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# Impact of a National Multicentric Strategy to Support Kidney Transplant Patients During the COVID-19 Pandemic in Latin America: FUTAC Team Creation and Activities

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## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had a significant worldwide impact, with over 230 000 000 infected people and 4 800 000 deaths as of September 2021.<sup>1</sup> Patients with chronic disease and that are chronically immunosuppressed are among the most vulnerable, as they have an increased risk of complications such as respiratory failure with >30% of patients requiring mechanical ventilation.<sup>2-4</sup> Transplant recipients are particularly at high risk because of the chronic immunosuppression related to transplant medications.<sup>5</sup> A multicenter cohort study of transplanted patients with COVID-19 in the United States and Europe indicated that 78% required hospitalization, 31% required mechanical ventilation, and 28% died during the first 28 d after diagnosis.<sup>3</sup>

Consequently, to prevent recipient exposure to immunosuppression and reduce risk of infection and death related to COVID-19, a significant reduction of transplants has occurred worldwide.<sup>6</sup> For example, at the beginning of the pandemic, several transplant societies recommended suspending living-donor kidney transplantation (because of potential infection risks for both donors and receptors) and reserving deceased-donor transplantation for likely lifesaving indications,<sup>7</sup> resulting in a consequent decrease of over 50% in kidney transplantation worldwide in living donors.<sup>8</sup>

While this is a worldwide situation, it has had an especially negative impact in Latin America that is not only due to the direct and indirect effects of the pandemic but also due to the ever-present socioeconomic and public health issues in the region.

## COVID-19 PANDEMIC IN LATIN AMERICA: EFFECTS OF POVERTY AND SOCIOECONOMIC INEQUALITY

Latin America is a region with the highest per capita death rate due to COVID-19 in the world,<sup>9</sup> with over 1.5 million recorded deaths as of September 2021.<sup>10</sup> These adverse outcomes may be explained by several factors,<sup>11,12</sup> including the low socioeconomic conditions and inequality present before the pandemic. According to global inequality data, Latin America is one of the most unequal regions in the world.<sup>13</sup> This economic impairment is associated with social disparity, including a lack of access to public health including health system preparedness, and a weak social welfare system. One report that evaluated countries in Latin America and Africa showed that areas with higher poverty rates had an increased transmission rate of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) compared with those with a lower poverty rate.<sup>14</sup> Also, a recent study in Brazil has shown that socioeconomic inequalities, besides other risk factors, have affected the

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course of the epidemic, with an increased death rate in communities with high socioeconomic vulnerability.<sup>15</sup>

Moreover, strategies designed to manage the COVID-19 pandemic have had indirect adverse effects such as being in lockdown and social distancing, which have had massive adverse social consequences.<sup>16</sup> These have contributed to increasing poverty levels as incomes decrease because of the high number of people unable to work outside the home, together with an increased rate of high-risk casual labor in the region.<sup>17</sup> Additionally, an increase in higher educational desertion is expected in Latin America, along with a decrease in secondary education levels, particularly for the most vulnerable children.<sup>18</sup>

Regarding public health data in Latin America, there has been a decrease in non-COVID-19-related healthcare during lockdown. This includes the suspension of nontransmissible diseases and mental health primary care services<sup>19</sup> and a reduction in stroke consultations in emergency rooms,<sup>20</sup> together with decreases in cancer screening tests and therapies (chemotherapy and oncologic surgery).<sup>21</sup>

In relation to transplant patients in Latin America, an increased rate of infection and death caused by COVID-19 has also been reported, where increased age and comorbidities such as diabetes and obesity are risk factors for adverse outcomes in Latin America.<sup>22,23</sup> Also, during the pandemic, there has been a severe reduction in the number of transplants performed due to the lack of appropriate in-hospital units for posttransplant management and the closure of several transplant centers. This situation has caused a severe reduction in organ transplantation, decreased organ donation, and reduced admission to the transplant waiting list.<sup>24</sup>

In Chile, >80% of transplant centers closed during the first months of the pandemic. Also, preliminary data indicate that there was a significant decrease in transplant list admissions (>75%) with a slight increase in the number of patients on the waiting list (estimated at 20%) in 2020; however, this slight increase may be biased given the reduction in the number of patients being added to the transplant list. In 2021, most transplant centers started working, especially those focused on deceased-donor transplantation; however, the number of transplant list admissions and living-donor transplantations continues to be low, which is especially relevant for kidney transplantation. Currently, living-donor kidney transplantation is being performed in private clinics where appropriate postoperative care is available. Unfortunately, most living-donor transplant programs at public hospitals are still closed because of the lack of appropriate management for posttransplant care and the collapse of public hospitals due to the high number of COVID-19 patients in critical care units.

## **SOCIOECONOMIC CHARACTERISTICS AND DISPARITY IN CHILE**

Chile is in southern Latin America and has 19 500 000 inhabitants.<sup>25</sup> It has a mixed health system; 78% of the population is treated by the public system, and 22% is treated in private systems.<sup>26</sup> As of December 2019, 9390 kidney transplants were performed, with an estimated activity of 400 transplants per year before the pandemic. The first reported case of COVID-19 was on March 3, 2020, with the first peak of 295 active cases per 100 000 inhabitants in June 2020 and a second peak in April 2021 with 399

active cases per 100 000 inhabitants. By September 2021, >1 600 000 people were infected, and 37 000 deaths have been reported.<sup>27</sup>

Although Chile is classified as a high-income country by the World Bank with a per capita income of \$15 000 USD,<sup>28</sup> it is a country with the highest socioeconomic disparity in Latin America with a Gini coefficient of 44.4; 10% of the wealthiest people in the country hold 60% of the total income.<sup>13</sup> This situation has immense social consequences that have resulted in massive social protests in recent years,<sup>29,30</sup> causing a political and constitutional change that is currently underway.<sup>31</sup>

The current social unrest has had immeasurable, detrimental repercussions on the public health system. For example, a 2019 study conducted in 6 Latin American cities showed an inverse association between socioeconomic status and life expectancy.<sup>32</sup> It was concluded that in Santiago, the capital of Chile, the 10% with the highest income in the population had a longer life expectancy of between 8.0 and 11.8 y compared with the 10% with the lowest income, and this was the highest disparity in all the evaluated cities.

Concerning the pandemic, the first cases of COVID-19 occurred in the highest socioeconomic status population in people returning from overseas vacations<sup>33</sup>; however, the virus spread mainly to the lower-income populations, where most cases and deaths have been observed. A recent publication has shown that in Chile, social disparity is a risk factor for COVID-19 mortality in the general population<sup>34</sup>; however, the socioeconomic effect in other vulnerable groups, such as transplanted patients, has not been studied.

## **FUTAC TEAM: A MULTICENTER NATIONAL STRATEGY TO HELP RENAL PATIENTS**

In March 2020, the Chilean Society of Nephrology created the FUTAC team (Fuerza de Trabajo Anti COVID-19—anti-COVID-19 working force). This initiative includes nephrologists, transplant specialists, nurses, and patients throughout the country. The main objective is to support patients in renal replacement therapy, including hemodialysis, peritoneal dialysis, and kidney transplant patients. To achieve this, the FUTAC team originally had 2 primary goals: first, to create and implement strategies to prevent COVID-19 infection in dialysis patients and renal transplant patients and second, to identify and follow up patients with COVID-19 infection to determine the epidemiology of COVID-19 infection and clinical outcomes, including hospitalization rates and mortality, and to evaluate potential predictors of adverse outcomes to detect high-risk groups. To achieve this, 4 prospective registries have been developed: a hemodialysis patient registry, a peritoneal dialysis patient registry, an acute kidney injury with hemodialysis requirements patient registry, and a kidney transplant patient registry. Each registry has a different director and evaluates specific relevant data related to each group.

To perform the activities, the FUTAC team has support from the Ministry of Health of Chile with direct communication to share information and develop public health strategies. In addition, there have been donations from nongovernmental organizations such as the Vientosur Foundation, which has provided economic resources to

purchase supplies such as personal protective equipment for patients and health professionals. Also, the FUTAC team has active communication with patient communities to educate, support, and improve pandemic management and prevent contagion.

### KIDNEY TRANSPLANT PATIENTS WITH COVID-19 REGISTRY IN CHILE: THE PANDEMIC'S FIRST 12-MO RESULTS

This registry includes data from a national, multicenter, prospective, observational study of kidney transplant centers throughout the country, which began in March 2020 and continues to date. The centers follow up kidney transplant patients in their respective centers, covering over 98% of the national population of kidney transplant patients. Once a case is detected, clinical follow-up is performed with a clinical data evaluation, laboratory tests, a need for hospitalization, and outcomes, including hospitalization, requirements for mechanical ventilation, and death. To evaluate the socioeconomic impact, a national classification (Encuesta de Caracterización Socioeconómica Nacional - National Socioeconomic Characterization Survey) on the multidimensional poverty of the community where the patient lived was used.<sup>26</sup>

As of March 2020, there were 4305 living patients with a functioning kidney graft, all of whom have been followed up. As of March 3, 2021 (12 mo after the first reported case in Chile), 262 kidney transplants had been infected with COVID-19 (Table 1), with a cumulative infection rate of 6086 out of 100000 people aged  $49.1 \pm 14.1$  y; 118 were female, (45.0%), 153 lived in low-income communities (58.4%), and 38 died (annual mortality rate of 14.5%). This mortality rate reached 35% in hospitalized patients and 52% in cases admitted to intensive care units. Compared with the general population, kidney transplants have a 1.2- and 5.1-fold increased risk of infection and mortality, respectively. Multivariate logistic regression (Table 2) showed that the principal factors associated with an increased risk of death were being of an age  $>65$  y (odds ratio [OR], 2.9;  $P=0.021$ ), living in a low-income community (OR, 2.4;  $P=0.039$ ), and presenting with diabetes (OR, 4.9;  $P=0.047$ ). Figure 1 shows that patients from low-income locations had a higher mortality rate than those from higher-income locations (18.7% versus 9.3%;  $P=0.034$ ).

### IMPACT OF THE FUTAC TEAM IN CHILE AND LATIN AMERICA: ACHIEVEMENTS AND FUTURE CHALLENGES

The FUTAC team has achieved several goals within Chile and Latin America. One of the first achievements was acquiring and distributing personal protective equipment during the first 8 mo of the pandemic, which there was a massive lack of due to increased costs that were not affordable for most institutions in our country. These were distributed to dialysis and kidney transplant centers throughout the country, helping to decrease the infection rate in both patients and health providers.

Another important goal was developing the COVID-19 registry, where our data are being used to support decision-making processes at the public health level. The main

**TABLE 1.**  
Characteristics of the cohort

	Total
No. of patients, n (%)	262 (100)
Age, mean $\pm$ SD, y	$49.1 \pm 14.1$
Age $>65$ y, n (%)	43 (16.4)
Time after renal transplantation, median (IQR)	6.7 (0.1–38.9)
Sex, n (%)	
Female	118 (45.0)
Male	144 (55.0)
Comorbidities, n (%)	
Hypertension	116 (44.3)
Diabetes	18 (6.9)
Coronary heart disease	15 (5.7)
Lung disease	6 (2.3)
Previous renal function, mean $\pm$ SD	
Serum creatinine, mg/dL	$1.39 \pm 0.64$
eGFR, mL/min/1.73 m <sup>2</sup>	$51.9 \pm 24.1$
Health system, n (%)	
Public	203 (77.5)
Private	59 (22.5)
Community socioeconomic situation, n (%)	
Low-income (below p50 of the country)	153 (58.4)
Mid-high-income (above or equal to p50 of the country)	109 (41.6)
Time between symptoms initiation and diagnosis, mean $\pm$ SD, d	$4.9 \pm 2.6$
Clinical outcomes, n (%)	
Hospitalizations	127 (48.4)
Oxygen requirements	87 (33.2)
Invasive ventilation	43 (16.4)
In-hospital stay, median (IQR), d	13 (1–113)
Deaths, n (%)	38 (14.5)

eGFR, estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration formula); IQR, interquartile range; p50, 50th percentile (median).

achievement of the registry was to contribute to defining the national vaccination strategy. In February 2021, a massive vaccination campaign against COVID-19 initially aimed at elderly patients began in Chile.<sup>35</sup> This campaign included the inactivated SARS-CoV-2 vaccine CoronaVac (Sinovac) and the BNT162b2 mRNA vaccine (Pfizer-BioNTech). Registry results have demonstrated that kidney transplant patients (and dialysis patients) had an increased risk of COVID-19 and death related to COVID-19. Therefore, the Ministry of Health included kidney transplant patients and dialysis patients in vaccination priority groups regardless of age.<sup>36</sup>

Recently, the Ministry of Health of Chile started a vaccination campaign with a booster dose using the BNT162b2 vaccine for selected populations. Following advice from the FUTAC team, kidney transplant patients (together with dialysis patients) were included in the priority groups for the booster vaccination.<sup>37</sup> As a result, by the end of September 2021, vaccination coverage in these patients was over 90% with completed doses and a vaccine refusal rate of lower than 5% was recorded.

Given the characteristics of our group, international societies such as the Latin American Society of Nephrology and Hypertension and the Pan American Health Organization

**TABLE 2.****Multivariate logistic regression of potential determinants of mortality in kidney transplant patients with COVID-19**

Variable	OR	P	95% CI	
Male	1.237	0.618	0.536	2.857
Age >65 y	2.975	0.021	1.179	7.502
Low socioeconomic status	2.465	0.039	1.093	6.896
Previous serum creatinine	1.511	0.070	0.966	2.363
Diabetes	4.942	0.047	1.024	23.830

CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio.

are interested in the activities and results of the FUTAC team. This initiative is considered as a model of a national group in Latin America that has achieved significant patient benefits. We have provided the information obtained by our group to push the Ministries of Health throughout all of Latin America to prioritize the vaccination of dialysis and kidney transplant patients as a high-risk group. This activity is especially relevant considering that as of September 2021, only 1 in 4 people had been fully vaccinated in our region.<sup>38</sup>

Future FUTAC team objectives include the evaluation of cellular and humoral immune response after anti-SARS-CoV-2 vaccination (2 doses plus an additional booster dose), and the follow-up of surviving COVID-19 patients by evaluating mid-long-term clinical outcomes, especially in kidney transplant patients. Also, we are still evaluating the proposal designs to prevent COVID-19 infection in dialysis and kidney transplantation patients and are primarily focusing on the most disadvantaged socioeconomic groups with the Chilean Ministry of Health and Latin American societies.

## CONCLUSIONS

The COVID-19 pandemic has had a significant impact on kidney transplant patients in Latin America, who have a higher risk of infection and death than the general population. This risk is higher in low-income populations due to socioeconomic impairments, the lack of appropriate prevention measures, and reduced access to public health.

This situation motivated the creation of the FUTAC team, a multidisciplinary national group in Chile, to

support these patients. As a result, this group has accomplished goals by delivering prevention supplies to patients and health providers plus prioritizing kidney transplant patients for COVID-19 vaccination with a high compliance of over 90% of completed doses.

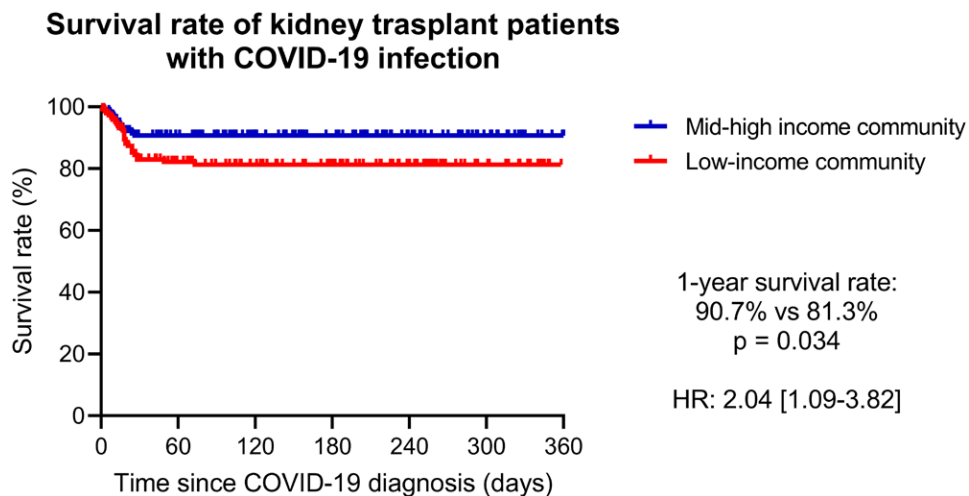
These results demonstrate that the collaboration between different groups, including physicians, health providers, patients, and public health representatives, is a viable and effective strategy to support the most vulnerable populations in Latin America, which can be applied to all transplantation populations. Therefore, the FUTAC team will continue working to support dialysis patients and kidney transplant patients in Chile and Latin America during and after this pandemic.

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## IN MEMORIAM

This publication is dedicated to Dr Andres Boltansky, MD, who died in December 2020 from a COVID-19 infection. Dr Boltansky was an expert nephrologist dedicated to kidney transplantation, a Chilean Society of Nephrology directive, and a cofounder of the FUTAC team.



**FIGURE 1.** Kaplan-Meier curve of COVID-19 infection survival rate in kidney transplant patients according to admission to the location of origin (named comunas in Spanish). Patients below the 50th percentile (red line) and above the 50th income percentile (blue line) are shown. The 12-mo survival rate and the HR are indicated. COVID-19, coronavirus disease 2019; HR, hazard ratio.



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