



Original article

# In-hospital clinical outcomes in kidney transplant recipients with COVID-19 infection

Sonia Celis-Conde <sup>1</sup>, Jessica Pinto-Ramirez <sup>1,2</sup>, Andrea García-Lopez  <sup>2</sup>, Nasly Patino-Jaramillo <sup>2</sup>, Alejandro Camargo-Salamanca <sup>1</sup>, Marco Anaya-Taboada <sup>1</sup>, Fredy Lozano-Castañeda <sup>1</sup> y Fernando Giron-Luque <sup>3</sup>

<sup>1</sup>Department of Transplant Nephrology, Colombiana de Trasplantes, Bogotá, Colombia

<sup>2</sup>Department of Transplant Research, Colombiana de Trasplantes, Bogotá, Colombia

<sup>3</sup>Department of Transplant Surgery, Colombiana de Trasplantes, Bogotá, Colombia

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## Abstract

**Introduction:** The coronavirus 19 disease (COVID-19) increased mortality in organ solid transplant patients due to chronic immunosuppression and significant comorbidity burden. We aim to evaluate patient and graft survival in kidney transplant (KT) recipients who were hospitalized or treated in Intensive Care Units (ICU) after contracting COVID-19.

**Keywords:** Kidney Transplantation, COVID-19, Pandemic, Graft Survival, Patient Survival, Mechanical Ventilation.

✉ **Corresponding author:** Andrea García López, Colombiana de Trasplantes, Av. Carrera 30 # 47A-47, Bogotá, Colombia. E-mail: [aegarcia@colombianadetrasplantes.com](mailto:aegarcia@colombianadetrasplantes.com)



**Methods:** A retrospective analysis was conducted on adult KT recipients diagnosed with COVID-19 between June 1 and July 31, 2021. The study reported demographics, symptoms, laboratory parameters, and clinical outcomes 30 days after a positive test. Risk factors for mortality were identified through comparisons between hospitalization-in-wards and ICU groups. The Kaplan-Meier method was used to calculate graft and patient survival.

**Results:** 55 KT patients were analysed, recipient age and history of diabetes showed significant differences between groups ( $p = 0.0124$  and  $p = 0.0506$ , respectively). Multivariate analysis revealed that diabetes ( $p = 0.002$ ) and dialysis requirement ( $p = 0.0006$ ) were significantly associated with mortality risk. The overall mortality rate was 25.5 %, with graft loss at 12.7 %. Patient survival after 30 days was 74.5 %, with significantly higher survival in the hospitalization-in-wards group ( $p = 0.0001$ ) compared to the ICU group.

**Conclusions:** KT patients diagnosed with COVID-19 are at higher mortality risk than the general population. Our study found that patients in the ICU group experienced worse clinical outcomes and higher mortality rates compared to those in the hospitalization-in-wards group. These findings underscore the importance of closely monitoring COVID-19-implicated KT patients and tailoring treatment plans to minimize risk and improve outcomes.

## Desenlaces clínicos en pacientes con trasplante renal hospitalizados por COVID-19

### Resumen

**Introducción:** la enfermedad por coronavirus 19 (COVID-19) aumentó la mortalidad en pacientes con trasplante renal (TR) debido a inmunosupresión crónica y carga significativa de comorbilidad. Nuestro objetivo es evaluar la supervivencia del paciente y del injerto en receptores de TR hospitalizados o tratados en Unidades de Cuidados Intensivos (UCI) por COVID-19.

**Métodos:** estudio observacional retrospectivo en adultos receptores de TR diagnosticados con COVID-19 entre junio 1 a julio 31 de 2021. Reportamos variables demográficas, sintomatología, laboratorios y desenlaces a los 30 días del resultado positivo. Comparamos hospitalización general y UCI, identificando factores de riesgo asociados a mortalidad. La supervivencia del injerto y del paciente fueron calculadas con el método de Kaplan-Meier.

**Resultados:** se analizaron 55 pacientes, la edad y tener diabetes mostraron diferencias significativas entre los grupos ( $p = 0,0124$  y  $p = 0,0506$  respectivamente). El análisis multivariante reveló que la diabetes ( $p = 0,002$ ) y la necesidad de diálisis ( $p = 0,0006$ ) se asociaron significativamente con mortalidad. La tasa de mortalidad global fue 25,5 %, con pérdida del injerto del 12,7 %. La supervivencia de los pacientes a 30 días de infección fue 74,5 %, siendo significativamente mayor en el grupo de hospitalización en salas ( $p = 0,0001$ ) comparado con tratamiento en UCI.

**Conclusión:** los pacientes con TR diagnosticados con COVID-19 tienen mayor riesgo de mortalidad que la población general. Nuestro estudio encontró que el grupo en UCI experimentó peores desenlaces y tasas de mortalidad más altas. Estos hallazgos subrayan la importancia de monitorear COVID-19 en pacientes con KT.

**Palabras clave:** trasplante renal, COVID-19, pandemia, supervivencia del injerto, supervivencia del paciente, ventilación mecánica.

## Introduction

The coronavirus disease 2019 (COVID-19) was detected in China and has rapidly become a pandemic [1]. So far, there are 523 million cases of COVID-19 and approximately 6.7 million deaths worldwide [2]. Kidney transplant (KT) recipients are at greater risk of developing severe disease in viral respiratory infections due to chronic immunosuppression and a significant comorbidity burden [3]. The literature has reported an increase in COVID-19-related mortality in hospitalized KT patients compared to the immunocompetent population, 30 % [4–11] versus 15 % [12,13], respectively. Moreover, ICU admission is higher in KT patients than in the general population [14].

Before the development of the COVID-19 vaccines, the literature reported that kidney transplant patients had worse clinical outcomes and that the transplant groups were focused on prevention measures and immunosuppressive adjustment to treat kidney transplant recipients. Thus, the immunosuppressive status was considered a risk factor to predispose to severe COVID-19 disease, with mortality rates from 13 % to 30 % in solid organ transplant recipients [15]. Therefore, immunosuppressive therapy was evaluated and adjusted according to the degree of severity of COVID-19 disease and the consensus of transplant societies that determined whether the take-off of antimetabolite agents comes first or the suspension of calcineurin inhibitors [16].

Conversely, Linares et al. reported that the clinical characteristics of transplant recipients and non-transplant populations could be alike. The literature showed that the main risk factors in mortality for patients with COVID-19 were advanced age, diabetes mellitus, arterial hypertension, elevated C-reactive protein, elevated D-dimer, and impaired renal function. Still, these risk factors were not associated with worse prognosis in transplant recipients compared to the general population with COVID-19 [17].

Locally, there is no publication about risk factors associated with KT recipients with COVID-19. In the first phase of our research, our transplant group published a descriptive study about KT recipients with COVID-19 without the association analysis of risk factors and clinical outcomes [18]. We aim to evaluate patient and graft survival in kidney transplant (KT) recipients who were hospitalized or treated in Intensive Care Units (ICU) after contracting COVID-19. Additionally, demographics, symptoms, laboratory parameters, and clinical outcomes were evaluated as potential associated factors related to mortality.

## Methodology

### *Study design and participants*

A retrospective observational analysis was performed with adult kidney transplant recipients (KT) ( $\geq 18$  years old) with COVID-19 diagnosis in Colombiana de Trasplantes. Our institution is a transplant centre with 4 headquarters in the main cities of Colombia that performs 21 % of the national transplant activity. The study period was from June 1, 2020, to July 31, 2021. Demographics, symptoms, laboratory parameters, and clinical outcomes were collected from institutional medical records for our database. COVID-19 infection was defined as a patient with or without clinical symptoms and a positive result in nasopharyngeal swabs using SARS-CoV-2 real-time reverse transcription-polymerase chain reaction (RT-PCR) or a positive SARS-CoV-2 antigen test. The results of these tests were reviewed in a database associated with the National Health Institute in Colombia (Instituto Nacional de Salud- INS). The national health administrator confirmed every mortality case of KT recipients with COVID-19. We excluded the COVID-19 KT patients without clinical data and follow-up in our medical records. We determined the complete vaccination state as at least one dose of the COVID-19 vaccine for the period of study.

### *Variables and measurements*

The sociodemographic, clinical and paraclinical variables and the outcomes of mortality, graft loss, and acute cell rejection were considered. Likewise, the definition under which acute kidney injury was estimated was according to the criteria set forth in the Acute Kidney Injury Network [19]. On the other hand, the definition adopted for graft loss will be the requirement of dialysis for at least 12 weeks after transplant. Also, symptoms and outcomes were evaluated 30 days after the result of a positive COVID-19 test.

### *Statistical analysis*

Descriptive statistics were used to report the demographic characteristics: frequencies and percentages for categorical variables, numerical variables using mean and standard deviation for normally distributed variables, and median and interquartile range (IQR) for nonnormally distributed variables. The death event was measured in the number of days from the first day of COVID-19 diagnosis to the date of patient death.

Comparisons between the two groups (the hospitalization-in-wards group and ICU group) were performed using Pearson's chi-square test for categorical variables and the t-test for numerical variables. We performed a univariate and multivariate model and calculated

odds ratios (OR) with 95 % confidence intervals (CI) to identify independent risk factors for mortality associated with COVID-19 infection between two risk groups (hospitalization-inwards group and ICU group).

Statistical analysis was performed using R version 4.0.3. Data on mortality and graft loss rate were collected up to day 30 following a positive COVID-19 test. Based on this information, we utilized the Kaplan-Meier curve to estimate graft and patient survival. Additionally, we compared the survival distributions using a log-rank test.

### ***Immunosuppressive protocol***

The immunosuppression scheme is based on induction with polyclonal anti-thymocyte globulin. Protocol of maintenance immunosuppression included tacrolimus and mycophenolate mofetil, and steroids-free unless patients were transplanted by a different centre, where they might receive immunosuppression schemes with steroids.

### ***Ethical Considerations***

This study was approved by the Institutional Research Committee, acting in concordance with local [20] and international regulations [21].

## **Results**

### **Sociodemographic and clinical characteristics**

A total of 55 KT patients were analysed during the study period. Most patients were male in both groups (hospitalization-inwards and ICU). The overall mean age for hospitalized and ICU patients were  $48.4 \pm 13.5$  and  $59.7 \pm 9.6$  years, respectively. There were no significant differences in the bivariate analysis of sex, clinical history of hypertension, smoking, heart disease, thyroid disease, and obesity. The recipient's age and the clinical history of diabetes mellitus had a significant difference between the hospitalization-inwards and ICU groups in the bivariate analysis ( $p = 0.0124$  and  $p = 0.0506$ ), respectively. Neurological and cardiovascular symptoms of COVID-19 were more prevalent in ICU patients. Table 1 describes the demographics and clinical characteristics of KT patients with COVID-19. In addition, we evaluated the antibiotic requirement, which was more prevalent in the ICU (77.8 %), although there were no significant differences between both groups ( $p = 0.315$ ).

**Table 1.** Demographic and clinical characteristics of KT patients with COVID-19

Variable	Hospitalization-in-wards	ICU	Total	P-value
	(N=37)	(N=18)	(N=55)	
<b>Demographics</b>				
Gender, n (%)				0,792
Male	19 (51.4)	11 (61.1)	30 (54.5)	
Female	18 (48.6)	7 (38.9)	25 (45.5)	
Age, mean (SD)	48.4 (13.5)	59.7 (9.66)	52.1 (13.4)	0,0124
BMI, mean (SD)	24.8 (3.86)	24.9 (2.41)	24.9 (3.43)	0,997
<b>Comorbidities, n (%)</b>				
Hypertension	26 (70.3)	16 (88.9)	42 (76.4)	0,313
Diabetes Mellitus	4 (10.8)	7 (38.9)	11 (20.0)	0,0506
Smoking	3 (8.1)	2 (11.1)	5 (9.1)	0,936
Heart disease	5 (13.5)	2 (11.1)	7 (12.7)	0,969
Thyroid disease	14 (37.8)	6 (33.3)	20 (36.4)	0,948
Obesity	6 (16.2)	1 (5.6)	7 (12.7)	0,538
<b>The immunosuppressive scheme, n (%)</b>				
Tacrolimus / Mycophenolate	25 (67.6)	14 (77.8)	39 (70.9)	NA
Tacrolimus / Mycophenolate /Prednisone	4 (10.8)	1 (5.6)	5 (9.1)	
Cyclosporine / Mycophenolate	2 (5.4)	0 (0)	2 (3.6)	
Other	6 (16.2)	3 (16.6)	9 (16.3)	
<b>Reported symptoms, n (%)</b>				
Fever	26 (70.3 %)	11 (61.1 %)	37 (67.3 %)	0,794
Respiratory	29 (78.4 %)	17 (94.4 %)	46 (83.6 %)	0,319
Gastrointestinal	26 (70.3 %)	13 (72.2 %)	39 (70.9 %)	0,989
Neurological	1 (2.7 %)	3 (16.7 %)	4 (7.3 %)	0,174
Cardiovascular	1 (2.7 %)	3 (16.7 %)	4 (7.3 %)	0,174
<b>Note:</b> SD: Standard deviation; ICU: intensive unit care; NA: Not applicable				

**Source:** The authors.

## Laboratory parameters

A higher mean level of C-reactive protein (CRP) was noted in KT recipients with COVID-19 in the ICU group compared to KT recipients with COVID-19 in the hospitalization-in-wards group ( $p = 0.01$ ). In addition, the ICU group had a higher elevation in the mean absolute white blood cell count and neutrophil count than the hospitalization-in-wards group ( $p = 0.00593$  and  $p = 0.0785$ , respectively). In terms of lymphocyte count, KT recipients in the ICU group developed a lower mean count than the KT recipients in the hospitalization-in-wards group ( $p = 0.0502$ ). No significant associations were found for the mean concentration of haemoglobin, thrombocyte count, and D-dimer levels in the bivariate analysis. Laboratory parameters are shown in Table 2.

**Table 2.** Laboratory parameters in KT patients with COVID-19

Laboratory parameters, median (min-max)	Hospitalization -in-wards	ICU	Total	P-value
	(N=37)	(N=18)	(N=55)	
Haemoglobin (g/dl)	12.0 [6.70, 16.4]	10.2 [4.70, 17.0]	11.3 [4.70, 17.0]	0.301
C-reactive protein (CRP) (mg/l)	38.5 [4.80, 113]	117 [22.5, 327]	49.8 [4.80, 327]	0.01
White blood cell count (mm <sup>3</sup> /dl)	5370 [3080,14000]	10100 [950,24000]	5890 [950,24000]	0.00593
Neutrophil count (mm <sup>3</sup> /dl)	3960 [1500,14600]	6120 [1130,17400]	5010 [1130,17400]	0.0785
Lymphocyte count (mm <sup>3</sup> /dl)	835 [1.44, 2220]	808 [0,17600]	835 [0, 17600]	0.0502
Thrombocyte count (mm <sup>3</sup> /dl)	248000 [14000,512000]	251000[75000,544000]	248000 [14000,544000]	0.986
D-dimer (ng/ml)	767 [0.400,32800]	1400 [552,4670]	1070 [0.400,32800]	0.625

**Note:** ICU: intensive unit care.

**Source:** The authors.

**Table 3.** Clinical outcomes in KT patients with COVID-19

Clinical outcomes and in-hospital complications, n(%)	Hospitalization- in-wards	ICU	Total	P-value
	(N=37)	(N=18)	(N=55)	
Graft loss	1 (2.7)	6 (33.3)	7 (12.7)	0.00601
Mortality	4 (10.8)	10 (55.6)	14 (25.5)	0.00168
Acute kidney injury	16 (43.2)	14 (77.8)	30 (54.5)	0.0543
Dialysis requirement	4 (10.8)	9 (50.0)	13 (23.6)	0.00579
Pulmonary embolism	1 (2.7)	1 (5.6)	2 (3.6)	0.869
Arrhythmia	3 (8.1)	1 (5.6)	4 (7.3)	0.943
Concomitant infection	21 (56.8)	16 (88.9)	37 (67.3)	0.0585
Vasopressor infusion	4 (10.8)	13 (72.2)	17 (30.1)	0.001
Mechanical ventilation requirement	1 (2.7)	16 (88.9)	17 (30.1)	0.001

**Note:** ICU: intensive unit care.

**Source:** The authors.

## Clinical Outcomes and in-hospital complications Associated with COVID-19

During the study period, KT patients with COVID-19 were analysed for clinical outcomes and in-hospital complications. One case of graft loss was registered in the hospitalization-in-wards group compared to six cases of graft loss in the ICU group ( $p = 0.006$ ). A significant difference in mortality was found comparing the hospitalization-in-wards group with the ICU

group ( $p = 0.0001$ ). The bivariate analysis revealed that acute kidney injury, dialysis requirement, and concomitant infection were significant hospitalization complications that occurred more frequently in the ICU group compared to the hospitalization-in-wards group. The KT recipients in ICU had significantly major mechanical ventilation requirements ( $p < 0.001$ ) and vasopressor infusion ( $p < 0.001$ ).

## Associated risk factors for mortality in KT recipients with COVID-19

We performed a multivariate Cox analysis to identify risk factors associated with mortality in KT patients within 30 days after COVID-19 positive test. KT recipients with a clinical history of diabetes mellitus ( $p = 0,002026$ ) and dialysis requirement ( $p = 0,0006$ ) within the hospitalization-in-wards or ICU stay were significantly associated with risk of death (Table 4).

**Table 4.** Multivariate Cox analysis for mortality within 30 days after COVID-19 infection in KT patients

Parameters	Full analysis model [HR (95 % CI)]	P-value	Final model [HR (95 % CI)]	P-value
Sex (Male)	1.24 (0.34-4.48)	0.7421	-	-
Age (years)	1.03 (0.96-1.11)	0.2747	-	-
Diabetes	5.95 (1.02-34.5)	0.047	9.01 (2.2-36.4)	0.002026
Acute kidney injury	5.50 (0.61-49.5)	0.1281	-	-
Dialysis requirement	7.04 (1.3-35.6)	0.0183	10.32 (2.7-39.2)	0.000604
Smoking	2.66 (0.28-25.1)	0.3913	-	-
Heart disease	2.05 (0.19-22.2)	0.5525	-	-
Obesity	0.42 (0.04-3.7)	0.4377	-	-
Hypertension	2.70 (0.52-13.8)	0.232	-	-
Concomitant infection	3.80 (0.56-25.7)	0.1716	3.61 (0.65-20.01)	0.14104

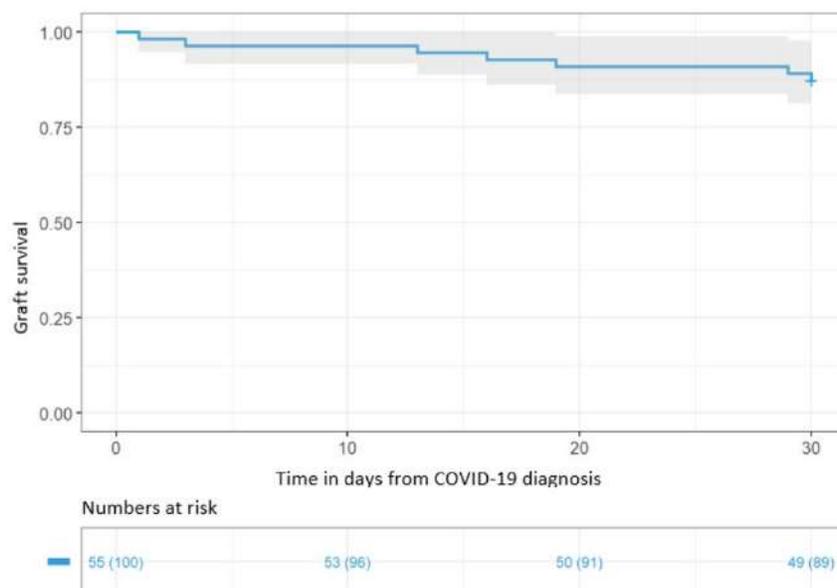
**Note:** KT – kidney transplant recipient. Variables are presented as hazard ratio (HR) with a 95 % confidence interval (95 % CI).

**Source:** The authors.

## Patient and graft survival

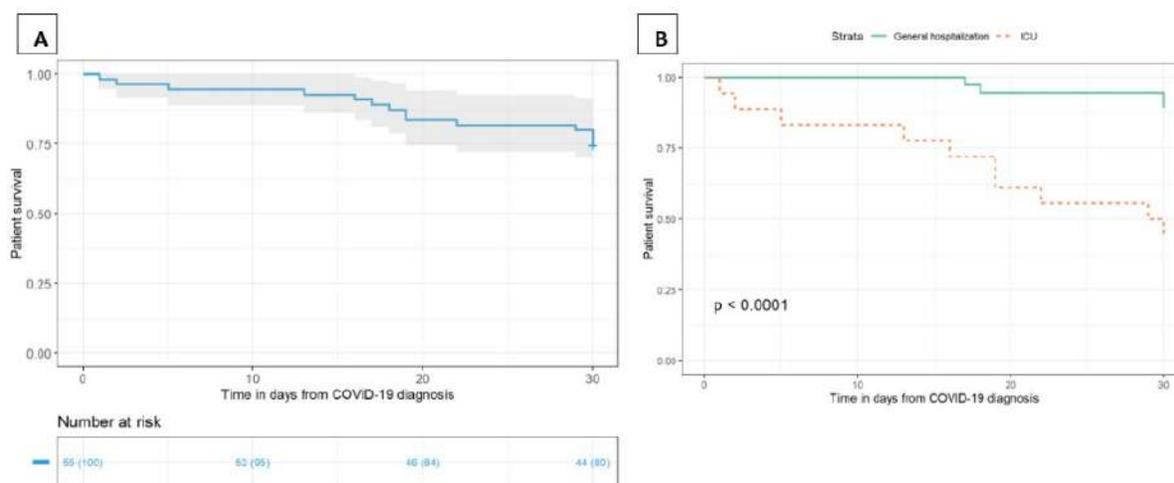
During the study period, 7 (12.7 %) KT patients with COVID-19 had graft loss. We performed a Kaplan-Meier survival analysis to determine the graft and patient survival in KT recipients of both study groups. The graft survival was 87.3 % at 30 days after a COVID-19 positive test (Figure 1).

The overall mortality rate was 25.5 % ( $n = 14$ ). The global patient survival was 74.5 % after 30 days of follow-up. In the comparison of hospitalization-in-wards and ICU groups, patient survival was significantly higher in KT patients with COVID-19 in the hospitalization-in-wards group versus the ICU group ( $p = 0.0001$ ) (Figure 2).



**Figure 1.** Global graft survival in KT patients with COVID-19 in the hospitalization-in-wards and ICU group

**Source:** The authors.



**Figure 2.** Patient survival in KT patients with COVID-19 after 30 days after a COVID-19 positive test

**Source:** The authors.

## Discussion

The COVID-19 pandemic caused by coronavirus, 2 of the severe acute respiratory syndromes (SARS-CoV-2), has changed the world. So far, there are 532 million cases of COVID-19, including 6,305,358 deaths, and a total of 11,854,673,610 doses of the COVID-19 vaccine that have been administered according to the World Health Organization (WHO) [22].

Additionally, organ transplantation was significantly affected by COVID-19 disease, decreasing organ donation rates and transplant activities, which mainly affected organ solid recipients [23]. COVID-19 infection has increased mortality, lethality, and morbidity rates in solid organ transplant patients. Also, the immunosuppression state of the organ solid transplant recipients has influenced their clinical outcomes after COVID-19 infection [23].

The first two articles that analysed the impact of COVID-19 on kidney transplant patients provided diverse results. The first case series was published in March 2020 and reported five cases of COVID-19 infection in kidney transplant patients in Wuhan, China. These patients had a good clinical evolution without death events. This study concluded that COVID-19 was not severe in these patients and calcineurin inhibitors were capable of blocking SARS-CoV-2 action [24].

The second publication was a case series reported by the transplant group of the Montefiore Hospital in New York (USA) in April 2020. This cohort included 36 kidney transplant patients with COVID-19 infection with a mortality rate of 27.7 % (n = 10). They concluded that the mortality rate in kidney transplant recipients was higher than in the general population (1 %-5 %) and higher in elderly people over 70 years of age (8 %-15 %) [12].

A systematic review and meta-analysis of solid organ transplant recipients (SOT) with COVID-19 infection included 1,500 kidney transplant patients. The most common symptoms were fever and cough (70.2 % and 63.8 %, respectively), with results like our study. In our findings, the mortality rate was 18.6 % versus 25.5 % [25]. Comparable to our results, a cohort of 11,875 KT patients from the Hospital do Rim at São Paulo-Brazil showed 491 cases of COVID-19 with a lethality rate of 28.5 % [26]. Interestingly, in this study, it was also observed that KT patients recovering from COVID-19 had permanent graft dysfunction (19 %) with a lower graft loss than our findings (4 % vs. 12,7 %, respectively).

In the characterization of our KT population, we found that the most frequent comorbidities were arterial hypertension, thyroid disease, and diabetes mellitus. In the literature, high blood pressure and diabetes mellitus have been described as risk factors for mortality and severity of COVID-19 in KT recipients [27].

Second, we found that the clinical presentation of COVID-19 in transplant patients is analogous to the general population, where fever and respiratory symptoms predominate. These findings are consistent with previous reports showing fever in 77 %-94 % and cough in 68 %-79 % [28-30] as the main presentation of COVID-19 symptoms. Gastrointestinal sym-

ptoms ranked third in the clinical presentation and were clearly due to acute diarrheal disease. Gastrointestinal symptoms in the initial symptoms of COVID-19 have been documented to be an associated factor with greater recovery and lower mortality [31]. Likewise, we found that a part of the patients was asymptomatic (10.2 %) and were treated in the outpatient division with a favourable outcome similar to other cohorts [32].

Among the paraclinical findings, some studies reported lymphopenia and thrombocytopenia in KT patients and COVID-19 as factors associated with increased mortality risk and COVID-19 severity [33–37]. In our cohort, the lymphocyte count was in the bivariate analysis, but it did not remain significant for the multivariate model. Thrombocytopenia was present in a low percentage of those evaluated. The procalcitonin level has also been associated as a predictor of mortality and severity in COVID-19 [5, 24, 38], but in our patients only one patient had procalcitonin value documented. Similarly, positive C-reactive protein (CRP) was identified in a quarter of our recipients. Although its association with mortality and severity was not analysed, it was related to higher mortality and COVID-19 severity in some studies [5, 38].

Regarding the main clinical outcomes, we found that most KT patients who lost the graft had severe COVID-19 disease. We found no evidence reporting a significant association between renal graft loss and COVID-19 infection. Other transplant groups have published similar survival analyses for graft loss [5, 35].

AKI ranked fourth in clinical presentation, requiring renal support therapy, specifically haemodialysis, in 10.2 % of cases. In other publications, the dialysis requirement for AKI has varied between 15.7 % and 28.8 % [36, 39, 40]. Compared to the general population, kidney transplant patients have up to a 4-fold increased risk of AKI [34, 40]. In our findings, although the frequency of AKI was high, most patients returned to adequate renal function 30 days after the diagnosis of COVID-19 with a positive test.

Regarding the severity of the disease, we found that some publications define the severity of COVID-19 by the need for ICU admission and mechanical ventilation [34, 35]. Our ICU admission compared to other publications was similar (14,2 % vs. 20 %-21 %) [35, 37]. The need for mechanical ventilation in our population was comparable with other results that presented frequencies between 12 % and 35 %. [33, 35, 36, 41]. The use of intravenous corticosteroids in COVID-19 patients with impaired oxygenation had lower mortality at 28 days follow-up, according to the RECOVERY study [42]. In our study, the use of dexamethasone was significantly higher in patients admitted to the ICU compared to those hospitalized on the

floor. However, its impact on patient mortality was not analysed. On the other hand, in the survival analysis of our kidney transplant and COVID-19 patients, significant differences were found between admission to hospitalization-in-wards vs. ICU, which is similar to the results of other publications [5, 33, 35].

Mortality in our population was lower than reported in previous international studies with transplant patients 18 %-32 % [5, 12, 43]. Thus, during the pandemic period, mortality has been variable given the diversity of individual patient factors, factors of the health system of each country and experience acquired during the pandemic for the care of patients with COVID-19. We performed a multivariate Cox analysis to identify risk factors associated with mortality in KT patients within 30 days after COVID-19 infection. KT recipients with a clinical history of diabetes mellitus ( $p = 0.002026$ ) and dialysis requirement ( $p = 0.0006$ ) within the hospitalization-in-wards or ICU stay was significantly associated with death risk. Monhan *et al.* found that nearly one in six deaths (16 %) among active transplant recipients in the United States in 2020 was attributed to COVID-19. Recipients who died of COVID-19 were younger, more likely to be obese, had lower educational attainment, and were likelier to belong to racial/ethnic minority groups than those who died of other causes in 2020 or 2019 [44].

The vaccination for COVID-19 was not completely available in the study period. A few percent of our population were vaccinated at the moment of admission to the hospital. That being the case, we could not measure the level of protection of the COVID-19 vaccination in our kidney transplant recipients. Benning *et al.* [45] reported lower seroconversion levels and impaired neutralization in kidney transplant patients with standard COVID-19 vaccination regimens against emerging COVID-19 variables (B.1.351 and B.1.617.2) in comparison with a healthy population ( $p < 0.001$ ). The aftermath of this study concludes that kidney transplant patients need an additional booster of COVID-19 vaccination to have better protection.

The limitations of our study include selection bias since patients for whom we did not have a complete follow-up clinical history were excluded. It is also possible that there is an underreporting of COVID-19 cases of those patients who did not undergo a PCR or antigen test for COVID-19. It should be noted that treatment protocols were not uniform for all patients, given the continuous changes based on new evidence on COVID-19 and the severity of each patient that was reported during the study period. In the study period that we analysed, the patients did not have wide access to vaccination against COVID-19, which did not allow us to measure the vaccine's efficacy in the formulated outcomes. Finally, the study's retrospective nature could give rise to information bias.

## **Conclusions**

KT patients diagnosed with COVID-19 are at higher mortality risk than the general population. Our study found that patients in the ICU group experienced worse clinical outcomes and higher mortality rates compared to those in the hospitalization-in-wards group. These findings underscore the importance of closely monitoring COVID-19-implicated KT patients and tailoring treatment plans to minimize risk and improve outcomes.

## **Conflicts of Interest**

The authors declare that there is no conflict of interest regarding the publication of this article.

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## **Author's contributions**

All authors conceived the study design. AG and NP supported protocol writing and managed the IRB approval process. SC, JP, AC, MA and FL collected clinical information. AG and NP performed data management and statistical analysis. SC, JP, AC, MA, FL and FG led data interpretation. AG and NP drafted article. SC, JP, AC, MA, FL and FG developed the critical revision of the article. FG supervised all aspects of the project.

## **Ethical statement**

The study adhered to national and international ethical guidelines and was approved by the Dexa Diab ethics committee. Informed consent was waived by the ethics committee, considering the retrospective collection and anonymized presentation of results.

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