

“SARS-CoV-2 Infection in Liver Transplant Recipients - Immunosuppression is the Silver Lining?”



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Background: COVID-19 is associated with higher mortality among patients who have comorbidities. However, evidences related to COVID-19 among post liver transplant recipients are scarce and evolving. **Methods:** Adult Indian patients who had undergone liver transplantation at our centre since 2006 and were under regular follow-up, were contacted either telephonically or on email. Data were recorded related to symptoms and diagnosis of COVID-19, need for hospitalization, and need for ICU stay and mortality. **Results:** Eighty one (3.71%) of the 2182 adult Liver transplant (LT) recipients on regular follow-up reported SARS-CoV-2 infection between 1st April 2020 and 31st May 2021. Mean age was 51.3(±9.8) years, and 74(91.4%) were males. Thirty five (43.2%) patients had one or more comorbidities. Twenty one (25.9%) patients were transplanted less than 1 year ago. Forty four (54.3%) patients had mild disease only while 23(28.4%) patients had severe COVID-19 disease. Of the 81 patients 14 patients died and overall mortality was 17.3% **Conclusion:** Uncomplicated liver transplant recipients without comorbidities who acquire SARS-CoV-2 do not have poor outcome. (J CLIN EXP HEPATOL 2022;12:384–389)

COVID-19 caused by SARS-CoV-2 has been shown to be associated with significant morbidity and high mortality among individuals who have pre-existing medical conditions such as obesity, diabetes, coronary artery disease, chronic kidney disease and nonalcoholic fatty liver disease.^{1,2} Patients who have undergone liver transplantation are on long-term immunosuppressive medications which predisposes them to infections.

Recent studies have suggested that patients with liver disease especially cirrhosis may have high mortality due to COVID-19.³ The data regarding impact of SARS-CoV-2 infection in post LT patients is conflicting, and risk factors for outcome are also not well defined.⁴ Initial studies suggested that patients on immunosuppressive medications, such as liver transplant recipients, are at increased risk of severe COVID-19 and mortality; however, subse-

quent evidence did not support this finding.^{5,6} Although immunosuppression has risk of increased viral replication; however, on the other hand, it may suppress immune dysregulation related cytokine storm in COVID-19. Data on SARS-CoV-2 infection in liver transplant recipients is very limited from India, which is one of the worst affected country in this pandemic. Here we are sharing the clinical characteristics, demographics and outcomes of SARS-CoV-2 infection in our post liver transplant population.

METHODS

Patients and follow-up

Ours is a high-volume liver transplant centre in New Delhi, India, doing about 250–300 living donor liver transplants (LDLT) annually, catering to both Indian and international patients. Transplant recipients are kept on regular monthly follow-up for the first year and subsequently at regular 3–6 monthly intervals through regular visits in persons, or telephonically or over emails as most patients return to their respective hometowns after first few months of the transplant. At the start of the pandemic, we reached out to all our post liver transplant patients through email to advise them on precautions to be taken during the pandemic and encouraged them to contact us in case of any health issue. During the pandemic, a close communication (either telephonically or through email) was maintained with them especially because they were discouraged to travel and physically visit the hospital. All patients were kept under closed supervision and advised

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Abbreviations: ARDS: Acute respiratory distress syndrome; CAD: Coronary artery disease; CKD: Chronic kidney disease; CNIs: Calcineurin inhibitors; COVID-19: corona virus disease 2019; LDLT: live donor liver transplants; LT: Liver transplant; NAAT: nucleic acid amplification test; NAFLD: Nonalcoholic fatty liver disease; NASH: Nonalcoholic steatohepatitis; OPD: Outpatients department; SARS-CoV-2: severe acute respiratory syndrome corona virus-2

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individually on precautions they needed to take to protect from exposure and encouraged to maintain communication if they developed any symptoms of SARS-CoV-2 infection. Data related to development of symptoms, testing for SARS-CoV-2, and need for hospitalization and outcomes were recorded through telephonic communication or emails.

Inclusion criteria

All post-liver transplant recipients (age > 18 year at time of transplant) on regular follow-up since 2006 who were on follow-up had laboratory confirmed SARS-CoV-2 infection between 1st April 2020 and 31st May 2021 were included in the study.

Exclusion criteria

Patients who had died or were lost to follow-up since their transplant surgery were excluded from the study. Patients with typical SARS-COV-2 symptoms; however, the negative laboratory report were also excluded. The study was approved by institute's ethical committee. (Approval number: RS/MSSH/MHIL/SKT-1/MHEC/CLBS/20-35).

Supervision protocol

Patients were encouraged to self-isolate themselves and get tested with a reverse transcription polymerase chain reaction (RT-PCR) assay or rapid antigen test for SARS-CoV-2 when either they or any of their close family members developed symptoms suggestive of COVID-19 or on contact with confirmed cases as per Indian council for medical research (ICMR) guidelines. A positive case was defined based on WHO guidelines with a positive reverse transcription polymerase chain reaction (RT-PCR) assay or rapid antigen test for SARS-CoV-2 in nasopharyngeal swab, sputum samples or bronchoalveolar lavage (BAL).⁷ The choice of the diagnostic test varied according to the local availability and hospital guidelines where patient consulted. Patients who tested positive for SARS-CoV-2 infection were referred to the concerned specialist as indicated and followed closely till recovery or death. For the patients who were hospitalized, all the necessary information on treatment or interventions was collected. Detailed clinical history of risk factors, symptoms and comorbidities was taken. Record was made if patient received any specific antiviral therapy for SARS-CoV-2 infection. Details of hospitalization, need for intensive care or respiratory support and final outcome were obtained. Demographic details, data regarding baseline immunosuppressive medications and any alterations made in it after SARS-CoV-2 infection were also recorded.

Chronic kidney disease (CKD) and its stages were defined as per standard KDOQI definitions.⁸

Severity of COVID-19 was classified according to WHO and national centre for disease control, India guidelines.^{7,9,10}

Mild disease – Upper respiratory tract symptoms (and or fever) without shortness of breath or hypoxia.

Moderate disease – Any one of the following: 1. respiratory rate >24/min, breathlessness and 2. SpO₂: 90% to <93% on room air.

Severe disease – Any one of the following: 1. respiratory rate >30/min, breathlessness and 2. SpO₂ < 90% on room air.

Patients were divided into three groups based on interval from liver transplantation till SARS-CoV-2 infection. Group A of the patients had SARS-CoV-2 infection within one year of liver transplant. Group B patients were transplanted 1–5 year ago, while group C included the patients who underwent transplant more than 5 year ago.

Primary outcome was survival after SARS-CoV-2 infection. Secondary outcomes were need for ICU care, need for mechanical ventilation. All data was recorded in standardized patient data collection sheets.

Patients who belonged to Delhi and nearby areas were treated in our centre only while remaining patients were managed in their hometown and close follow-up was kept via emails and telephonically. Management protocols at these different centres although not exactly similar but were fairly uniform and based on health ministry guidelines and evidence-based recommendations of WHO.

After SARS-CoV-2 infection in transplant recipients, immunosuppressive medications were modified. Dose of immunosuppression was reduced, and complete withholding was avoided. For most of the cases, mycophenolate mofetil was stopped in patients with moderate and severe disease while calcineurin inhibitors (CNIs) were continued in lower doses. All of the patients with moderately severe or severe disease received steroids most commonly dexamethasone or methylprednisolone. Eleven patients received favipiravir. Two patients were given remdesivir, and convalescent plasma therapy was used in one patient. Casirivimab + Imdevimab monoclonal antibody combination was used in one patient. No patient received tocilizumab drug.

Statistical analysis

All categorical data were expressed as frequency or proportions, and continuous data were expressed as mean (SD) or median (range). Statistical analysis was done using software SPSS version 17, Chicago. The data were documented in a predesigned proformas. The case record forms were kept at safe places. Computer files were created in Microsoft excel for windows. Statistical analysis was done using software SPSS version 17, Chicago. The normally distributed variables were expressed as mean \pm standard deviation (SD), and continuous variables with skewed

Table 1 Characteristics of Liver Transplant Recipients With SARS-CoV-2 Infection.

Parameters	Results
Patients, n	81
Age, Mean (±SD)	51.34 (±9.8) years
Male n (%)	74 (91.4%)
Female n (%)	7 (8.6%)
Duration since transplant n (%)	
Group A- Less than 1 year	21 (25.9%)
Group B –1 to 5 years	36 (44.4%)
Group C- More than 5 years	24 (29.6%)
Pretransplant liver disease n (%)	
ALD	24 (29.6%)
NASH	22 (27.2%)
Cryptogenic cirrhosis	15 (18.5%)
HBV cirrhosis	12 (14.8%)
Others	8 (9.9%)
Comorbidities n (%)	
No Comorbidities	46 (56.7%)
Diabetes mellitus	22 (27.1%)
DM2 and HTN	6 (7.4%)
Hypertension	3(3.7%)
DM2 CKD	4 (4.9%)
Baseline immunosuppression n (%)	
A-Tacrolimus only	11 (13.5%)
B-CNIs + Mycophenolate	59 (72.8%)
C-CNIs + Mycophenolate + Oral prednisolone	10 (12.3%)
D-Everolimus	1 (1.2%)
Specific antiviral therapy for SARS-CoV-2)	
Favipravir	11 (13.5%)
Remdesivir	2 (2.4%)
Plasma therapy	1(1.2%)
Casirivimab + imdevimab	1(1.2%)
Symptoms at presentation n (%)	
Fever	52 (76.5%)
Cough	35 (52.2%)
Shortness of breath	17 (25.8%)
Diarrhea	7 (10.6%)
Severity of COVID-19	
Mild	44 (54.3%)
Moderate	14 (17.3%)
Severe	23 (28.4%)
Hospitalization n (%)	35 (43.2%)
Need for ICU n (%)	28 (34.6%)
Need for mechanical ventilation	17 (20.9%)

Table 1 (Continued)

Parameters	Results
Death	14 (17.3%)

CNIs – calcineurin inhibitors.

distribution as median (interquartile range). Categorical data were presented as frequency and proportions. The comparison of continuous variables between two groups was done using the independent t-test and Mann-Whitney U test. Categorical variables were analyzed using the chi-square test and Fisher’s exact test. Logistic regression analysis was done to determine risk factors for mortality. A P value of <0.05 was considered as statistically significant.

RESULTS

Demographic characteristics

Of the 3096 patients who underwent liver transplantation (>95% live donor related transplant) at our centre since year 2006, 2182 adult recipients were under regular follow-up and in communication with us at the start of the pandemic. Of these, 88 patients (3.71%) reported SARS-CoV-2 infection between 1st April 2020 and 31st November 2020. Six adult patients were excluded from the analysis as follow-up data about recovery from COVID-19 was not available. One child transplant recipient was also excluded, and 81 patients were included in the final analysis. At the time of writing of this manuscript, India had about 20,621 SARS-CoV-2 laboratory-confirmed cases per million population which is about 2.06% of the general population.¹¹ Average age of SARS-CoV-2-infected patients in our study was 51.3 years, and 74 patients (91.4%) were males. Twenty-one (25.9%) patients infected with SARS-CoV-2 underwent liver transplant within one year (group A). Thirty-six (44.4%) patients received transplant between 1 and 5 year while 24 (29.6%) patients were transplanted more than 5 year ago.

Pretransplant cirrhosis etiology

All 81 patients received transplant for liver cirrhosis. Most common etiology of pretransplant cirrhosis was alcohol-related liver disease (ALD) which was present in 24 (29.6%) patients. NASH related cirrhosis was seen in 22 (27.2%) while 15(18.5%) and 8(9.9%) patients had cryptogenic and HBV-related cirrhosis, respectively.

Comorbidities

Diabetes mellitus was the most common comorbidity, which was seen in 22 (27.1%) SARS-CoV-2 infected patients. Hypertension alone was present in 3(3.7%) patients while 6 (7.4%) patients had DM2 with hypertension. Four

Table 2 Comorbidities and Time Since Transplantation in Died and Survived Group.

Variables	Died (n=)	Survived (n=)	Total	P value
Patients with comorbidity n (%)	11 (31.4%)	24 (68.5%)	35 (43.2%)	0.003
Patients without comorbidity n (%)	3 (6.5%)	43 (93.4%)	46 (56.7%)	
Less 1 year since liver transplant (Group A) n (%)	1 (4.7%)	20 (95.2%)	21 (25.9%)	0.102
1–5 year since liver transplant (Group B) n (%)	6 (16.6%)	30 (83.3%)	36 (44.4%)	
More than 5 years since liver transplant (Group C) n (%)	7 (29.1%)	17 (70.8%)	24 (29.6%)	

patients had chronic kidney disease along with DM2. Out of these four patients one had stage 2 CKD and other three patients had stage 3 CKD. Details of patient characteristics and patient’s outcome have been shown in Table 1 and Table 2.

Base line immunosuppression

Most of the patients [59 (72.8%)] were on two immunosuppressants, that is, CNIs and mycophenolate mofetil. 10(12.3%) patients were receiving three immunosuppressive drugs calcineurin inhibitors (CNIs), mycophenolate mofetil and prednisolone. Eleven (13.5%) patients were taking single immunosuppressive medication (tacrolimus) only. One patient was on steroids with tacrolimus and everolimus due to recent rejection episode.

Presentation and course of SARS-CoV-2 infection in liver transplant recipients

Most common symptom at presentation was fever (76.5%) followed by cough (52.2%). Seventeen (25.8%) patients had shortness of breath at presentation. Diarrhea was seen only in 7 (10.6%) patients. No patients reported anosmia or dysgeusia.

Most of the patients had mild disease only which was present in 44 (54.3%) patients. Moderately severe and severe disease was seen in 14 (17.3%) and 23(28.4%) patients, respectively. Of the 81 patients 35 (43.2%) received in hospital care. Patients with mild disease mostly managed on OPD basis with home isolation. Some COVID-19 patients with moderately severe disease also received OPD based care and virtual consultation as at the peak of pandemic hospitalization became difficult. Patients with mild disease who contracted SARS-CoV-2 infection during early post-transplant period were managed in our hospital only.

28 (34.6%) patients received ICU care and 17 of them needed mechanical ventilation. Overall, 14(17.3%) patients died because of COVID-19. All COVID-19 related deaths occurred secondary to ARDS and respiratory failure. No patient had liver failure or graft rejection during the course of COVID-19. No thromboembolic complication was seen in our patients.

COVID-19 mortality association with time since transplant

Based on duration since liver transplant, patients were divided in to three groups. Group A (n = 21) included the patients who infected with SARS-CoV-2 within one year of liver transplant. Group B (n = 36) and group C (n = 24) patients received transplant 1–5 year ago and more than 5 years ago, respectively. One (4.8%) Patient died in group A as compared to 6 (16.7%) and 7 (29.2%) in group B and C respectively. Although mortality was higher in group C than other two groups, difference was not statistically significant (P = 0.102).

Mortality in patients with or without comorbidities

In our study group, 35 (43.2%) patients had one or more comorbidities. Eleven (31.4%) patients died because of COVID-19 in this group. Only 3 (6.5%) patients death occurred due to SARS-CoV-2 infection among transplant recipients without any comorbidity. (P = 0.003).

Predictors of mortality

On logistic regression analysis advanced age and presence of comorbidities were independent predictors of death due to COVID-19.

DISCUSSION

In our observational study of 81 liver transplant recipients with SARS-CoV-2 infection, 14 (17.3%) patients died because of COVID-19. Most of the patients had mild disease only and recovered completely.

Eighty-one (3.71%) adult liver transplant recipients reported SARS-CoV-2 infection as compared to the 2.06% prevalence of laboratory confirmed cases in general population. However, true seroprevalence in general population is likely to be much higher due to undertesting and large proportion of asymptomatic cases.

Deaths were more common in patients with comorbidities and advance age. Presence of DM2, chronic kidney disease has been strongly associated with poor outcomes in individuals with SARS-CoV-2 infection. Thus, rather than the post–liver transplantation status, it was the presence of comorbidities, or other risk factors such as advanced age which may have been responsible for mortality.

Published data on the course and outcome of COVID-19 in LT recipients are controversial and still evolving.

Complications like pneumonia in COVID-19 are driven by abnormal immune response, therefore patients on immunosuppressive medications are likely to have a favorable outcome.^{6,12} A recent study published by Webb *et al* demonstrated that LT recipients are not at risk for higher mortality in SARS-CoV-2 infection.¹³ Another study from India reported favorable outcome of SARS-CoV-2 infection in liver transplant recipients. In this series, of the 12 adult LT recipients with COVID-19, one patient died and 11 patients recovered.¹⁴

Although difference in mortality was not statistically significant in three groups based on duration from liver transplantation. In our study all patients except one who died received liver transplant more than one year ago. After 1-year of transplant doses of immunosuppressive medications are usually significantly reduced. This supports the hypothesis that patients who are on regular immunosuppression may be protected from getting severe COVID-19 disease. Bhoori *et al* also in the initial months of the pandemic had described higher mortality among long-term LT recipients.¹⁵

However, in a series of solid-organ transplant recipients, Coll *et al* demonstrated that the transplant recipients not only have increased risk of mortality but are also more prone to SARS-CoV-2 infection although details of comorbidities were not provided in this study.¹⁶ Furthermore, they studied a heterogeneous group and did demonstrate that the independent risk factors for mortality were age >60 years, acquired nosocomial infection and post-lung transplantation. In our cohort, none of the patients acquired any nosocomial infection, and the mean age (51.3 years) was lower than 60 years. In another study by Belli *et al* COVID-19-related overall mortality was 20% among LT recipients while 25% of hospitalized patients died. Average age of patients was higher (63 year) in this study, and 77% had comorbidities.¹⁷ Previously published studies have also shown that mortality in transplant recipients mainly occurred in older patients, with comorbidities and those who were on minimal immunosuppression.^{5,15}

In our study population COVID-19-related mortality was 17.3%. Although overall mortality in Indian general population is much lower (1.24%), our study group's mean age was much higher than general population and, 35% patients had one or more comorbidity. Studies from India have reported 18.2% mortality in hospitalized COVID-19 patients.¹⁸ Despite being older in age and higher proportion of comorbidities deaths in our patients were not higher. In a study from Spain mortality in transplant recipients was 18%, which was lower than matched general population.¹⁹

There are some limitations in our study. Although testing for SARS-CoV-2 infection was liberal in our country it may still be underdiagnosed in our study population as asymptomatic and mildly symptomatic patients who recovered swiftly may have avoided testing.

We did not compare mortality in our liver transplant recipients with immunocompetent matched COVID-19 patients. That could have provided better understanding of role of immunosuppressants in COVID-19-related immune dysregulation. This should be addressed in future studies. We could not study the impact of individual comorbidities on mortality due to limited number of patients. In addition, details of inflammatory markers and serum level of immunosuppressive medications were not included in the study as only 43% patients were hospitalized and remaining patients were managed at home.

In conclusion, of the 2182 adult Indian liver transplant recipients on regular follow-up 81(3.71%) had infection with SARS-CoV-2 since the occurrence of pandemic. Most of the patients had only mild disease. The mortality due to COVID-19 in our study group was 17.3%, and mostly associated with underlying comorbidities such as diabetes and advanced age. Our study shows that uncomplicated liver transplant recipients who acquire SARS-CoV-2 do not have poor outcome and immunosuppression may play a protective role in liver transplant recipients. However more studies are needed with larger patients population and matched control groups to reach a firm conclusion.

ETHICAL APPROVAL STATEMENT

Study was conducted with prior approval from institute ethical committee.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Dr. Shekhar Singh Jadaun- Writing - Original Draft, Investigation, Analysis. Dr Shweta A. Singh: Conceptualization, Writing - Original Draft, Supervision, Analysis, Validation. Dr Kaushal Madan: Conceptualization, Supervision, Writing - Review & Editing. Dr Subhash Gupta: Conceptualization, Review & Editing, Supervision, Resources.

CONFLICTS OF INTEREST

The authors have none to declare.

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REFERENCES

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020 Mar;395:1054–1062.
2. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its impact on patients with COVID-19. *Sn Compr Clin Med*. 2020 Jun 25:1–8.
3. Sarin SK, Choudhury A, Lau GK, Zheng M-H, Ji D, et al, APASL COVID Task Force, APASL COVID Liver Injury Spectrum Study (APCOLIS Study-NCT 04345640). Pre-existing liver disease is associated with poor outcome in patients with SARS CoV2 infection; the APCOLIS Study (APASL COVID-19 Liver Injury Spectrum Study). *Hepatol Int*. 2020 Sep;14(5):690–700.
4. Fix OK, Hameed B, Fontana RJ, et al. Clinical best practice advice for hepatology and liver transplant providers during the COVID-19 pandemic: AASLD expert panel consensus statement. *Hepatology*. 2020 Apr 16;72(1):287–304. hep.31281.
5. Becchetti C, Zambelli MF, Pasulo L, et al. COVID-19 in an international European liver transplant recipient cohort. *Gut*. 2020 Oct;69(10):1832–1840. gutjnl-2020-321923.
6. Verma A, Khorsandi SE, Dolcet A, et al. Low prevalence and disease severity of COVID-19 in post-liver transplant recipients—a single centre experience. *Liver Int*. 2020 Aug;40(8):1972–1976. liv.14552.
7. WHO COVID-19 Case definition [Internet]. [cited 2020 Sep 6]. Available from: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Surveillance_Case_Definition-2020.1.
8. NKF KDOQI Guidelines [Internet]. [cited 2021 Jun 14]. Available from: https://kidneyfoundation.cachefly.net/professionals/KDOQI/guidelines_ckd/p4_class_g1.htm.
9. Case definitions : National Centre for Disease Control (NCDC) [Internet]. [cited 2020 Sep 6]. Available from: <https://www.ncdc.gov.in/index1.php?lang=1&level=1&sublinkid=685&lid=547>.
10. Information on COVID-19 Treatment, Prevention and Research [Internet]. COVID-19 Treatment Guidelines. [cited 2021 Jun 6]. Available from: <https://www.covid19treatmentguidelines.nih.gov/>.
11. India COVID: 29,419,405 Cases and 367,577 Deaths - Worldometer [Internet]. [cited 2021 Jun 12]. Available from: <https://www.worldometers.info/coronavirus/country/india/>.
12. Choudhury A, Reddy GS, Venishetty S, et al. COVID-19 in liver transplant recipients - a series with successful recovery. *J Clin Transl Hepatol*. 2020 Dec 28;8:1–7.
13. Webb GJ, Marjot T, Cook JA, et al. Outcomes following SARS-CoV-2 infection in liver transplant recipients: an international registry study. *Lancet Gastroenterol Hepatol*. 2020 Nov;5:1008–1016.
14. Dhampalwar S, Saigal S, Choudhary N, et al. Outcomes of coronavirus disease 2019 in living donor liver transplant recipients. *Liver Transplant*. 2020 Dec;26(12):1665–1666. It.25909.
15. Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol*. 2020 Jun;5:532–533.
16. Coll E, Fernández-Ruiz M, Sánchez-Álvarez JE, et al. Covid-19 in transplant recipients: the Spanish experience. *Am J Transplant*. 2021 May;21(5):1825–1837. ajt.16369.
17. Belli LS, Fondevila C, Cortesi PA, et al. Protective role of tacrolimus, deleterious role of age and comorbidities in liver transplant recipients with Covid-19: results from the ELITA/ELTR multi-center European study. *Gastroenterology*. 2021 March;160(4):1151–1163.
18. Aggarwal R, Bhatia R, Kulshrestha K, et al. Clinicoepidemiological features and mortality analysis of deceased patients with COVID-19 in a tertiary care centre. *Indian J Crit Care Med*. 2021 Jun;25:622–628.
19. Colmenero J, Rodríguez-Perálvarez M, Salcedo M, et al. Epidemiological pattern, incidence, and outcomes of COVID-19 in liver transplant patients. *J Hepatol*. 2021 Jan;74:148–155.