ORIGINAL ARTICLE

Recovery of kidney function after AKI because of COVID-19 in kidney transplant recipients

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Clinical trials of India CTRI registration no. – CTRI/2020/06/026000.

SUMMARY

Evidence on the evolution of graft function in kidney transplant recipients recovering from coronavirus disease-2019 (COVID-19) is lacking. This multicenter observational study evaluated the short-term clinical outcomes in recipients with acute kidney injury (AKI) secondary to COVID-19. Out of 452 recipients following up at five centers, 50 had AKI secondary to COVID-19. 42 recipients with at least 3-month follow-up were included. Median follow-up was 5.23 months [IQR 4.09–6.99]. Severe COVID-19 was seen in 21 (50%), and 12 (28.6%) had KDIGO stage 3 AKI. Complete recovery of graft function at 3 months was seen in 17 (40.5%) patients. Worsening of proteinuria was seen in 15 (37.5%) patients, and 4 (9.5%) patients had new onset proteinuria. Graft failure was seen in 6 (14.3%) patients. Kidney biopsy revealed acute tubular injury (9/11 patients), thrombotic microangiopathy (2/11), acute cellular rejection (2/11), and chronic active antibody-mediated rejection (3/11). Patients with incomplete recovery were likely to have lower eGFR and proteinuria at baseline, historical allograft rejection, higher admission SOFA score, orthostatic hypotension, and KDIGO stage 3 AKI. Baseline proteinuria and the presence of orthostatic hypotension independently predicted incomplete graft recovery. This shows that graft recovery may remain incomplete after AKI secondary to COVID-19.

Transplant International 2021; 34: 1074–1082

Key words
acute kidney injury, COVID-19, graft function, kidney transplantation, outcomes, recovery

Received: 15 February 2021; Revision requested: 8 April 2021; Accepted: 15 April 2021

Introduction

Emerging evidence suggests that kidney transplant recipients are at an increased risk of severe coronavirus disease-2019 (COVID-19) [1], with a higher rate of hospital admissions [2], mortality [2,3], and acute kidney injury [4]. However, data on clinical outcomes of transplant recipients recovering from COVID-19 are lacking.

The in-hospital mortality is largely related to the severity of COVID-19, but various factors affect the graft function in the long term—underlying (pre-COVID-19) graft function, hemodynamic or septic insults, and use of nephrotoxic drugs. Also, recipients with COVID-19 are at higher immunological risk because of reduction in immunosuppression, transfusion of blood products, and virus-related immunomodulation [5]. In this study, we included a cohort of recipients who had AKI secondary to COVID-19 with at least 3-month follow-up, with an aim to identify the evolution of clinical outcomes after recovery from

doi:10.1111/tri.13886

COVID-19 and to recognize the predictive factors for adverse clinical outcomes.

Patients and methods

Study design and participants

This cohort study included all adult (>18 years) kidney transplant recipients at five tertiary referral centers in western Maharashtra, who were diagnosed with COVID-19 between March 22, 2020, and September 22, 2020, (6 months) and had acute kidney injury during their course of admission. Patients with a presumed and suspected diagnosis of COVID-19, those with an estimated glomerular filtration rate (eGFR) <15 ml/min/1.73 m^2 before admission, and who did not complete at least 3 months of follow-up were excluded. The study was approved by the Institutional ethics committee (EC/OA-112/2020) with a waiver of consent. It was registered with Clinical Trials Registry – India (CTRI/2020/06/026000). The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Data collection

We obtained data on demographics, comorbidities, past medical history, concomitant medication use, clinical presentation, hospital course, laboratory parameters, treatment, and outcomes. All the patients were admitted to the renal high dependency unit managed by nephrologists. After discharge, patients were followed up weekly in the transplant clinic till the graft function stabilized, and monthly thereafter. During these visits, patients underwent thorough physical examination, investigations (complete blood count, serum creatinine, serum electrolytes, liver function tests, urine routine, and urine protein quantification), and outcomes were recorded.

Clinical outcome assessment and definitions

The primary outcome was complete recovery of graft function at 3 months. It was defined as serum creatinine and proteinuria reaching the baseline value. Baseline Serum creatinine and proteinuria were calculated by taking an average of three values before the diagnosis of COVID-19. Proteinuria more than 300 mg above the baseline was considered as raised above the baseline. The secondary outcomes were patient survival, acute graft rejections, transient worsening of proteinuria (<3 months). Severe COVID-19 was defined as oxygen saturation (SpO_2) ≤94% at room air or acute respiratory distress syndrome [Partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) < 300]. Baseline graft function was assessed by estimated glomerular filtration rate (eGFR) using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula. The presence of proteinuria at baseline was defined as protein excretion of more than 300 mg in a day. Acute kidney injury was classified as per Kidney Diseases Improving Global Outcomes (KDIGO) staging. The Sequential Organ Failure Assessment (SOFA) score was used to the assess severity of organ dysfunctions [6]. Anemia was defined at hemoglobin <12 g/dl, and severe anemia was defined as hemoglobin <9 g/dl. Tacrolimus trough levels more than 7 ng/ml after the first year post-transplant were considered supratherapeutic.

Statistical analysis

We presented categorical variables as count and percentages. We calculated mean and standard deviation for continuous variables which were normally distributed (Shapiro Test) and median and interquartile range (IQR) for those which were not. For comparison of categorical variables, we have used the Fisher's exact test when observations were <5, and the Pearson's chi-square test when they were not. For continuous variables that were normally distributed, we have used *t*-test and for not-normally distributed data, we have used the Mann–Whitney test. Predictors of the primary outcome were calculated using multivariable binary logistic regression. The significance level was fixed at $P < 0.05$, and all tests were two tailed.

Results

Out of 452 transplant recipients on regular follow-up, 60 transplant recipients were hospitalized with COVID-19 from March 22, 2020, to September 22, 2020. Of these, 50 (83.3%) recipients had acute kidney injury, of which eight patients succumbed. The remaining 42 had a follow-up of a minimum of three months and were included in this analysis (Fig. 1). The median follow-up was 5.23 months [IQR 4.09–6.99 months]. Thirty-two (76.2%) were males, and the mean age was 41.33 ± 11.5 years (Table 1). Hypertension was the most common co-morbid condition (71.4%). The median duration from transplant to the diagnosis of COVID-19 was 5.37 years (IQR 27–87 months). Baseline eGFR was

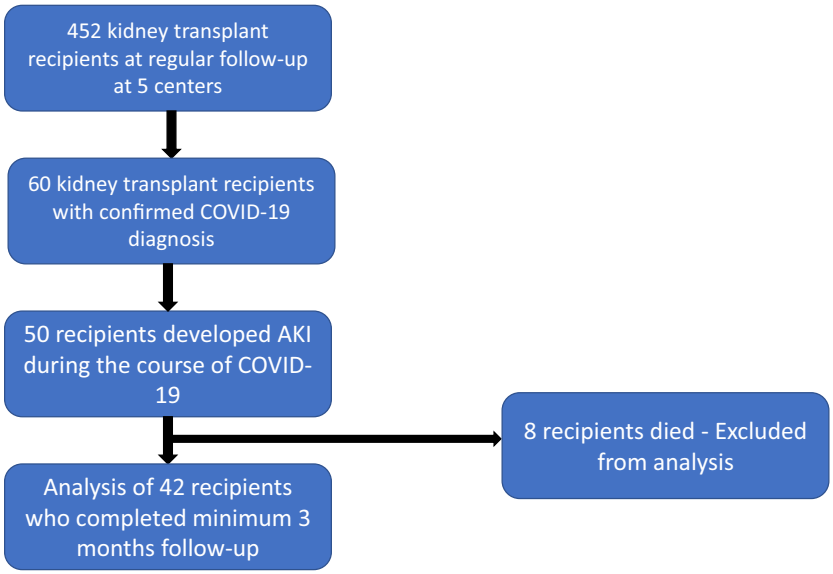

Figure 1 Flowchart of study population selection.

57.96 ± 20.21 ml/min/1.73 m^2. Twelve (28.6%) patients had received treatment for allograft rejection in the past, these patients had a lower eGFR at baseline (47.90 ± 23.86 ml/min/1.73 m^2 vs. 65.34 ± 18.23 ml/min/1.73 m^2; $P = 0.014$). Their tacrolimus trough level before COVID-19 was not significantly different from those without rejection (5.73 ± 2.26 ng/ml vs. 5.46 ± 1.49 ng/ml; $P = 0.731$) l/min/1.73 m^2. 16 (38.1%) had proteinuria (>300 mg/day) at baseline.

Clinical presentation and management

Twenty-one (50%) patients developed severe COVID-19 (Table 2). The median [IQR] SOFA score on admission was 3 [1–4.25]. Diarrhea as a presenting feature was seen in 23 (54.8%) patients. Orthostatic hypotension was present in 13 (31%) of patients and two developed shock requiring inotropes. Twelve (28.6%) patients developed KDIGO stage 3 AKI and three required hemodialysis. Antimetabolite was withdrawn in 84.6% of patients, and calcineurin inhibitors (CNI) were decreased or stopped in 25/40 patients (62.5%). Twenty (47.6%) patients with severe COVID-19 received intravenous dexamethasone 6 mg or methylprednisolone 40 mg for a period of 7 or 10 days as per clinical condition, in other patients, the steroid dose was maintained the same. Remdesivir was given to 13 (31%) patients with severe COVID-19. The dose administered was 600 mg over 5 days for 12 patients, and one patient received 1100 mg over 10 days. On recovery, the steroid was tapered to the original dose, and antimetabolite was reintroduced at reduced doses in the first week after discharge. CNI dosing was guided by trough concentrations.

Clinical outcomes

Complete recovery of graft function at 3 months was seen in 17 (40.5%) patients. Median [IQR] days for AKI to recover was 21 [14.5–39]. Median [IQR] eGFR at 3 months was 49.9 ml/min/1.73 m^2 [32.1–62.75 ml/min/1.73 m^2]. Worsening of pre-existing proteinuria (>300 mg above the baseline) was seen in 15 (37.5%) patients with a median [IQR] of 1675 mg/day [957.5–2550 mg/day]. In 3 of these patients, proteinuria recovered to baseline within 3 months. New onset proteinuria was present in 4 (9.5%) patients. As compared to patients with complete recovery those with incomplete recovery had significantly lower eGFR and higher proteinuria at baseline, on admission, at 3-month follow-up, and at last follow-up (Fig. 2, Table 3). There was no significant difference in tacrolimus trough concentrations between these two groups at these time points. Six (14.3%) patients had progressive worsening of graft function and remained on maintenance hemodialysis at 3 months. Of these, three patients had required hemodialysis during COVID-19 and three patients were initiated on dialysis subsequently on follow-up visits. One patient having persistent graft dysfunction (eGFR 57.4 ml/min/1.73 m^2 at 3 months) developed sudden onset chest discomfort at home and succumbed after 4 months of COVID-19. The cause of death could not be identified.

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Table 1. Baseline demographics and medication use.

Variable	Total (n = 42)	Graft function recovered (n = 17)	Graft function not recovered (n = 25)	P value
Age (years)	41.33 ± 11.5	44.25 ± 13.47	39.36 ± 9.78	0.183
Male	32 (76.2%)	13 (76.4%)	19 (76.0%)	0.999
Time since transplant to SARS-CoV-2 positivity (months)	49.5 [25.5–87]	34 [13.5–89]	59 [38–87]	0.093
Time from SARS-CoV-2 positivity until last follow-up (months)	5.23 [4.09–6.99]	5.62 [4.40–6.57]	4.86 [3.84–7.13]	–
Comorbidities				
Diabetes mellitus (pre- or post-transplant)	12 (28.6%)	6 (35.3%)	6 (24.5%)	0.498
Hypertension	30 (71.4%)	11 (64.7%)	19 (76.0%)	0.498
Heart disease	1 (2.4%)	0	1 (4%)	1.0
Lung disease	5 (11.7%)	2 (11.8%)	3 (12%)	0.982
Tuberculosis (active or historical)	8 (19%)	2 (11.8%)	6 (24%)	0.439
Type of transplant (LRDT vs. DDT)	35 (83.3%)	14 (82.4%)	21 (84%)	1
Kidney from marginal donors*	4 (9.5%)	1 (5.9%)	3 (12%)	0.789
Etiology of kidney disease				
Diabetes	1 (2.4%)	0	1 (4%)	
Glomerular	5 (11.9%)	2 (11.7%)	3 (12%)	
Polycystic kidney disease	1 (2.4%)	1 (5.8%)	0	–
CAKUT	6 (14.2%)	1 (5.8%)	5 (20%)	
Unknown	29 (69%)	13 (76.4%)	16 (64%)	
BMI (kg/m^2)	25 + 5.7	25 + 7.13	25 ± 4.40	0.971
Medications				
Antibody induction (anti-thymocyte globulin/basiliximab/garfalon)	25 (59.5%)	13 (76.5%)	12 (48%)	0.137
Calcineurin inhibitor	40 (95.3%)	17 (100%)	23 (92%)	0.507
Mycophenolate mofetil	33 (78.6%)	14 (82.5%)	19 (76%)	0.713
Azathioprine	6 (14.3%)	2 (11.7%)	4 (16%)	0.979
mTOR inhibitor	2 (4.8%)	1 (5.8%)	1 (4%)	1
Steroids	42 (100%)	17 (100%)	25 (100%)	–
ACEi/ARB	7 (16.7%)	2 (11.8%)	5 (20%)	0.685
Tacrolimus trough levels prior to COVID-19	5.54 ± 1.72	5.06 ± 1.22	5.87 ± 1.95	0.178
Baseline eGFR [CKD-EPI] ml/min/1.73 m^2	60.36 ± 21.25	68.6 ± 21.17	54.76 ± 19.79	0.037
Baseline proteinuria (>300 mg/day)	16 (38.1%)	2 (11.8%)	14 (56%)	0.004
Historical allograft rejection	12 (28.6%)	1 (5.9%)	11 (44%)	0.013

CAKUT, congenital anomaly of kidney and urinary tract; CKD-EPI, chronic kidney disease epidemiology collaboration; DDT, ecease donor transplant; LRDT, Live related donor transplant.

*Data not available for marginal donors (n = 5), antibody induction (n = 1).

Evaluation and management of graft dysfunction

Pending biopsy report, 5 (12%) patients received injectable methylprednisolone, and oral prednisone dose was increased in 6 (14.3%) patients. Antimetabolite was increased in 7 (16.7%) patients. Ten (23.8%) patients had supratherapeutic tacrolimus trough levels and required a dose reduction. One (2.4%) patient developed de novo donor-specific antibody (DSAs) (Antibody against HLA-DQA1*02:01 with background corrected MFI = 14 819). His DSAs were negative one year back when he was evaluated for borderline acute cellular rejection and was treated with anti-rejection therapy.

Kidney histopathology

Eleven patients underwent kidney biopsy for evaluation of graft dysfunction (Tables S1 and S2). Nine patients had features of acute tubular injury in the form of denudation of tubular cells and loss of brush borders. Three patients had chronic active antibody-mediated rejection. One patient had a borderline acute cellular rejection with chronic antibody-

Table 2. Clinical presentation, laboratory parameters, and management strategies.

Variable	Total (n = 42)	Graft function recovered (n = 17)	Graft function not recovered (n = 25)	P value
Presence of severe COVID-19	21 (50%)	8 (47.1%)	13 (52%)	0.999
Presence of diarrhea	23 (54.8%)	7 (41.2%)	16 (64%)	0.209
Hypotension requiring inotropes	2 (4.8%)	1 (5.8%)	1 (4%)	1
Presence of orthostatic hypotension*	13 (31%)	2 (11.8%)	11 (44%)	0.041
SOFA score on admission	3 [1–4.25]	2 [1–3.5]	3 [2.5–5]	0.011
Median [IQR]				
Severe anemia	12 (28.6%)	2 (11.8%)	10 (40%)	0.081
Drop in hemoglobin from baseline (g/dl)	2.17 ± 1.18	1.75 ± 0.95	2.45 ± 1.25	0.059
Leukopenia (WBC <4000/μl)	24 (57.1%)	8 (47.1%)	16 (64%)	0.348
Peak serum creatinine (mg/dl)	2.40 [1.77–3.70]	1.80 [1.60–2.45]	2.80 [2.35–5.70]	0.002
Acute kidney injury				
KDIGO stage 1	24 (57.1%)	15 (88.2%)	9 (36%)	0.004
KDIGO stage 2	6 (14.3%)	0	6 (24%)	
KDIGO stage 3	12 (28.6%)	2 (11.8%)	10 (40%)	
Raised AST/ALT	8 (19%)	4 (23.5%)	4 (16%)	0.694
Diffuse (>50%) lung involvement on imaging	10 (24.4%)	3 (17.7%)	7 (29.2%)	0.480
C-reactive protein (mg/l)	38.8 [15.22–68]	44 [8.9–68]	33.6 [17.68–64]	0.756
Lactate dehydrogenase, U/l	600 [409–855]	601 [373–778]	599 [432–1317]	0.458
D-dimer (μg/ml)*	0.89 [0.59–1.98]	0.87 [0.50–1.67]	0.89 [0.79–2.23]	0.745
Serum ferritin (μg/l)*	931 [317–1201]	531 [215–4201]	1002 [931–1202]	0.116
IL-6 (pg/ml)*	29.5 [9.25–166.1]	97.4 [9.50–292.0]	19.8 [3.49–41.8]	0.372
Presence of supratherapeutic tacrolimus trough levels [C_0]*	10 (23.8%)	3 (17.6%)	7 (28%)	0.490
C_0 level*	6.69 ± 4.73	7.41 ± 6.36	6.26 ± 3.56	0.516
Management strategies				
MMF/AZA withdrawal†	33/39 (84.6%)	14 (87.5%)	19 (82.6%)	1
CNI withdrawal or decrease‡	25/40 (62.5%)	11 (64.7%)	14 (60.9%)	1
Increased steroids	20 (47.6%)	9 (52.9%)	11 (44%)	0.754
Remdesivir	13 (31%)	7 (41.2%)	6 (24%)	0.314
Days of oxygen supplementation	3.33 ± 5.12	2.76 ± 3.68	3.72 ± 5.95	0.999
mean ± SD; Median [IQR]	0 [0–6.25]	0 [0–7.5]	0 [0–6]	
Hemodialysis	3 (7.1%)	0	3 (12%)	0.260

AZA, azathioprine; KDIGO, kidney diseases improving global outcomes; MMF, mycophenolate mofetil; NIPPV, noninvasive positive pressure ventilation; SOFA, sequential organ failure assessment.

*Data missing for lung involvement (n = 1); D-dimer (n = 40); C-reactive protein (n = 12); lactate dehydrogenase (n = 14); serum ferritin (n = 26); interleukin 6 (n = 30); tacrolimus trough levels C_0 (n = 5).

†Not on antimetabolite: n = 3; decreased AZA but not stopped for n = 1.

‡Not on CNI (calcineurin Inhibitor) n = 2.

mediated rejection which was not present in the previous biopsy done 2.5 years back. One patient had borderline acute cellular rejection. Two patients had biopsy features of acute thrombotic microangiopathy along with acute tubular injury, one of them also had chronic active antibody-mediated rejection. Both these patients were treated with intravenous immunoglobulin (IVIG) and plasmapheresis, one patient lost the graft and the other patient's eGFR at 3 months was 18.6 ml/min/1.73 m^2. A focal segmental glomerulosclerosis pattern of injury (non-collapsing) was seen in one patient. All the patients had interstitial fibrosis and tubular atrophy, which was worsened in 4 of them as compared with the previous biopsy. Two patients had features of chronic CNI toxicity. Six patients had mesangial matrix expansion, and 3 of them had de novo mesangial deposition of IgA (+3) and C3 (+).

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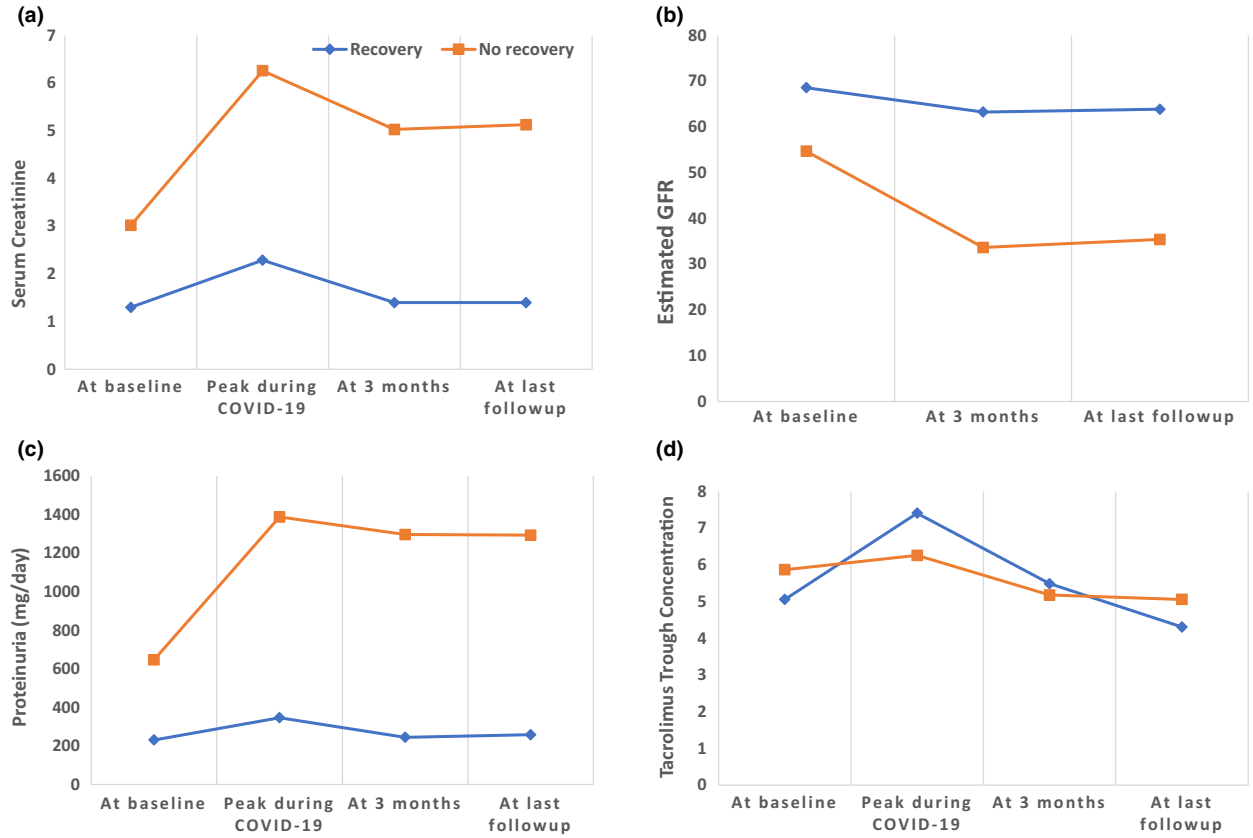

Figure 2 Evolution of graft function (a. serum creatinine, b. estimated GFR, c. proteinuria and d. tacrolimus trough levels) with time before and after COVID-19 infection.

Risk factors associated with incomplete recovery of kidney function

In univariate analysis, patients with incomplete recovery were more likely to have lower baseline eGFR ($P = 0.043$), proteinuria at baseline ($P = 0.004$), and a history of allograft rejection ($P = 0.013$; Table 1). They had a higher SOFA score at admission ($P = 0.011$), larger drop in hemoglobin from baseline ($P = 0.059$), and were more likely to have orthostatic hypotension ($P = 0.041$) and KDIGO stage 3 AKI ($P = 0.004$). There was no difference in the groups with respect to the severity of COVID-19, hepatic dysfunction, inflammatory markers, and treatment strategies including Remdesivir. On multivariable binary logistic regression (Table S3), the presence of proteinuria at baseline ($P = 0.009$) and orthostatic hypotension during the course of COVID-19 ($P = 0.042$) independently predicted incomplete recovery of graft at 3 months.

Discussion

We report short-term (median 5 months) outcomes of 42 kidney transplant recipients who had AKI because of COVID-19. In 25 (59.5%) patients, the graft function did not recover to baseline at 3 months. 15 (37.5%) patients had worsening of pre-existing proteinuria, and 4 (9.5%) patients had new onset proteinuria. Six (14.2%) patients had progressive graft failure and were initiated on maintenance hemodialysis. Graft rejection was seen in 4 (9.5%) patients. Patients with incomplete recovery of graft function were more likely to have lower baseline eGFR, proteinuria at baseline, historical graft rejection, higher SOFA score at admission, orthostatic hypotension, larger drop in hemoglobin from baseline, and KDIGO stage 3 AKI during COVID-19 admission.

Acute kidney injury in COVID-19 has been attributed to various factors including direct injury because of SARS-CoV-2, hemodynamic insults, cytokine-related injury, and coagulation dysfunction [7]. Histological lesions described in the native kidneys are acute tubular injury, pigmented tubular casts, focal segmental glomerulosclerosis (collapsing variant), and segmental glomerular fibrin thrombi, and "Viral-like" particles in the glomerulus and tubules [8]. The kidney allograft is at an additional risk of AKI because of the above COVID-19-related factors and transplant-related factors like graft rejection and CNI toxicity. Histological data

Table 3. Evolution of graft function and CNI levels with time in patients with recovery vs. no recovery.

Variable	Graft function recovered (n = 17)	Graft function not recovered (n = 25)	P value
Serum creatinine (mg/dl)			
At baseline	1.30 ± 0.38	1.72 ± 0.89	0.045
Peak during COVID-19	2.29 ± 1.23	3.97 ± 2.64	0.009
At 3-month follow-up	1.40 ± 0.36	3.63 ± 3.24	0.008
At last follow-up	1.42 ± 0.54	3.73 ± 3.25	0.002
Estimated GFR CKD-EPI (ml/min/1.73 m^2)			
At baseline	68.60 ± 21.17	54.70 ± 19.79	0.037
At 3-month follow-up	63.27 ± 19.7	33.67 ± 18.18	<0.001
At last follow-up	63.87 ± 19.90	35.42 ± 20.45	<0.001
Proteinuria(mg/day)			
At baseline	100 [65–216]	400 [110–1200]	0.015
Peak during COVID-19	120 [64–305]	890 [135–2400]	0.002
At 3-month follow-up	110 [65–330]	960 [120–2250]	<0.001
At last follow-up	100 [70–405]	1100 [119.5–2400]	0.001
Tacrolimus trough concentration (ng/ml)			
At baseline*	5.06 ± 1.22	5.87 ± 1.95	0.178
Peak during COVID-19†	7.41 ± 6.36	6.26 ± 3.56	0.516
At 3-month follow-up‡	5.49 ± 1.82	5.18 ± 2.72	0.742
At last follow-up§	4.31 ± 2.04	5.06 ± 1.82	0.509

Missing data for *N = 8, †N = 10, ‡n = 12, §n = 28.

from allograft biopsies are lacking. Features of acute tubular injury were seen in all of our patients in varying degrees. One patient had focal segmental glomerulosclerosis but not the collapsing variant. Thrombotic microangiopathy has been reported in native kidneys in COVID-19 [9] and is linked to the hypercoagulable state. In our cohort, two patients had features of thrombotic microangiopathy but it was found after recovery from COVID-19 and was also associated with other features of graft rejection (Table 3). Evidence of graft rejection episodes in recipients with COVID-19 is lacking with only two studies have reported an incidence of 1% [10] and 8% [11] (in recipients within 60 days after transplant). Graft rejection as seen in 9.5% of our patients and the presence of de novo donor-specific antibodies in one patient can be attributed to the reduction of immunosuppression made during the period of COVID-19 and also because of immunological dysregulation associated with COVID-19.

There is evidence suggesting that kidney function may not completely recover after COVID-19 in the general population. In a cohort of 1655 US veterans with AKI because of COVID-19, 47% did not recover to baseline by discharge [12]. In the STOP-COVID study of 637 critically ill adults with COVID-19 who developed AKI, 34% of those who survived remained dialysis dependent at discharge and 18% remained dialysis dependent 60 days after ICU admission [13]. Similar data of long-term kidney outcomes of COVID-19 in transplant recipients are lacking. Our data are in contrast with Paula *et al.* [14], who reported 3-month outcome of 26 kidney transplant recipients with AKI during COVID-19, with all patients recovering to baseline at the end of follow-up. There were no rejection episodes of graft rejection, and none of the patients developed de novo donor-specific antibodies. These differences can be attributed higher prevalence of stage 3 AKI in our cohort (12/42 vs. 2/26).

In our study, recovery of kidney function was not associated with baseline comorbidities, use of renin-angiotensin inhibitors, baseline immunosuppression, the severity of COVID-19, and presence of diarrhea. More patients treated with remdesivir had complete recovery (41% vs. 24%). Though this was not statistically significant, it points toward the safety of remdesivir in this population as we have previously reported [15]. More patients with incomplete recovery had supratherapeutic tacrolimus trough levels (28% vs. 18%), but this was not significant. The presence of proteinuria at the baseline was an independent predictor of incomplete graft recovery. This highlights the need for close monitoring of graft function in such patients. Similarly, clinical parameters like orthostatic hypotension and a larger drop in hemoglobin from baseline portended poor kidney recovery. These can serve as red flags in transplant recipients with COVID-

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19 and warrant prompt treatment and frequent monitoring.

Viral infections like CMV, BKV, and adenovirus have been associated with increased risk of rejection [5,16–18]. Though the exact mechanism is not clear, it has been attributed to viral cross-reactivity with HLA class I leading to T-cell activation, direct endothelial cell damage, and release of proinflammatory cytokines. Whether similar association is seen with COVID-19 needs to be confirmed in future studies. Four patients in our cohort required blood transfusion for symptomatic anemia. This can lead to development of de novo donor-specific antibodies augmenting the graft injury. We found de novo mesangial deposits of IgA and C3 in 3/9 patients which warrant further evaluation in future studies.

Comprehensive evaluation and meticulous follow-up of 100% of patients are the notable merits of our study. To our knowledge, this is the largest longitudinal cohort reporting the outcome of AKI because of COVID-19 in transplant recipients. Still, small sample size averts the establishment of the association and makes our study hypothesis generating, the findings of which need to be confirmed in future larger studies.

In conclusion, we found that more than half of patients who develop AKI because of COVID-19 have incomplete recovery of graft function. They are at risk for rejection, the appearance of de novo DSAs, and graft loss. They constitute a high-risk group that warrant more frequent follow-up in the transplant clinic than 2–3 months as suggested by guidelines (KDIGO 2009). They should get serial measurements of eGFR and proteinuria and should have a low threshold for screening for DSAs and for graft biopsy.

Authorship

All the authors contributed toward the study and read and approved final manuscript. DB and TEJ: designed the study and analyzed the data. SD, SB, CG, TM, AK, NS, AP, ST, AEP, AH, VK, SJ and AS: involved in the data collection and performance of the study. DB, TEJ and VK: prepared the manuscript.

Funding

The authors have declared no funding.

Conflict of interests

The authors have declared no conflicts of interests.

Acknowledgements

We acknowledge the support from Dr Hemant Deshmukh (Dean, Seth GSMC & KEM H, Mumbai) and Dr M.Y. Nadkar (Head, Department of medicine, Seth GSMC & KEM H) for setting up and maintaining a COVID-19 high dependency kidney unit free of charge to the patients. We acknowledge the help from Dr Pratap Jadhav in statistical analysis. We acknowledge the help of Mr Kishore Wardhan in data collection for this study.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Graft biopsy positive findings of transplant recipients.

Table S2. Summary of kidney histopathology findings.

Table S3. Multivariable binary logistic regression for predictor of non recovery of graft function.

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