

Living donor liver transplant outcomes during the COVID-19 pandemic: does a decrease in case volume impact the overall outcomes?

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Background: High-volume centers (HVCs) are classically associated with better outcomes. During the coronavirus disease 2019 (COVID-19) pandemic, there has been a decrease in the regular liver transplantation (LT) activity at our center. This study analyzed the effect of the decline in LT on posttransplant patient outcomes at our HVC.

Methods: We compared the surgical outcomes of patients who underwent LT during the COVID-19 pandemic lockdown (April 1, 2020 to September 30, 2020) with outcomes in the pre-pandemic calendar year (April 1, 2019 to March 31, 2020).

Results: During the 6 months of pandemic lockdown, 60 patients underwent LT (43 adults and 17 children) while 228 patients underwent LT (178 adults and 50 children) during the pre-pandemic calendar year. Patients in the pandemic group had significantly higher model for end-stage liver disease (MELD) scores (24.39±9.55 vs. 21.14±9.17, P=0.034), Child-Turcotte-Pugh scores (11.46±2.32 vs. 10.25±2.24, P=0.03), and incidence of acute-on-chronic liver failure (30.2% vs. 10.2%, P=0.002). Despite performing LT in sicker patients with COVID-19-related challenges, the 30-day (14% vs. 18.5%, P=0.479), 3-month (16.3% vs. 20.2%, P=0.557), and 6-month mortality rates (23.3% vs. 28.7%, P=0.477) were lower, but not statistically significant when compared to the pre-pandemic cohort.

Conclusions: During the COVID-19 pandemic lockdown the number of LT procedures performed at our HVC declined by half because prevailing conditions allowed LT in very sick patients only. Despite these changes, outcomes were not inferior during the pandemic period compared to the pre-pandemic calendar year. Greater individualization of patient care contributed to non-inferior outcomes in these sick recipients.

Keywords: Liver transplantation; SARS-CoV-2; Health care outcome assessment; Hospital bed capacity

HIGHLIGHTS

- Liver transplant outcomes can be affected by case volume at transplant center.
- Volume of liver transplants reduced by half at our center during severe acute respiratory syndrome coronavirus 2 pandemic.
- We compared liver transplant outcomes in pandemic period with pre-pandemic period.
- Transplant recipients in pandemic were sicker with higher model for end-stage liver disease and Child-Turcotte-Pugh score.
- Transplant outcomes in pandemic period were non-inferior to outcomes during pandemic period.

INTRODUCTION

Case volume at liver transplantation (LT) centers has been classically associated with posttransplant outcomes. Compared to low-volume centers (LVCs), high-volume centers (HVCs) are known to have better outcomes, including lower in-hospital mortality after LT [1], simultaneous liver and kidney transplantation (SLKT) [2], and other gastrointestinal surgical procedures [3]. How case volume affects posttransplant outcomes is not clear, although case volume can be associated with a protocolized approach, surgical experience, postoperative critical care, and the availability of radiologic and endoscopic expertise, all of which affect the transplant outcomes. However, some studies suggest that transplant center case volume is no longer a significant predictor of posttransplant survival in the model for end-stage liver disease (MELD) era [4].

Although the term "HVC" is used in the literature, the definition of HVC varies widely in different countries and even within different geographic regions of a country. In Korean studies, HVCs were defined as those conducting 30 to 50 transplants per year [5], and in the West the definition of 65 to 175 cases per year has been used [6]. The criteria for high- or low-volume transplant centers have not yet been defined in India, however, centers like ours that perform >100 LTs per year are considered HVCs [7].

The coronavirus disease 2019 (COVID-19) pandemic caused tremendous morbidity and mortality worldwide and reduced transplant work in India, with only the sickest patients being operated on. The volume of trans-

plants reduced by half at our center with the onset of the COVID-19 pandemic in 2020. This unique situation gave us an opportunity to study the effect of case volume on posttransplant outcomes at our center, which may not have been possible otherwise. Our study analyzed the impact of case volume reduction during the COVID-19 pandemic on posttransplant outcomes at our center by comparing results with the previous year.

METHODS

This study was approved by the Institutional Review Board of Max Super Speciality Hospital (IRB No. BHR/RS/MSSH/MHIL/SKT-1/MHEC/ANES/22-05). The requirement for informed consent was waived by the institutional ethics committee in view of retrospective nature of study.

This was a retrospective analysis of a prospectively maintained departmental database. Patients undergoing LT between April 1, 2020, and September 30, 2020 were included in the pandemic group (PG). The PG was further subdivided into the adult PG (APG; ≥ 18 years of age) and the pediatric PG (PPG; < 18 years of age). Similarly, patients undergoing LTs between April 1, 2019, and March 31, 2020, were grouped in the pre-PG (P-PG), which was further subdivided according to age into the adult P-PG (AdP-PG) and the pediatric P-PG (PedP-PG). The data of the APG was compared with the AdP-PG and the PPG was compared with the PedP-PG. The collected data included the transplant recipients' demographics, the details and extent of liver disease and other ailments, preoperative laboratory parameters, donor details, and details of the recipients' preoperative intensive care unit (ICU) stay. The patients' alcohol-related liver diseases included decompensated cirrhosis, acute-on-chronic liver failure (ACLF), and severe alcoholic hepatitis. All patients with alcohol-related liver disease underwent comprehensive assessment for posttransplant relapse of drinking behaviors as per our center's protocol. ACLF in adult patients was defined according to the European Association for the Study of Chronic Liver Failure criteria [8]. The intraoperative details noted were graft-to-recipient weight ratio, cold and warm ischemia time, graft steatosis (fat estimation on imaging), intraoperative blood transfusion, duration of transplant surgery, and type of donor surgery (open or laparoscopic). Postoperative data included the duration of ICU stay and hospital stay; postoperative complications

including biliary and vascular complications (i.e., hepatic artery thrombosis, portal vein thrombosis (PVT), middle hepatic vein/right hepatic vein thrombosis, bile leak) and sepsis; postoperative interventions performed (e.g., dialysis, plasmapheresis); and surgical, endoscopic, and radiological interventions conducted prior to discharge. The mortality rates at 30 days, 3 months, and 6 months were the primary outcomes of the study and complication rates were the secondary outcomes.

Statistical Analysis

The data were documented in a pre-designed form. Data were entered and analyzed using SPSS ver. 21 (IBM Corp., Armonk, NY, USA). Normally distributed variables were expressed as mean±standard deviation, and categorical data were presented as frequency and proportions. Continuous variables between two groups were compared using the independent t-test. Categorical variables were analyzed using the chi-square test and the Fisher exact test. Kaplan-Meier analysis was used to estimate the 1-year survival of patients. The log-rank test was used for comparing survival curves. P-values of <0.05 were considered to indicate statistical significance.

RESULTS

During the 6-month lockdown period, only 60 living donor LT (LDLT) procedures were performed in our unit, of which 43 were adult recipients (APG) and 17 were pediatric recipients (PPG) (Fig. 1). Five transplants were deferred

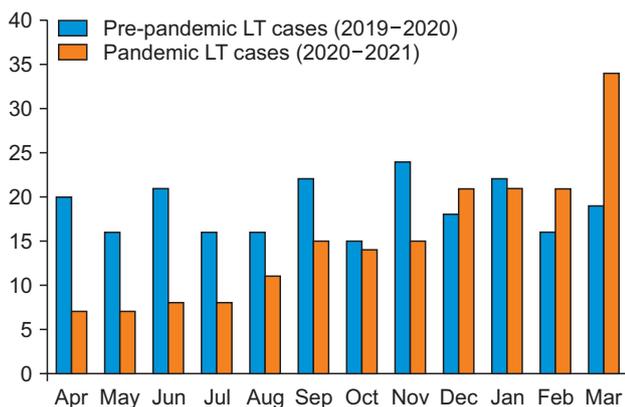


Fig. 1. Bar graph depicting the number of liver transplantation procedures performed by month. LT, liver transplantation.

during the pandemic when the donors tested positive during preoperative screening for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Three of these patients underwent LDLT at a later date. One of the two patients with ACLF and SARS-CoV-2 infection underwent LDLT after recovery from COVID-19. In contrast, 228 LT procedures were performed in our unit during the pre-pandemic year, of which 178 were in adults (AdP-PG) and 50 were in pediatric patients (PedP-PG). Three of these were deceased donor LT (DDLT) procedures, and three involved SLKT.

The demographics, including baseline recipient and donor characteristics and the preoperative and intraoperative details of adult LT recipients (APG and AdP-PG) are depicted in Table 1, and those of the pediatric age group (PPG and PedP-PG) are depicted in Table 2. The age, sex, and body mass index (BMI) of adult and pediatric recipients were found to be comparable between the two groups (Tables 1 and 2). Foreign nationals seeking treatment decreased significantly during the lockdown due to travel restrictions (14% in APG vs. 37.1% in AdP-PG, $P=0.003$ and 53% in PPG vs. 72% in Ped-PG, $P=0.024$) (Tables 1 and 2).

The most common etiology for cirrhosis among adults was alcohol use in the APG (37.2%) and viral infection in the AdP-PG (hepatitis B and C; 28.6%). The number of recipients with comorbidities (stroke, seizure disorders, interstitial lung disease) was higher in the APG. The mean MELD score of patients in the APG was significantly higher (24.39 ± 9.55 vs. 21.14 ± 9.17 , $P=0.034$) compared to the AdP-PG (Table 1). More APG patients than AdP-PG patients had complications of cirrhosis in the form of spontaneous bacterial peritonitis (SBP; 11.6% vs. 4.5%, $P=0.073$), PVT (8.4% vs. 2.3%, $P=0.277$), hepatic encephalopathy (HE; 46.5% vs. 34.27%, $P=0.131$), and hepatorenal syndrome (HRS; 13.95% vs. 7.3%, $P=0.163$), though these results were not statistically significant (Table 1). More patients with ACLF (30.2% vs. 10.2%, $P=0.002$) underwent transplantation in the APG, including ACLF-3 (i.e., three or more organs failing), compared to the AdP-PG (5.5% vs. 5%, $P=0.001$) (Table 1).

In the pediatric groups, the number of foreign nationals was significantly lower in the PPG than in the PedP-PG (53.57% vs. 72%, $P=0.024$). Patients in the PPG had higher pediatric end-stage liver disease (PELD) scores than the PedP-PG, but this difference was not statistically significant (24.93 ± 16.54 vs. 18.21 ± 17.59 , $P=0.477$). The most common etiology was biliary atresia in both pediat-

Table 1. Comparison of the demographics and preoperative and intraoperative parameters of adults who underwent liver transplantation in the COVID-19 pandemic period versus the pre-pandemic year

Parameter	APG (n=43)	AdP-PG (n=178)	P-value
Recipient			
Age (yr)	51.09±10.23	48.56±11.03	0.160
Sex			0.345
Male	39 (83.5)	148 (83.1)	
Female	4 (16.5)	30 (16.9)	
Donor			
Age (yr)	35.78±10.83	34.59 ±10.39	0.124
BMI (kg/m ²)	25.58±4.05	25.41±4.61	0.656
ABO incompatible	2 (4.7)	11 (6.2)	0.702
Nationality			0.003
Indian	37 (86)	112 (62.9)	
Foreign	6 (14)	66 (37.1)	
Diagnosis			
ALF	0	4 (2.2)	0.975
CLD	30 (69.8)	156 (87.6)	0.005 ^{a)}
ACLF	13 (30.2)	18 (10.2)	0.002 ^{a)}
ACLF-grade 3	7 (5.5)	9 (5)	0.001 ^{a)}
Etiology			
Alcohol	16 (37.2)	48 (26.9)	0.184
Viral	11 (25.6)	51 (28.6)	0.688
NASH	15 (34.9)	47 (26.4)	0.207
Cryptogenic	1 (2.3)	19 (10.7)	0.087
Others	0	13 (7.3)	0.068
CTP score	11.46±2.32	10.25±2.24	0.030 ^{a)}
MELD score	24.39±9.55	21.14±9.17	0.034 ^{a)}
HCC	4 (9.3)	43 (24.16)	0.037 ^{a)}
PVT			0.277
Partial	3 (6.97)	7 (3.9)	
Complete	1 (2.3)	15 (8.4)	
Past abdominal surgery	10 (23.3)	26 (14.61)	0.156
Cirrhosis complications			
HE	20 (46.5)	61 (34.27)	0.131
HRS	6 (13.95)	13 (7.3)	0.163
SBP	5 (11.6)	8 (4.5)	0.073
Preoperative dialysis	5 (11.6)	5 (2.8)	0.012 ^{a)}
Comorbidities			
DM	17 (39.5)	65 (36.52)	0.251
HTN	9 (20.9)	28 (15.73)	0.499
CAD	1 (2.3)	4 (2.25)	0.251
COPD/TB	5 (11.6)	5 (2.80)	0.548
Others (stroke, seizure, ILD)	1 (2.3)	1 (0.5)	0.110

Table 1. Continued

Parameter	APG (n=43)	AdP-PG (n=178)	P-value
Preoperative ICU stay (day)	11 (25.5)	45 (25.28)	0.043 ^{a)}
Preoperative functional status			
Ambulatory	27 (62.7)	130 (73.03)	0.183
Assisted mobility	5 (11.6)	34 (19.10)	0.248
Bedbound	11 (25.58)	14 (7.87)	<0.001 ^{a)}
Preoperative Hb (mg/dL)	9.50±2.05	9.96±2.29	0.091
Preoperative creatinine (mg/dL)	1.23±0.86	0.96±0.65	0.031 ^{a)}
GRWR	1.01±0.26	1.02±0.23	0.748
Graft steatosis			
Liver attenuation index on CT			
>5	36 (83.7)	139 (78.1)	0.414
≤5 or ≥-10	6 (13.9)	38 (21.3)	0.276
<-10	1 (2.3)	1 (0.6)	0.273
Fat fraction on MR (>10%)	3 (6.97)	10 (5.62)	0.611
CIT (min)	93.65±53.19	89.26±37.6	0.558
WIT (min)	42.58±8.78	32.42±11.62	0.933
Duration of surgery (hr)	10.26±1.46	9.80±1.58	0.151
Laparoscopic donor surgery	2 (4.7)	22 (12.35)	0.142
Blood transfusion (PRBC, unit)	5.81±4.65	7.84±9.45	0.044 ^{a)}

Values are presented as mean±standard deviation or number (%).

COVID-19, coronavirus disease 2019; APG, adult pandemic group; AdP-PG, adult pre-pandemic group; BMI, body mass index; ALF, acute liver failure; CLD, chronic liver disease; ACLF, acute-on-chronic liver failure; NASH, non-alcoholic steatohepatitis; CTP, Child-Turcotte-Pugh; MELD, model for end-stage liver diseases; HCC, hepatocellular carcinoma; PVT, portal vein thrombosis; HE, hepatic encephalopathy; HRS, hepatorenal syndrome; SBP, spontaneous bacterial peritonitis; DM, diabetes mellitus; HTN, hypertension; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; TB, tuberculosis; ILD, interstitial lung disease; ICU, intensive care unit; Hb, haemoglobin; GRWR, graft-to-recipient weight ratio; CT, computed tomography; MR, magnetic resonance; CIT, cold ischemia time; WIT, warm ischemia time; PRBC, packed red blood cell.

^{a)}P<0.05 indicate statistical significance.

ric groups and all other parameters were comparable as well (Table 2).

Although duration of surgery was longer in the APG compared to the AdP-PG, mean intraoperative packed red blood cell transfusions were significantly less in the APG compared to the AdP-PG (6.18±4.65 vs. 7.84±9.45 units, P=0.044). The incidence of postoperative complications were similar in the APG and the AdP-PG (25.58% vs. 35.96%, P=0.197), with similar needs for radiological (35% vs. 37%, P=0.597), endoscopic, and surgical interventions

Table 2. Comparison of the demographics and preoperative and intraoperative parameters of pediatric patients who received liver transplants during the COVID-19 pandemic period versus the pre-pandemic year

Variable	PPG (n=17)	PedP-PG (n=50)	P-value
Age (yr)	3.13±3.83	3.69±4.07	0.573
Sex			0.139
Male	5 (35.71)	30 (60)	
Female	12 (64.29)	20 (40)	
Donor age (yr)	30.03±5.72	33.46±7.48	0.125
Nationality			0.024 ^{a)}
Indian	9 (46.42)	14 (28)	
Foreign	8 (53.57)	36 (72)	
Etiology			
Biliary atresia	11 (60.71)	32 (64)	0.786
Caroli disease	1 (3.57)	0	0.253
Malignancy	1 (3.57)	2 (4)	1
Metabolic liver disease	1 (10.71)	5 (10)	0.617
PFIC	2 (10.71)	5 (10)	0.572
Viral	1 (3.57)	1 (2)	1
Others	0	5 (10)	0.318
Diagnosis			
ACLF	0	1 (2)	0.567
ALF	1 (7.14)	2 (4)	0.756
CLD	16 (92.86)	47 (94)	0.986
CTP score	9.7±2.14	9.6±2.05	0.494
PELD score	24.93±16.54	18.21±17.59	0.477
Past abdominal surgeries	6 (35.17)	14 (28)	0.278
Preoperative ICU stay (day)	3 (17.86)	5 (10)	0.323
GRWR	2.62±1.10	2.37±0.98	0.293
CIT	50.32±29.60	62.76±32.21	0.312
WIT	23.68±5.61	25.04±10.54	0.944
ABO incompatible	2 (14.29)	3 (6)	0.572

Values are presented as mean±standard deviation or number (%).

COVID-19, coronavirus disease 2019; PPG, pediatric pandemic group; PedP-PG, pediatric pre-pandemic group; PFIC, progressive familial intrahepatic cholestasis; ACLF, acute-on-chronic liver failure; ALF, acute liver failure; CLD, chronic liver disease; CTP, Child-Turcotte-Pugh; PELD, pediatric end-stage liver disease; ICU, intensive care unit; GRWR, graft-to-recipient weight ratio; CIT, cold ischemia time; WIT, warm ischemia time.

^{a)}P<0.05 indicate statistical significance.

(16.27% vs. 16.29%, P=0.994) in the early postoperative phase. While bile leaks were the most common early postoperative complication in the AdP-PG (14.6% vs. 4.7%, P=0.121), the incidence of postoperative bleeds (11.6% vs. 8.9%, P=0.596) and sepsis (9.3% vs. 7.3%, P=0.749) was similar in the APG and the AdP-PG. Postoperative ICU stays were significantly longer in the APG compared to

Table 3. Comparison of liver transplant outcome parameters between APG and AdP-PG

Parameter	APG (n=43)	AdP-PG (n=178)	P-value
Postoperative			
Complication	11 (25.58)	64 (35.96)	0.197
Bleeding	5 (11.6)	16 (8.99)	0.596
HAT	0	3 (1.69)	1.000
PVT	0	4 (2.25)	1.000
MHV block	0	8 (4.5)	0.359
RHV block	1 (0)	1 (0.56)	1.000
Bile leak	2 (4.7)	26 (14.60)	0.121
Sepsis	4 (9.3)	13 (7.3)	0.749
Intervention			
Radiological	14 (32.55)	67 (37.64)	0.597
Surgical re-exploration	7 (16.27)	29 (16.29)	0.994
Postoperative dialysis	8 (18.6)	29 (16.23)	0.712
Postoperative ICU stay (day)	17.19±10.09	13.54±11.18	0.045 ^{a)}
Day of extubation			
Day 0	2 (4.7)	27 (15.17)	0.300
Day 1	33 (76.7)	139 (78.09)	-
Postoperative hospital stay (day)	26.37±12.30	22.72±9.86	0.398
Tracheostomy	9 (20.9)	19 (10.67)	0.120
Retransplant	1 (2.3)	0	0.715
30-Day outcome			0.479
Death	6 (14)	33 (18.5)	
Survival	37 (86)	145 (81.5)	
3-Month outcome			0.557
Death	7 (16.3)	36 (20.2)	
Survival	36 (83.7)	142 (79.8)	
6-Month outcome			0.477
Death	10 (23.3)	51 (28.7)	
Survival	33 (76.7)	127 (71.3)	

Values are presented as number (%) or mean±standard deviation.

APG, adult pandemic group; AdP-PG, adult pre-pandemic group; HAT, hepatic artery thrombosis; PVT, portal vein thrombosis; MHV, middle hepatic vein; RHV, right hepatic vein.

^{a)}P<0.05 indicate statistical significance.

the AdP-PG (16.06±10.09 vs. 13.54±11.82 days, P=0.045) (Table 3).

In both pediatric groups (PPG and PedP-PG), biliary atresia was the most common etiology. The mean PELD score (24.93±16.54 vs. 18.21±17.59, P=0.477) was higher in the PPG. Although not statistically significant, patients in the PPG had more postoperative complications than the PedP-PG (32.14% vs. 18.0%, P=0.502) (Table 4). Postoperative ICU stays and hospital stays were significantly

Table 4. Outcome parameters of pediatric patients in the COVID-19 pandemic group versus the pre-pandemic pediatric group

Parameter	PPG (n=17)	PedP-PG (n=50)	P-value
Complication	6 (32.14)	9 (18)	0.502
Bleeding	0	1 (2)	0.654
HAT	2 (7.14)	3 (6)	0.573
PVT	0 (3.57)	3 (6)	0.492
MHV block	0	1 (2)	0.654
Bile leak	5 (17.86)	2 (4)	0.203
Sepsis	3 (10.71)	1 (2)	0.571
Postoperative intervention			
Radiological	5 (39.28)	18 (36)	0.336
Re-exploration	2 (25)	9 (18)	0.433
Postoperative dialysis	1 (0)	1 (2)	0.654
Retransplantation	1 (3.57)	0	0.432
Postoperative hospital stay (day)	41±18.04	24±12.68	0.007 ^{a)}
Postoperative ICU stay (day)	28.6±15.17	15.34±7.77	0.001 ^{a)}
30-Day outcome			0.618
Death	1 (3.57)	5 (10)	
Survival	16 (96.43)	45 (90)	
3-Month outcome			0.715
Death	3 (14.29)	7 (14)	
Survival	14 (85.17)	43 (86)	
6-Month outcome			0.713
Death	3 (14.29)	7 (14)	
Survival	14 (85.17)	43 (86)	

Values are presented as number (%) or mean±standard deviation. COVID-19, coronavirus disease 2019; PPG, pediatric pandemic group; PedP-PG, pediatric pre-pandemic group; HAT, hepatic artery thrombosis; PVT, portal vein thrombosis; MHV, middle hepatic vein; ICU, intensive care unit.

^{a)}P<0.05 indicate statistical significance.

longer in the PPG than in the PedP-PG (28.6±15.17 vs. 15.34±7.77 days, P=0.001) (Table 4).

The 30-day, 3-month, and 6-month outcomes were not significantly different in both the adult and pediatric groups (Tables 3 and 4, Fig. 2). Fig. 2 shows the 1-year Kaplan Meier survival analysis of the adult (Fig. 2A) and pediatric (Fig. 2B) populations in the pandemic and pre-pandemic periods. In the pediatric cohort, the 30-day mortality rate was lower in the PPG, whereas the 3-month and 6-month mortality rates were similar in both groups (Table 4, Fig. 2B).

DISCUSSION

It has been classically observed that centers dealing with higher surgical volumes have better outcomes. Mortality at HVCs is lower than at centers with lower surgical volumes, perhaps due to better surgical techniques, established protocols, and team organization [5,9]. However, these same HVCs also operate on sicker patients and accept borderline grafts so that the outcomes in these centers eventually even out [10,11]. The cut-off for designating a center as high-volume varies across different geographical regions. The cut-off for HVCs in the Indian subcontinent has yet to be formally defined; however, a large center in India typically conducts >100 LT procedures per year [7]. Our center is one of the high HVCs in India, consistently performing >200 LDLT procedures annually.

Axelrod et al. [6] investigated how the volume of cases

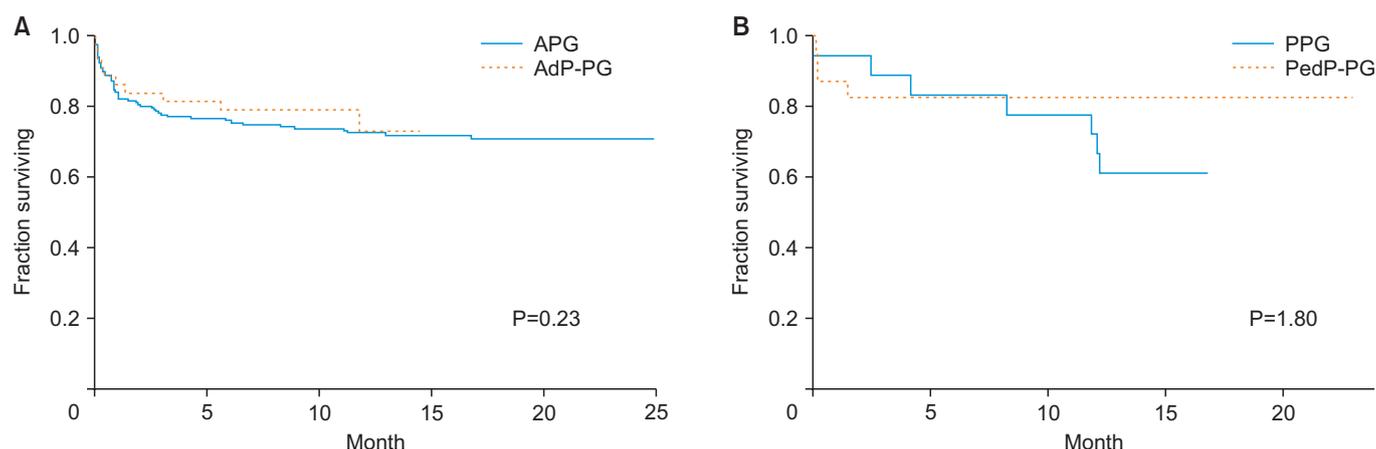


Fig. 2. Kaplan-Meier 1-year survival curves for pandemic and pre-pandemic groups. (A) Adult 1-year survival curve. (B) Pediatric 1-year survival curve. APG, adult pandemic group; AdP-PG, adult pre-pandemic group; PPG, pediatric pandemic group; PedP-PG, pediatric pre-pandemic group.

impacted liver and kidney transplant outcomes by analyzing data from the American Scientific Registry of Transplant Recipients over 4 years (1996–2000). They found that the unadjusted 1-year mortality rate following LT was significantly different in HVCs (defined as those conducting 93 transplants per year, 15.9%) compared to LVCs (defined as those conducting 21 transplants per year, 16.9%) and medium volume centers (those conducting 48 transplants per year, 14.7%). LVCs were associated with a significantly higher risk of death (adjusted odds ratio, 1.30; $P=0.0036$). The unadjusted rate of renal graft loss within 1 year was significantly lower at HVCs (167 per year, 8.6%) than at centers with very low (20 per year, 9.6%), low (58 per year, 9.9%), and medium (93 per year, 9.7%) volumes ($P=0.0014$) [6].

Macomber et al. [12] analyzed the Universal Health Coverage database in the US from 2009 to 2010 and identified 63 liver transplant centers and 5,130 transplants. Mortality was also found to be lower at HVCs (>76 cases in 2009 and >71 cases in 2010) than at LVCs (11–47 cases in 2009 and 13–43 cases in 2010); 2.9% and 3.4%, respectively. HVCs had a shorter median length of stay than LVCs (9 vs. 10 days, $P<0.0001$) and shorter median ICU stays than LVCs (2 vs. 3 days, respectively; $P<0.0001$). Their study showed that increased center volume resulted in improved long-term LT outcomes and more efficient use of hospital resources, thereby lowering the cost [12].

A study analyzing outcomes in patients who underwent liver retransplantation between 2007 and 2016 from the Korean National Healthcare Insurance Service database reported similar results. In-hospital mortality after liver retransplantation was lower in HVCs than LVCs (25% and 36%, respectively; $P=0.069$) [13]. LT centers were categorized as HVCs (≥ 64 LTs per year) or LVCs (< 64 LTs per year) based on annual LT case volume. In India, with imposition of a lockdown in March 2020, healthcare workers geared up to cope with the largely unknown pandemic. An advisory issued by the Indian Council of Medical Research (ICMR) recommended operating in emergencies only, as all healthcare resources were being diverted to manage those affected by the pandemic [14].

For several reasons, referrals to our center decreased significantly, leading to a drop in the total number of transplants performed. Patients and their families were reluctant to visit a hospital for fear of contracting infection. The general public postponed health-related matters, and physician availability in the hospitals was reduced as the workforce was diverted to take care of patients affect-

ed by COVID-19. Interstate and international travel restrictions also prevented patients from reaching transplant centers. The transplant community updated its treatment guidelines [15], stating that only sick patients with advanced liver failure such as ACLF, acute liver failure, and hepatocellular carcinoma (HCC) should be scheduled for transplant since a delay in their surgery was perceived to be life-threatening. Only very sick patients were referred to our transplant unit during the pandemic and the number of LT procedures performed in our unit was reduced by half. Delman et al. [16] reported that the COVID-19 pandemic did not significantly affect overall transplant outcomes. However, those eligible patients who could not receive transplants due to the overwhelmed health care system during the pandemic should be considered.

At our center, only 60 LT procedures were conducted over 6 months during the pandemic, compared to 228 patients in the pre-pandemic year. Since the caseload at our HVC was reduced by half during the pandemic, we decided to analyze the effect of the caseload reduction on patient outcomes. At our center, only sick cirrhotic patients with various types of decompensation, high MELD scores, and ACLF were admitted. LT was performed in those selected patients who, despite all medical management, were too sick to be discharged from the hospital. Although the PGs had higher rates of postoperative bleeding, sepsis, and longer ICU stays, the posttransplant outcomes were comparable in the pandemic and pre-pandemic patients for both adult and pediatric groups. We saw a higher percentage of patients with alcoholic hepatitis and alcohol-induced ACLF (Table 2), perhaps with the prevailing lockdown, uncertainty, and economic slowdown leading to excessive alcohol consumption. More patients were also referred with unresectable HCC (beyond Milan criteria), whom we managed with oral chemotherapy, chemo-embolization, or radio-embolization.

The COVID-19 pandemic and the national lockdown period presented new challenges. India's blood banks were tasked with arranging plasma therapy for COVID-19 patients. Thus, in the absence of blood donation camps and the inability of the family and friends of patients undergoing LT to reach the hospital for blood donation, arranging blood and blood components for surgery became a major challenge. During the pandemic, all patients were screened for infection with SARS-CoV-2 before admission to the hospital and within 48 hours of surgery. Strict personal protective equipment policies were followed by healthcare personnel. The hospital did not permit visitors.

Despite all precautions, five elective transplants were deferred the day prior to elective LDLT when their asymptomatic donors tested positive for SARS-CoV-2 infection on routine mandatory preoperative screening. The surgeries were deferred for 6 weeks to ensure full recovery from COVID-19 as per the Liver Transplant Society of India guidelines. Three of the surgeries were subsequently rescheduled after ensuring the absence of COVID-19 sequelae in the donors, while two of the patients with liver disease died while awaiting transplant in the absence of another potentially healthy donor in the family. Two patients presented to our unit with COVID-19 induced ACLF. One of these underwent LDLT 4 weeks after recovery from the SARS-CoV-2 infection. Five of the chronic liver disease patients admitted for LT also tested positive for SARS-CoV-2 prior to their scheduled surgery. All five were managed with oxygen therapy and other supportive care and, over the course of a year, we were able to transplant three of these five patients after their full recovery. Two of the five died due to sepsis and multi-organ failure and could not be transplanted.

Our study was the first to compare the high and low case volume outcomes at the same center, thereby avoiding many confounding factors such as differences in the operative team and geographical factors. However, there were some limitations to our study. First, the time periods for the pandemic and PedP-PGs were not similar, which may have affected the number and type of patients included in both groups. The follow-up time was relatively short and some long-term complications like biliary stricture may have affected long-term outcomes. We also need to consider those patients who did not receive a transplant and died while the healthcare system was overwhelmed due to COVID-19. That loss is difficult to assess.

Despite these challenges, the 30-day, 3-month, and 6-month outcomes in adult patients during the pandemic were non-inferior to the pre-pandemic calendar year (Tables 3 and 4). This reflects how a reduction in the number of cases at an HVC led to the highly focused care of those patients who received LT despite adverse circumstances, which led to acceptable outcomes and graft survival in sicker patients. The COVID-19 pandemic affected transplant activity during the national lockdown in India, allowing only acutely ill patients to receive transplants at our facility. Although sicker patients were eventually transplanted at our center, the outcomes were not inferior. This indicates that a reduction in the usual number of

operations at an otherwise busy HVC, allowed better individualized patient care for very sick transplant patients, which translated into equally good outcomes. Although HVCs traditionally have better outcomes, a reduction in their usual volume of operations need not result in inferior outcomes.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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