

Outcome of COVID-19 in Kidney Transplant Patients from Eastern India: A Single Center Study

Abstract

Introduction: COVID-19 in kidney transplant recipients (KTR) had been associated with high incidence of acute kidney injury and higher mortality. Management of these patients is still evolving. **Methods:** A retrospective observational study was done that included all KTR aged ≥ 18 years and ≤ 65 years who had COVID-19 diagnosis via RTPCR test between 1 June 2020 and 30 May 2021. Severity of COVID-19 was determined as per the guidelines given by Government of India. Acute kidney injury was defined according to KDIGO guideline. Data was collected and analyzed using SPSS version 16.0 (Chicago, SPSS Inc.). **Results:** Out of 34 patients, 29 were men. Median age of patients was 39.9 years and median time since transplantation was 34 months. Presenting symptoms were fever (100%), cough (79.4%), gastrointestinal symptoms (23.5%), and dysgeusia/anosmia (23.5%). COVID-19 was severe in 17.6%, moderately severe in 32.4%, and mild in 50% of patients. Time since transplantation, duration of symptoms, hospital stay and inflammatory markers like CRP, LDH, ferritin and d-dimer were significantly associated with disease severity ($P < 0.05$). Steroids were increased in 55%, antiproliferative agents stopped in 97%, and calcineurin inhibitors stopped in 26% of patients. 70.6% of the patients were managed in home isolation. Acute kidney injury occurred in 58.8% cases. 75% of the AKI patients recovered by 28 days after discharge. **Conclusion:** Our study showed that outcome of COVID-19 in kidney transplant patients was reasonably good.

Keywords: Acute kidney injury, COVID-19, kidney transplant recipients, outcome, severity

Introduction

The novel corona virus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of *Coronaviridae* family. The disease started at Wuhan, China in December 2019 leading to the ongoing global pandemic.^[1] The record spike, noted in COVID-19 since March 2021 in India, has crippled lives and overwhelmed available health infrastructure. The government imposed “strict lockdown” in most of the states again in April 2021. Till 31 August 2021, India had reported 32,810,845 cases of COVID-19 with 439,020 (1.34%) deaths and Bihar state had 725,708 cases with 9653 deaths (1.33%).^[2] The virus usually involves the respiratory tract; in severe cases, renal dysfunction and multi-organ failure are also seen. Kidney transplant recipients (KTR) are at higher risk of infection.^[3-7] Recent studies have shown higher incidence of acute

kidney injury (AKI) and significantly higher morbidity and mortality from COVID-19 in KTR as compared to general population and cohorts with other risk factors.^[4-9] Management of KTR with COVID-19 remains challenging. There is no clear consensus on how to modify immunosuppression. Although interventions like HCQS, steroids, convalescent plasma transfusion and other experimental drugs were used in general population, their role in transplant patients remains uncertain. Recent studies have shown no significant benefit of these interventions except steroids.^[10,11] In contrast to higher mortality shown in various studies in India and abroad,^[4-9] one case series of nine patients from eastern India showed no mortality or significant sequelae.^[12] With this background, we studied the outcome, clinical and laboratory parameters, and management of COVID-19 in KTRs in Bihar, a resource-constrained state^[13] of eastern part of India.

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Methods

This is a retrospective observational study done at Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study was approved by the institute ethics committee (letter no. 132/IEC/IGIMS/2021). All kidney transplant recipients aged more than 18 years and less than 65 years evaluated at IGIMS and tested positive on RT-PCR test for SARS-CoV-2 between 1 June 2020 and 30 May 2021 were included in the study. Severity of the COVID-19 was determined as per “CLINICAL MANAGEMENT PROTOCOL FOR COVID-19”, published by Ministry of Health and Family Welfare, Government of India.^[14] AKI was defined as increase in serum creatinine ≥ 0.3 mg/dl within 24 hours or ≥ 1.5 times the baseline.^[15]

Clinical data including age, sex, transplant vintage, immunosuppressive treatment, comorbidities, signs and symptoms, severity, and biochemical parameters including kidney function tests, liver function tests, and inflammatory markers were noted. Data were collected at the time of hospitalization, at the time of discharge, and at follow up done one month after discharge, from hospital records and electronic communications (e.g., telephone/SMS/WhatsApp®/emails).

Data was collected, compiled, processed, and analyzed using SPSS for Windows, version 16.0 (Chicago, SPSS Inc.). The categorical variables were expressed as number and percentage, and continuous variables were shown as mean, standard deviation, median and interquartile range (IQR), where appropriate. For comparing categorical variables, Chi-squared test or Fisher’s exact test (when expected frequencies of cells were < 5) were used. Shapiro–Wilk test of normality was performed and data was found to be not normally distributed for many independent variables. As the assumptions of ANOVA were violated due to non-normality and outliers in the data, Kruskal–Wallis H test was performed. P value of < 0.05 was considered significant.

Results

We had 194 KTRs in our active follow up in 2020–2021. Out of 194 KTRs, 34 (17.5%) were detected COVID-positive by RT-PCR method over 12 months period from 1 June 2020 to 31 May 2021. 29 patients (85%) were men with a median age of 39.9 years. Baseline characteristics of the patients and transplantation are given in Table 1. All but one had received live kidney donation. 28 patients (82.4%) had received anti-thymocyte globulin (ATG) induction at the time of transplant and all were on triple immunosuppressive agents (ISA) including prednisolone, calcineurin inhibitors (CNI)/mTOR inhibitors, and mycophenolate mofetil (MMF). History of graft rejection was present in six patients (acute antibody mediated and acute cellular rejections in three each).

Presenting symptoms were fever (100%), cough (79.4%), shortness of breath (38.2%), gastrointestinal symptoms (23.5%), and dysgeusia and/or anosmia in 23.5% cases [Table 2]. None of the patients

Table 1: Baseline characteristics of kidney transplant recipients with COVID-19

Characteristics	<i>n</i> (%) or Median (IQR)
Man/Woman	29/5 (85/15)
Mean Age (years)	39.9 (Range 23-66)
Time since transplant (months)	34 (16.75-70.75)
Induction	29 (85.3)
Basiliximab	1 (2.9)
Anti-thymocyte Globulin	28 (82.4)
None	5 (14.7)
Maintenance Immunosuppressants (<i>n</i> %)	
Prednisolone	34 (100%)
Tacrolimus/cyclosporin	33/1 (97/3)
Mycophenolate/Azathioprine	32/2
Baseline serum creatinine (mg/dL)	1.1
Basic kidney disease	
CIN	17 (50)
DKD	6 (17.6)
HTN	5 (14.7)
IgA nephropathy	3 (8.8)
CGN	3 (8.8)
COMORBIDITIES	
HTN	27 (79.4)
DM	9 (26.5)
CAD	2 (5.9)
Hypothyroidism	5 (14.7)
More than one	12 (35.3)
None	6 (17.6)

Abbreviations: CAD, coronary artery disease; CGN, chronic glomerulonephritis; CIN, chronic interstitial nephritis; DKD, diabetic kidney disease; DM, diabetes mellitus; HTN, hypertension; *n*, numbers; IQR, interquartile range

Table 2: Clinical parameters of kidney transplant recipients with COVID-19

Characteristics	Median (IQR) or <i>n</i> (%)	<i>P</i>
Time since transplant (months)	34 (16.75-70.75)	0.034
Duration of symptoms before presentation (days)	5 (4-7)	0.054
Duration of hospital stay (days)	11 (7.5-17)	0.001
Fever	34 (100%)	-
Cough	27 (79.4)	0.103
Shortness of breath	13 (38.2)	0.000
Gastrointestinal symptoms	8 (23.5)	0.889
Dysgeusia/Anosmia	6/2 (17.6/5.9)	0.088
Severity		
Mild	17 (50)	
Moderate	11 (32.4%)	
severe	6 (17.6%)	
Acute kidney injury	20 (58.8)	0.078
Hospitalization	10 (29%)	0.000

developed complications related to bleeding diathesis or hypercoagulation. Laboratory parameters according to severity of COVID-19 are presented in Table 3. COVID-19 was severe in six (17.6%), moderately severe in 11 (32.4%) and mild in 17 (50%) patients. In mild, moderate and severe cases, median oxygen saturation (SPO₂) was 97%, 93%, and 84% respectively. Overall, 24 patients (70.6%) were managed in home isolation. Out of ten hospitalized patients, one patient each needed BiPAP and mechanical ventilation.

Dose of prednisolone was not changed in 15 patients (44.1%) and increased in 12 (35.3%). Prednisolone was substituted with dexamethasone in 6 patients (17.6%) while with intravenous methyl prednisolone in 1 patient. Antiproliferative drugs were stopped in 33 patients and additionally CNi was stopped in 9 patients (26%) who had severe COVID-19 and/or had AKI. Three patients received remdesivir and one received favipiravir. AKI developed in 20 patients (58.8%). AKI occurred in 47%, 54.5% and 100% of mild, moderate and severe cases, respectively.

One patient who needed mechanical ventilation died and one patient who had chronic graft dysfunction and needed hemodialysis remained dialysis dependent even after 28 days since discharge.

Discussion

India is among the most severely COVID-affected countries globally. COVID-19 overwhelmed the existing health system several weeks. Kidney transplant recipients are susceptible to COVID-19 infection with worst outcome as shown in few Indian studies [7,16,17] and also in various

studies from different countries.[4-6,8,18] Although data regarding transplant recipients are now emerging in the form of case series and registries worldwide, the same from India are still limited. There is no published data on KTR with COVID-19 from eastern part of the India to the best of the authors' knowledge.

We present data on 34 kidney transplant patients affected with COVID-19. IGIMS is a low volume transplant center situated in a resource-constrained state. COVID positivity rate at our center is 17.5% which is much higher than that shown in various studies.[8,9,16,17] 85% of kidney transplant recipients (KTRs) were male while 80% live donations came from women, reflecting prevalent gender bias in kidney transplant.[9] We had a relatively younger cohort of transplant recipients with a median age of 39.9 years.[8,9] Apart from immunosuppressive state, two most important risk factors for COVID-19 namely hypertension and diabetes were seen in approximately 80% and 25% patients, respectively. Disease severity varied from severe (17.6%), moderately severe (32.4%), to mild (50%) patients similar to that observed in Indian reports.[4,16] The incidence of AKI (58%) was at par with other studies reporting incidence of AKI ranging from 42%–57%.[4,7-9,19] Out of 20 AKI patients, only seven (35%) had serum creatinine declined to their pre-COVID serum creatinine at the time of discharge, but follow up after 28 days showed recovery to pre-COVID serum creatinine in 15 (75%) patients.

Although there was no clear consensus on how to manage immunosuppression in these cases, learning from the past, we discontinued antimetabolites in all patients and decreased the dose of tacrolimus in almost half of the patients, including withdrawal of tacrolimus in one-fourth

Table 3: Laboratory parameters according to severity of COVID-19

Variables	Mild (n=17)	Moderate (n=11)	Severe (n=6)	H (df)	P
Time since transplant (months)	22 (15-50)	30 (15-61)	93.5 (52-165.5)	6.754 (2)	0.034
Duration of symptoms before presentation (days)	4 (3-6.5)	5 (4-8)	6.5 (5-9.25)	5.826 (2)	0.054
Duration of hospital stay* (days)	-	9.5 (7.5-14)	15.5 (8-19)	13.799 (2)	0.001
TLC	8230 (5897-10212)	7430 (5360-9120)	9000 (7950-14355)	3.457 (2)	0.178
Platelets (×1000)	173 (143-183)	158 (144-167)	157 (95-190)	0.713 (2)	0.700
S. Cr during infection (mg/dl)	1.7 (1.3-1.7)	1.6 (1.2-1.92)	2.19 (1.74-4.2)	3.492 (2)	0.174
S Cr. At the time of discharge/recovery (mg/dl)	1.35 (1.13-1.61)	1.47 (0.31)	1.59 (1.3-3.1)	2.465 (2)	0.292
Serum albumin (g/dl)	4.2 (3.9-4.3)	3.8 (3.5-4.1)	3.7 (0.7)	4.331 (2)	0.115
SGOT (U/L)	34 (21-63)	29 (20-54)	40 (35-61)	1.649 (2)	0.439
SGPT (U/L)	34 (16-100)	32 (18-58)	55 (38-107)	1.754 (2)	0.416
LDH (U/L)	296 (218-390)	654 (304.68)	590 (467-724)	13.112 (2)	0.001
CRP (mg/L)	26 (11.1-51.1)	40.5 (26.37)	50.1 (41-98.7)	6.085 (2)	0.048
D-dimer (µg/ml)	0.5 (0.31-0.57)	1.9 (0.6-3.2)	1.44 (0.87-10.57)	10.173 (2)	0.006
Ferritin (ng/ml)	339.3 (205-586)	639.1 (478-1368)	891 (583-1454)	10.204 (2)	0.006
Procalcitonin (ng/ml)	0.45 (0.3-0.57)	0.6 (0.5-1.26)	0.5 (0.17)	4.252 (2)	0.119
Interleukin-6 (pg/ml)	-	17.85 (4-34)	31.55 (40.09)	1.333 (1)	0.248

*Number of patients hospitalized: Mild- 0, Moderate- 6, Severe - 4. Data are n (%) or median (IQR); H statistic=Kruskal-Wallis Test.

Abbreviations: SpO₂, % oxygen saturation; CRP, C-reactive protein; IQR, interquartile range; LDH, lactate dehydrogenase; n, number; S. Cr, serum creatinine; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; TLC, total leucocyte count.

of cases with moderate-to-severe disease and in those with AKI. Prednisolone dose was increased in 35% cases while intravenous dexamethasone was used for short-term in 6 patients (17%) in accordance with RECOVERY trial recommendations.^[11] 70% of kidney transplant recipients were managed at home with telemedicine support, 30% were admitted in the hospital and overall, 97% recovered from COVID-19.

Conclusion

Kidney transplant recipients are at a high risk of contracting COVID-19 and acute kidney injury. Duration of symptoms and level of inflammatory markers were significantly associated with severity. Most of the patients were managed successfully at home and outcome of COVID-19 in kidney transplant patients was better in terms of higher recovery rate and lesser mortality.

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Conflicts of interest

There are no conflicts of interest.

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