Outcomes of COVID-19 in Kidney Transplant Recipients: The Sri Lankan Experience

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Abstract

Coronavirus disease 2019 (COVID-19) causes severe illness in the immunocompromised. This study aimed to describe the severity and outcomes of kidney transplant recipients (KTRs) treated for COVID-19 during the first 16 months of the pandemic in Sri Lanka. We conducted a cross-sectional survey of all nephrology centers in Sri Lanka using a self-administered electronic data collection sheet. All practicing nephrologists were invited. KTRs who had been treated/were under treatment for COVID-19 between March 1, 2020 and June 30, 2021 were included. Data on patient demographics, management practices, and outcomes were collected. Outcomes included graft loss, requirement of kidney replacement therapy (KRT), duration of hospital stay, highest level of treatment setting, highest level of respiratory support, and mortality. Fifteen nephrologists (12 centers) responded with data regarding 58 KTRs with COVID-19, 10 of whom were receiving ongoing treatment; 47/58 (81%) were male. Forty (69%) were between 30 and 59 years of age and 15 (25.9%) were aged 60 years or above. Fourteen (24.1%) were within 1 year of transplantation. Fifty-three (91.4%) were on triple immunosuppression. Antiproliferative was reduced/withheld in 89.1% and calcineurin inhibitor was reduced/withheld in 42.1%. Overall mortality was 16/48 (33.3%). Seventeen (29.3%) required intensive care. Six (10.3%) received noninvasive ventilation, and 11 (19.0%) received invasive ventilation. Ten of the ventilated patients died. Six needed acute KRT, five of whom died. One patient survived with a loss of graft. There was no association between modifications to the immunosuppression and outcomes. COVID-19 causes poor outcomes and severe illness in KTRs. Special preventive and therapeutic strategies are urgently required.

Keywords: *COVID-19, kidney transplant recipients, posttransplant*

Introduction

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in over 4.5 million deaths worldwide.[1] It was declared a pandemic by the World Health Organization in March 2020.[2] As of October 14, 2021, Sri Lanka reported over 500,000 confirmed cases and 13,000 deaths due to COVID-19.[3] This has resulted in a large medical, economic, and humanitarian strain on the nation.

SARS-CoV-2 infection can range from an asymptomatic infection to multi-organ failure and death.[4] It has been well recognized that those with comorbidities such as diabetes, hypertension, and cardiovascular disease are at a higher risk of developing severe illness, prolonged hospitalization, and mortality.[5-7] The Centers for Disease Control and Prevention (CDC) has recognized that immunocompromised patients are at a higher risk of developing severe illness.[8] Kidney transplant recipients (KTRs) are one such at-risk population due to their immunocompromised state.[7,9]

In addition to being immunocompromised, KTRs may also have other comorbidities such as diabetes and hypertension, which increases the risk of severe illness.[5]

The COVID-19 pandemic has placed a strain on the Sri Lankan health system. We conducted this study to identify the impact of the COVID-19 infection on KTRs in Sri Lanka to assess the vulnerability of this group. This study aimed to determine the severity and outcomes of KTRs who received in-hospital or outpatient care for COVID-19 in Sri Lanka during the period from March 2020 to June 2021.

Materials and Methods

This study was a cross-sectional survey carried out among the practicing nephrologists caring for KTRs infected with SARS-CoV-2 in Sri Lanka. All practicing

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nephrologists in Sri Lanka were invited to participate in the survey via email. Those who consented were expected to fill out a self-administered electronic Google form. No data which allowed identification of individual patients were collected.

Data of KTRs positive for SARS-CoV-2 by polymerase chain reaction (PCR) test between March 1, 2020 and June 30, 2021 were collected. The survey gathered information regarding socio-demography of the patients (age category, sex), current practices in COVID-19 management, and patient outcomes. The outcomes included highest level of healthcare required, duration of hospital stay, need for respiratory support and kidney replacement therapy (KRT), graft loss, and mortality. Information on changes made to transplant immunosuppressants was also collected.

Statistical Package for Social Sciences (SPSS) version 26.0 was used for statistical analysis. Descriptive statistics were generated. Categorical variables were compared using Pearson's Chi-square test. *P* value of less than 0.05 was considered significant.

This study was approved by the ethics review committee of the Faculty of Medicine, University of Colombo, Sri Lanka (reference number: EC-21-062).

Results

Thirty-seven nephrologists were invited to participate in the study and 19 responded. Fifteen of them had treated KTRs with COVID-19 infection in 12 nephrology and transplantation units from five districts (5/25) in Sri Lanka.

Data were reported on 58 KTRs infected with SARS-CoV-2. The majority were male (81%). Most (69%) were aged between 30 and 59 years, with 15 patients (25.9%) aged 60 years or older. Only three (5.2%) patients were below the age of 30 years. Fourteen (24.1%) of the patients had been transplanted within the previous year. Twenty-six of the patients had been transplanted 1–5 years before (44.8%), while the rest of the patients had been transplanted more than 5 years before (31.0%).

At the time of survey, 48 had completed treatment and 10 were still receiving treatment. The majority of the patients had been/were being managed within a hospital ward (63.8%), with 17 (29.3%) requiring intensive care [Table 1]. Four patients (4/58, 6.9%) had received treatment for more than 4 weeks, 20 patients for 2–4 weeks, and 58.6% for less than 2 weeks. Eleven (19%) patients received mechanical ventilation, and six (10.3%) received noninvasive ventilation. Ten of the ventilated patients (90.0%) were dead at the time of survey, with the remaining patients receiving ongoing care. Overall mortality was 16/48 (33.3%).

Six (6/58, 10.3%) had required acute KRT and at the time of survey, five of whom died following intensive care with invasive ventilation. The sixth was receiving ongoing respiratory support with noninvasive ventilation in the ward setting at the time of survey.

Fifty-three patients were on triple immunosuppression on admission. Changes made to baseline immunosuppression at any point in the disease course are summarized in Figure 1. The antiproliferative drug dose was reduced or withheld in 49/55 patients (89.1%), whereas the calcineurin inhibitor (CNI) dose was either reduced or withheld in 24/57 patients (42.1%).

There was no association between reduction or withholding of the dose of the steroid, CNI, or antiproliferative agent and outcome or graft loss.

Table 1: Outcomes of patients

Care given and outcomes of the patients (*N*=58)	Number of patients	Percentage (%)
Required kidney replacement therapy	6	10.3
Graft loss	5	8.6
Highest level of care required		
Intensive care	17	29.3
Hospital ward	37	63.8
Home care	4	6.9
Maximum level of respiratory support needed		
Intubation and ventilation	11	19.0
Noninvasive ventilation	6	10.3
Oxygen via face mask/nasal cannula	23	39.7
None	18	31.0
Duration of hospital stay/home care		
>4 weeks	4	6.9
2-4 weeks	20	34.5
<2 weeks	34	58.6
Final outcome of patients		
Died	16	27.6
Ongoing care	10	17.2
Recovered	32	55.2

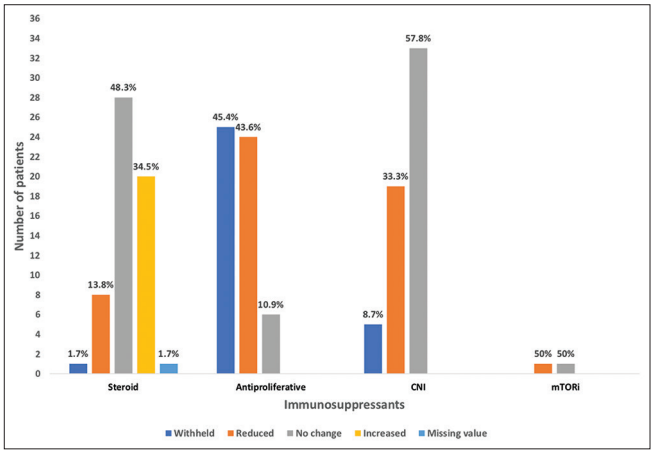

Figure 1: Changes made to immunosuppression in kidney transplant recipients treated for COVID-19. CNI = calcineurin inhibitor, COVID-19 = coronavirus disease 2019, mTORi = mammalian Target of Rapamycin inhibitor

Discussion

The results of our cross-sectional survey portray the impact of COVID-19 in 58 KTRs in Sri Lanka during the first 16 months of the pandemic. During this period, the country focused on a preventive strategy with enforcement of strict lockdowns, rigorous contact tracing, and hospitalization of positive cases for monitoring and isolation. Therefore, it is likely that many with no or mild symptoms were detected and hospitalized and are included in this cohort of 58 patients.

Despite this, the mortality of KTRs with COVID-19 infection at the time of this survey was 33.3% (16/48), with 10/58 patients still receiving ongoing care. The case fatality rate for COVID-19 in Sri Lanka as of October 14, 2021 was 2.5%.[10] This figure includes data from the more recent stages of the pandemic, including the spread of the more virulent delta variant. During this period, the case detection was lower and milder cases are more likely to have been unreported.

Reported mortality has been variable across studies and likely reflects the differing criteria used for inclusion of cases and duration of follow-up. This discrepancy has been highlighted in a systematic review of COVID-19 in KTRs which collected data between April and August 2020. In the 20 studies included in this review, in-patient mortality ranged from 18% to 45%.[11] Considering the likely inclusion of milder cases of COVID-19 in our survey, our mortality appears to be relatively high. Furthermore, much of the data in this meta-analysis is from earlier days during the pandemic, compared to our cohort, when healthcare for COVID-19 may not have been streamlined and many social and service factors may have played a role in high mortality.

The cause for higher mortality in our cohort is not immediately clear. Though there were scattered cases of COVID throughout 2020, the peak in cases in Sri Lanka, related to this cohort, was around April to June 2021. Our data is not able to differentiate between deaths during these two phases of the pandemic. However, higher mortality during the early phase might be explained by lack of consensus treatment and lack of experience in dealing with critically ill COVID patients. Between April and June 2021, health services were overwhelmed by the caseloads, and limitations in resources may have delayed or prevented treatment of some patients. Though our study did not investigate this, issues such as social stigmatization associated with COVID diagnosis and fear of rigid quarantine laws could have led to delays in presentation and diagnosis.

Reducing mortality in this vulnerable group should be considered a priority. Vaccination is known to be less effective in this cohort and may need a different approach to that of the general population, including multiple boosters.[12] Efforts must be taken to vaccinate patients and their immediate contacts before transplantation. As pandemic fatigue sets in, patient education and re-education on preventing the spread of disease, identifying symptoms, and the importance of early presentation to a health-care service is essential. Majority of our patients had their antiproliferative reduced or withheld. This is similar to the reported practices from other study groups and is in keeping with current recommendations.[4,6,13] We were not able to collect data on specific use of antivirals and immunomodulatory therapies among our study participants. However, use of remdesivir during this period was very limited. Dexamethasone was commonly used for patients with low arterial oxygen saturation and tocilizumab for selected patients with severe pneumonia.[14,15] A multidisciplinary approach to adjusting immunomodulation or immunosuppression on a case-by-case basis may be helpful as there is limited high-quality evidence on how to balance the risks of infection, "cytokine storm," and graft rejection in these patients. Antivirals and monoclonal antibodies with immunomodulatory effect should be made readily accessible for urgent use.

One strength of this study is that it is a multicenter study. Though the response rate was only 19/37 (51.4%), all transplant centers responded, and it is most likely that nonresponders had not encountered KTRs with COVID-19. A limitation is that the number of reported cases is small, which is likely a reflection of the small KTR population in the country. As the data regarding previously treated patients was gathered retrospectively, there is a risk of recall bias, particularly with the milder cases going unreported. Due to the nature of our survey, we were also not able to collect specific clinical, demographic, and outcome data. This included data on illness severity at presentation and comorbidity, which are known to influence outcomes in COVID-19. Finally, as this is an observational study, we cannot make any inference regarding the effect of management strategies and treatment outcomes. However, this study is the first to be published from South Asia and provides valuable information to guide planning of future care.

In conclusion, our study depicts severe illness and poor outcomes in KTRs infected with COVID-19. Urgent and effective preventive and therapeutic strategies must be explored and implemented for this vulnerable group to minimize the infection and prevent complications.

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Conflicts of interest

There are no conflicts of interest.

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