicated patients) and 22 patients (40.74%) developed pneumonia, of which 17 (31.48%) recovered and 5 (9.26%) died (Figure 1). The demographic characteristics and immunosuppression regimens of the patients according to their groups are shown in Table 1. The mean age of the group with pneumonia was higher than that of the group without pneumonia ($P = .05$). Male gender was observed to be a risk factor for the development of pneumonia ($P = .011$). In terms of donor type, it was observed that the number of patients who received a kidney from a living donor was significantly higher in the group without pneumonia ($P = .001$). The post-transplant follow-up period and chronic kidney disease (CKD) etiology were not determined to have any effect on the development of pneumonia ($P > .05$). Comorbid diseases other than chronic obstructive pulmonary disease had no effect on the development of pneumonia. Smoking was determined to be a risk factor for the development of pneumonia ($P = .021$). It was observed that drug treatments other than mTOR inhibitors had no effect on the development of pneumonia ($P > .05$).

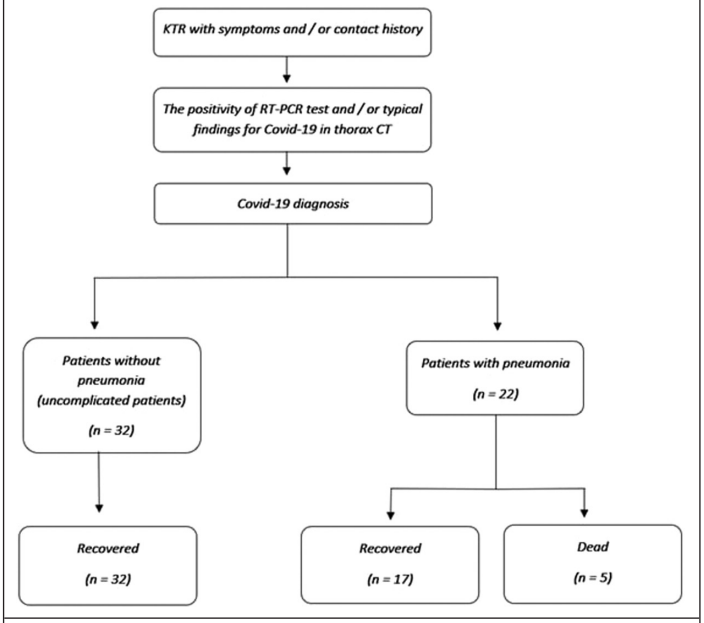

Figure 1. Flowchart of the patients in the study. COVID-19, coronavirus disease 2019; CT, computed tomography; KTR, kidney transplant recipient; RT-PCR, reverse transcription-polymerase chain reaction.

Clinical Characteristics and Laboratory Results

The clinical characteristics and laboratory results of the patients according to their groups are shown in Table 2. It was stated by the patients that the most common source of COVID-19 infection was the family–home environment (n = 35, 64.81%) and social life (n = 11, 20.37%). Myalgia (n = 41, 75.93%), loss of taste and smell (n = 29, 53.7%), fever (n = 26, 48.15%), and cough (n = 25, 46.3%) were the most frequent symptoms in all of the patients. According to the laboratory tests, no significant difference was found between the groups in terms of hemoglobin, platelet, white blood cell, and neutrophil (Neu) values ($P > .05$). Creatinine, blood urea nitrogen (BUN), ferritin, LDH, aspartate aminotransferase, C-reactive protein (CRP), neutr ophil-to-lymphocyte ratio (NLR), and lactate dehydrogenase-t o-lymphocyte ratio (LDH/lymph) were significantly higher in the group with pneumonia ($P < .05$). Chronic kidney disease epidemiology collaboration (CKD-EPI), albumin, and lymphocyte values were significantly higher in the group without pneumonia ($P < .05$).

Outcomes

Of the 54 patients, 36 (66.66%) were followed up as outpatients and 18 (33.33%) were hospitalized, of which 13 (24.07%) were followed up in the service and 5 (9.26%) needed intensive care. All 5 patients (9.26%) in need of intensive care died, and the remaining 49 patients (90.74%) recovered (Table 2). According to the univariate logistic regression analyses, smoking pack-years, male gender, creatinine, BUN, LDH, Neu/lymph, and CRP were significant risk factors for COVID-19 pneumonia, and age and ferritin were found to be borderline significant risk factors. In the univariate logistic regression analysis, living donor,

Table 1. Patients' Demographic Characteristics and Immunosuppression Regimen

	All Patients (n = 54)	Patients Without Pneumonia (n = 32; Group 1)	Patients With Pneumonia (n = 22; Group 2)	*P* (Groups 1 and 2)
Age (mean ± SD, years)	46.09 ± 11.68	43.53 ± 11.98	49.82 ± 10.39	.050
Sex (n, %)				
Female/male	18 (33.33)/36 (66.67)	15 (46.88)/17 (53.13)	3 (13.64)/19 (86.36)	.011
Post-transplant follow-up, months [median (Q1–Q3)]	80.87 ± 50.99 [71.5 (5-188)]	79.13 ± 54.89 [72 (5-177)]	83.41 ± 45.86 [69 (28-188)]	.616
Type of donor (n, %)				
Living	40 (74.07)	29 (90.63)	11 (50)	.001
Deceased	14 (25.93)	3 (9.38)	11 (50)	.001
Etiology of CKD (n, %)				
Hypertensive nephrosclerosis	11 (20.4)	7 (21.9)	4 (18.2)	
Diabetic nephropathy	5 (9.3)	1 (3.1)	4 (18.2)	
Primary glomerular disease	8 (14.8)	6 (18.8)	2 (9.1)	.285
Other	18 (33.3)	12 (37.5)	6 (27.3)	
Unknown	12 (22.2)	6 (18.8)	6 (27.3)	
Comorbidities (n, %)				
Diabetes mellitus	10 (18.52)	4 (12.5)	6 (27.27)	.285
Hypertension	31 (57.41)	18 (56.25)	13 (59.09)	.836
Ischemic heart disease	6 (11.11)	2 (6.25)	4 (18.18)	.211
Heart failure	3 (5.56)	1 (3.13)	2 (9.09)	.560
COPD	4 (7.41)	0 (0)	4 (18.18)	.023
Cancer	2 (3.7)	1 (3.13)	1 (4.55)	1
Chronic liver disease	1 (1.85)	0 (0)	1 (4.55)	.407
Smoking				
Never smoked (*n*, %)	38 (70.37)	27 (84.38)	11 (50)	
Former smoker (*n*, %)	14 (25.93)	4 (12.5)	10 (45.45)	.021
Current smoker (*n*, %)	2 (3.7)	1 (3.13)	1 (4.55)	
Smoking pack-years	5.96 ± 16.66	1.25 ± 3.98	12.82 ± 24.38	.003
Medications (*n*, %)				
ACEIs, ARBs	17 (31.48)	10 (31.25)	7 (31.82)	.965
Other antihypertensives	28 (51.85)	15 (46.88)	13 (59.09)	.377
Insulin	11 (20.37)	5 (15.63)	6 (27.27)	.324
Oral antidiabetics	5 (9.26)	3 (9.38)	2 (9.09)	1
Statins	15 (27.78)	8 (25)	7 (31.82)	.583
Antiaggregant or anticoagulants	24 (44.44)	11 (34.38)	13 (59.09)	.073
Maintenance immunosuppression at admission (n, %)				
Tacrolimus	49 (90.74)	30 (93.75)	19 (86.36)	.388
Cyclosporine A	2 (3.7)	1 (3.13)	1 (4.55)	1
mTOR inhibitors	6 (11.11)	1 (3.13)	5 (22.73)	.020
Mycophenolate derivatives	51 (94.44)	32 (100)	19 (86.36)	.062
Steroids	53 (98.15)	31 (96.88)	22 (100)	1

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; mTOR, mammalian target of rapamycin; SD, standard deviation.
**P*-value of <.05 was considered statistically significant.

Table 2. Patients' Clinical Characteristics and Laboratory Results

	All Patients (n = 54)	Patients Without Pneumonia (n = 32; Group 1)	Patients With Pneumonia (n = 22; Group 2)	*P* (Groups 1 and 2)
Possible source of COVID-19 (n, %)				
Family–home environment	35 (64.81)	20 (62.5)	15 (68.18)	.667
Workplace/nursing home, etc.	6 (11.11)	2 (6.25)	4 (18.18)	.211
Social life	11 (20.37)	9 (28.13)	2 (9.09)	.167
Healthcare center	2 (3.7)	1 (3.13)	1 (4.55)	1
COVID-19-related clinic presentation at the time of diagnosis (n, %)				
Mild–moderate disease	45 (83.33)	32 (100)	13 (59.09)	.0001
Severe–critical disease	9 (16.67)	0 (0)	9 (40.91)	.0001
Positive nasopharyngeal swab RT-PCR	51 (94.44)	32 (100)	19 (86.36)	.062
Presentation symptoms (n, %)				
Fever	26 (48.15)	10 (31.25)	16 (72.73)	.003
Cough	25 (46.3)	9 (28.13)	16 (72.73)	.001
Dyspnea	10 (18.52)	1 (3.13)	9 (40.91)	.001
Diarrhea	3 (5.56)	2 (6.25)	1 (4.55)	1
Headache	19 (35.19)	15 (46.88)	4 (18.18)	.03
Myalgia	41 (75.93)	26 (81.25)	15 (68.18)	.27
Loss of taste–smell	29 (53.7)	17 (53.13)	12 (54.55)	.918
Laboratory results at admission				
Creatinine (mg/dL)	1.87 ± 1.13	1.45 ± 0.59	2.48 ± 1.43	.002
BUN (mg/dL)	29.04 ± 22.31	21.19 ± 11.07	40.45 ± 29.08	.005
CKD-EPI (mL/min)	52.69 ± 23.56	59.06 ± 19.87	43.41 ± 25.8	.015
Albumin (g/dL)	41.31 ± 5.09	42.84 ± 3.56	39.1 ± 6.17	.016
Ferritin (mg/L)	414.26 ± 452.16	312.83 ± 399.08	561.78 ± 492.34	.008
LDH (U/L)	259.96 ± 138.44	207.13 ± 81.11	336.82 ± 167.99	.0001
AST (U/L)	23.48 ± 29.06	17.16 ± 7.48	32.68 ± 43.58	.015
CRP (mg/L)	53.47 ± 74	20.92 ± 37.59	100.81 ± 88.17	.0001
HB (g/dL)	12.8 ± 2.62	12.63 ± 3.15	13.06 ± 1.6	.798
PLT ($\times 10^3$/μL)	246.44 ± 105.71	260 ± 110.16	226.73 ± 97.99	.105
WBC (/μL)	9020.19 ± 4936.18	8356.88 ± 2693.06	9985 ± 7010.2	.923
Neutrophil (/μL)	6325.19 ± 4064.01	5383.75 ± 2399.98	7694.55 ± 5464.98	.231
Lymphocyte (/μL)	1795.93 ± 1472.61	2172.5 ± 928.61	1248.18 ± 1915.66	.0001
Neu/Lymph	6.77 ± 9.55	3.23 ± 3.04	11.93 ± 13.01	.0001
LDH/Lymph	0.34 ± 0.7	0.12 ± 0.09	0.66 ± 1.01	.0001
The course of the disease (n, %)				
Followed by ambulatory	36 (66.66)	32 (100)	4 (18.18)	.0001
Hospitalization	18 (33.33)	0 (0)	18 (81.82)	.0001
Service	13 (24.07)	0 (0)	13 (59.09)	.0001
Intensive care	5 (9.26)	0 (0)	5 (22.73)	.008
Cure	49 (90.74)	32 (100)	17 (77.27)	.011
Dead	5 (9.26)	0 (0)	5 (22.73)	.008

AST, aspartate aminotransferase; BUN, blood urea nitrogen; CKD-EPI, chronic kidney disease epidemiology collaboration; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase; Neu, Neu/Lymph, neutrophil-to-lymphocyte ratio; PLT, platelet; RT-PCR, reverse transcription-polymerase chain reaction; WBC, white blood cell.

Table 3. Logistic Regression Analysis of Pneumonia Risk Factors for Kidney Transplant Recipients

	Univariate Analysis		
	Odds Ratio	**CI**	***P***
Age	1.051	0.999-1.106	.056
Male sex	5.588	1.376-22.700	.016
Living donor	0.103	0.024-0.442	.002
Smoking pack-years	1.126	1.006-1.259	.039
Creatinine (mg/dL)	2.966	1.374-6.400	.006
BUN (mg/dL)	1.057	1.013-1.102	.010
CKD-EPI (mL/min)	0.970	0.945-0.995	.020
Albumin (g/dL)	0.850	0.748-0.965	.012
Ferritin (mg/L)	1.001	1.000-1003	.059
LDH (U/L)	1.012	1.004-1.021	.002
CRP (mg/L)	1.026	1.011-1.041	.001
Neu/Lymph	1.329	1.068-1.652	.011

BUN, blood urea nitrogen; CKD, EPI chronic kidney disease epidemiology collaboration; CRP, c-reactive protein; LDH, lactate dehydrogenase; Neu/Lymph, neutrophil-to-lymphocyte ratio.
**P*-value of <.05 was considered statistically significant.

CKD-EPI, and albumin were found to be protective factors against COVID-19 pneumonia (Table 3). In the univariate logistic regression analysis performed in terms of mortality due to COVID-19, smoking pack-years, creatinine, BUN, LDH, and Neu/lymph were found to be significant risk factors (Table 4).

DISCUSSION

Coronavirus disease 2019 has affected the whole world, and this retrospective study presented a single-center experience of the course of COVID-19 infection in KTx recipients, who constitute a special group. The study included 54 KTx recipients, followed up in our center, who were diagnosed with COVID-19 infection, between April 1, 2020, and February 1, 2021. Of the 54 patients, 32 (59.25%) survived the disease without pneumonia (uncomplicated patients) treated as outpatients, 22 patients (40.74%) developed pneumonia, of which 17 (31.48%) recovered and 5 (9.26%) died (Figure 1). The case fatality rate thus far has ranged widely from 1% to 7.2% in the general population.[13,14] In a multicenter study conducted on KTx recipients in Istanbul, the mortality rate was found to be 12.5%.[10] In the current study, 5 of 54 patients died, giving a mortality rate of 9.26%. Anti-cytokine, pulse steroid, and plasmapheresis treatments were not used on any of the 54 KTx patients with COVID-19 infection.

Table 4. Logistic Regression Analysis of Mortality Risk Factors for Kidney Transplant Recipients

	Univariate Analysis		
	Odds Ratio	**CI**	***P***
Smoking pack-years	1.061	1.004-1.120	.034
Creatinine (mg/dL)	1.927	1.009-3.682	.047
BUN (mg/dL)	1.037	1.004-1.071	.026
LDH (U/L)	1.008	1.001-1.016	.027
Neu/Lymph	1.103	1.024-1.188	.01

BUN, blood urea nitrogen; LDH, lactate dehydrogenase; Neu/Lymph, neutrophil-to-lymphocyte ratio.
**P*-value of <.05 was considered statistically significant.

Similar to the series reported by Demir et al, the average age of the current study patients was 46 years. In the same study, the frequencies of hypertension and diabetes mellitus were 65% and 5%, respectively,[10] and in the current study, these frequencies were 57.41% and 18.52%, respectively. There was no significant difference between the groups with and without pneumonia in terms of post-transplant follow-up time, etiology of CKD, medications, or maintenance immunosuppression at admission, except for mTOR inhibitors (Table 1). The use of mTOR inhibitors was found to be significantly higher in the group with pneumonia (*P* = .02). Shi et al[15] demonstrated that mTOR inhibitors boost the first step of the SARS-CoV-2 infection cycle, cell entrance, by causing the degradation of antiviral proteins that defend against virus invasion. This could make COVID-19 infection worse in KTx patients who are currently on immunosuppressive drugs. When the patients were compared according to the donor type, there was a significantly higher rate of living donor types in the group without pneumonia (*P* = .001). This suggested that lower induction therapy and lower cumulative immunosuppression therapy may be effective in reducing pneumonia and mortality.

In the assessment made in terms of the possible source of COVID-19, it was observed that the family–home environment was reported at 64.81%, social life at 20.37%, workplace/nursing home at 11.11%, and healthcare centers at 3.7%. These results suggested that patients consider their relatives and friends to be disease-free and compromise personal protective measures. Of course, more frequent contact with these people when compared to the other situations may also have been effective in the occurrence of these results. When the symptoms on presentation were questioned, the most common was myalgia in 75.93% of patients, followed by loss of taste and smell in 53.7%, fever in 48.15%, and cough in 46.3% of patients. These results demonstrated that myalgia and loss of taste and smell are complaints which are just as important as fever, cough, and shortness of breath.

There have also been studies published on the biology of COVID-19 infection and clinical management of the disease, with some demonstrating that differences in COVID-19 disease prevalence and severity are associated with male gender, and smoking is linked to a higher expression of angiotensin-converting enzyme 2 (ACE2; the receptor for SARS-CoV-2); thus,

that could also be a factor.[16] The expression of ACE2 was discovered to be more prevalent in Asian men in a prior study utilizing single-cell sequencing, which could explain why COVID-19 is more common in this subset of patients than in women and patients of other races.[17] In a study of 1099 patients with COVID-19 from 552 hospitals in 30 provinces in China, 58% of the patients were male.[18] In the current study, the rate of male patients in the group with pneumonia was 86.36%, while it was 53.13% in the group without pneumonia (Table 1). Male gender was predominant in both groups with and without pneumonia, but the difference was more pronounced in the group with pneumonia (*P* = .01). In terms of smoking, the rate of patients who had never smoked was 84.38% in the group without pneumonia, while it was 50% in the group with pneumonia (*P* = .021). A significant increase was found in the group with pneumonia in terms of smoking pack-years (*P* = .003). Similar to previous studies, these results showed that male gender and smoking are risk factors for COVID-19 infection.

According to the univariate logistic regression analyses, smoking pack-years, male gender, creatinine, BUN, LDH, NLR, and CRP were significant risk factors for COVID-19 pneumonia, and age and ferritin were found to be borderline significant risk factors. It was observed in the univariate logistic regression analysis that living donor, CKD-EPI, and albumin were protective factors against COVID-19 pneumonia (Table 3). In the univariate logistic regression analysis performed in terms of mortality due to COVID-19, smoking pack-years, creatinine, BUN, LDH, and NLR were found to be significant risk factors (Table 4). In a group of 452 hospitalized patients, Qin et al[19] discovered a significantly greater NLR in individuals with severe forms of COVID-19. A greater NLR upon hospital admission was related to a more severe result in research by Ciccullo et al.[20] and an NLR of >4 was a predictor of admission to the intensive care unit. Similarly, in the current study, the NLR in the group with pneumonia (mean 11.93) was found to be significantly higher than that of the group without pneumonia (mean 3.23) (*P* = .0001). Serin et al[21] looked at LDH/lymph in terms of diagnosis and death, using specific CT involvement as the gold standard approach, which was shown to be more sensitive due to PCR false negativity, and found 0.06 and 0.21 as cut-off values for diagnosis and mortality, respectively. In the current study, the mean LDH/lymph value was 0.12 in the group without pneumonia and it was 0.66 in the group with pneumonia (*P* = .0001).

Even slightly symptomatic transplant recipients should have quick outpatient SARS-CoV-2 PCR testing and/or thorax CT with early hospital admission, based on our experience to date. During the COVID-19 pandemic, unfortunately, the best immunosuppressive technique is yet unknown. Protecting against graft rejection while maintaining adequate immunity to prevent overwhelming infection is the optimum technique for continuous immunosuppressive medication. Antimetabolites (mycophenolate derivatives and azathioprine) were not used in any of the instances, as per our protocol. Early on, steroid doses were increased to a stress level, then reduced to a maintenance level. The levels of calcineurin and mTOR were not modified, and medication levels were tested twice a week to maintain stability. During any patient's follow-up, no irreversible kidney injury or transplant loss was identified. Acute renal damage occurs in 21%-30% of KTx recipients, according to recent studies.[2,22] As a result, stopping all immunosuppression in patients with high immunological risk should be approached with caution because this could result in graft rejection and loss.

There were some limitations to this retrospective study. The number of patients was limited as KTx recipients are a specialized group. There was no control group and the follow-up period was short. Hence, these findings are preliminary and will need to be confirmed in large-scale prospective cohort studies with longer follow-up periods. Thus, a standard diagnosis and treatment protocol can be established for KTx recipients with COVID-19.

The results of this study showed that the mortality rates due to COVID-19 were higher in KTx recipients than those in the normal population. Therefore, it can be recommended that even mildly symptomatic KTx recipients should undergo rapid outpatient SARS-CoV-2 PCR testing and/or thorax CT with early hospital admission. The results indicated that NLR and LDH/lymph values can be used to support the diagnosis and determine prognosis in KTx recipients with suspected COVID-19. Immunosuppressive treatments and supportive treatments should be carefully regulated in this patient group. Induction therapy with lymphocyte-depleting agents should be avoided in KTx recipients during the pandemic period. In addition, both in group comparisons and in the univariate logistic regression analysis, smoking was seen to be a significant risk factor for the development of pneumonia and mortality due to COVID-19. Therefore, all patients must be strongly reminded and encouraged to stop smoking. To date, there is no antiviral or anti-cytokine therapy available for the treatment of COVID-19. However, a few vaccines are being used to try to keep the disease under control.

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Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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