

# Short Term Donor Outcomes After Hepatectomy in Living Donor Liver Transplantation

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## ABSTRACT

**Objective:** To determine the outcome of living-donor liver transplant (LDLT) donors from the first liver transplant program in Pakistan.

**Study Design:** Cohort study.

**Place and Duration of Study:** Shifa International Hospital, Islamabad, from April 2012 to August 2014.

**Methodology:** A total of 100 live donors who underwent hepatectomy were included. Demographics, etiologies, graft characteristics and operative variables were retrospectively assessed. Outcome was assessed based on morbidity and mortality.

**Results:** Median donor age was 28 (17 - 45) years and median body mass index (BMI) was 24 kg/m<sup>2</sup> (15 - 36). Male to female ratio was 1.5:1. Hepatitis B and C were the most common underlying etiologies and accounted for 79/100 (79%) of LDLT's. Overall, 93/100 (93%) donors donated a right lobe graft. Median estimated graft weight to recipient body weight (GW/BW) ratio was 1.03 (0.78 - 2). Standard arterial anatomy was present in 56% donors. The 90-day morbidity was 13/100 (13%) and overall morbidity was 17/100 (17%). Bile leak was encountered in 3 (3%) patients. There was no donor mortality.

**Conclusion:** Acceptable short-term donor outcomes were achieved in an LDLT program in Pakistan with careful donor selection and planning.

**Key Words:** Liver transplantation. Morbidity. Mortality. Donors.

## INTRODUCTION

The first successful living donor liver transplantation (LDLT) was performed in 1989 and was followed by successful adult LDLT in 1994.<sup>1,2</sup> Since then it has become a widely accepted treatment option for patients with end stage liver disease (ESLD) with restricted deceased donor availability.<sup>3</sup> It is also an acceptable alternative in western countries experiencing cadaveric organ shortage.<sup>4</sup> Liver transplantation is a major undertaking, consumes significant hospital resources and requires team approach. In developing countries, certain non-medical factors also pose challenges to inception and sustenance of a transplant program. These include complex legislation for organ donation, gross national product (GNP), economic status of the concerned population and prevalence of insurance policies etc.<sup>5</sup> The state of affairs is further complicated when the only mode of organ donation is a living relative. It is difficult for healthy donors to trust a new program for such a major undertaking. Indeed, it has been shown

that for centers with less than 20 LDLT experience, graft failure rate is significantly worse.<sup>6</sup>

According to burden of disease study, chronic liver disease is the 5th most common cause of premature mortality and 11th most common cause of disability in Pakistan.<sup>7</sup> With a massive liver disease burden in Pakistan, there was a desperate need of a transplant program. Although the first liver transplant in Pakistan was performed in 2003, for various reasons no further transplants could be performed. In April 2012, the authors performed the first pediatric LDLT. The purpose of this study was to report short-term outcomes of first 100 live donors who underwent voluntary liver donation at Shifa International Hospital, Islamabad.

## METHODOLOGY

Until October 2014, 120 LDLT have been performed. The outcomes of voluntary donors who underwent donor hepatectomy between April 2012 and August 2014 at Shifa International Hospital were retrospectively reviewed. A total of 100 living donors were included in the study with a minimum follow-up of 3 months. All donors were included in the study.

Potential donors had no co-morbidities, were blood group compatible, related to the recipient and fell within 18 - 50 years age group. Donors with a BMI < 30 were preferred unless exceptional circumstances prevailed.

The protocol for donor evaluation used in our center is

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*Received: May 07, 2015; Accepted: December 11, 2015.*

**Table I:** Donor evaluation process.

<b>Step 1</b>	
Consultation:	Transplant Surgeon
Blood tests:	Blood grouping, complete blood count, prothrombin time/international normalized ratio, liver function tests, urea, glucose, albumin, creatinine, magnesium, electrolytes, urine R/E, hepatitis C virus antibody, hepatitis B profile (Hbs Ag, HBC Ab, Hbs Ab, HIV 1 and 2 screen, Thyroid function tests
Radiology:	Chest X-ray PA view
Cardiology:	Electrocardiogram (ECG)
<b>Step 2</b>	
Radiology:	Liver dynamic CT scan, echo-2D with pulmonary pressure readings
<b>Step 3</b>	
Radiology:	Magnetic resonance cholangiopancreatography (MRCP)
Thrombotic screen:	lupus anticoagulant, anti-thrombin III, Protein S and C, anti-cardiolipin IgG, resistance V (factor V)
Biochemistry:	G6PD, reticulocyte count, sickle cell, Hb A1C, lipid profile, serum ferritin, ceruloplasmin, alpha-1 anti-trypsin
Immunology:	IgA, IgG, IgM, ANCA, ANA group (ANA, ASMA, AMA), antibody screen, coomb's test (direct and indirect), cytomegalovirus IgG, toxoplasma IgG, Epstein-Barr virus IgG, human T-cell lymphoma virus 1 and 2, methicillin resistant <i>Staphylococcus aureus</i> swab, herpes IgG
Consultations:	Psychiatrist, anesthetist, hepatologist, independent assessor

shown in Table I. A detailed history and physical examination were followed by routine laboratory investigations. If the results were satisfactory, computed tomography scan (CT) was performed with dynamic liver protocol on a multi-detector scanner (Aquilion ONE™ 320 Slice CT). Unenhanced images were acquired followed by arterial and portal venous phases. Data obtained was analyzed on work station (VitreaFx, Toshiba, Japan). A 3-dimension (3D) reconstruction was performed and liver volumes were assessed using middle hepatic vein as cut plane. To delineate biliary anatomy, magnetic resonance cholangiopancreatography (MRCP) was performed aided by 3D reconstruction. The minimum acceptable residual donor liver volume was taken 30%. Conventional angiography was not considered essential. Liver biopsy was performed if liver attenuation index (LAI) was less than 5. Liver attenuation index (LAI) was defined as the difference between mean hepatic and mean splenic attenuation. All donors were evaluated by a physician and psychiatrist. A surgical plan was drawn on a template with all anatomical and volumetric details. An informed consent was taken ensuring the donors knowledge and understanding of voluntary nature of donation and their right to refuse donation at any time, if they choose too. Final approval of donation was given by the Hospital Ethics Committee and then by Human Organ and Tissue Transplantation Authority (HOTA) of Pakistan. Ethics committee comprised of transplant surgeons, hepatologists, radiologists, nutritionists and transplant coordinators.

Donor hepatectomy was performed under low central venous pressure. A J-shaped incision was used for exposure, Thompson retractors were used. Retrograde cholecystectomy was followed by intra-operative cholangiogram. Hepatic transection was performed along the Cantlie's line with Cavitron Ultrasonic Surgical Aspirator (CUSA). Middle hepatic vein (MHV) was generally preserved but if required, partial or complete MHV was taken with the graft. After procurement, graft was weighed and flushed with university of Wisconsin

solution. Residual donor liver was fixed to anterior abdominal wall with falciform ligament. A single drain was placed near cut surface of the liver. Mass closure of the abdominal wall was performed with Loop Nylon and skin was approximated with Monocryl subcuticular sutures.

Donors were shifted to intensive care unit (ICU) after the procedure. Central venous pressure was kept at 5 - 10 cm of water. Liver doppler scan was performed on post-operative day 1 to ensure patency of arterial, portal inflow and hepatic venous outflow. Donors were advised to refrain from resuming a right lateral position in the early postoperative period. They were generally shifted to floor on the second postoperative day.

Characteristics of our donors, graft characteristics and operative variables were retrospectively reviewed and collected from patients' files. Categorical variables were represented as frequencies and percentages while interval variables as median and range. Outcome was assessed on the basis of overall morbidity and mortality. All significant (Grade-2 and above) complications on Clavien-Dindo grading system were included as morbidity.<sup>8</sup> Data analysis was performed on SPSS version 20.

## RESULTS

Median donor age was 28 (17 - 45) years and median BMI was 24 kg/m<sup>2</sup> (15 - 34). Male to female ratio was 1.5:1. Hepatitis B and C were the most common etiologies for which donation was performed and accounted for 79/100 (79%) of LDLTs. Six (6%) transplants were performed for acute liver failure. All donors were related to recipient. Son (19%), nephew (14%) and siblings (26%) were the most common relatives. In addition, around 15% donors were 3rd degree relatives of the recipient. Table II describes donor characteristics and etiologies of liver failure in recipients.

Overall, 93/100 (93%) donors donated a right lobe graft. MHV was not taken with the graft in 61/93 (65.5%) donors, while partial MHV was taken in 27/93 (29%)

**Table II: Donor characteristics.**

	Number	Percent (%)
<b>Gender</b>		
Male	61	61
Female	39	39
<b>Etiology</b>		
Hepatitis C	73	73
Cryptogenic	9	9
Hepatitis B	6	6
Autoimmune	3	3
Crigler-Najjar syndrome	2	2
Wilson disease	2	2
Primary hyperoxaluria	1	1
Primary biliary cirrhosis	1	1
Extrahepatic biliary atresia	1	1
Veno-occlusive	1	1
Unknown	1	1
<b>Onset</b>		
Acute	6	6
Chronic	94	94
<b>Donor's relation</b>		
Son	19	19
Nephew	14	14
Brother	13	13
Sister	13	13
Daughter	9	9
Wife	4	4
Niece	4	4
Mother	3	3
First cousin	3	3
Father	2	2
Husband	1	1
Other	15	15
<b>Liver attenuation index</b>		
≤5	13	13
6-10	30	30
>10	57	57
	Median	Range
Age	28	17-45
Body mass index	24	15-34

grafts. Full MHV was taken in 5 patients. Left lateral sector was used in 4 (4%) while left lobe in 2 (2%) patients. One whole liver was transplanted in domino setting. Standard arterial anatomy was encountered only in 56% donors. More than 1 hepatic veins were anastomosed in 60/100 (60%) recipients. On intra-operative cholangiogram, biliary anatomy was conventional in 60% donors. Around 22% recipients required more than 1 biliary anastomosis. Median estimated graft weight to recipient body weight (GW/BW) ratio was 1.03 (0.78 - 2). Table III shows the graft characteristics and operative variables.

The 90-day morbidity rate was 13/100 (13%) while overall morbidity was 17/100 (17%). Bile leak was encountered in 3 patients. One patient required ERCP with stent placement, while the other 2 were managed conservatively. There were 4 donors with non-specific intra-abdominal collection that required percutaneous

**Table III: Graft characteristics and operative variables.**

	Number	Percent (%)
<b>Type of graft</b>		
Right lobe/no MHV	61	61
Right lobe/partial MHV	27	27
Right lobe/full MHV	5	5
Left lateral sector	4	4
Left lobe	2	2
Whole liver	1	1
<b>Arterial anatomy</b>		
Standard	56	56
Right hepatic from SMA	16	16
Accessory arteries	9	9
Left hepatic from left gastric	6	6
Others	13	13
<b>Number of outflow anastomosis</b>		
1	40	40
2	53	53
3	7	7
<b>Cholangiogram findings</b>		
Conventional	60	60
Right posterior in LHD	27	27
Right anterior in LHD	1	1
Others	12	12
<b>Number of biliary anastomosis</b>		
1	78	78
2	22	22
<b>Ductoplasty</b>		
Yes	17	17
	Median	Range
Estimated GW/BW ratio	1.03	0.78-2
Operative time (minutes)	537	300-925
Blood loss (milliliters)	400	200-2000
ICU stay (days)	2	1-6
Total hospital stay (days)	9	5-18

**Table IV: Outcomes in 100 living donors.**

	Number	Percent
Overall mortality	0	0
90-day morbidity	13	13
Overall morbidity	17	17
Bile leak	3	3
Abdominal collection	4	4
Psychosis	4	4
Pneumonia	2	2
Incisional hernia	1	1
Sub-acute intestinal obstruction	1	1
Renal insufficiency	1	1
Conjunctivitis	1	1

aspiration or drain placement. Four patients developed significant psychological symptoms resulting in prolonged ICU stay or a shift back to ICU along with anti-psychotic medications. One patient developed incisional hernia 7 months after operation and required re-operation. No donor mortality was encountered in 100 donors included in the study. One patient with sub-acute intestinal obstruction was successfully managed with nasogastric tube placement and nothing per oral. Two

patients with pneumonia required prolonged course of antibiotics. A patient with renal insufficiency responded to fluid management and medicines modification. One patient with conjunctivitis required eye drops and was well at the time of discharge (Table IV).

## DISCUSSION

The current study highlights outcomes of voluntary donors who underwent donor hepatectomy in Pakistan's first liver transplant program. No donor mortality was observed and morbidity comparable with previous reports was achieved. Increasing number of transplants performed at the study center over the time not only demonstrate a developing trust but a tremendous burden of end-stage liver disease in Pakistan.

In Asian countries, hepatitis C has been shown to be the major etiology for ESLD. Frequency in the current study was higher; and more than two-third of these patients were cirrhotic, secondary to hepatitis C.<sup>9,10</sup> Clavien-Dindo grading system is an effective method for grading postoperative complications. A grade-2 and above complication rate of 10 - 40% has been previously reported in LDLT donors.<sup>11-14</sup> A complication rate of 17% was observed in these donors, which falls well within the range of previous reports. Only one donor required re-operation for repair of incisional hernia. All other patients were managed with medications, percutaneous or radiological interventions. This low complication rate can be attributed to strict donor criteria with relatively younger donors and thorough attention to peri-operative care.

Biliary complications can be the most frequent complications in live donors.<sup>15</sup> However, in the current study psychiatric problems were the most common morbidity. Patients required prolonged ICU stay along with antipsychotic medications culminating in prolonged overall hospital stay. Although these patients were evaluated and cleared by psychiatrist before operation, postoperative psychosis in this patient cohort is difficult to explain. All these patients were postoperatively reviewed by psychiatry team and managed medically. It was thought that ICU related psychosis and adverse effects of medications might have been contributory. However, a detailed analysis of this finding is mandated.

With more than 15 donor deaths reported so far and a significant morbidity rate, donor safety has evolved as a controversial issue in LDLT setting.<sup>16-18</sup> In adult LDLT, it is a frequently employed technique since it provides greater volume to the recipient to meet his metabolic demands. For a new transplant center, ensuring donor safety is of paramount importance as it is a decisive factor in future success of the program. Good donor outcomes were possible because of ample training of members of transplant team in high volume centers thus reducing the learning curve. Para-medical staff was also

sent to established transplant centers to gain appropriate exposure. Donor selection criteria were stringent to ensure inclusion of individuals for donation with no underlying co-morbid conditions and relatively younger age (18 - 50). The present donor age cut-off of 50 years is lower than many other centers that perform LDLT.<sup>19</sup> Younger age is associated with better regenerative ability of remnant liver and may protect against liver failure in the donor.<sup>20</sup> Since it has been shown that a donor remnant liver volume < 30 - 35% is associated with higher rate of complications, the minimum donor residual volume at the study center was 30%.<sup>21,22</sup>

Recently, recipient outcomes from this program were published and demonstrated acceptable recipient outcomes comparable to international standards.<sup>23</sup> In addition, quality of life in donors (N=60) was also determined and the outcomes were promising.<sup>24</sup> Technically challenging donor procedures have also been performed in author's center with success.<sup>25</sup> The high volume of transplants performed in our center, more than 30 transplants in the last 5 months, reflects a reduction in learning curve as very early in our experience we crossed the threshold of 20 LDLTs; a number that has been linked with worse outcomes.<sup>6</sup>

It is important to remain aware of possible long-term complications and quality of life issues in donors which require long-term follow-up. Future studies, addressing quality of life in donors in developing countries and frequency of long-term complications, are required to accurately determine safety of a living donor hepatectomy in LDLT donors in a developing country.

Limitations of the current study include its retrospective design and the potential to have missed significant data. Follow-up is relatively short and it is difficult to comment upon frequency of long-term complications.

## CONCLUSION

The current study shows that acceptable short-term outcomes can be achieved in a new liver transplant program in a developing country with reasonable donor safety profile. Meticulous planning and adherence to pre-defined protocols produce expected outcomes.

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