Original Article

Early Outcomes Of Living Donor Liver Transplant Recipients In A University Teaching Hospital Of Nepal

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Abstract

Introduction: The burden of chronic liver disease (CLD) is on the rise and liver transplantation remains the best treatment modality for the end stage liver disease (ESLD). Tribhuvan University Teaching Hospital has started doing living donor liver transplantation (LDLT) and we aim to report our experience and early postoperative outcomes of the first 10 living donor liver transplants performed in our institute.

Methods: This is a retrospective review and included all patients who were operated for LDLT from the year 2019 to 2023 for various indications. Demographic data, Model for End-Stage Liver Disease score, Child score, etiology of CLD, liver graft type, graft-to-recipient weight ratio, operative time, blood transfusion and complications were analysed.

Results: From 2019 to 2023, in total, 10 patients underwent LDLT, including one paediatric transplant. The most common etiology was alcohol (50%) and right lobe was the preferred graft. The average operative time was 7.9 ± 2.56 hours. There were no re exploration or re transplantation. The mean duration of hospital stay was around 21.37 ± 6.43 days. All patients were followed for one to five years. Four recipients had Clavien Dindo Grade II and above complications, including bile leak and post-operative bleeding. One mortality occurred on 27th post-operative day due to covid infection.

Conclusions: Living donor liver transplantation is a feasible option for patients with end stage liver disease and is safe to be performed in low volume centre with the help of expertise and good team work.

Keywords: Early outcomes; liver transplantation; Living donor liver transplantation; recipient.

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Introduction

The prevalence of chronic liver disease (CLD) is on the rise with cirrhosis currently being the 11th most common cause of death worldwide and 15th leading cause of morbidity.[1] Even in Nepal, the incidence is rising, with alcohol being one of the commonest reason.[2,3] Transplantation of liver is a lifesaving procedure and has been proposed as the best treatment modality for end stage liver disease (ESLD) with a 1, 3 and 5-year survival rates as 91.8%, 83.8% and 76.1%, respectively.[4]

Nepal saw its first case in December 2016 by Human Organ Transplant Centre Bhaktapur.[5] Similarly, on 31st May 2019, Tribhuvan University Teaching Hospital (TUTH), amidst huge challenges was successful in doing its first case of living donor liver transplantation (LDLT), with the help from the Indian team. This study has been conducted to report our experience of the first 10 recipients of LDLT in our institute and report the early perioperative outcomes of these patients.

Methods

This was a retrospective review of patients who had diagnosis of chronic liver disease and underwent LDLT from 2019 – 2023 in Department of Surgical Gastroenterology, TUTH. It included all patients who had CLD with paediatric end stage liver disease (PELD) score >10 in age less than 12 years or model for end stage liver disease (MELD) score more than 15 in those above 12 years according to the AASLD guidelines.[6]

A detailed history was taken and computed tomography scan of abdomen and pelvis was done. All patients underwent routine phase wise investigations which included LAI index, CT Volumetry, and blood investigations and departmental clearances. Blood group matching was mandatory with donors. Donors also went through evaluation as per standard international living liver donation guidelines.[7] Vaccination, economic and social assessment, and transplant education was done and clearance from the hospital legal committee was obtained.

For the recipient hepatectomy, peripheral access, central line, and A-line were placed. Modified Makuuchi incision was given. After mobilization, dissection was done in the porta and portal structures were looped and later divided during explantation. For benching, Histidine-tryptophan-ketoglutarate (HTK) solution was used. Neo Middle hepatic vein (MHV) was made using PTFE Graft. Anastomosis of right portal vein (PV) was done with the recipient's main PV and followed by anastomosis of hepatic artery and biliary anastomosis respectively. Doppler ultrasound of the liver was done to see the inflow and outflow patency and satisfactory perfusion of the graft.

Injection Piperacillin/Tazobactam was given for anti-bacterial prophylaxis and fluconazole was used as prophylaxis for fungal infection. If CMV PCR positive then Valganciclovir was given for three months. Hepatic Doppler was done twice a day for first week after transplant and then as required. Induction immunotherapy was done with Methylprednisolone and maintenance was done with Prednisolone, Tacrolimus and Mycophenolate mofetil. Serum Tac levels were monitored regularly and level of 7-10 ng/mL was maintained.

Demographic data, blood group of patients, MELD and Child score, etiology, liver graft type and GRWR were recorded. Warm ischemia and cold ischemia time, duration of operation, blood transfusion and complications according to the (Clavien-Dindo) were recorded. Patients were followed up for at least one year.

Statistical Analysis was done by collecting data and the data was then analysed using SPSS version 25. Mean ± standard deviation was calculated for quantitative variables. Frequencies were calculated for qualitative variables. P-value of ≤0.05 was considered statistically significant.

Results

Ten living donor liver transplants were performed from 31st May 2019 to 30th may 2024. The first year there were three LDLTs followed by one LDLT in 2020. During the COVID-19 pandemic, the liver transplantation program was stopped temporarily. In the following three years, two LDLT cases were done per year. The patient's demographic profile has been shown in **Table 1**. The youngest patient was 11 months. The most common etiology was Alcohol (50 %) followed by Cryptogenic in 20% and there was one case each of Hepatocellular carcinoma, Biliary Atresia and Wilson's disease. All the donor recipients' pair were genetically related.

Table 1. Demographic Profile of the patients

Variable		Value
Age, mean ± SD (years)		42.6 ± 16.07
M: F		9:1
BMI, mean ± SD		23.3 ± 4.2
CTP Score	A	1
	B	2
	C	7
MELD Na, range		16 – 31
ECOG	0	1
	1	8
	2	1

Intraoperative details are mentioned in **Table 2**, where the most common graft was right lobe and in one case, left lateral sectionectomy was done for paediatric transplant. The average operative time was 7.9 ± 2.56 hours with no critical events during the procedure. In one patient, intraoperative Doppler study showed unsatisfactory flow of hepatic artery. Revision hepatic artery anastomosis was done.

Table 2. Intraoperative details

Variable	Value (N=10)	
Graft type	Right	9
	Lt lateral	1
Graft weight (gm), mean ± SD	615 ± 170.6	
GRWR, mean ± SD	1.2 ± 0.4	
MHV conduit	PTFE graft	7
	Portal vein	1
	None	2
Bile Duct Anastomosis	Single	6
	Double	4

Surgical characteristics are shown in **Table 3**, where average blood loss was around 1.5 litres with an average operative time of 8 hours. Four patients had post-operative complications and shown in **Table 4**. The first transplant recipient had cut surface collection of around 558ml, in post-operative period, for which a pigtail drain was placed. Patient was discharged without any issues. The fifth case, paediatric transplant, had bilious drain on 6th post-operative day (POD) and was suspected of jejunojejunostomy leak. He was managed conservatively and had clear drain from 11th post-operative day. Seventh transplant patient had sanguineous drain output on 7th POD. His CT Angiography was normal and drain cleared by 13th POD.

Table 3. Surgical characteristics

Variable	Value (mean ± SD)
Blood loss	1.45 ± 1.27 L
Cold ischemia time	75.4 ± 39.45 min
Warm ischemia time	32.12 ± 10.69 min
Operative time	7.9 ± 2.56 hrs
ICU stay	12.12 ± 6.6 days
Total hospital stay	21.37 ± 6.43 days

There was one mortality in our series. Patient initially had early graft dysfunction but on 17th POD, patient developed increased oxygen requirement and by 19th POD patient was intubated. Her COVID test came as positive and patient succumbed on 27th POD due to multi organ dysfunction.

The mean duration of hospital stay was 21.37 ± 6.43 days. All patients were followed up for minimum of one year. The first transplant recipient had incisional hernia for which mesh repair was done. Readmission was done for two patients, one for pancreatitis and another for urosepsis, both were managed conservatively. None of the cases developed chronic rejection, infectious or vascular complications, re exploration or re transplantation.

Discussion

Liver transplantation is a definitive treatment for ESLD and with an increase in incidence, the demand for the donor liver grafts is also rising. There has been shortage of organ donation and the West have favoured deceased donor organ

Table 4. Post-Operative Complications

Complication	Clavien-Dindo Grade	Number
Bile leak	II	1
Postoperative bleeding	II	1
Intra-abdominal collection	III a	1
Mortality	V	1

donation, whereas in Asia LDLT has been preferred.[8] The first LDLT was described by Raia and colleagues in 1989 and was done for paediatric recipients.[9] Initially there was ethical dilemma and concerns for LDLT but slowly it got accepted and expanded from paediatrics to adult transplantation.

Liver transplantation is a necessity in developing countries but poor infrastructure, shortage of trained manpower and limited resources have said to be significant factors for slow development.[10] Kidney transplantation, started in 2008 in TUTH.[11] First living donor liver transplantation was done on 31st May 2019 with help from Apollo hospital, Delhi. Similarly, other cases followed and there was significant support from Fortis Hospital team, New Delhi.

In Nepal, LDLT is the common choice. All the 10 cases in this series are LDLT. Till now only HOTC has done deceased donor liver transplantation.[5] Human Body Organ Transplantation (Regulation and Prohibition) Act in December 2016 allowed organ donation from brain dead donors but it still hasn't gained popularity mainly due to less awareness, various religious beliefs, family barriers and logistic issues.[12]

Globally, incidence of NASH is rising[13] but in Asian countries alcohol still seems to be the main cause of CLD.[14] Most of the patients admitted to our centre with CLD for LDLT were due to alcoholic liver disease and this may be attributed to the cultural acceptance of alcohol. Amongst the 10 cases of LDLT, one was a paediatric transplant for biliary atresia. Improvement in technology, experience and logistical improvements in liver surgery has led to better patient and graft survival outcomes. This case was the first paediatric transplant in our country and we hope to get more case referrals and do more cases in future.

Bile leak and anastomotic stricture is said to be one of the major complications for any LDLT with a incidence rates reported from 5.1% to 21.5% and 6.5% to 21.5%, respectively.[15] In our series, bile leak developed in one patient and there were no case of biliary stricture in follow up. Our institute is still in early phase of starting the program and a greater number of transplants and long duration of follow up will be required to reflect the true post-operative outcomes in future.

The in-hospital mortality rate after liver transplantation has been reported from 3.6 to 18.9%.[16] Factors leading to mortality include a high MELD score, hepatic artery and portal vein thrombosis and infections.[17] No vascular complications were seen in our small series but there

was one mortality due to COVID related pulmonary complications. COVID-19 pandemic lead to reduction in number of transplants worldwide and the safety and timing of LT in the individuals who recovered from COVID was also unknown.[18] The first mortality in early stage of starting the program and that to during the pandemic lead to major setback in our transplant program with decrease confidence level and many questioned the capability and sustainability of the program. However, with proper leadership and multidisciplinary integration and organization management, we were able to look beyond the setback and give continuity to the program.

Limitations of this study is that it is a retrospective study with small numbers of LDLT patients and follow-up is relatively short thus it is also difficult to comment on long-term complications.

The current challenge for us is the sustainability of the liver transplant program. TUTH being the country's largest referral centre has an advantage of having a huge manpower support and a dedicated and trained team members and hopes to increase the numbers gradually. The success of the limited numbers has encouraged the team to work together to make it a sustainable liver transplantation program and has overcome the disbeliefs prevailing in many that liver transplantation is not possible in Nepal.

Conclusions

Living donor liver transplantation is a feasible option for patients with end stage liver disease in Nepal and is safe to be performed in low volume centre with the help of expertise and good team work.

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