The adverse effects of high-dose corticosteroid on infectious and non-infectious sequelae in renal transplant recipients with coronavirus disease-19 in India

Vamsidhar Veeranki | Narayan Prasad | Jeyakumar Meyyappan | Dharmendra Bhadauria | Manas R. Behera | Ravi Kushwaha | Manas R. Patel | Monika Yaccha | Anupama Kaul

Abstract

Introduction: The corticosteroid dosing modulation in renal transplant recipients (RTRs) with coronavirus disease-19 (COVID-19) is not well defined. We aimed to analyze the outcomes and infectious and non-infectious sequelae in RTR with COVID-19 with reference to corticosteroid dosing and the first and second pandemic waves of COVID-19.

Materials and methods: This study included RTRs admitted during two pandemic waves between March 25, 2020, and July 31, 2021. Patients were categorized into mild, moderate, and severe COVID-19. The outcomes and predictors of survival at 4 weeks were analyzed. The survivors were also followed for 6 months and were studied for mortality, readmission rates, and infectious and non-infectious sequelae with reference to high-dose and standard-dose corticosteroids.

Results: A total of 251 RTRs, 104 during the first wave and 147 during the second wave, were treated. Overall mortality was 15.1% (11.5% in the first wave vs. 17.5% in the second wave, \(p = .23\)). The use of high-dose steroids was also significantly high in non-survivors (85.8% vs. 11.3%, \(p = .001\)). On multivariate analysis, the severity of COVID-19, graft dysfunction, and high dose of corticosteroid therapy were associated with increased odds of mortality. Among survivors, 6-month mortality (17.3% vs. 0.5%, \(p = .001\)), readmission rate (91.3% vs. 23.7%, \(p = .001\)), fungal infection (30.4% vs. 2.2%, \(p < .001\)), and post-COVID lung sequelae (21.7% vs. 4.4%, \(p = .008\)) were significantly higher in the high-dose corticosteroid group than in the standard-dose group.

Conclusion: High-dose corticosteroid dosing in RTRs with COVID-19 was associated with increased infections, particularly fungal infections, and non-infectious sequelae with higher mortality on subsequent follow-up.
1 INTRODUCTION

Immunosuppressed renal transplant recipients (RTRs) are at high risk for acquiring infection, hospitalization, and mortality. The coronavirus disease-19 (COVID-19) pandemic, one of the biggest tragedies of the current century for a human being, did not spare the RTRs. During the pandemic, the community spread of SARS-CoV-2 overwhelmed the healthcare resources in many countries, particularly in low-middle socioeconomic countries such as India. It aggravated the situation manifold in an already resource constraint healthcare setting. Despite the Ministry of Health and Family Welfare guideline, Government of India (MOHFW, GOI) for indoor treatment of all RTRs suffering from COVID-19, many patients did not get admission, and the healthcare system was overwhelmed by the huge case burden.3

The second wave worsened the situation, with a sudden surge, high virulence, and severity of SARS-CoV-2 dominated by the delta variant. The changing virulence of the virus, differences in immunity levels, particularly after prior infection and vaccination, and changes in management strategies, including the titration of immunosuppression and hiking up steroids, also affected outcomes during the second wave. By the second wave, however, the transplant physicians had experience of the modulation of immunosuppression from the first wave.4 The strategy of reducing immunosuppression to reduce viral replication predisposed them to rejection on many occasions.5 On the other hand, the hiked-up dose of steroids to combat systemic inflammatory response syndrome (SIRS) in severe COVID-19 predisposes them to viral replication, and bacterial, fungal, and other opportunistic infections, common causes of morbidity and mortality in RTRs. Corticosteroids were increasingly used during the second pandemic wave after the RECOVERY trial,6 and many other shreds of evidence also suggested mortality benefit in moderate to severe COVID-19.7,8 However, the data were mainly limited to the non-immunosuppressed population and extrapolated to transplant recipients.

Moreover, the guidelines were not unanimous on the use of corticosteroids and dosing of corticosteroids, more so in the transplant population who are already on long-term steroids along with other maintenance immunosuppression. Whether the use of high-dose corticosteroids during the second pandemic wave has consequences post-COVID remains undiscovered. The post-COVID sequelae usually seen with severe COVID-19 have been well described in the general population but remain unevaluated in the transplant population.9 We have already shown the poor outcomes and quality of life of RTRs with severe COVID-19 during the first wave.10 The outcome and follow-up data of the patients who had recovered from the second pandemic wave, where the use of steroids and COVID severity per se was relatively higher than in the first wave, are yet not fully established.11 The current study aims to analyze the overall outcomes of RTRs affected by COVID-19 during the two pandemic waves, and in standard-dose versus high-dose corticosteroids, in terms of mortality and infectious and non-infectious sequelae at 4-week and 6-month follow-ups.

2 MATERIALS AND METHODS

2.1 Study design and setting

This single-center retrospective study included RTRs admitted to Rajdhani Corona Hospital (RCH) of the institute between March 25, 2020, and January 31, 2021, during the first pandemic wave and from March 1, 2021, to July 31, 2021, during the second wave. RCH is equipped to capture all data electronically from admission to discharge, with all laboratory investigations and clinical courses of the patients. After entry to RCH, each patient’s data were prospectively entered by the treating physicians and the supervising transplant team into the electronic system without any prior plan for such study. The previous records of the transplant-related data were retrieved from the electronic record of the hospital information system of the institute during both waves. All RTRs were categorized into mild, moderate, and severe COVID groups as per the Indian Council of Medical Research, the MOHFW, GOI, and guidelines for treating COVID-19 by the Indian Society of Organ Transplantation.12,13 The disease was classified as mild when symptoms were present without features of viral pneumonia on imaging (x-ray chest or high-resolution computed tomography scans), moderate if manifestations were present, while severe disease refers to the presence of hypoxia with respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air, including acute respiratory distress syndrome (ARDS).14

The patients were considered to be suffering from coronary artery disease (CAD) if they had a past or present history of acute coronary syndrome or chronic stable angina requiring medical, endovascular, or surgical interventions, including antiplatelet therapy or thrombolysis, percutaneous stenting, and coronary artery bypass surgery. Hypertension was considered if the patients were receiving anti-hypertensives or if the patients had a systolic pressure of >140 mmHg and diastolic blood pressure >90 mmHg.15 Diabetes mellitus (DM) was considered if they had a past history of diabetes, post-transplant DM, patients receiving anti-diabetic medicines, and if they had HbA1C ≥6.5% or fasting plasma glucose ≥126 mg/dl or 2-h plasma glucose ≥200 mg/dl on evaluation.16

All surviving patients were considered recovered and discharged if their report was negative for reverse transcription-polymerase chain reaction. After discharge, all surviving patients were followed up every 4 weeks for at least 6 months either in-person or through the telemedicine services of the institute. RTRs with a failed allograft
and on dialysis were excluded from the study. The institutional ethics committee approved the study. The study was completed with ethics standards as per the Declaration of Istanbul and Declaration of Helsinki.

2.2 Management

All RTR with COVID-19 had been treated in multiple domains, including the management of COVID-19, titration of immunosuppression, monitoring of graft function, glycemic control, and fluid status. Other specific treatments given to patients are shown in Table 1. All patients in the moderate and severe categories received anticoagulation prophylaxis. The trained physicians and nursing staff managed all COVID-19-affected RTRs under the supervision of transplant physicians.

2.3 Modification in immunosuppression and dosing of steroids

The doses of antimetabolites were reduced to half in patients with mild–moderate COVID-19 and stopped in patients with severe COVID-19. Calcineurin inhibitors (CNIs) were reduced to half in patients with severe disease. Trough levels of tacrolimus were targeted toward lower recommended levels, between 3 and 5 ng/ml if beyond 6 months post-transplant and between 6 and 8 ng/ml within 6 months post-transplant. The titration of the immunosuppression remained the same during both waves of COVID-19, except varying doses of corticosteroid dosages were used to suppress SIRS that varied during both waves as seen in another study. RTRs were categorized into two groups based on corticosteroid dosing: (1) standard-dose corticosteroid category, those who received corticosteroids equivalent to 6 mg of dexamethasone or less per day for 14 days; and (2) high-dose corticosteroids category, those who received corticosteroids more than 6 mg dexamethasone or equivalent doses per day, including intravenous methylprednisolone (IV-MPS) for 3 days followed by 50 mg per day prednisolone or its equivalent for 14 days. The patients were shifted back onto the previous dose of prednisolone at the time of discharge in survivors. They were admitted to non-COVID facility if further evaluations and graft kidney biopsy were required between during both waves after discharge and follow-up as part of the institute's protocol. Various infectious complications, such as fungal infections (pulmonary or extrapulmonary fungal infections) and non-fungal severe infections requiring hospitalization (SIRH), including urinary tract infections (UTIs), lower respiratory tract infection (LRTI), and tuberculosis, were also monitored during follow-up and noted. Fungal infections were diagnosed if they fulfilled the criteria for the category of possible fungal infections as per the revised EORTC and MSGERC consensus. Among the non-infectious complications, the graft dysfunction/rejection rates and post-COVID lung sequelae were monitored. Acute graft dysfunction was defined as an increase in serum creatinine of ≥25% from the baseline values. By graft biopsy as indicated, and the biopsy-proven acute rejections (BPAR) were also recorded and compared between the two waves.

2.4 Statistical analysis

All continuous data were expressed as the mean or median depending on the normality of the data. Categorical data were expressed as percentages. The chi-square test or Fischer’s exact test was used to compare the categorical values between the groups, as per the requirements. Student’s t-test was used to compare the mean values and continuous variables if they were normally distributed. Mann-Whitney’s U-test was used to analyze whether the data were not normally distributed. Univariate and multivariate Cox regression analyses were used to analyze the factors predicting mortality. Cox regression analysis was performed to investigate the predictors of mortality, using mortality as the dependent variable. Age, gender, induction regimen, immunosuppressive maintenance regimen, history of rejection, diabetes, use of steroids, and other comorbidities were used as independent variables. Statistical analysis was performed by SPSS software, version 25.

3 RESULTS

A total of 251 RTRs, 104 during the first wave and 147 during the second wave, were treated during the study period (Table 1). The baseline characteristics of the RTRs with COVID-19 between the first and second pandemic waves were similar in age, gender distribution, duration after transplantation, and comorbidities. The comorbidities, such as diabetes, hypertension, and CADs, were actively managed as per clinical indication and requirement, as all these patients were admitted to the hospital. The proportion of patients with hypertension and DM was significantly higher during the second wave (70.2% vs. 87.7%, \( p = .002 \); 34.6% vs. 49.6%, \( p = .03 \), respectively). The maintenance immunosuppression regimen was similar; however, a higher proportion of patients in the first wave had anti-thymocyte globulin induction at the time of transplantation and basiliximab induction during the second wave. In addition, there was a trend toward increased male gender and a lower proportion of CAD in the second wave, although it did not reach statistical significance. The severity of COVID-19 was similar across the two waves.

3.1 Modifications in immunosuppression and management of COVID-19

The corticosteroid dose was increased in a significantly higher proportion of patients in the second wave than in the first wave (95.9% vs. 76.9%, \( p = .002 \)) (Table 1). More specifically, the use of IV-MPS pulse significantly increased in the second wave compared to the first wave (22.4% vs. 11.5%, \( p = .03 \)). Overall, of all the cases of mild–moderate
| Variable                                             | Total (n = 251) | Wave 1 (n = 104) | Wave 2 (n = 147) | p-Value |
|------------------------------------------------------|-----------------|------------------|------------------|---------|
| Age (mean ± SD)                                       | 43.3 (12.8)     | 44.09 (± 12.8)   | 42.8 (± 12.9)    | .41     |
| Gender (male, %)                                      | 210 (83.6%)     | 88 (84.6%)       | 122 (93.1%)      | .07     |
| Type of transplant                                    |                 |                  |                  |         |
| • ABOc live donor                                     | 233 (92.8%)     | 96 (92.3%)       | 137 (93.2%)      | .8      |
| • ABOi live donor                                     | 18 (7.1%)       | 8 (7.7%)         | 10 (6.8%)        | .7      |
| Duration since transplant (months), mean ± SD         | 65.9 ± 8.2      | 64.33 ± 48.1 (2–280) | 66.6 ± 52.2 (15 days–335 months) | .9      |
| Comorbidity                                           |                 |                  |                  |         |
| • DM                                                 | 109 (43.4%)     | 36 (34.6%)       | 73 (49.6%)       | .03     |
| • HTN                                                | 202 (80.4%)     | 73 (70.2%)       | 129 (87.7%)      | .002    |
| • CAD                                                | 10 (4%)         | 7 (6.7%)         | 3 (2%)           | .06     |
| • Past history TB                                     | 34 (13.5%)      | 13 (12.5%)       | 21 (14%)         | .11     |
| • Past history fungal pneumonia                      | 9 (3.5%)        | 4 (3.8%)         | 5 (3.4%)         | .8      |
| Induction                                             |                 |                  |                  |         |
| • ATG                                                | 52 (20.7%)      | 28 (26.9%)       | 24 (16.3%)       | .04     |
| • Basiliximab                                         | 156 (62.1%)     | 48 (46.2%)       | 108 (73.4%)      | .001    |
| • Unknown/no induction                                | 43 (17.1%)      | 28 (26.9%)       | 15 (10.2%)       | .001    |
| Maintenance immunosuppression                         |                 |                  |                  |         |
| • Triple (T/C + M + P)                                | 248 (98.8%)     | 102 (98%)        | 146 (99.3%)      | .8      |
| • Dual (T/C + P)                                      | 3 (1.2%)        | 2 (2%)           | 1 (0.6%)         | .3      |
| Disease severity                                      |                 |                  |                  |         |
| • Mild to moderate                                    | 187 (74.5%)     | 75 (72.1%)       | 112 (76.1%)      | .6      |
| • Severe                                              | 64 (25.5%)      | 29 (27.8%)       | 35 (23.8%)       |         |
| Antimetabolite alteration                             |                 |                  |                  |         |
| • Reduced                                             | 153 (60.9%)     | 60 (57.6%)       | 93 (63.2%)       | .38     |
| • Stopped                                             | 82 (32.7%)      | 33 (31.8%)       | 49 (34%)         | .71     |
| • No alteration                                       | 16 (6.4%)       | 11 (10.6%)       | 5 (3%)           | .01     |
| CNI alteration                                        |                 |                  |                  |         |
| • Reduced                                             | 56 (22.3%)      | 23 (22.1%)       | 33 (22.4%)       | .95     |
| • Stopped                                             | 16 (6.3%)       | 3 (2.9%)         | 13 (8.8%)        | .06     |
| • No alteration                                       | 179 (71.4%)     | 78 (75%)         | 101 (68.7%)      | .27     |
| Steroids increased                                    |                 |                  |                  |         |
| • Standard dose                                       | 176 (70.1%)     | 68 (65.4%)       | 108 (73.5%)      | .18     |
| • High dose                                           | 45 (17.9%)      | 12 (11.5%)       | 33 (22.4%)       | .03     |
| Antiviral strategies                                   |                 |                  |                  |         |
| • Ivermectin                                          | 188 (74.9%)     | 89 (85.6%)       | 99 (67.3%)       | .005    |
| • Azithromycin                                        | 216 (86%)       | 91 (87.5%)       | 125 (85%)        | .5      |
| • Convalescent plasma                                 | 1 (0.3%)        | 1                 | 0                 | .7      |
| • Tocilizumab                                         | 2 (0.7%)        | 0                 | 2 (1.5%)         | .4      |
| • Tofacitinib                                         | 6 (2.4%)        | 0                 | 6 (4.0%)         | .04     |
| • IVIG                                                | 12 (4.8%)       | 0                 | 12 (7.3%)        | .005    |
| • Remdesivir                                          | 86 (34.3%)      | 46 (44.2%)       | 40 (27.2%)       | .005    |

Abbreviations: ABOc, ABO-compatible transplant; ABOi, ABO-incompatible transplant; ATG, anti-thymocyte globulin; CAD, coronary artery disease; CNI, calcineurin inhibitors; DM, diabetes mellitus; HTN, hypertension; IVIG, intravenous immunoglobulin; TB, tuberculosis; T/C + M + P, tacrolimus/cyclosporine + mycophenolate mofetil + prednisolone.
COVID (n = 187), 172 (92%) received standard-dose corticosteroids, and only 8% received high-dose corticosteroids (p = .0001). However, the use of standard-dose and high-dose corticosteroids was similar in severe COVID-19 cases. Of all the cases of severe COVID-19 (n = 64), 46.9% received standard-dose corticosteroids and 53.1% received high-dose corticosteroids (p = .48).

In contrast, the use of remdesivir in the first wave was higher than that in the second wave (44.2% vs. 27.2%, p = .005) due to nonavailability issues in the second wave. However, 12 patients (7.3%) with severe COVID-19 during the second wave received intravenous immunoglobulin compared to none during the first wave, and six of them survived. Anti-COVID therapy, such as azithromycin and ivermectin, was also used as per guidelines issued with emerging evidence. Other anti-COVID therapies, such as tofacitinib, were infrequently used during the second wave.

3.2 | Outcome analysis

A total of 38 (15.1%) of the 251 RTRs with COVID-19 died during the initial hospitalization. Thirteen patients (11.5%) died during the first wave, and 25 (17.5%) died during the second wave (p = .23). The comparison of clinical and laboratory parameters of the survivors and non-survivors, at the time of discharge or death during both pandemic waves is shown in Table 2. A total of four patients with mild, one with moderate, and 33 with severe COVID-19 died. The risk of death with severe disease was 6.34 (95% confidence interval 2.5–15.9), which was higher than that with mild–moderate COVID-19. The cause of death in mild COVID-19 was cardiovascular, two patients had an acute myocardial infarction, one patient had a cerebrovascular accident, and one had a sudden death. In addition, one more death in the moderate category of COVID-19 was also due to a sudden cardiac arrhythmia. Although these cardiovascular-related deaths among the mild category patients do not seem directly due to COVID-19, they could have been precipitated secondary to SARS-CoV-2 infection. As they were monitored regularly for any QT prolongation (secondary to various drugs such as tacrolimus and azithromycin), conduction abnormalities were unlikely to be the cause of death for them. On the other hand, the causes of death in 33 patients with severe COVID were ARDS and associated complications. All patients with moderate and severe disease received anticoagulant prophylaxis.

The mean age of the patients, proportion of cadaveric transplantation, diabetes, and CADs were significantly higher in the non-survivor group. Graft dysfunction rates were also considerably higher among the non-survivors. The inflammatory markers serum ferritin and C-reactive protein were elevated in non-survivors than in survivors. High-dose steroids were also significantly higher among the non-survivors (85.8% vs. 11.3%, p = .001). As expected, the oxygen requirement, vasopressor, or ventilator requirement was significantly higher among the non-survivors.

3.3 | Predictors of mortality

The predictors of mortality on univariate and multivariate Cox regression analyses are shown in Table 3. Elderly patients aged >60 years had high odds, and those younger than 40 years had low odds for mortality on univariate analysis. Among the comorbidity factors, diabetes and CAD were significant risk factors for mortality, while hypertension was not associated with mortality. Other factors such as the severity of COVID-19, graft dysfunction at presentation, high-dose corticosteroid therapy, vasopressor requirement, and non-invasive and invasive ventilation were also significantly associated with mortality. However, on multivariate analysis, only severity of COVID-19, graft dysfunction, and high dose of corticosteroid therapy were associated with an increased risk of death.

3.4 | Infectious and non-infectious sequelae in surviving patients with reference to high-dose versus standard-dose corticosteroids on follow-up

3.4.1 | Additional mortality on follow-up after discharge at the end of 6 months

In addition to the 13 (12.5%) deaths during the first wave and 25 (17%) during the second wave, there was one more death from the first wave and three deaths from the second wave during the 6-month follow-up period. The 6-month mortality among the survivors was 17.3% (n = 4) in the high-dose steroid group compared to 0.5% (n = 1) in the standard-dose group (p = .001). The hazard ratio of death within 6 months with high-dose corticosteroids was 35.6 (3.8–333.6), p = .002 (Table 4).

Of the four deaths in the high-dose group, three patients had a severe fungal infection, while one patient had severe bacterial LRTI and sepsis. One death from the standard-dose corticosteroid group was due to cavitary fungal pneumonia and pneumothorax. The readmission rates over a 6-month follow-up period were 91.3% among the survivors of high-dose corticosteroids compared to 23.7% of the patients who had received standard-dose steroids (p = .001).

3.5 | Fungal infections

A total of 11 (5.1%) patients (one in first wave and 10 in second wave) developed fungal infections after recovery from COVID-19, and four (all from the second wave) of them died due to invasive fungal infections (Supplementary Table 1). Fungal infections were noticed in a significantly higher proportion of patients in the high-dose corticosteroid group than in the standard-dose group (7 [30.4%] vs. 4 [2.2%], p = .001). The hazard ratio of fungal infections in patients with high-dose corticosteroids compared to standard-dose steroids was 17.2 (5.07–58.5), p = .001.
**TABLE 2** Comparison of survivors and non-survivors across both pandemic waves among renal transplant recipients with COVID-19

| Variable                         | Survivors (n = 213) | Non-survivors (n = 38) | p-Value | p-Value |
|----------------------------------|---------------------|------------------------|---------|---------|
| **Age (mean, years) ± SD**       | 41.9 ± 12.6         | 43.2 (12.4)            | .22     |
| **Gender (male, %)**             | 189 (88.7%)         | 74 (83.1%)             | .029    |
| **Type of transplant**           |                     |                        |         |
| • ABOc live donor                | 197 (92.5%)         | 34 (89.5%)             | .71     |
| • ABOi live donor                | 16 (7.5%)           | 4 (10.5%)              |         |
| **Type of transplant**           | .37                 |                        | .016    |
| • Live                           | 210 (98.6%)         | 35 (92.1%)             |         |
| • Cadaveric                      | 3 (1.4%)            | 3 (7.9%)               |         |
| **Induction**                    |                     |                        |         |
| • ATG                            | 40 (18.8%)          | 173 (81.2%)            | .09     |
| • Basiliximab                    | 133 (62.4%)         | 25 (65.8%)             | .14     |
| • No induction                   | 40 (18.8%)          | 2 (16.7%)              | .10     |
| **Maintenance immunosuppression**| .09                 |                        | .03     |
| • Triple                         | 211 (84.7%)         | 38 (15.3%)             |         |
| • Dual                           | 2 (0.9%)            | 0                      |         |
| **Duration since transplant (months), mean (range)** | 65.3 ± 49.1 | 69.08 ± 43.1 | .09     |
| **Comorbidity**                  |                     |                        |         |
| • DM                             | 84 (39.4%)          | 25 (65.8%)             | .14     |
| • HTN                            | 168 (78.9%)         | 32 (84.2%)             | .01     |
| • CAD                            | 5 (2.3%)            | 4 (10.5%)              | .93     |
| • History of PTB                 | 28 (13.1%)          | 4 (10.5%)              | .26     |
| • History of fungal pneumonia    | 4 (1.9%)            | 3 (7.9%)               | .73     |
| **History of rejection within the last 1 year** | 31 (14.6%) | 30 (33.7%) | .06     |
| **COVID-19 severity category**   | .03                 |                        |         |
| • Mild                           | 162 (76.1%)         | 162 (76.1%)            | .92     |

(Continues)
| Variable                                      | Survivors (n = 213) | Non-survivors (n = 38) | p-Value |
|-----------------------------------------------|---------------------|------------------------|---------|
|                                              | Total               | Wave 1 (n = 89)        | Wave 2 (n = 124) | p-Value |
|                                              | Total               | Wave 1 (n = 13)        | Wave 2 (n = 25)  | p-Value |
|                                              | Total               | Wave 1 (n = 13)        | Wave 2 (n = 25)  | p-Value |
| • Moderate                                    | 22 (10.3%)          | 6 (6.7%)               | 16 (12.9%)      | .14     |
|                                              | 1 (4.3%)            | 0                      | 1 (3.8%)        | .49     |
| • Severe                                      | 29 (13.6%)          | 15 (16.9%)             | 14 (11.3%)      | .24     |
|                                              | 33 (86.8%)          | 12 (36.4%)             | 21 (63.6%)      | .10     |
| Serum ferritin                                | 1026.8 (2753)       | 626.9 (472.3)          | 1363.9 (3690.5) | .13     |
|                                              | 5294.4 (5499.1)     | 1067.6 (606.1)         | 6213.3 (5666.01) | .05   |
| C-reactive protein                            | 40.2 (58.7)         | 51.7 (72.8)            | 30.8 (42.4)     | .04     |
|                                              | 139.3 (91.3)        | 199.5 (111.7)          | 103.2 (71.6)    | .006    |
| Graft dysfunction at presentation             | 78 (36.6%)          | 40 (44.9%)             | 38 (30.6%)      | .03     |
|                                              | 30 (78.9%)          | 12 (100%)              | 18 (69.2%)      | .03     |
| Steroids                                      | 24 (11.3%)          | 6 (6.7%)               | 18 (14.5%)      | .27     |
|                                              | 25 (65.8%)          | 6 (50%)                | 19 (73.1%)      | .16     |
| • High-dose steroids                          | 189 (88.7%)         | 83 (93.3%)             | 116 (85.5%)     | .04     |
| • Low-dose–medium-dose steroids               | 13 (34.2%)          | 6 (50%)                | 7 (26.9%)       | .17     |
| Antimetabolite alteration                     |                     |                       |               | <.001   |
| • Reduced                                     | 150 (70.4%)         | 59 (66.3%)             | 91 (73.3%)      | .27     |
| • Stopped                                     | 34 (15.9%)          | 14 (15.7%)             | 20 (16.1%)      | .93     |
| • Unaltered                                   | 0                   | 0                      | 0               | .34     |
| CNI alteration                                | 34 (15.9%)          | 14 (15.7%)             | 20 (16.1%)      | .27     |
| • Reduced                                     | 22 (57.9%)          | 6 (50%)                | 16 (61.5%)      | .51     |
| • Stopped                                     | 16 (42.1%)          | 2 (16.7%)              | 4 (15.3%)       | .91     |
| ICU requirement at admission                  | 7 (3.3%)            | 2 (2.2%)               | 5 (4%)          | .47     |
| Oxygen requirement at admission               | 51 (23.9%)          | 21 (23.6%)             | 30 (24.1%)      | .93     |
| Ventilator requirement during the course      | 2 (0.9%)            | 1 (1.1%)               | 1 (0.8%)        | .813    |
| (including NIV)                               | 38 (100%)           | 12 (31.6%)             | 26 (68.4%)      | .15     |
| Vasopressor requirement during course         | 2 (0.9%)            | 1 (1.1%)               | 1 (0.8%)        | .813    |
| (including NIV)                               | 35 (92.1%)          | 9 (25.7%)              | 26 (74.3%)      | .008    |
| Abbreviations: ABOc, ABO-compatible transplant; ABOi, ABO-incompatible transplant; ATG, anti-thymocyte globulin; CAD, coronary artery disease; CNI, calcineurin inhibitors; DM, diabetes mellitus; HTN, hypertension; ICU, intensive care unit; NIV, non-invasive ventilation; PTB, pulmonary tuberculosis.
3.6 | Non-fungal infectious complications

3.6.1 | Serious infections requiring hospitalization post-COVID-19

The overall major non-fungal SIRH were similar between the two groups [5 (21.7%) vs. 29 (31.8%), \( p = .32 \)]. We found that a total of 19 (9.1%) patients in the high-dose group had UTIs. More specifically, *Escherichia coli* was the causative organism found in nine cases, while *Pseudomonas* was found in three patients and *Proteus* sp. in two more patients were the causative organisms found. Notably, three cases of UTI due to *Morganella morgagni* were noted. Of the patients who were hospitalized for UTIs, 13 patients (76.4%) had UTIs within 1 month of recovery from COVID-19. The LRTI rate was found to be significantly higher in the high-dose group than in the standard-dose group [1 (4.3%) vs. 1 (0.2%), \( p = .02 \)]. The rate of tubercular and viral infections among the two groups was similar (Table 4).

3.7 | Non-infectious sequelae in surviving patients

3.7.1 | Post-COVID lung sequelae

A total of 13 patients (three in first wave and 10 in second wave) had post-COVID lung sequelae. The proportion of patients with lung sequelae was similar during both waves; however, it was significantly higher among the patients who had received high-dose steroids [5 (21.7%) vs. 8 (4.4%), \( p = .008 \)]. All these patients presented with persistent breathlessness after recovery from COVID-19. All patients had focal to diffuse lung fibrosis with a subpleural honeycombing appearance as a part of the lung sequelae (representative Figure 1). All patients with post-COVID lung sequelae had severe COVID-19 and required oxygen support, and two of them required ventilator support during COVID-19.

3.7.2 | Biopsy-proven graft rejections post-COVID

As shown in Table 4, a total of 10 (4.8%) patients (three in first wave and seven in second wave), three (13%) from the high-dose group and seven (3.8%) from the standard-dose group (\( p = .05 \)) had biopsy-proven graft rejections (BPAR). All three patients in the high-dose corticosteroid group had severe COVID-19 and received a reduced dose of tacrolimus without mycophenolate mofetil (MMF). In the standard-dose group, five patients had moderate COVID-19 with reduced MMF and CNI by 50%, and two patients had severe COVID-19 with reduced CNI and stopped MMF. The mean duration post-transplant among these patients was 54.2 ± 26.8 months. Six patients (60%) had chronic active antibody-mediated rejection (ABMR), three patients (40%) had T-cell-mediated rejection (TCMR), and one (10%) had mixed rejection. All cases of ABMR were treated with plasmapheresis and intravenous immunoglobulin. Patients with TCMR were treated with pulse MPS of 500 mg for 3 consecutive days. Nine patients (six ABMR and three TCMR) responded to the anti-rejection therapy; however, one patient from the second wave with severe ABMR had graft loss and did not respond to treatment.

4 | DISCUSSION

In this study, we observed that more RTRs (\( n = 147 \) patients) were admitted over a short period of 5 months during the explosive and hard-hit second wave, compared to only 104 over 10 months during the first wave that slowly evolved to grip the entire world. The differences in the preparedness-related issues during the two waves across India were briefly summarized in previous studies from India that are also applied here.\(^{21}\) While the essential accessories such as personal protective equipment (PPE)-kit were limited during the first wave, the sudden surge of cases during the second wave outweighed the availability of oxygen supply, drugs such as remdesivir, and hospital and intensive care unit (ICU) beds. The unavailability of remdesivir was highlighted in print and electronic media during that period.\(^{22}\) We observed less use of remdesivir during the second wave, mainly because of unavailability. Although we do not have data on sequencing for our cohort of patients, multiple variants, including the delta variant, have been reported during the second wave.\(^{23,24}\) This study showed that the number of patients admitted with diabetes and hypertension was high during the second wave. However, the overall severity of COVID-19 was similar between the two waves, and more importantly, there was no difference in the mortality rate.
between the two waves. The mortality rate found in our cohort is similar to the prior studies on COVID-19 in RTRs. With evolving evidence of various therapeutic armamentariums in COVID-19, the treatment regimen has been changed from time to time and therefore varied in the first and second waves. The modulation of maintenance immunosuppression, including the titration of CNIs and antimetabolites, remains the same during both waves, which could be because of the carry-over learning experience from the first wave (Table 1). However, the use of corticosteroids increased during the second wave. The increase in the use of steroids was based on the pieces of evidence from numerous small studies and recommendations from the RECOVERY trial. Compared to dexamethasone, the concept of better penetration of MPS into the lung was published, leading to higher MPS use during the second wave. The RECOVERY trials and other studies supported the use of dexamethasone and its equivalent corticosteroid for the treatment of COVID-19 pneumonia and associated ARDS. The recovery trial showed that corticosteroids reduced SIRS and ARDS severity and prevented COVID-19-associated mortality in the general population. However, these trials did not explore the consequences of a high dose of corticosteroids on other outcomes in the transplant population, a group of patients where the add-on amount of steroids over the long-term background immunosuppression might be harmful.

In addition, the higher use of corticosteroids could lead to unwelcoming post-effects, particularly infectious sequelae. Fungal infections, particularly invasive fungal infections such as mucormycosis and aspergillosis, were reported in 11 surviving patients with COVID-19 after discharge from the COVID-19 hospital (Figure 2). Four of them subsequently died. There was a sudden surge in “black fungus” mucormycosis across India in non-transplant recipients. A similar study by Kute and coworkers also reported 11 cases of post-COVID mucormycosis among RTRs, and an approximately equal mortality of 27% was reported within that cohort. To our surprise, we did not observe a significant association with DM and other induction regimens associated with a substantial risk of these fungal infections in the post-COVID period. Steroids are a double-edged sword, and infectious sequelae, especially in our immunocompromised subgroup, could be a plausible explanation.

However, non-fungal SIRH rates were not significantly different between the two steroid groups. Even though the UTI is uncommon after long-term post-transplant, UTI was observed in 8.1% of these patients post-COVID. The study could not pinpoint the exact reasons for the high incidence of UTIs in the post-COVID period. However, personal hygiene, isolation in the COVID-19 ward, and limited toilet facilities in isolation wards may be the speculated risk factors for UTI in these patients. In addition, M. morgagni infection was seen in three patients (17.6% of all cases of UTI), an uncommon etiology for UTI. The prolonged hospital stay and higher use of broad-spectrum antibiotics might have led to high UTI rates due to nosocomial organisms. Each episode of SIRH poses some adverse effects on graft function and shortens graft life, affecting overall graft survival. Such findings merit further investigation.

Post-COVID lung sequelae were noted in 6.2% of RTRs in our study, more so in the patients who had received high-dose corticosteroids (22%). We have also observed that a significant number of patients developed other non-infectious sequelae post-COVID-19, including post-COVID lung sequelae and BPAR. This could probably be due to higher secondary infection rates in immunosuppressed RTR.

The after-effects of COVID-19 specific to RTRs are graft dysfunction and rejection rates. We found that the graft rejection rate was higher in the second wave than in the first wave and was higher among the high-dose corticosteroid group, probably because of the
TABLE 3  Predictors of 4-week mortality in COVID-19 affected renal transplant recipients using univariate and multivariate Cox regression analyses

| Independent variables | Odds ratio | 95% CI | p-Value |
|-----------------------|------------|--------|---------|
| **Univariate analysis** |            |        |         |
| Age                   |            |        |         |
| • <40 years           | 0.3        | 0.16–0.806 | .013   |
| • 40–60 years         | 1.7        | 0.86–3.5 | .12     |
| • >60 years           | 2.6        | 1.2–6.7 | .04     |
| Male gender           |            | 0.67   | .53     |
| Comorbidities         |            | 0.67   | .53     |
| • Diabetes mellitus   | 2.95       | 1.4–6.09 | .003   |
| • Hypertension        | 1.43       | 0.56–3.62 | .453   |
| • Coronary artery disease | 4.89 | 1.25–19.1 | .022   |
| • Past history of tuberculosis | 0.77 | 0.25–2.35 | .656   |
| • Past history of fungal pneumonia | 0.22 | 0.04–1.1 | .062   |
| Live transplant       | 0.16       | 0.03–0.85 | .01    |
| Induction regimen     |            | 0.64   | .28     |
| • ATG                 | 0.64       | 0.29–1.44 | .69    |
| • Basiliximab         | 0.86       | 0.42–1.78 | .69    |
| COVID-19 disease severity |      |        |         |
| • Mild category       | 0.03       | 0.01–0.10 | <.001  |
| • Moderate category   | 0.235      | 0.03–1.79 | .163   |
| • Severe category     | 41.86      | 15.1–115.9 | <.001  |
| Graft dysfunction at presentation | 6.49 | 2.83–14.85 | <.001  |
| High-dose steroid versus standard dose | 15.14 | 6.86–33.48 | <.001  |
| O2 requirement at presentation | 27.71 | 9.3–81.8 | <.001  |
| Requirement of mechanical ventilation including NIV | 86.33 | 29.1–256.1 | <.001  |
| Requirement of vasopressor support | 295.4 | 61.5–1417.7 | <.001  |
| **Multivariate analysis** |            |        |         |
| Age 20–40 years       | 0.33       | 0.96–1.14 | .08    |
| Age >60 years         | 0.79       | 0.30–5.17 | .74    |
| Diabetes mellitus     | 2.0        | 0.68–5.8 | .2     |
| Coronary artery disease | 0.59  | 0.08–4.15 | .603   |
| Live transplant       | 0.38       | 0.02–5.40 | .477   |
| Mild category         | 1.2        | 0.01–138.1 | .91   |
| Severe category       | 10.48      | 1.16–94.5 | .03    |
| Graft dysfunction at presentation | 4.23 | 1.33–13.4 | .01    |
| Oxygen requirement    | 1.16       | 0.01–125.4 | .95   |
| Requirement of mechanical ventilation including NIV | 22.9 | 13.7–88.3 | .001  |
| High-dose versus low-dose corticosteroids | 5.70 | 1.97–16.4 | .001  |

Abbreviations: ATG, anti-thymocyte globulin; CI, confidence interval; NIV, non-invasive ventilation.

The modulation of MMF and CNIs in these patients (Table 4). A total of 10 patients developed rejections, mostly during the second wave. All patients had severe COVID-19, and MMF was reduced or stopped. However, CNI was decreased in seven patients and was not changed in three patients. All three patients without CNI reduction had cellular rejection and responded to treatment. It is possible that modulation in CNI and MMF in these patients led to ABMR, and one patient had graft loss. At present, there are limited data on graft sequelae post-COVID. The study highlights that patients who had immunomodulation need to be followed up for a more extended period, as they have a predisposition to chronic graft dysfunction. The 35.6-fold increased risk of death in the high-dose steroid group that was not found in the
TABLE 4  Follow-up data of infectious and non-infectious sequelae among high-dose and standard-dose corticosteroids during COVID-19 (n = 208)

| Variables                              | Total (n=208) | High-dose corticosteroids (n=23) | Standard-dose corticosteroids (n=185) | p-Value |
|----------------------------------------|---------------|----------------------------------|---------------------------------------|---------|
| 6-month mortality                      | 5 (2.4%)      | 4 (17.3%)                        | 1 (0.5%)                             | <.001   |
| Readmission rate                       | 65 (31.2%)    | 21 (91.3%)                       | 44 (23.7%)                           | <.001   |
| Fungal infections                      | 11 (5.2%)     | 7 (30.4%)                        | 4 (2.2%)                             | <.001   |
| Major infections requiring hospitalization | 34 (25%)     | 5 (21.7%)                        | 29 (31.8%)                           | .32     |
| 1. UTI                                 | 17 (8.1%)     | 2 (8.7%)                         | 15 (8.3%)                            | .94     |
| 2. LRTI                                | 2 (0.9%)      | 1 (4.3%)                         | 1 (0.2%)                             | .02     |
| 3. Tuberculosis                        | 6 (2.8%)      | 1 (4.3%)                         | 5 (2.7%)                             | .66     |
| 4. Viral infections                    | 9 (4.3%)      | 1 (4.3%)                         | 8 (4.3%)                             | 1.0     |
| A) BKV                                 | 4 (1.9%)      | 0                                | 4 (2.2%)                             | .4      |
| B) CMV                                 | 2 (0.9%)      | 0                                | 2 (1.1%)                             | .6      |
| C) Others                              | 3 (1.4%)      | 0                                | 2 (1.6%)                             | .44     |
| a. Dengue                              | 2 (0.9%)      | 1 (4.3%)                         | 1 (0.6%)                             | .09     |
| b. Herpes simplex                      | 1 (0.5%)      | 0                                | 1 (0.6%)                             | .77     |
| Non-infectious complications           |               |                                  |                                       |         |
| 1. Post-COVID lung sequelae            | 13 (6.2%)     | 5 (21.7%)                        | 8 (4.4%)                             | .008    |
| 2. BPARa                               | 10 (4.8%)     | 3 (13%)                          | 6 (3.8%)                             | .05     |

Abbreviations: BPAR, biopsy-proven acute rejection; BKV, BK virus; CMV, cytomegalovirus; LRTI, lower respiratory tract infection; UTI, urinary tract infection.

*Donor-specific antibody (DSA) by single antigen bead assay was available for four patients and was positive for class II antibodies. Two patients with antibody-mediated rejection and one with mixed rejection were treated based on biopsy reports, as DSA could not be performed due to financial constraints.

prior studies could be due to the very low overall event rate and more so in the standard-dose group.

4.1  | Strengths and limitations

The study is limited to single-center experience; however, it is one of the largest studies highlighting the infectious and non-infectious sequelae outcomes in RTRs post-COVID-19. In addition, the comparability of the two groups across the two pandemic waves may be limited by various confounding factors, including overwhelmed resources, different variants, change in policy to give higher doses of steroids during the delta wave, remdesivir shortage during the delta wave, shortages of oxygen, ICU beds and hospital bed shortage. The study also highlights the adverse effects of high doses of corticosteroids in already immunosuppressed RTRs.

5  | CONCLUSION

To conclude, there was no difference in the mortality of RTRs during the first and second waves of the COVID-19 pandemic. The severity of COVID-19, graft dysfunction at presentation, and high-dose corticosteroids were independently associated with mortality in RTRs. Higher doses of corticosteroids were associated with higher infectious complications, particularly fungal infections post-COVID-19, and more deaths.

5.1  | Future research

There is a need for a trial to standardize the dose of corticosteroids in RTRs with COVID-19. Inadvertent use of high-dose corticosteroids should be avoided in RTRs.

ACKNOWLEDGMENTS

We acknowledge the nodal officer Dr. RK Singh, Emergency Medicine, and Dr. Alok Nath, Pulmonary Medicine, for their contribution to the management of patients during admission. We also acknowledge Dr. Prabhakar Mishra of the Department of Biostatistics for statistical analysis input.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors have not received any funding for this project.
AUTHOR CONTRIBUTIONS
Narayan Prasad and Vamsidhar Veeranki conceptualized, analyzed, and wrote the manuscript. Jeyakumar Meyyappan, Dharmendra Bhadauria, Manas R. Behera, and Ravi Kushwaha collected data and performed the analysis. Manas R. Patel, Monika Yaccha, and Anupama Kaul looked after the clinical management and helped in the follow-up of the patients.

DATA AVAILABILITY STATEMENT
The data are available with the first author and corresponding authors. The data can be made available upon reasonable request. The data cannot be made public due to ethical issues.

ORCID
Narayan Prasad https://orcid.org/0000-0001-9801-0474
Dharmendra Bhadauria https://orcid.org/0000-0002-1273-8294

REFERENCES
1. Toapanta N, Torres IB, Sellarés J, Chamoun B, Serón D, Moreso F. Kidney transplantation and COVID-19 renal and patient prognosis. Clin Kidney J. 2021;14(1):sup11:1-29.
2. Revised Guidelines for Home Isolation. Accessed January 2022. https://www.mohfw.gov.in/pdf/RevisedHomeIsolationGuidelines0502022.pdf
3. The Lancet. India’s COVID-19 emergency. Lancet. 2021; 397(10286):1683.
4. Yi SG, Rogers AW, Saharia A, et al. Early experience with COVID-19 and solid organ transplantation at a US high-volume transplant center. Transplantation. 2020;104(11):2208-2214.
5. Pascual M, Theruvath T, Kawai T, Tolkoff-Rubin N, Cosimi AB. Strategies to improve long-term outcomes after renal transplantation. N Engl J Med. 2002;346(8):580-590.
6. RECOVERY Collaborative Group; Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384(8):697-704.
7. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Sterne JAC, Murthy S, Diaz JV, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. JAMA. 2020;324(13):1330-1341.
8. Ma S, Xu C, Liu S, et al. Efficacy and safety of systematic corticosteroids among severe-19 patients: a systematic review and meta-analysis of randomized controlled trials. Signal Transduct Target Ther. 2021;6(1):83.
9. Caruso D, Guido G, Zerunian M, et al. Post-acute sequelae of COVID-19 pneumonia: six-month chest CT follow-up. Radiology. 2021;301(2):E396-E405.
10. Meyyappan J, Prasad N, Kushwaha R, et al. Health-related quality of life score and outcomes in living donor renal transplant recipients with COVID-19. Exp Clin Transplant. 2022;20(1):42-51.
11. Kute VB, Bhalia AK, Guleria S, et al. Clinical profile and outcome of COVID-19 in 250 kidney transplant recipients: a multicenter cohort study from India. Transplantation. 2021;105(4):851-860.
12. Clinical Guidance for Management of Adult COVID-19 Patients. Accessed January 29, 2022. https://www.icmr.gov.in/pdf/covid/technoc/COVID_Clinical_Management_14012022.pdf
13. Kute V, Guleria S, Prakash J, et al. NOTTO transplant specific guidelines with reference to COVID-19. Indian J Nephrol. 2020;30:215-220.
14. Clinical Guidance for Management of Adult COVID-19 Patients. Accessed June 4, 2022. https://www.icmr.gov.in/pdf/covid/technoc/COVID_Clinical_Management_14012022.pdf
15. Jones NR, McCormack T, Constanti M, McManus RJ. Diagnosis and management of hypertension in adults: NICE guideline update 2019 [published correction appears in Br J Gen Pract. 2020;70(692):111]. Br J Gen Pract. 2020;70(691):90-91.
16. American Diabetes Association. Standards of medical care in diabetes—2011. Diab Care. 2011;34(suppl 1):S11-S61.
17. Azzi Y, Bartash R, Scalea J, Loarte-Campos P, Akalin E. COVID-19, and solid organ transplantation: a review article. Transplantation. 2021;105(1):37-55.
18. Elec F, Bolboacă SD, Muntean A, et al. Comparing the first and second wave of COVID-19 in kidney transplant recipients: an east-European perspective. Eur Surg Res. 2022;63(1):25-32.
19. Peter Donnelly J, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Diseases. 2020;71(6):1367-1376.
20. Kadambi PV, Brennan DC, James Chon W. Kidney Transplantation in Adults: Evaluation and Diagnosis of Acute Kidney Allograft Dysfunction. UpToDate. https://www.uptodate.com/contents/kidney-transplantation-in-adults-evaluation-and-diagnosis-of-acute-kidney-allograft-dysfunction
21. Jain VK, Iyengar KP, Vaishya R. Differences between first wave and second wave of COVID-19 in India. Diabetes Metab Syndr. 2021;15(3):1047-1048.
22. What Remdesivir Shortage Says About India’s Preparedness. Accessed January 30, 2022. https://www.livemint.com/news/india/remdesivir-short-supply-shows-lack-of-preparedness-11618331985612.html
23. Iftimie S, López-Azcona AF, Vallverdu I, et al. First and second waves of coronavirus disease-19: a comparative study in hospitalized patients in Reus, Spain. PLoS One. 2021;16(3):e0248029.
24. Vaidyanathan G. Coronavirus variants are spreading in India—what scientists know so far. Nature. 2021;593(7859):321-322.
25. Kremer D, Pieters TT, Verhaar MC, et al. A systematic review and meta-analysis of COVID-19 in kidney transplant recipients: lessons to be learned. Am J Transplant. 2021;21(12):3936-3945
26. Raja MA, Mendoza MA, Villavicencio A, et al. COVID-19 in solid organ transplant recipients: a systematic review and meta-analysis of current literature. Transplant Rev. 2021;35(1):100588.
27. Mahalingasivam V, Craik A, Tomlinson LA, et al. A systematic review of COVID-19 and kidney transplantation. Kidney Int Rep. 2021;6(1):24-45.
28. Ranjbar K, Moghadami M, Mirahmadizadeh A, et al. Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial. BMC Infect Dis. 2021;21(1):337.
29. Black Fungus: Here is a List of States with the Highest Number of Mucormycosis Cases. Accessed January 30, 2022. https://www.hindustantimes.com/india-news/black-fungus-states-with-highest-number-of-mucormycosis-cases-101621559394002.html
30. Sharma S, Grover M, Bharagwa S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. J Laryngol Otol. 2021;135(5):442-447.
31. Meshram HS, Kute VB, Chauhan S, et al. Mucormycosis as SARS-CoV2 sequelae in kidney transplant recipients: a single-center experience from India. Int Urol Nephrol. 2021;54(7):1693-1703.
32. Behzad D, Hakimeh A, Hossein R, Khaledi A. A middle east systematic review and meta-analysis of bacterial urinary tract infection among renal transplant recipients; Causative microorganisms. Microb Pathog. 2020;148:104458.
33. Camargo LF, Esteves ABA, Ulisses LRS, Rivelli GG, Mazzali M. Urinary tract infection in renal transplant recipients: incidence, risk factors, and impact on graft function. Transplant Proc. 2014;46(6):1757-1759.
34. Liu H, Zhu J, Hu Q, Rao X. Morganella morganii, a non-negligent opportunistic pathogen. Int J Infect Dis. 2016;50:10-17.
35. Britt NS, Hagopian JC, Brennan DC, et al. Effects of recurrent urinary tract infections on graft and patient outcomes after kidney transplantation. Nephrol Dial Transplant. 2017;32(10):1758-1766.

36. Aiello FB, Calabrese F, Rigotti P, et al. Acute rejection and graft survival in renal transplanted patients with viral diseases. Mod Pathol. 2004;17(2):189-196.

37. Groff D, Sun A, Ssentongo AE, et al. Short-term and long-term rates of postacute sequelae of SARS-CoV-2 infection: a systematic review. JAMA Netw Open. 2021;4(10):e2128568.

SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Veeranki V, Prasad N, Meyyappan J, et al. The adverse effects of high-dose corticosteroid on infectious and non-infectious sequelae in renal transplant recipients with coronavirus disease-19 in India. Transpl Infect Dis. 2022;24:e13908. https://doi.org/10.1111/tid.13908