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Effect of the COVID-19 Pandemic on Kidney Transplant and on Chronic Dialysis Patients

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ABSTRACT

Background. The reported fatality rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in patients receiving maintenance dialysis or kidney transplant are higher than in the general population. The aim of this study was to evaluate the impact of SARS-CoV-2 infection in chronic dialysis patients (DPs) compared with kidney transplant recipients (KTxRs).

Methods. A study evaluating 266 COVID-19-positive patients (112 DPs and 154 KTxRs) was conducted in a single center from March 1, 2020, to June 30, 2021. All patients were confirmed for COVID-19 infection by reverse transcription polymerase chain reaction or antigen test.

Results. KTxRs were younger (49 ± 12.4 vs 61 ± 14.6 years; $P < .0001$) and had significantly fewer coexisting disorders than the DPs. A higher percentage of KTxRs required hospitalization (70% vs 49.4%, $P = .002$) and intensive care unit admission (39% vs 25%, $P = .01$). The fatality rate was 24% in both groups.

Discussion. There is no consensus among studies about the higher fatality rate between KTxRs and DPs who develop COVID-19. In our study, we also did not find a different fatality rate.

Conclusion. In spite of KTxRs being younger and having fewer coexisting disorders, compared with DPs, they presented a higher hospitalization and intensive care unit necessity rate but a similar fatality rate.

COVID-19 was first reported in Wuhan, China, in December of 2019 and became a world health emergency [1]. In February 2020, the first case of COVID-19 was reported in Brazil, which then became one of the most affected countries. The country had more than 21 million confirmed cases and more than 600,000 deaths, corresponding to an overall case fatality rate of 2.8% [2]. Because of underlying chronic kidney disease associated with comorbid conditions, chronic dialysis patients (DPs) and kidney transplant recipients (KTxRs) are at high risk for COVID-19 [3]. Brazil has the world's third highest number of chronic DPs and the second highest absolute number of KTxRs worldwide, which both focus attention on COVID-19 in these Brazilian cohorts [4,5].

The long-term use of immunosuppression in KTxRs is a matter of debate, with some arguing that the immunosuppression

would predispose them to a greater risk of severe infection [6]. Others speculate that immunosuppressive therapy may be protective against the COVID-19-induced cytokine storm [7]. DPs are at high risk of COVID-19 infection because they require frequent travel to the dialysis facility using public transportation and because they have close contact with the staff and other patients within the dialysis unit [8].

The aim of the present study was to compare the outcomes of DPs and KTxRs with COVID-19.

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METHODS

Study Population

We conducted a prospective, observational, single-center study, and data were collected from registry files of 266 patients who tested positive for COVID-19, 154 KTxRs and 112 DPs, during the period from March 1, 2020, to June 30, 2021. Patients suspected with having COVID-19 were tested with real-time reverse transcription polymerase chain reaction (RT-PCR) or SARS-CoV-2 antigen test (Ag-Test) on 1380 kidney replacement therapy patients (500 DPs and 880 KTxRs) from a metropolitan region comprising 2 million inhabitants. The study protocol was approved by the institutional review board (4212395) and was performed in accordance with the Declaration of Helsinki as well as the Declaration of Istanbul 2008.

Statistical Analysis

The parametric data group comparisons were made using a *t* test or one-way analysis of variance. Group comparisons of nonparametric data were carried out using the Mann-Whitney or Kruskal-Wallis test. The data were analyzed using Statistica 9.0 software (Statsoft Inc., Tulsa, OK, USA). Data are presented as mean \pm standard deviation, and *P* < .05 was considered statistically significant.

RESULTS

Dialysis Patients

Of 511 patients suspected to have COVID-19, 112 tested positive for COVID-19 by RT-PCR. The majority, 85%, were undergoing hemodialysis, and 15% were undergoing home peritoneal dialysis, having an average dialysis time of 43 \pm 41 months.

Kidney Transplant Recipients

Out of 526 KTxRs tested, 154 had COVID-19 confirmed by RT-PCR (89%) or Ag-Test (11%). Of the KTxRs positive with COVID-19, 79% received transplants from deceased donors, with an average time of transplant of approximately 85 \pm 67 months. Immunosuppression regimen was based on calcineurin inhibitors (71%) associated with mycophenolic acid (51%) or mammalian target of rapamycin inhibitors (5.3%) or azathioprine (13%). Only 1.3% were receiving a steroid-free regimen.

DP vs KTxR groups

KTxRs were younger, presented higher body mass index, and had fewer coexisting disorders (cardiovascular disease, hypertension, diabetes mellitus, lung disease; [Table 1](#)) than DPs.

Classical symptoms, such as fever, cough, and dyspnea, were more frequent in the DPs than in KTxRs. Changes in biochemistry and hematological and inflammatory markers were higher in the KTxRs than the DPs. Interestingly, lower hemoglobin and higher alkaline phosphatases were seen more frequently in the DPs ([Table 1](#)).

KTxRs required more hospitalization and intensive care unit admissions, and no significant differences were found between the 2 groups concerning the fatality rate. The mean age at death was higher in the DP group ([Table 1](#)).

The incidence rate of COVID-19 in the DP group was 2240/10,000 patients with a mortality rate of 480/10,000 patients and a fatality rate 24%. In the KTxR group, the incidence rate was 1750/10,000 patients with a mortality rate of 420.4/10,000 patients and a fatality rate of 24%. <H1>Discussion

The incidence of COVID-19 infection in the general Brazilian population is 1002.8/10,000 inhabitants, much lower than in the DP group (2240/10,000 inhabitants) and the KTxR group (1750/10,000 inhabitants). The highest incidence found in the DP may be because of the higher exposure during the shared transport and frequently close contact with staff and other patients, and in KTxR possibly because of the consultation and hospitalization contamination [2,9].

The general Brazilian population mortality was of 28/10,000 inhabitants and a fatality rate of 2.8% [5], lower than the DPs (mortality of 480/10,000 inhabitants and a fatality rate of 24%) and the KTxRs (mortality rate of 420.4/10,000 inhabitants and a fatality rate of 24%), showing the higher risk of death for COVID-19 infection in these populations.

Even with the higher incidence and mortality rates observed in the DPs and the KTxRs, their fatality rate did not differ. The KTxR and DP fatality rates (24%) in our study were similar in the DPs (24.9%) of the Spanish study, but higher in the KTxRs (18.6%) found in the same Spanish study [10]. However, these findings were higher in both DPs and KTxRs than in the multicenter European group study (21.2% and 20.2%, respectively) [11]. The high fatality rate found in DPs can be explained by the fact that this population is older and has more coexisting disorders ([Table 1](#)), in agreement with other studies [3,10,11]. In spite of the KTxRs being younger and with fewer comorbidities than the dialysis group, these results are similar to the multicenter European group study [11].

Comparing other outcomes, the KTxRs presented more hospitalization and more intensive care unit need than the DPs. In addition, a European study comparing the mortality between the KTxRs and DPs shows that the mortality risk in KTxRs with COVID-19 was 28% higher than in the selected matched group of DPs [11].

A recent study from Madrid reported some inflammatory markers as predictors of severe COVID-19 in the general population [12]. A COVID-19 analysis in DPs in the same hospital in Brazil showed that those markers were significantly higher in the severe form of COVID-19, whereas hemoglobin and lymphocyte counts were significantly lower [9]. Our study found that the neutrophil lymphocyte ratio, C-reactive protein, lactic dehydrogenase, and liver enzymes were more frequently higher in the KTxRs than in the DPs, which could mean more severe disease.

CONCLUSIONS

Our results suggest that the clinical spectrum of COVID-19 between KTxRs and DPs has much higher fatality and mortality rates compared with the general Brazilian population. Additionally, KTxRs, in spite of having fewer comorbidities and younger age, had similar mortality and fatality rates, as well as incidence of COVID-19, as the DP group.

Table 1. Demographic Characteristics and Outcomes of Patients With COVID-19 in Dialysis or Kidney Transplant

Characteristics and Outcomes	DP Group (n = 112)	KtxR Group (n = 154)	P Value
Age (y), mean (SD)	61 ± 14.6	49 ± 12.4	<.0001
Sex, male [n (%)]	63 (56)	93 (60)	.52
Race (W/NW)	88/24	109/45	–
BMI (kg/m ²), mean (SD)	24.3 ± 4.6	27.7 ± 4.8	<.0001
Coexisting disorder [n (%)]			
Cardiovascular disease	46 (41)	23 (15)	<.0001
Hypertension	105 (94)	130 (88.4)	.02
Diabetes mellitus	55 (49)	51 (33)	.01
Lung disease	25 (22.3)	8 (5.2)	<.0001
Symptoms [n (%)]			
Fever	68 (61)	52 (34)	<.0001
Cough	68 (61)	58 (37.7)	.0003
Dyspnea	55 (49)	13 (8.4)	<.0001
Laboratory findings, median (IQR)			
Hemoglobin, g/dL	10.4 ± 2	12.3 ± 2	<.0001
Platelets, per mm ³	189 ± 124	182 ± 76	.09
Leukocytes, per mm ³	5365 ± 2447	7048 ± 4923	.007
Lymphocytes, per mm ³	966 ± 556	832 ± 520	.008
Neutrophils, per mm ³	3809 ± 2200	5571 ± 4414	<.0001
Neutrophil lymphocyte ratio	6.15 ± 10	9.3 ± 9.6	.004
C-reactive protein, mg/dL	8.05 ± 9.5	11 ± 14.4	.04
Aspartate aminotransferase, U/L	28.4 ± 29	40 ± 30	<.0001
Alanine aminotransferase, U/L	20.4 ± 27	30.4 ± 24	<.0001
Total serum bilirubin, mg/dL	0.30 ± 0.19	0.38 ± 0.29	.005
Gamma-glutamyl transpeptidase, IU/L	107.8 ± 234	134.6 ± 171	.01
Alkaline phosphatase, IU/L	126 ± 104	94 ± 46	.0006
D-dimer, μg/mL	1.86 ± 1.5	1.98 ± 2.2	.22
Lactate dehydrogenase, U/L	293.6 ± 105	382.2 ± 190	.0001
Hospitalization [%]	70%	49.4%	.002
ICU [%]	39%	25%	.01
Death [n (%)]	27 (24)	37 (24)	.55
30-day fatality rate [n (%)]	4 (3.6)	2 (1.3)	.24
Age at death, mean (SD)	63 ± 15	54 ± 10.6	.007
Incidence rate/10,000	2.240	1.750	–
Mortality rate/10,000	480	420.4	–
Fatality rate, %	24	24	.55

The incidence, mortality and case fatality rates were calculated as follows: Incidence = number of cases from March 1, 2020 until the end of the current report (June 31, 2021)/number of exposed people per 10,000. Mortality = number of deaths due to COVID-19/number of exposed people per 10,000. Fatality = (number of confirmed deaths owing to COVID-19/number of confirmed COVID-19 cases) × 100.

DP, dialysis patients; KtxR, kidney transplant recipient; SD, standard deviation; M, male; W, white; NW, nonwhite; BMI, body mass index; ICU, intensive care unit; IQR, interquartile range.

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