# Management strategies and outcomes in renal transplant recipients recovering from COVID-19: A retrospective, multicentre, cohort study

Vivek B. Kute,[a]* Deepak S. Ray,[b] Feroz Aziz,[c] Suraj M. Godara,[d] Umapati Hegde,[e] Anil Kumar BT,[f] Anil K. Bhalla,[g] Dinesh Kumar Yadav,[h] Sarbpreet Singh,[i] Vivek Pathak,[j] Sonal Dalal,[k] Madan M. Bahadur,[l] Urmila Anandh,[m] Abi Abraham M,[n] Vishwanath Siddini,[o] Sushree Sashmita Das,[b] Sharmila Thukral,[b] Arvind Krishnakumar,[c] Ashish Sharma,[i] Vijay Kher,[h] Shyam B. Bansal,[h] Ashay Shingare,[l] Ranjit Narayanan,[c] Himanshu Patel,[a] Sanjeev Gulati,[p] Shailesh Kakde,[q] Dinesh Bansal,[h] Sandeep Guleria,[r] Dinesh Khullar,[s] Manoj R. Gumber,[t] Umesh Varyani,[u] Swarnalatha Guditi,[v] Prakash Khetan,[w] Rutul Dave,[k] Vineet V. Mishra,[a] Stefan G. Tullius,[x] Sanshriti Chauhan,[a] and Hari Shankar Meshram[a]

[a]Department of Nephrology, Institute of Kidney Diseases and Research Centre, Dr. HL Trivedi Institute of Transplantation Sciences (IKDRC-ITS), Ahmedabad, Gujarat 380016, India
[b]Department of Nephrology, Rabindranath Tagore International Institute of Cardiac Sciences, Kolkata, West Bengal, India
[c]Department of Nephrology, IQRAA International Hospital and Research Centre Calicut, Kozhikode, Kerala, India
[d]Department of Nephrology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India
[e]Department of Nephrology, Muljibhai Patel Urological Hospital, Nadiad, Gujarat, India
[f]Department of Nephrology BGS Global Hospital, Bengaluru, Karnataka, India
[g]Department of Nephrology, Sir Ganga Ram Hospital, New Delhi, India
[h]Department of Nephrology, Medanta Institute of Kidney and Urology, Medanta-The Medicity, Gurugram, Haryana, India
[i]Department of Renal Transplant Surgery; Postgraduate Institute of Medical Education and Research, Chandigarh, India
[j]Department of nephrology, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India
[k]Department of Nephrology, Gujarat Kidney Foundation, Ahmedabad, Gujarat, India
[l]Department of Nephrology, Jaslok Hospital and Research Centre, Mumbai, Maharashtra, India
[m]Department of Nephrology, Yashoda Hospitals, Secunderabad, Telangana, India
[n]Department of Nephrology, VPS Lakeshore Hospital, Kochi, India
[o]Department of Nephrology, Manipal Hospital, Bangalore, India
[p]Department of Nephrology, Fortis Group of Hospitals, New Delhi, India
[q]Department of Nephrology, Jupiter Hospital, Pune, India
[r]Department of Transplantation Surgery, Indraprastha Apollo Hospital, New Delhi, Delhi, India
[s]Department of Nephrology, Max Saket Complex, Max Super Speciality Hospital, Saket, Delhi, India
[t]Department of Nephrology, Indraprastha Apollo Hospital, Ahmedabad, Gujarat, India
[u]Department of Nephrology, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, India
[v]Department of Nephrology, Nizam's Institute of Medical Sciences Panjagutta, Hyderabad, India
[w]Department of Nephrology, Kingsway Hospitals, Nagpur, India
[x]Department of Surgery, Division of Transplant Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

## Summary

**Background** There is an enormous knowledge gap on management strategies, clinical outcomes, and follow-up after kidney transplantation (KT) in recipients that have recovered from coronavirus disease (COVID-19).

**Methods** We conducted a multi-center, retrospective analysis in 23 Indian transplant centres between June 26, 2020 to December 1, 2021 on KT recipients who recovered after COVID-19 infections. We analyzed clinical and biopsy-confirmed acute rejection (AR) incidence and used cox-proportional modeling to estimate multivariate-adjusted hazard ratios (HR) for predictors of AR. We also performed competing risk analysis. Additional outcome measures included graft loss, all-cause mortality, waiting time from a positive real-time polymerase test (RT-PCR) to KT, laboratory parameters, and quality of life in follow-up.

**Findings** Among 372 KT which included 38(10·21%) ABO-incompatible, 12(3·22%) sensitized, 64(17·20%) coexisting donors with COVID-19 history and 20 (5·37%) recipients with residual radiographic abnormalities, the incidence of AR was 34 (9·1%) with 1(0·26%) death censored graft loss, and 4(1·07%) all-cause mortality over a median

*Corresponding author.
*E-mail address:* drvivekkute@rediffmail.com (V.B. Kute).

(interquartile range) follow-up of 241 (106−350) days. In our cox hazard proportional analysis, absence of oxygen requirement during COVID-19 compared to oxygen need [HR = 0·14(0·03−0·59); *p*-value = 0·0071], and use of thymoglobulin use compared to other induction strategies [HR = 0·17(0·03−0·95); *p*-value = 0·044] had a lower risk for AR. Degree of Human leukocyte antigen (HLA) DR mismatch had the highest risk of AR [HR = 10.2(1·74−65·83); *p*-value = 0·011]. With competing risk analysis, with death as a competing event, HLA DR mismatch, and oxygen requirement continued to be associated with AR. Age, gender, obesity, inflammatory markers, dialysis vintage, steroid use, sensitization and ABO-incompatibility have not been associated with a higher risk of AR. The median duration between COVID-19 real time polymerase test negativity to transplant was 88(40−145) days (overall), and ranged from 88(40−137), 65(42−120), 110(49−190), and 127(64−161) days in World Health Organization ordinal scale ≤ 3, 4, 5, and 6−7, respectively. There was no difference in quality of life, tacrolimus levels, blood counts, and mean serum creatinine assessed in patients with a past COVID-19 infection independent of severity.

**Interpretation** Our findings support that the outcomes of KT after COVID-19 recovery are excellent with absence of COVID-19 sequelae during follow-up. Additionally, there does not seem to be a need for changes in the induction/immunosuppression regimen based on the severity of COVID-19.

### Research in context

*Evidence before this study*

We searched PubMed and Google scholar through December 1, 2021, for articles published with the following MeSH terms: "COVID-19" or "SARS-CoV-2" and "recovery", or "recovered", and "transplantation". There was no restriction of language or date or type of articles in our literature search. With coronavirus disease (COVID-19) spreading in all regions of the world, the condition became an inevitable concern for transplantation. Existing publications prior to our analysis yielded only case reports with limited and short-term follow-up.

*Added value of this study*

We performed a multicentre, retrospective, observational cohort study representing the largest analysis of 372 COVID-19 recovered recipients and 64 donors with co-existing COVID-19 history reporting the longest median (interquartile range) follow-up duration of 241 (106−350) and 373(243−446) days after kidney transplantation and COVID-19 infection, respectively. The median duration between COVID-19 negativity by real time polymerase testing to transplantation was 88(40−145) days (overall); this time period increased in parallel to COVID-19 severity. We found that the acute rejection, graft loss, and patient survival was excellent. Furthermore, outcomes were similar for high-risk transplants including sensitized and ABO incompatible recipients. The outcomes of cases where both donor and recipient had COVID-19 were also favourable. In our multivariable analysis, recipients who did not require oxygen during COVID-19 infection and those who received thymoglobulin had lower rates of rejection.

Human leukocyte antigen DR mismatch was associated with highest risk of rejection. In addition, we successfully performed transplantation in 20 (5.37%) recipients with residual radiographic abnormalities. We did not observe post-COVID-19 sequelae during our follow-up.

*Implications of all the available evidence*

This report suggests that there is no need for any alteration in induction or immunosuppressive regimen in recipients of kidney transplants who have recovered from COVID-19. The outcome and follow-up course of these patients are excellent and also not complicated by any COVID-19 sequelae.

## Introduction

According to data accessible on the Global Observatory on Donation and Transplantation website, the total annual number of organ transplants performed in India has increased from 4990 in 2013 to 12,666 in 2019. Similarly, the rate of organ donation has increased two-fold since 2013 (340 in 2013 versus 715 in 2019).[1] Currently, India is ranked third for transplantation activities behind the United States, and China. The coronavirus disease (COVID-19) pandemic has had a negative influence on organ donation, and transplantation activities in India with total organ transplant rates of 7443 in 2020 compared to 12,666 in 2019.[2] As of December 1, 2021, India had the second-most COVID-19 cases worldwide. Since the emergence of the pandemic, solid organ transplantation (SOT) has been recognized as particularly impacted by COVID-19 with

higher rates of mortality and morbidity in transplant recipients.[3] Patients waiting for organ transplants have also been shown to be adversely affected.[4] Owing to the logistics and changing priorities during the pandemic, a marked decline in transplantation rates have been observed across the globe.[5,6] Indian transplant centers have the largest living donation programs worldwide and transplant volume declined the most during this pandemic.[1,2,7] With higher risks of COVID-19 affecting immunocompromised patients, it has also not been clear if a modification of immunosuppression is required. Of particular relevance, it has also been unclear on how to treat patients that have recovered from COVID-19 awaiting transplantation. The existing literature has been limited to a few case reports and series with short term follow up.[8] Of interest, many reports on living donor transplants during COVID-19 originate from developing nations.[9−11] Many data on deceased donation during COVID-19, in turn, originate from the developed world due to their robust deceased donation program.[12−21]

The authors have previously reported a multicentre cohort study from India with 75 kidney transplantation (KT) in recipients recovered after COVID- 19 during the first wave.[10] The study included only 22(29·33%) patients requiring oxygen, and had a limited median follow-up 81(56−117) days. Also, the previous study was conducted in the initial wave of pandemic where variants had not emerged. Longer follow-up and a standardized characterization of the severity of patient and donor COVID-19 is therefore necessary to better understand the impact of prior severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections on SOT recipients. We aimed to explore management strategy, transplant outcomes, safety, short and long-term follow-up of KT conducted in COVID-19 recovered patients. This report provides useful insights to transplant professionals across the globe supporting decisions on optimal timing to proceed with transplants and optimal immunosuppressive protocols that will critically determine outcomes.

## Methods

### Study design and population

This multicentre, retrospective, cohort study was conducted at transplant centres across India between June 26, 2020 (the index transplant date of the study) to December 1, 2021 (last follow-up date). Through a nationwide collaboration of 23 participating centres (**Supplementary Table 1**), data of a total of 372 KT in COVID-19 recovered patients were collected. The study was approved by the ethical committee of Institute of Kidney Diseases and Research center and Dr. HL Trivedi Institute of Transplantation Sciences, Ahmedabad, Gujarat, India. We abided with the declaration of

Helsinki, the declaration of Istanbul, and the Transplantation of Human Organs and Tissues Act in conducting transplantation throughout all the centres. We strictly adhered to the Strengthening the Reporting of Observational studies in Epidemiology guidelines for reporting of observational studies. Written informed consent was taken from donor-recipient pairs prior transplantation. We included all recipients that recovered from SARS-CoV-2 prior to transplantation based on nasopharyngeal SARS-CoV-2 real-time polymerase chain reaction (SARS-CoV-2 RT-PCR) sample. We excluded cases with the following criteria: 1) Patients who were diagnosed with COVID-19 through an antibody test. 2) Patients who met only clinical criteria for COVID-19.

### Procedures

We defined acute COVID-19 as the time from symptoms onset in a donor/recipient to clinical recovery with or without RT-PCR positive. Data were retrieved from case files, and electronic medical records, including but not limited to demographic characteristics (age, sex, height, weight, and body mass index), blood group, comorbidities, dialysis vintage, native kidney disease, mode of dialysis, cytomegalovirus serology, donor-specific antibody(DSA), induction regimen used, Human leukocyte antigen (HLA) mismatches at different loci (A, B, DR), laboratory test results (pre-transplant routine tests, and inflammatory markers during COVID-19), timeline from COVID-19 to surgery, and treatment received during COVID-19 (corticosteroids, anti-coagulation, and remdesivir). COVID-19 severity was graded based on the World Health Organization 7-point ordinal scale[22] which included the following categories: 1 - at home with resumption of normal activities; 2 - at home but difficulty to resume normal activities; 3 - hospitalized without requiring supplemental oxygen; 4 - admitted to hospital, and requiring low flow oxygen devices; 5 - requiring high-flow nasal cannula (HFNC)/ non-rebreather mask (NRBM); 6 - needing non-invasive mechanical ventilation(NIV); 7 - needing the support of invasive mechanical ventilation (MV). The EuroQol five-dimension five-level (EQ-5D-5 L) questionnaire and the EuroQol Visual Analogue Scale (EQ-VAS) were used to assess quality of life (QOL). The EQ-5D-5 L is a validated questionnaire, which has also been previously used in organ transplantation[23] to evaluate the patient quality of life based on five domains: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Categorization within each domain was divided further from 1 to 5, where 1 represents no difficulty and 5 stands for extreme difficulty.[24] The EQ-VAS is a patient's subjective assessment of overall health, ranging from 0 (worst) to 100 (best health). QOL was assessed at the last follow-up time of recipient at participating transplant centres. In addition, we assessed a retrospective pre-operative QOL. Primary outcomes included the rate

of AR (both clinical and biopsy-proven) and risk factors for rejection. The secondary outcomes included graft loss (defined as return to maintenance dialysis or re-transplantation), patient's death (mortality due to any cause), COVID-19 after transplant (defined as a repeat RT-PCR confirmed COVID-19 infection which is irrespective of the clinical severity), blood counts (white blood cell counts (WBC) and Lymphocyte counts trends at follow-up), immunosuppression levels (tacrolimus levels), quality of life (addressed by EQ-5D-5 L and EQVAS scores).

Evaluation of donors—recipient pairs have been detailed in our previous publications[9,10] We adhere to the Indian Society of Organ Transplantation consensus statement for kidney transplant recipients and living donors with a previous diagnosis of COVID-19 and adhere to the National Organ and Tissue Transplant Organization transplant specific guidelines with reference to COVID-19.[25] It suggests, using standard drugs and doses of induction and maintenance immunosuppressive regimen based on the recipient's immune risk stratification as was being practised before COVID-19 in the respective transplant centres. We did not modify our immunosuppression in patients with COVID-19, irrespective of severity or gap from recovery. We did not use any induction (including interleukin-2(IL-2) blocker) in well-matched recipients who received transplants from related donors.[10] In brief, transplants were performed with prior COVID-19 with the following prerequisite (a) two documented negative PCR tests including or additional one negative test at the time of transplant surgery, (b) complete symptom resolution for at least 28 days, (c) normal chest imaging by high resolution computed tomography scan or Roentgenogram chest which are showing no signs of active infection (d) written, and informed consent of the unknown risks including, but not limited to, reactivation or recrudescence of COVID-19 symptoms, impact on the kidney allograft, and potential for poor long-term outcome. (e) COVID-19 free transplant pathway with dedicated transplant team to reduce the risk of transmission. (f) Adherence to established COVID-19 protections at all times for donor, recipient, caretakers, and health care workers.

## Statistical methods, and analysis

All statistical analysis were done with the International Business Machines Statistical Package for the Social Sciences Software version 25, and StataCorp STATA: statistical software of data science version 16. A two-tailed $p$-value of less than 0.05 was considered statistically significant. No computation was done for achieving the sample size reached. Missing data were handled by listwise deletion. Data was expressed as median with interquartile range (IQR) or mean, and standard deviation (SD) for continuous variables. For categorical

variables, absolute value along with the percentage were used. Recipients were categorized into four groups according to their COVID-19 severity scale during their hospital stay: ≤3, not requiring supplemental oxygen; scale: 4, requiring supplemental oxygen through low flow device; scale: 5, requiring HFNC/NRBM; scale: 6—7 NIV- MV. For comparison of baseline data, COVID-19 course, and outcomes (laboratory, and quality of life), we used $\chi 2$ test or Fisher's exact test, analysis of variance (ANOVA) test, or Kruskal Wallis test as appropriate depending on the type of data, and normality distribution. Kaplan Meier curves were generated along with lifetime table analysis [numbers at risk (censored)] reporting for AR, and compared between oxygen status during COVID-19 severity, different pandemic waves (The definition, and timeline of waves in India is described in previous studies[26]), COVID-19 history of donor, DSA, ABO incompatibility, and induction regimen used. Breslow test has been used for survival function instead of a classical log-rank (Mantel cox), as the event of interest (AR) was clustered at early time points. Transplant-related covariates (donor age, recipient age, recipient sex, donor sex, HLA mismatches, dialysis vintage, DSA, ABO incompatibility and induction protocol (thymoglobulin, anti-Human T-lymphocyte immunoglobulin, IL-2 blocker, or no induction agent used) The selection of covariates was based on current evidence of risk factors for rejection. COVID-19 related factors like COVID-19 oxygen requirement, steroids use, and inflammatory markers were also included as covariates in the model to assess their association. For the assessment of survival times, the interval from transplantation to AR was selected as time to event and AR was chosen as failure event. Cox proportional hazard analysis was performed with stcox command of STATA version 16. Method for handling tied failures in the regression model was efron. Proportional hazard assumption testing for the model fit was estimated by estat phtest command. Model fitness was assessed with log likelihood, chi square and $p$-values. Effects of competing risks (with Death as a competing event) were assessed by stcreg command. The multivariable time to event analysis was expressed as hazard ratio (HR) with accompanying 95% confidence interval (CI), standard errors and z values.

## Role of the funding source

The funder of this descriptive study had no role in study conceptualization, design, data collection, data handling, data analysis, data interpretation, or scientific writing of the report.

## Results

A total of 372 KT with COVID-19 history were performed between June 26, 2020 to December 1, 2021,

including 365(98·11%) living, and 7(1·89%) deceased donor KT. Duration from COVID-19 to last follow-up was 373 (243−446) days. The study population for recipients was compiled of all grades of COVID-19 severity including scales of ≤ 3, 4, 5, 6, and 7 in 272 (73·12%), 59 (15·86%), 29 (7·80%), 7 (1·88%), and 5 (1·34%) patients, respectively. The cohort was almost evenly distributed during the pandemic with 171 patients (45·96%) corresponding to the first wave, and 201 (54·04%) to the second wave. The number of negative RT-PCR tests done before surgery in the recipients included 2, 3, and 4 in 105(28·22%), 117(31·45%), and149(40·05%) recipients respectively. (Supplementary Table 4 and Supplementary Figure 1). The demographic and acute COVID-19 phase of the recipients, and donors are detailed comprehensively in Table 1, and Table 2, respectively. The median (IQR) age of recipients was 39 (32−48) years, with 305 (81·98%) males, and 67 (18·02%) females. There was no statistical difference for age, or sex among different COVID-19 scales. Only 32 (8·60%) cases had obesity. The median (IQR) dialysis vintage for the study population was 11 (6−14·7) months with no difference per COVID-19 severity (p-value = 0·78). The mode of dialysis was predominantly hemodialysis through arteriovenous fistula followed by non-tunneled catheter, tunneled cuffed venous catheter, continuous ambulatory peritoneal dialysis, and pre-emptive transplants in 297 (79·84%), 28 (7·53%), 32 (8·60%),6 (1·61%), and 9 (2·42%) patients, respectively. Only 14 (3·76%) of the recipients were completely vaccinated for COVID-19 before transplant surgery. Covishield (Oxford/AstraZeneca) was the predominant vaccine with 30(81·08%) doses, and Covaxin (Bharat Biotech BBV152) was applied in only seven (18·92%) of the 37 doses given including the first dose. We assessed pre-transplant COVID-19 antibodies in only 56(15·05%) recipients due to resource limitations. The median (IQR) antibody levels developed through different grades of severity [31(10−325) vs 31(10−325) vs 38 (31−48) vs 115 (58−172) AU/ml; p-value = 0·86] was comparable. The minimum waiting time from SARS-CoV-2 RT-PCR positivity to transplant surgery varied according to the disease severity (scale ≤3, 4, 5, and ≥ 6 was 17, 36, 42, and 37 days, respectively). The minimum waiting time from SARS-CoV-2 RT-PCR negative report to transplant surgery on scales of ≤3, 4, 5, and ≥ 6 was 7, 28, 32, and 30 days, respectively. Pre-transplant radiological abnormalities persisted in 20(5·37%) of recipients. There were no statistically significant differences for the pre-transplant laboratory blood tests among different grades of severity of COVID-19 (Supplementary Table 5). However, forty-three (11·55%) cases had high C-reactive protein (CRP) at the time of transplant of which 24(55·81%), 10 (23·26%), 9(20·93%) cases belonged to scale of 3, 4 and 5, respectively.

In our report, the median (IQR) age of donors was 48(40−55) years with 240 (64·5%) donations

originating from females. The pre-donation serum creatinine was 0·8(0·8−0·8) mg/dl. The mean (SD) HLA mismatches for the study were 1·16 (0·5), 1·14 (0·5), and 1·15 (0·5) for HLA A, B, and DR loci, respectively. Sixty-four (17·20%) cases had both donor, and recipient with a history of COVID-19. The COVID-19 severity for donors had a scale of 3, and 4 in 62(96·87%), and 2 (3·13%) cases, respectively.

QOL (Table 3) was measured in recipients, with prominent findings reported in the anxiety domain (21·3%). Collectively, for all the domains of EQ-5D-5 L, only five recipients had a scale of 3 (moderate) while the rest all had a scale of 2 (sight difficulties). There was no difference in quality of life as per scales. The quality of life of the donor was also satisfactory as shown in Supplementary Table 6. No other neurological, pulmonary, and cognitive impairment was noted in recipients and donors with a COVID-19 history. Few recipients had post-transplant complications in the form of 17(4·56%) urinary tract infections [10(58·82%) Escherichia coli, and 7(41·18%) Klebsiella], four (1·07%) post-transplant diabetes mellitus, one (0·26%) polycythaemia, two (0·53%) acute pancreatitis, one (0·26%) urinary leak, one (0·26%) capsular tear, one (0·26%) catheter-related blood stream infection, one (0·26%) Klebsiella pneumonia immediate post-transplant, one (0·26%) dengue, and one (0·26%) parvo-virus infections. Two (0·53%) patients developed pyelonephritis with one (0·26%) patient death. There was no complication related to COVID-19 in recipients and donors except for two (0·53%) cases. One (0·26%) case each with a COVID-19 oxygen scale of 2, and 4 developed a second COVID-19 infection by day 10 and 3-months, respectively without molecular diagnostics, and typing confirmation for re-infection/reactivation due to resource limitations. Both patients recovered successfully. Four (1·07%) deaths unrelated to COVID-19 were reported, and their detailed analysis is outlined as Supplementary Table 7. AR episode were detected in 34 (9·13%) cases with a median (IQR) time between transplant and acute rejection of 7·5 (5−12) days after transplantation. The time distribution of the AR episodes was as follows: Twenty-three (67·65%) AR events before 10 days, seven (20·59%) between 10 and 20 days, and four (11·76%) AR events reported beyond 20 days.

Kaplan Meier estimates assessing AR association COVID-19 related factors showed a lower risk of acute rejections in patients that never required oxygen (Figure 1A) during the COVID-19 infection (Breslow test; p-value = 0·019) compared to patients who required oxygen. Estimated censored largest mean survival time for rejection free episode was higher for cases that never required oxygen compared to cases with oxygen [480 (464−495) vs 404(371−437) days]. Different pandemic waves of COVID-19 (Figure 1B) and co-existing history of COVID-19 in donor (Figure 1C) showed no predictive value with AR in the study. In Kaplan Meier analysis,

| | Total (n = 372) | Ordinal scale: 3 (n = 272) | Ordinal scale: 4 (n = 59) | Ordinal scale: 5 (n = 29) | Ordinal scale: 6−7 (n = 12) | p-value |
|---|---|---|---|---|---|---|
| **Demographics** | | | | | | |
| Age, years | 39(32−48) | 39(32−48) | 38(32−48) | 38(31−48) | 46(39·5−47) | 0·27 |
| Male Sex | 305(82·2) | 229(84·2) | 44(74·6) | 24(82·8) | 8(72·7) | 0·28 |
| Height, cm | 166(159−172) | 166(159−172) | 166(159−172) | 166(159−172) | 168(159−172) | 0·13 |
| Weight, kg | 64(54−74) | 64(54−74) | 63(54−73) | 61·5(54−72) | 69·5(57·7−77·2) | 0·58 |
| Body mass index, kg/m$^2$ | 23(20−25) | 23·4(20·6−25·7) | 23·2(20·5−25·5) | 23(20·4−25) | 24·6−21·1−26·2) | 0·42 |
| Obesity | 32(8·6) | 21(7·7) | 7(11·9) | 3(10·3) | 1(8·3) | 0·75 |
| **ABO Blood group typing, n = 369** | | | | | | |
| A | 95(25·5) | 64(23·5) | 16(27·1) | 12(41·4) | 3(25) | 0·21 |
| B | 101(27·2) | 74(27·2) | 15(25·4) | 8(27·6) | 4(33·3) | 0·95 |
| AB | 35(9·4) | 25(9·2) | 8(13·6) | 2(6·9) | 0(0) | 0·44 |
| O | 138(37·1) | 108(39·7) | 18(30·5) | 7(24·1) | 5(41·7) | 0·25 |
| **Native kidney disease** | | | | | | |
| Re-transplant | 10(3·2) | 6(2·7) | 3(5·3) | 1(4·2) | 0(0) | 0·73 |
| Hypertensive nephropathy | 116(31·2) | 86(31·6) | 19(32·2) | 10(34·5) | 1(8·3) | 0·37 |
| Diabetic kidney disease | 74(19·9) | 53(19·5) | 12(20·3) | 3(10·3) | 6(50) | 0·036 |
| Obstructive uropathy | 16(4·3) | 14(5·1) | 0(0) | 1(3·4) | 1(8·3) | 0·303 |
| Cystic kidney disease | 16(4·3) | 13(4·8) | 0(0) | 3(10·3) | 0(0) | 0·11 |
| IgA nephropathy | 29(7·8) | 23(8·5) | 5(8·5) | 1(3·4) | 0(0) | 0·57 |
| Focal segmental glomerulosclerosis | 14(3·8) | 11(4) | 2(3·4) | 1(3·4) | 0(0) | 0·906 |
| Lupus nephritis | 6(1·6) | 5(1·8) | 0(0) | 1(3·4) | 0(0) | 0·603 |
| Chronic glomerulonephritis | 83(22·3) | 62(22·8) | 13(22) | 6(20·7) | 2(16·7) | 0·95 |
| Unknown | 17(19·1) | 47(17·3) | 15(25·4) | 6(20·7) | 3(25) | 0·48 |
| Chronic interstitial nephritis | 12(3·2) | 8(2·9) | 1(1·7) | 3(10·3) | 0(0) | 0·13 |
| Alport syndrome | 5(1·3) | 4(1·5) | 1(1·7) | 0(0) | 0(0) | 0·88 |
| **Co-morbid conditions** | | | | | | |
| Hypertension | 337(90·6) | 247(90·8) | 55(93·2) | 25(86·2) | 10(83·3) | 0·59 |
| Diabetes | 98(26·3) | 70(25·7) | 17(28·8) | 5(17·2) | 6(50) | 0·17 |
| Past Myocardial infarction | 35(9·4) | 24(8·8) | 5(8·5) | 2(6·9) | 4(33·3) | 0·037 |
| Hypothyroid | 57(15·3) | 40(14·7) | 11(1·6) | 3(10·3) | 3(25) | 0·57 |
| Chronic liver disease | 6(1·6) | 4(1·5) | 1(1·7) | 0(0) | 1(8·3) | 0·26 |
| Peripheral vascular disease | 5(1·3) | 4(1·5) | 0(0) | 1(3·4) | 0(0) | 0·57 |
| Peptic ulcer disease | 8(2·2) | 4(1·5) | 0(0) | 4(13·8) | 0(0) | <0·0001 |
| Chronic obstructive pulmonary disease | 13(3·5) | 6(2·2) | 5(8·5) | 1(3·4) | 1(8·3) | 0·089 |
| Cerebrovascular accident | 17(4·6) | 11(4) | 4(6·8) | 1(3·4) | 1(8·3) | 0·72 |
| Malignancy | 3(0·8) | 3(1·1) | 0(0) | 0(0) | 0(0) | 0·77 |
| Leukaemia | 3(0·8) | 2(0·7) | 1(1·7) | 0(0) | 0(0) | 0·81 |
| **Viral marker status** | | | | | | |
| Hepatitis C virus | 24(6·5) | 18(6·6) | 1(1·7) | 5(17·2) | 0(0) | 0·034 |
| Hepatitis B virus | 8(2·2) | 6(2·2) | 2(3·4) | 0(0) | 0(0) | 0·72 |
| Human immunodeficiency virus | 3(0·8) | 2(0·7) | 0(0) | 0(0) | 1(8·3) | 0·026 |
| **Cytomegalovirus serology (n = 361)** | | | | | | |
| Donor -/ recipient + | 20(5·5) | 17(6·4) | 1(1·8) | 1(3·6) | 1(10) | 0·48 |
| Donor +/ recipient - | 12(3·3) | 7(2·6) | 2(3·6) | 2(7·1) | 1(10) | 0·38 |
| Donor +/ recipient + | 171(47·4) | 122(45·7) | 34(60·7) | 13(46·4) | 2(20) | 0·056 |
| Donor -/ recipient - | 79(21·9) | 54(20·2) | 16(28·6) | 8(28·6) | 1(10) | 0·32 |
| **ABO incompatible** | 38(10·2) | 29(10·7) | 7(11·9) | 1(3·4) | 1(8·3) | 0·63 |
| **COVID-19 symptoms** | | | | | | |

*Table 1* (Continued)

| | Total (n = 372) | Ordinal scale: 3 (n = 272) | Ordinal scale: 4 (n = 59) | Ordinal scale: 5 (n = 29) | Ordinal scale: 6−7 (n = 12) | p-value |
|---|---|---|---|---|---|---|
| Fever | 260(70) | 173(63·8) | 54(91·5) | 25(86·2) | 8(66·7) | <0·0001 |
| Cough | 202(54·3) | 117(43) | 54(91·5) | 23(79·3) | 8(66·7) | <0·0001 |
| Dyspnea | 95(25·5) | 26(9·6) | 32(54·2) | 26(89·7) | 11(91·7) | <0·0001 |
| Anosmia/ageusia | 140(37·6) | 97(35·7) | 26(44·1) | 13(44·8) | 4(33·3) | 0·52 |
| Diarrhea | 49(13·2) | 36(13·2) | 2(3·4) | 8(27·6) | 3(25) | 0·0082 |
| **Radiological abnormalities detected (n = 361)** | 185(51·2) | 104(39·2) | 46(80·7) | 23(85·2) | 12(100) | <0·0001 |
| **Anti-COVID-19 regimen** | | | | | | |
| Remdesivir | 102(27·5) | 43(15·9) | 34(57·6) | 17(58·6) | 8(66·7) | <0·0001 |
| Anticoagulation | 153(41·5) | 76(28·3) | 43(72·9) | 24(82·8) | 19(83·3) | <0·0001 |
| Steroid | 153(41·2) | 70(25·8) | 48(81·4) | 25(86·2) | 10(83·3) | <0·0001 |
| **Peak laboratory abnormalities, (n)** | | | | | | |
| Hemoglobin, g/dl (n = 344) | 9·050(8−10) | 9(8−10) | 9(8−10) | 9(8−10) | 9·1(7·45−9·9) | 0·013 |
| Total leukocyte count x 10³ cells (n = 328) | 4·8(3·84−6·37) | 4·8(3·8−6·3) | 4·8(3·9−6·35) | 4·8(3·9−6·4) | 4·3(3·7−6) | 0·45 |
| Neutrophil,% (n = 342) | 72(67−79) | 72(67−79) | 72(67−79) | 72(67−80) | 76(70−81) | 0·14 |
| Lymphocyte,% (n = 341) | 22(15−27) | 22(15−27) | 22(15−27) | 22(13−26) | 20(19·5−22) | 0·051 |
| Neutrophil lymphocyte ratio (n = 341) | 3·3(2·5−5·3) | 3·3(2·5−5·3) | 3·3(2·5−5·3) | 3·3(2·5−5·8) | 3·5(3·3−4·15) | 0·0099 |
| C-reactive protein, g/L (n = 244) | 22·7(8−54) | 22·7(8−54) | 27·3(9−55·2) | 33(12−61) | 46(33−67·5) | <0·0001 |
| D-dimer, micromol/L (n = 188) | 583(357−1220) | 583(357−1220) | 566(357−1220) | 567(359−1226) | 1200(668−1545) | 0·029 |
| Interleukin-6, pg/ml (n = 51) | 36·6(12·9−60) | 36·7(13−1100) | 36·6(13−58) | 36·6(13−58) | 8(8−8) | 0·62 |
| Ferritin, ng/ml (n = 131) | 687(368−1101) | 326(239−439) | 687(372−1100) | 687(372−1100) | 794(645−890) | 0·015 |
| Lactate dehydrogenase, IU/L (n = 120) | 326(237−439) | 326(239−439) | 326(239−439) | 326(239−439) | 441(377−561) | 0·12 |
| **SARS-CoV-2 vaccine status** | | | | | | |
| One dose | 23(6·2) | 16(5·9) | 3(5·1) | 3(10·3) | 1(8·3) | 0·77 |
| Two doses | 14(3·8) | 10(3·7) | 2(3·4) | 1(3·4) | 1(8·3) | 0·86 |

*Table 1*: **Demographic and acute COVID-19 course of recipient.**
**Abbreviations**: Data expressed as numbers, percentages, median, and interquartile range· p-value was calculated using Chi square test, Kruskal Wallis test or Analysis of variance test as appropriate· Obesity was defined as Body mass index > 30 kg/m²*, Ordinal scale for COVID-19 severity in recipient is ≤3 = no oxygen needed; 4 = oxygen through low-flow oxygen device; 5 = high-flow nasal cannula for oxygen therapy; 6 = non-invasive ventilation and 7 = mechanical ventilation·.

thymoglobulin (Breslow test; p-value = 0·0030) as induction (Figure 2A) was associated with fewer AR episodes compared to others, while no induction (Breslow test; p-value = 0·011) had a higher risk of AR (Figure 2B). Estimated censored largest mean survival time for rejection free episode was higher for thymoglobulin compared to others [486(470−501) vs 438(411−465) days], and contrarily lower for cases with no induction [352(319−384) vs 478(462−493)]. Cox hazard proportional analysis (Table 4) showed that no oxygen requirement during COVID-19 [HR = 0·14(0·03−0·59); p-value = 0·0071] and thymoglobulin use had lower risk for AR [HR = 0·17(0·03−0·95); p-value = 0·044]. Degree of HLA DR mismatch had the highest risk of AR [HR = 10·2(1·74- 65·83; p-value = 0·011]. In competing risk analysis (Supplementary Table 2) which included death as competing event, HLA DR mismatch and absence of oxygen requirement compared to oxygen

requirement during COVID-19 confirmed our Cox hazard proportional analysis. Demographic parameters (age, gender), inflammatory markers (D-dimer, highly sensitive C reactive protein, neutrophil lymphocyte ratio), sensitization and ABO-incompatibility, dialysis vintage, obesity, and steroid use were not associated with rates of AR. There was no donor-derived SARS-CoV-2 infection in our cohort.

Twelve (3.22%) KT (Supplementary Table 3) were performed in sensitized cases, and their outcomes were comparable to those of our non-sensitized groups (Figure 2C). Thirty-eight (10.21%) cases were ABO-incompatible KT and they had similar outcomes compared to non-ABO-incompatible KT (Figure 2D, and Supplementary Figure 2). A total of 64(17.20%) KT were performed in which both donor, and recipient had a previous history of COVID-19 with no deaths or graft loss. The AR rates 8(12.50%) were similar to cases in

| | Total ($n$ = 372) | Ordinal scale: 3 ($n$ = 272) | Ordinal scale: 4 ($n$ = 59) | Ordinal scale: 5 ($n$ = 29) | Ordinal scale: 6−7($n$ = 12) | $p$-value |
|---|---|---|---|---|---|---|
| **Age, years** | 48(40−55) | 49(40−55) | 48(42−55) | 45(38−52) | 47.5(37−52.5) | 0·47 |
| **Female sex, n (%)** | 240(64·5) | 179(65·8) | 41(69·5) | 16(55·2) | 4(33·3) | 0·0706 |
| **Height, cm** | 158·6(157·5−159·7) | 158·7(157·4−160) | 158·5(155·5−161·5) | 158·3(154·1−162·5) | 158·9(152·6−165·2) | 0·99 |
| **Weight, kg** | 59·3(58·3−60·3) | 58·4(57·3−59·5) | 61·9(59·4−64·3) | 60·3(57·2−63·4) | 64·8(57·3−72·2) | 0·013 |
| **Pre-donation SBP, mmHg** | 122·2(117·4−127·1) | 123·1(116·6−129·7) | 117·6(112·5−122·7) | 121·5(119·3−123·6) | 127·2(121·4−132·9) | 0·85 |
| **Pre-donation S· creatinine, mg/dl** | 0·8(0·8−0·8) | 0·8(0·8−0·8) | 0·8(0·8−0·8) | 0·8(0·7−0·8) | 0·8(0·7−0·9) | 0·42 |
| **DTPA GFR (Left kidney), ml/min/1·72/m²** | 66·6(64·2−69) | 67·5(64·7−70·3) | 62·1(56·3−67·9) | 66·2(56·6−75·7) | 70·5(53·7−87·4) | 0·409 |
| **DTPA** | 68·2(65·7−70·7) | 68·8(65·9−71·7) | 63·9(57·8−69·9) | 69·2(59·5−78·9) | 72·1(54·3−89·9) | 0·501 |
| **GFR (Right kidney), ml/min/1·72/m²** | | | | | | |
| **HLA mismatches ($n$ = 325)** | | | | | | |
| A | 1·16(0·5) | 1·16(0·5) | 1·18(0·5) | 1·14(0·6) | 1·09(0·3) | 0·95 |
| B | 1·14(0·5) | 1·15(0·5) | 1·16(0·5) | 1·07(0·6) | 1(0) | 0·66 |
| DR | 1·15(0·5) | 1·1(0·5) | 1·34(0·6) | 1·25(0·6) | 0·9(0·3) | 0·016 |
| **Past COVID-19 status, n (%)** | 64(17·2) | 49(18) | 11(18·6) | 3(10·3) | 1(8·3) | 0·608 |

*Table 2*: **Baseline features of the donors.**

**Abbreviations:** Data reported as numbers(percentages) or median (IQR) or mean (SD). IQR: interquartile range; SD: standard deviation; SBP: systolic blood pressure; DTPA: Diethylene Triamine Pentaacetic Acid; GFR: glomerular filtration rate; BMI: body mass index; HLA: human leukocyte antigen; SD: standard deviation. Only 2 cases had low flow oxygen requirement among the donors with COVID-19 Ordinal scale for COVID-19 severity in recipient is ≤3 = no oxygen needed; 4 = oxygen through low-flow oxygen device; 5 = high-flow nasal cannula for oxygen therapy; 6 = non-invasive ventilation and 7 = mechanical ventilation.

| | Total (n = 372) | Ordinal scale: 3 (n = 272) | Ordinal scale: 4 (n = 59) | Ordinal scale: 5 (n = 29) | Ordinal scale: 6−7 (n = 12) | p-value |
|---|---|---|---|---|---|---|
| **Days from initial negative SARS-CoV-2 RT-PCR to surgery** | 88(40−145) | 88(40−137) | 65(42−120) | 110(49−190) | 127(64−161) | 0·18 |
| **Days from SARS-CoV-2 RT-PCR positive to surgery** | 100(54−159) | 100(51−155) | 94(54−130) | 144(59−197) | 141(97−177) | 0·46 |
| **Induction regimen** | | | | | | |
| IL-2 blocker | 55(14·8) | 38(14) | 10(16·9) | 3(10·3) | 4(33·3) | 0·25 |
| Thymoglobulin | 218(58·6) | 160(58·8) | 38(64·4) | 17(58·6) | 3(25) | 0·093 |
| No induction | 78(21) | 66(24·3) | 4(6·8) | 4(13·8) | 4(33·3) | 0·012 |
| Anti-Human T-lymphocyte immunoglobulin | 21(5·6) | 8(2·9) | 7(11·9) | 5(17·2) | 1(8·3) | 0·0013 |
| **EQ-5D-5 L questionnaire, n = 248** | | | | | | |
| Mobility: problems during walking around | 24(6·9) | 11(4·3) | 7(12·5) | 4(16) | 2(18·2) | 0·013 |
| Personal care: problems with washing or dishing | 8(2·3) | 5(2) | 0(0) | 3(8) | 1(9·1) | 0·062 |
| Usual activity: problems in usual activity | 12(3·4) | 4(1·6) | 5(8·9) | 2(8) | 1(9·1) | 0·015 |
| Pain/discomfort | 9(2·6) | 3(1·2) | 3(5·4) | 3(12) | 0(0) | 0·0078 |
| Anxiety/depression | 74(21·3) | 51(19·9) | 15(26·8) | 7(28) | 1(9·1) | 0·44 |
| **EQ-VAS before transplant** | 60·6(11·2) | 60·8(11·3) | 60·1(9·8) | 61·3(14·2) | 54·6(5·3) | |
| **EQ-VAS after transplant** | 84·4(20) | 84·6(19·9) | 83(23) | 83·3(18·7) | 87·5(5·9) | <0.0001 |
| **Serum creatinine, mg/dl** | | | | | | |
| Post-operative days to nadir creatinine | 4(3−6) | 4(3−6) | 5(4−5) | 4(3−6) | 4(3−5·25) | 0·65 |
| Nadir creatinine (n = 307) | 0·98(0·8−1·2) | 1(0·8−1·2) | 1(0·8−1·2) | 1(0·8−1·23) | 0·9(0·8−1·13) | 0·76 |
| Discharge, (n = 306) | 1·1(0·9−1·307) | 1·1(0·9−1·3) | 1·1(0·9−1·3) | 1·1(0·9−1·35) | 1(0·87−1·2) | 0·96 |
| 1-m, (n = 251) | 1·1(0·9−1·2) | 1·1(0·9−1·2) | 1·1(0·9−1·2) | 1·1(0·9−1·3) | 1·1(1·05−1·13) | 0·83 |
| 3-m, (n = 196) | 1·1(1−1·2) | 1·1(1−1·2) | 1·1(1−1·2) | 1·1(1−1·5) | 1·1(1·1−1·12) | 0·63 |
| 6-m, (n = 155) | 1·1(1·1−1·2) | 1·1(1·1−1·2) | 1·1(1−1·3) | 1·27(1·1−1·5) | 1·1(1·1−1·2) | 0·064 |
| ≥ 1 yr, (n = 66) | 1·1(1−1·2) | 1·1(1−1·2) | 1·1(1·1−1·2) | 1·15(1·12−1·17) | 1·5(1·45−1·55) | 0·24 |
| **Total leucocyte count, x 10³ cells mm³** | | | | | | |
| Discharge, (n = 307) | 7·8(6·1−9·5) | 7·7(6−9·4) | 7·6(6·7−8·9) | 8(6·8−9·8) | 7·3(5·4−9) | 0·77 |
| 1-m, (n = 298) | 6·8(5·6−8·8) | 6·8(5·6−8·8) | 7·8(5·3−8·7) | 6·8(6−8·7) | 5·6(5−7·7) | 0·28 |
| 3-m, (n = 257) | 7(5·6−8·9) | 7·2(5·7−9) | 6·9(5·7−7·9) | 5·7(5·25−8·85) | 7(3·95−9·4) | 0·47 |
| 6-m, (n = 84) | 6·8(5·6−8) | 7·1(5·9−8·8) | 6(5·6−7) | 6·75(6·37−7·8) | 4·4(3·25−4·6) | 0·28 |
| ≥ 1 yr, (n = 38) | 6·85(5·925−7·5) | 7(6−7·8) | 6·8(6·2−6·9) | 8·1(8·1−8·1) | 3·4(2·8−4) | 0·15 |
| **Lymphocyte,%** | | | | | | |
| Discharge, (n = 282) | 25(20−29) | 25(20−29) | 23(18·5−27·7) | 24(19−28) | 28(18·5−31·2) | 0·49 |
| 1-m, (n = 134) | 21·5(16−25) | 22(16−25) | 20(13·4−25·5) | 22(21−23·5) | 21(16·5−23) | 0·28 |
| 3-m, (n = 232) | 18(15−22) | 18(15−21·2) | 19(16−21·5) | 19(15·5−34·3) | 17(15−20) | 0·53 |
| 6-m, (n = 11) | 23·5(21−28) | 25(22−28) | 21(19−24) | 23(23−25·8) | 16(16−16) | 0·62 |
| 1 yr, (n = 11) | 22(20−24·6) | 20(20−24·6) | 24(24−24) | 22(22−22) | N/A | 0·308 |
| **Tacrolimus levels, ng/ml in follow-up** | | | | | | |
| 1-m, (n = 206) | 10·7(9−11·9) | 10·9(9−11·9) | 10·2(8·8−11·9) | 11·3(10−13) | 9·7(8·6−10·4) | 0·085 |
| 3-m, (n = 272) | 8·7(7·825−9·5) | 8·8(7·8−9·5) | 8·6(7·8−9·5) | 9·3(8·2−9·5) | 9·3(8·15−9·35) | 0·098 |
| 6-m, (n = 137) | 7·8(7−8·4) | 7·8(7·2−8·4) | 7·9(6·9−8·3) | 7·2(6·3−7·8) | 6·9(5·8−8·23) | 0·43 |
| ≥ 1 yr, (n = 31) | 6·2(6−7·3) | 6·9(6−7·6) | 6·8(6·2−7·2) | 5(4·7−5·5) | 5·6(5·4−5·8) | 0·11 |

***Table 3***: Outcomes and follow-up course of recipients after transplantation.

**Abbreviations**: Data reported as numbers(percentages) or median (IQR) or mean (SD). IQR: interquartile range; SD: standard deviation; m: months; yr: years; RT-PCR: real time polymerase test detected by nasopharyngeal sample; IL-2: interleukin 2; Ordinal scale for COVID-19 severity in recipient is ≤3 = no oxygen needed; 4 = oxygen through low-flow oxygen device; 5 = high-flow nasal cannula for oxygen therapy; 6 = non-invasive ventilation and 7 = mechanical ventilation; EQ-5D-5 L = EuroQol five-dimension five-level questionnaire which consists of five domains, each of which has points ranging from 1(No difficulty) to 5 (extreme difficulty)· All values reported of EQ-5D-5 L had score of 2; EQ-VAS: EuroQol Visual Analogue Scale, ranging from 0 (worst imaginable health) to 100 (best of health)· p-value for EQVAS values before and after transplant was calculated.
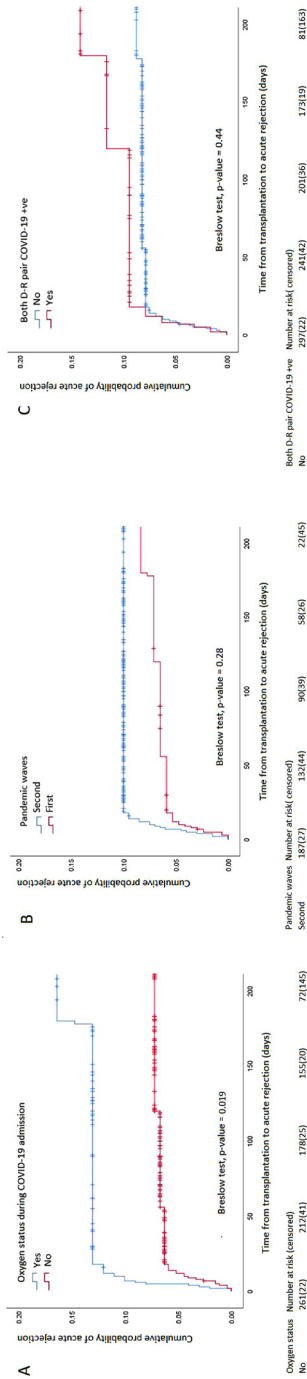
**Figure 1.** Kaplan Meier analysis for the association of acute rejections with COVID-19 related factors (1A: oxygen status during COVID-19 illness; 1B: Comparison of two pandemic waves, 1C: Both donor-recipient(D-R) had COVID-19 history before transplant).

which only recipients had a COVID-19 history (Figure 1C, and Supplementary Figure 3). There was no proteinuria, haematuria, any other renal or extra-renal abnormality on follow-up in living donors who donated kidney after recovery of COVID-19 at median (IQR) follow up duration 227(109−309) days, suggesting safety of donation without any postulated sequelae. As per the safety analysis, the data did not result in any safety signal or potential safety issue.

## Discussion

We report this multicentre cohort study from India of 372 KT in recipients recovered after COVID- 19 with favourable outcomes. These data collected during the first and second COVID-19 wave may help to increase the number of KT that can be performed in India. To the best of knowledge, this is the largest cohort study of KT of 372 COVID-19 recovered recipients and 64 donors with the longest follow-up duration assessing management strategy and outcomes. The incidence of AR was 34(9·13%) in which biopsy-proven rejection was 23(6·18%) which is comparable to previous reports and comparable to standard transplantation outcomes before the COVID-19 pandemic.[27,28] AR episodes tend to be more frequent in cases with higher severity. Furthermore, rejection episodes were less in cases with induction agents.

Patients with severe clinical COVID-19 symptoms requiring oxygen or those with a less potent induction treatment had more frequent AR in our report. This observation can be explained by the fact that, the patients with increasing COVID-19 severity, who are well known to have greater co-morbidities, had a trend for lower induction strategy. Based on our findings, we hypothesize that COVID-19 disease severity or recovery time may not serve as a criterion for reducing immunosuppression. Hence, we support no tailoring of induction agent even in cases who had history of oxygen requirement. Our report supports of an unmodified maintenance immunosuppressive regimen in relation to COVID-19. With only two COVID-19 infections in the post-transplant period, our report also suggests on the safety of current immunosuppression regimen.

We have also performed various high-risk transplantation including sensitized and ABO-incompatible patients with favourable outcomes in the absence of modified immunosuppressants. The four deaths reported during the study were non-COVID-19 related. Although various professional societies have suggested waiting for an extended period before surgery in severe COVID-19, we have found that a minimum waiting time of around 1 month would be safe for all grades of previous COVID-19 infections.

We included 20(5·37%) transplants with pre-surgery residual abnormalities, again with favourable outcomes in the absence of AR. Our report thus supports the
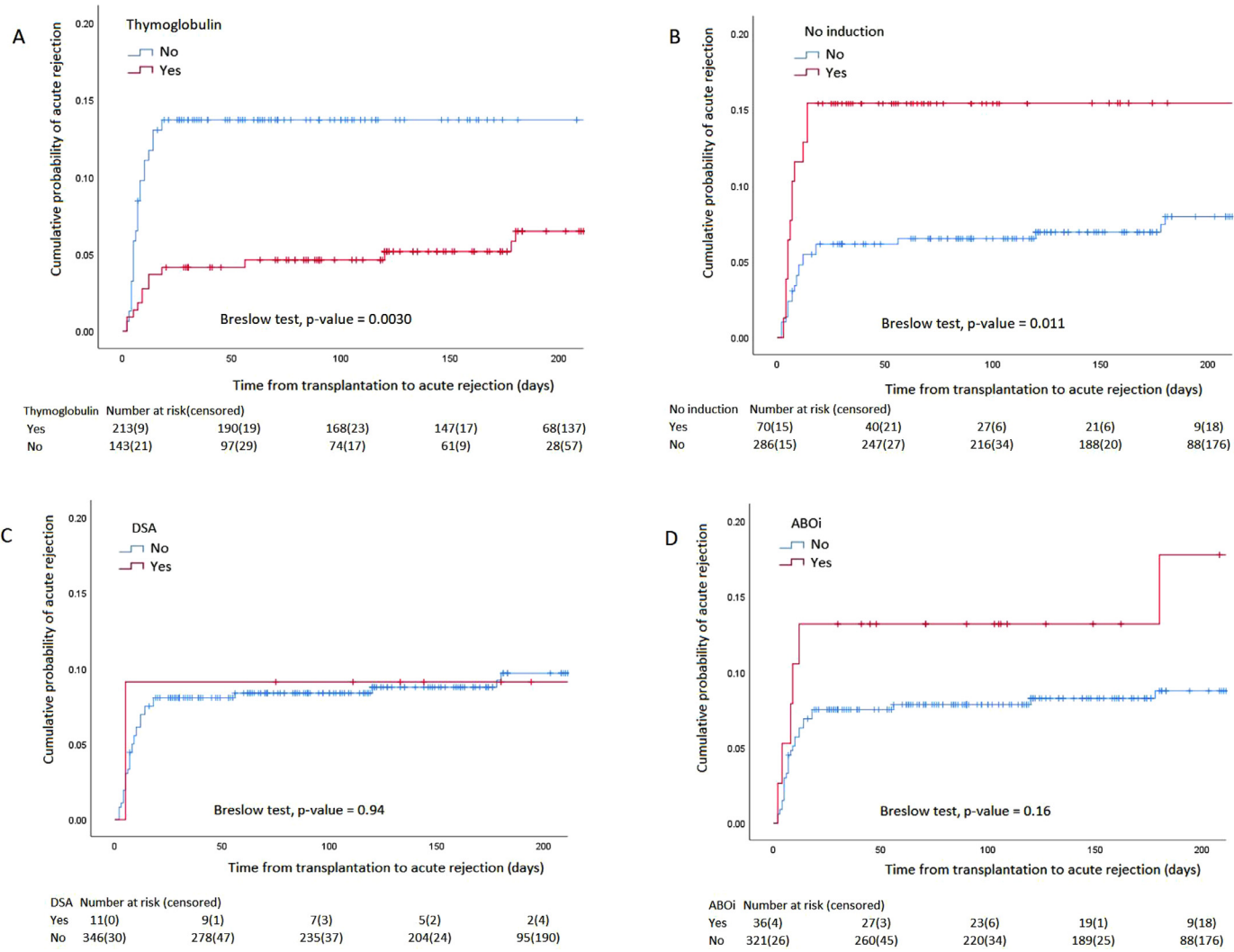
**Figure 2.** Kaplan Meier analysis for the association of acute rejections with transplant related factors (2A: Comparison of thymoglobulin vs other induction strategy, 2B: No induction vs other strategy; 2C: Donor specific antibody (DSA) existence; 2D: ABO incompatible transplant or not).

| Co-variates | HR | SE | z | *p*-value | 95% CI | |
|---|---|---|---|---|---|---|
| | | | | | LL | UL |
| **Chronology from COVID-19 infection to surgery** | | | | | | |
| Time from RT-PCR positive to surgery | 0.98 | 0.03 | −0.53 | 0.59 | 0.90 | 1.05 |
| Time from RT-PCR negative to surgery | 1.02 | 0.04 | 0.6 | 0.54 | 0.94 | 1.10 |
| **Treatment received for COVID-19** | | | | | | |
| No oxygen supplementation | 0.14 | 0.10 | −2.69 | 0.0071 | 0.03 | 0.59 |
| Steroid use | 0.68 | 0.73 | −0.36 | 0.72 | 0.08 | 5.59 |
| **Inflammatory and laboratory markers** | | | | | | |
| HS-CRP | 1.00 | 0.00 | 1.71 | 0.087 | 0.99 | 1.01 |
| D-dimer | 1.00 | 0.00 | −0.76 | 0.44 | 0.99 | 1.00 |
| NLR | 1.08 | 0.05 | 1.44 | 0.14 | 0.97 | 1.20 |
| **COVID-19 related general factors** | | | | | | |
| Pandemic waves (First wave versus second wave) | 0.92 | 0.67 | −0.11 | 0.91 | 0.22 | 3.86 |
| Both donor-recipient had COVID-19 history | 2.02 | 1.51 | 0.94 | 0.34 | 0.46 | 8.76 |
| **Biological and baseline factors** | | | | | | |
| Donor's age | 1.07 | 0.04 | 1.84 | 0.066 | 0.99 | 1.15 |
| Donor's sex | 0.64 | 0.59 | −0.48 | 0.63 | 0.10 | 3.87 |
| Pre-donation serum creatinine | 0.25 | 0.60 | −0.58 | 0.56 | 0.00 | 26.29 |
| Recipient's age | 0.98 | 0.02 | −0.69 | 0.49 | 0.92 | 1.03 |
| Recipient's sex | 4.31 | 3.90 | 1.62 | 0.106 | 0.73 | 25.40 |
| Recipient's obesity | 1.94 | 1.94 | 0.67 | 0.503 | 0.27 | 13.75 |
| Dialysis vintage | 1.01 | 0.00 | 2.51 | 0.012 | 1.00 | 1.02 |
| **Immunological factors** | | | | | | |
| HLA A mismatch | 0.26 | 0.24 | −1.47 | 0.14 | 0.04 | 1.55 |
| HLA B mismatch | 0.10 | 0.09 | −2.39 | 0.017 | 0.01 | 0.66 |
| HLA DR mismatch | 10.72 | 9.92 | 2.56 | 0.011 | 1.74 | 65.83 |
| DSA | 6.23 | 9.01 | 1.27 | 0.205 | 0.36 | 105.94 |
| ABOiTx | 0.65 | 0.56 | −0.49 | 0.62 | 0.12 | 3.59 |
| Thymoglobulin vs others* | 0.17 | 0.15 | −2.01 | 0.044 | 0.03 | 0.95 |
| No induction vs induction agents | 0.68 | 0.58 | −0.45 | 0.65 | 0.12 | 3.68 |

*Table 4*: **Cox proportional hazard model for acute rejection.**
Abbreviations: HR = hazard ratio; UL= upper limit; LL= lower limit; SE: standard error; RT-PCR: real time polymerase test detected by nasopharyngeal sample; HS-CRP = highly sensitive C reactive protein; HLA = human leukocyte antigen; NLR= neutrophil lymphocyte ratio; ABOiTx = ABO incompatible kidney transplantation; DSA = donor specific antibody;.
* = induction with anti-human T-lymphocyte immunoglobulin, Interleukin-2 blocker and no induction. Model fitness statistics (log likelihood = −69.702; LR chi = 44.1; global test's *p*-value = 0.036).

rationale that the presence of residual radiological abnormalities without active infections before transplant should not be an absolute contraindication for transplantation, rather than individualizing the assessment. There were extremely few surgical complications in the study which is encouraging in comparison to previously reported eventful post-operative period in COVID-19 recovered patients.[29] Of additional relevance, we have not detected any venous or arterial thromboembolic phenomena in the absence of anti-thrombotic prophylaxis. In our study, a repeat DSA done after COVID-19 infection was not positive. With the retrospective nature of this study during the pandemic, it was not possible to recover data from patients lost to follow-up. Of note, we did not observe cross-match positivity (by cytotoxic or flow crossmatch) in any of the donor-

recipient pairs after COVID-19 infection. This observation suggests that sensitization subsequent to COVID-19 infection is a rare event.[30] Moreover, transplants have not been denied in any recipient recovering from COVID-19 due to medical unsuitability.

The strength of this study is based on an extensive and detailed follow up, large number of 100(27%) moderate-severe cases, feasibility and safety of transplants in 20(5·37%) recipients with residual radiological abnormality in chest without active infection before transplant surgery, 38(10·21%) ABO-incompatible KT, 12 (3·22%) sensitised patients, and 64(17·20%) donor/recipient pairs who recovered from COVID-19. We tested and demonstrated that the outcomes in the above-mentioned high-risk transplantation are also safe while yielding favourable graft outcomes. The donor-

recipient pairs involved in the study remained at close and dedicated follow-up through in-person/telecommunication for any possible problems. One-year outcomes in transplant recipients and donors in COVID-19 survivors are without any long-term sequelae of COVID-19, and this further adds value to the study contrasting with previous reports.[31,32] The younger cohort of the study population may partly be responsible for the uneventful post-COVID-19 course. The available follow-up suggests that transplantation and immunosuppression appear to be safe even in severe cases of COVID-19 survivors. Our data also show favourable outcome of KT in the first, and second wave despite reliable less pre-transplant vaccinations. We emphasized with all our patients on the importance of COVID-19 protections.

The retrospective design is a limitation of our study. Our patient cohort has been young which is common in India.[27,28] We want to emphasize that there has not been any selection bias for the inclusion of patients. Nevertheless, our patient population may limit the generalizability of our data for older recipients. Our study population also includes predominantly live donor kidney transplants. In our approach, we kept the waiting time from SARS-CoV-2 RT-PCR negativity to surgery to a minimum as some patients wanted to move forward based on financial challenges, which is commoner in public sector. Moreover, some patients could have been COVID-19 negative, but due to legislation issues (regional differences in legal policy of documentation and verification), the transplant would have been delayed. Of additional relevance have been varying COVID-19 transmission rate at various time lines and various regions in addition to varying thresholds for restarting transplantation during the pandemic. Additionally, immunosuppression including maintenance and treatment for COVID-19 have been based on center policies. Some variables remain unexamined regarding safety such as neutralizing antibody testing in the majority of cases and protocol biopsy of patients, and donors with prior COVID-19. Also, only a few pediatric cases in the cohort. The exact waiting time from recovery to transplant for different scales of COVID-19 severity cannot be computed, as it depends on logistics, financial boundaries of patients, transplant center capacity, COVID-19 transmission rate, and legal issues during transplantation.

In conclusion, we report on our experience in 372 kidney transplants with a past medical history of COVID-19 (365 living and seven deceased donor transplants) across 23 transplant centres in India (Three public, and 20 private hospitals). Transplantation and established immunosuppression appear independent of past COVID-19 severity. Insights from our study may help transplants professionals in developing an early regional plan for transplanting patients with a past medical history of COVID-19.

## Contributors

All participating authors have full access to all the data in the study and consented to the final responsibility regarding the content of the manuscript before the submission. All authors contributed equally to the conception, design of the work, acquisition, data analysis, interpretation of data, drafting the work, revising it critically for important intellectual content, final approval of the version to be published, and have agreed to be accountable for all aspects of the work. VBK, DSR, FA & HSM have verified the underlying data before submission. VBK, and HSM decided for submission to the journal with input from all other authors.

## Data sharing statement

The data collected for the study, including a data dictionary defining each field in the set, individual de-identified participant data, other specified data set, any additional, related documents will be available (e.g., study protocol, statistical analysis plan, informed consent form) following the publication of this manuscript from the corresponding author on request

## Declaration of interests

All authors declare no competing interests

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101359.

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