

# A Multicentric Experience on Living Donor Liver Transplantation in Coronavirus Disease 2019 Hotspots in India

## TO THE EDITOR:

As of August 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected more than 213 countries, leading to more than 18 million cases and 690,000 deaths. India is the second most affected

country, with the majority of cases in metropolitan cities such as Mumbai, New Delhi, Chennai, and Bengaluru. There is limited literature on the outcomes and safety of performing living donor liver transplantation (LDLT) in coronavirus disease 2019 (COVID-19) epicenters.

## Patients and Methods

We conducted a multicenter, prospective cohort study that recruited consecutive LDLT recipients from 4 major transplant centers in Mumbai, Chennai, Hyderabad, and Bengaluru. The coordinating center was Gleneagles Global Health City in Chennai. This study conformed to the Declaration of Helsinki and was approved by the institutional ethics committee. Written informed consent was obtained from all patients. Both adult and pediatric recipients undergoing LDLT between April and July 2020 were included in the study. Recipient and donor data, including demographic variables, perioperative clinical and laboratory parameters, and postoperative outcome variables, were recorded. The overall survival rate at the end of 1 month post liver transplantation (LT) was recorded and analyzed.

## COVID-19 SAFETY MEASURES

COVID-19 safety measures for LDLT were divided into the following 3 standard operating protocols: patient related, staff related, and environment/equipment related. Emphasis was given to make the protocols safe and sustainable. A COVID-19-free transplant pathway was designed (Fig. 1). During the liver transplant intensive care unit (ICU) stay, donors and recipients were allowed to talk to their attenders through video calling. Caregivers underwent SARS-CoV-2 polymerase chain reaction (PCR) screening before coming into the liver unit. Home collection of blood samples and video consultations with the LT team were the

*Abbreviations: ACLF, acute-on-chronic liver failure; ALF, acute liver failure; CLD, chronic liver disease; CO-RADS, COVID-19 Reporting and Data System; COVID-19, coronavirus disease 2019; D0, Day of surgery; HRCT, high-resolution computed tomography; ICU, intensive care unit; LDLT, living donor liver transplantation; LT, liver transplantation; LTICU, Liver Transplant Intensive Care Unit; MAFLD, metabolic dysfunction-associated fatty liver disease; MELD, Model for End-Stage Liver Disease; NA, not applicable; PCR, polymerase chain reaction; PELD, Pediatric End-Stage Liver Disease; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.*

*Address reprint requests to Joy Varghese, M.D., D.M., Institute of Liver Disease & Transplantation, Gleneagles Global Health City, Cheran Nagar, Perumbakkam, Chennai 600100, India. Telephone: +91-44-22777000; FAX: +91 44 4477 7100; E-mail: joyvargese@gmail.com*

*Joy Varghese, Selvakumar Malleeswaran, and Chandhan Kumar Kedarisetty participated in the study concept and design. Joy Varghese, Selvakumar Malleeswaran, Rajanikanth V. Patcha, Chandhan Kumar Kedarisetty, Dharmesh Kapoor, Ravi Mohanka, Sunil D. Shenvi, and Bhaskaran Pillai Venugopal participated in the data acquisition. Joy Varghese participated in the statistical analysis. Selvakumar Malleeswaran, Chandhan Kumar Kedarisetty, and Ellango Appusamy participated in drafting the manuscript. Perumal Karnan, Balbir Singh, Prashantha S. Rao, Kota Venugopal, Babu Y. Raghavendra, Karan Kumar, Vinayak Nikam, Selvakumar Malleeswaran, Anurag Shrimal, and Nigel D. Heaton participated in critical revision of the manuscript. Selvakumar Malleeswaran and Rajanikanth V. Patcha participated in administrative and technical support.*

*Received August 17, 2020; accepted November 16, 2020.*

*Copyright © 2021 by the American Association for the Study of Liver Diseases.*

*View this article online at [wileyonlinelibrary.com](https://www.wileyonlinelibrary.com).*

*DOI 10.1002/lt.25957*

*Potential conflict of interest: Nothing to report.*

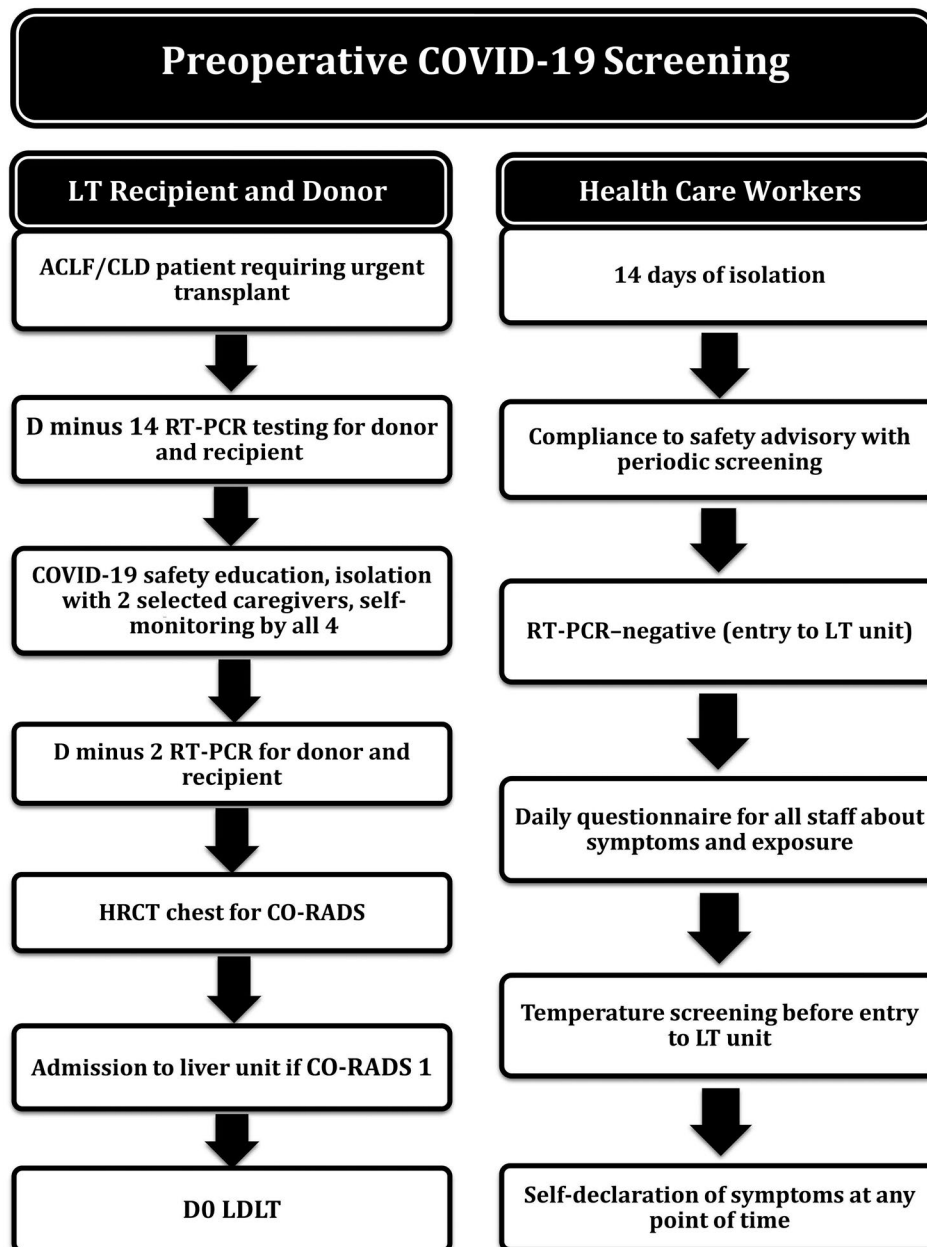


FIG. 1. Preoperative COVID-19 screening for LT recipients, donors, and staff members.

primary modalities of follow-up. If needed, patients came back to the dedicated liver unit, where all the emergency/elective queries were directed.

## STATISTICAL ANALYSIS

Descriptive statistics were expressed as median (interquartile range) or number (percentage). Comparisons

of continuous variables were done by Wilcoxon rank sum test, and categorical variables were compared by the Fisher's exact test or Pearson chi-square test. One-way and 2-way tables were computed. A *P* value of <0.05 was considered significant. Data were analyzed from Excel (Microsoft, Redmond, WA) sheets using Medcalc Software (Oostende, Belgium) statistical software.

TABLE 1. Demographic and Clinical Details of Recipients and Donors

Study Group	Adult LDLT (n = 21, mean ± SD)	Pediatric LDLT (n = 10, mean ± SD)	P Value
Recipient characteristics			
Age, years, median (range)	46 (18-59)	9 (0.5-17)	NA
Sex, male:female	18:3	5:5	0.03
Etiology of liver disease, n (%)	Ethanol related, 8 (38) MAFLD, 7 (33.3) Hepatitis B, 2 (9.5) Autoimmune hepatitis, 1 (4.7) Wilson's disease, 3 (14.3)	Wilson's disease, 3 (30) Post-Kasai, 1 (10) Hepatoblastoma, 3 (30) Progressive familial intrahepatic cholestasis, 2 (20) Cholesteryl esterase deficiency, 1 (10)	
Indication for LT, n (%)	ALF, 0 ACLF, 3 (14.3) MELD >15, 18 (85.7)	ALF, 1 (10) ACLF, 6 (60) Hepatoblastoma, 3 (30)	NA
Comorbidity, n (%)	Diabetes mellitus, 4 (19) Hypertension, 2 (9.5) Ischemic heart disease, 1 (4.7) Diabetes, hypertension, and morbid obesity, 1 (4.7)	Nil	NA
MELD/PELD score	20.3 ± 7.9	24.8 ± 9.5	0.33
Donor characteristics			
Age, years	39.1 ± 9.3	33.9 ± 7.7	0.14
Sex, male:female	9:12	0:10	0.02
Body mass index, kg/m <sup>2</sup>	25.3 ± 3.2	23.7 ± 3.1	0.20
Outcome variables			
ICU stay, days, median (range)	7 (4-28)	5 (3-8)	0.02
Hospital stay, days, median (range)	19 (12-51)	17 (10-23)	0.06
Morbidity, n (%)	7 (33.3)	1 (10)	0.17
Mortality, n (%)	2 (9.5)	0	0.32

## Results

A total of 31 LDLTs were conducted during the study period. Of these, 21 (67.7%) were adults and 10 (32.2%) were children. The demographic characteristics of donors and recipients and their clinical details are included in Table 1. In adults, ethanol-related chronic liver disease (CLD) was the predominant etiology followed by metabolic dysfunction-associated fatty liver disease (MAFLD). Of the children, 2 had progressive familial intrahepatic cholestasis presenting as secondary biliary cirrhosis, and 3 underwent LDLT for hepatoblastoma. Notably, 1 child presented with acute liver failure. The median postoperative ICU stay was 7 days in adults compared with 5 days in children ( $P = 0.02$ ). Of the adults, 2 patients died as a result of bacterial sepsis. Of the 7 adult recipients with postoperative morbidity, 4 had septicemia. One patient each developed bile leak, hepatic artery thrombosis, or polytetrafluoroethylene graft thrombosis respectively, all of which were managed successfully. One pediatric recipient had acute cellular rejection, which was

managed by pulse steroid therapy. One adult recipient was diagnosed with COVID-19 infection after discharge from the hospital, 46 days after surgery. The patient presented with fever and hypoxemia and had deranged transaminases. Chest computed tomography showed ground-glass opacities with COVID-19 Reporting and Data System (CO-RADS) 4 grading, and the PCR nasopharyngeal swab for COVID-19 was positive. Mycophenolate mofetil was discontinued, and the doses of steroid and tacrolimus were optimized. Antivirals were avoided because of hepatitis. The patient is currently in the hospital and recovering without ventilatory support. Notably, none of the donors, recipients, or transplant team members acquired nosocomial COVID-19 infection.

## Discussion

Timely LT in a patient with progressively decompensating cirrhosis or in a patient who is critically ill with acute-on-chronic liver failure (ACLF) is potentially

curative, with good long-term survival. However, the COVID-19 pandemic has raised many unanswered questions, including the risk and severity of perioperative COVID-19 in transplant recipients, the safety of the donors, and the safety of the LT team. In a large, online, cross-sectional survey<sup>(1)</sup> from 109 European transplant centers, the overall incidence of symptomatic COVID-19 and the crude death rate in transplant waitlist candidates versus LT recipients were 1.05% versus 0.3% and 18% versus 15%, respectively. The data from Mount Sinai Medical Center, New York, also showed similar results in 38 recipients infected with COVID-19, with an overall mortality of 18% and an in-hospital mortality of 29%.<sup>(2)</sup> Therefore, if we select patients who need urgent transplants and would be at higher risk of dying from liver failure than from COVID-19, LT could be safely performed with appropriate precautions.

During the study period, the average monthly incidence of COVID-19 in the 4 cities ranged between 955 and 2274 new cases per million population. The average hospital admission for COVID-19 in the 4 study centers ranged between 16% and 38% of the total available beds in each hospital. Despite this, because of stringent precautionary measures followed by the donor, recipient, and their accompanying caregivers; strict mitigation of the primary LT surgical, anesthesia, and supporting staff members from other duties to avoid unnecessary exposure; and the segregation of the donors and recipients in the liver transplant intensive care unit (LTICU), the chain of any possible transmission in the hospital was broken, and therefore nosocomial-acquired COVID-19 cases were avoided. Only those patients with urgent indications, such as high Model for End-Stage Liver Disease (MELD) scores, acute liver failure (ALF), acute-on-chronic liver failure (ACLF), primary hepatic malignancies, and so on were considered for timely LDLT after explaining the risks of COVID-19 and ensuring strict compliance to prevention protocols. Unfortunately, 1 adult recipient acquired COVID-19 infection from the community after discharge but is recovering. Similar encouraging results have also been reported from centers in India<sup>(3)</sup> and Korea.<sup>(4)</sup>

The possible limitation in the study is the small size of the study group. Further studies with long-term follow-up of these patients and donors can give us more information about the risk and severity of COVID-19 infections compared with the general population. In conclusion, this is the first

multicentric study highlighting the perioperative safety and good outcomes in carefully timed LDLT, even in COVID-19 hotspots, with stringent preventive protocols in place.

*Acknowledgment:* The authors thank Professor Vijaya Srinivasan, senior consultant epidemiologist, for statistical assistance.

Joy Varghese, M.D., D.M. <sup>1</sup>

Selvakumar Malleeswaran, M.D.<sup>1</sup>

Rajanikanth V. Patcha, M.S., F.R.C.S.<sup>1</sup>

Ellango Appusamy, M.D.<sup>1</sup>

Perumal Karnan, M.D.<sup>1</sup>

Dharmesh Kapoor, M.D., D.M.<sup>2</sup>

Kota Venugopal, M.S., F.R.C.S.<sup>2</sup>

Chandhan Kumar Kedarisetty, M.D., D.M.<sup>2</sup>

Balbir Singh, M.S., F.R.C.S.<sup>2</sup>

Prashantha S. Rao, M.S., F.R.C.S.<sup>2</sup>

Raghavendra Babu Yalakanti, M.S., F.R.C.S.<sup>2</sup>

Ravi Mohanka, M.S., F.R.C.S.<sup>3</sup>

Anurag Shrimal, M.S., F.R.C.S.<sup>3</sup>

Vinayak Nikam, M.S., F.R.C.S.<sup>3</sup>

Karan Kumar, M.D. <sup>4</sup>

Sunil D. Shenvi, M.S., F.R.C.S.<sup>4</sup>

Bhaskaran Pillai Venugopal, M.S., F.R.C.S.<sup>4</sup>

Nigel D. Heaton, M.D., F.R.C.S.<sup>5</sup>

<sup>1</sup>Institute of Liver Disease & Transplantation  
Gleneagles Global Health City  
Chennai

<sup>2</sup>Department of Hepatology & Transplantation  
Gleneagles Global Health City  
Hyderabad

<sup>3</sup>Department of Liver Transplant & Hepatobiliary  
Surgery  
Gleneagles Global Health City  
Mumbai, India

<sup>4</sup>Department of Hepato-pancreato-biliary &  
Transplant Surgery  
BGS Gleneagles Global Hospital  
Bengaluru, India

<sup>5</sup>Institute of Liver Studies  
King's College Hospital  
London, UK

## REFERENCES

- 1) Polak WG, Fondevila C, Karam V, Adam R, Baumann U, Germani G, et al. Impact of COVID-19 on liver transplantation in Europe: alert from an early survey of European Liver and

Intestine Transplantation Association (ELITA) and European Liver Transplant Registry (ELTR). *Transpl Int* 2020;33:1244-1252.

- 2) Lee BT, Perumalswami PV, Im GY, Florman S, Schiano TD, on behalf of the COBE Study Group. COVID-19 in liver transplant recipients: an initial experience from the US epicenter. *Gastroenterology* 2020;159:1176-1178.e2.
- 3) Verma S, Agarwal S, Chikkala BR, Dey R, Singh S, Varma S, et al. Living donor liver transplants for sick recipients during COVID-19 pandemic: an experience from a tertiary center in India. *Am J Transpl* 2020;20:3257-3258.
- 4) Lee JM. Effect of COVID-19 on liver transplantation in Korea. *Transpl Infect Dis* 2020;22:e13384.