



## Choose Well, Cut Well and Get Well Living Donor Liver Transplants

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### ABSTRACT

**Introduction:** LDLT is a potentially life-saving operation for the recipient, but at the same time it is a major surgical procedure applied to healthy donors and does not provide any direct medical advantage. The only advantage of this procedure for the donor is the psychological satisfaction of saving a loved one's life. So, the safety of the healthy donor should be the prime important concern and if possible the donor hepatectomy surgery should be done without any mortality or minimum morbidity. **Aims and Objectives:** The aim of this single-center study in Pakistan is to assess the complications linked to donor hepatectomy and to report donor outcome in our center where more than 130 transplants have been done since 2012. **Place and Duration of Study:** This Study was conducted in Shaikh Zayed Hospital on 100 patients who underwent liver transplant in our hospital from 2011 to May 2016. **Material and Methods:** Data was collected for the first 100 patients, who underwent liver transplantation in our hospital from 2011 to May, 2017. Demographics, etiologies, graft characteristics and operative variables were retrospectively assessed. Outcome was assessed based on morbidity and mortality. **Results:** Of the 100 donors Male to female ratio was 3.1:1. mean age of the donors was 25.78 Mean BMI of donors was  $22.26 \pm 2.77$  kg/m<sup>2</sup> (range, 16.60-29.00 kg/m<sup>2</sup>). Most common etiology for liver transplant was hep B and hep C, all the donors donated their right lobe with Estimated GRWR from liver volumetry of  $1.2 \pm 0.21$  (ranging from 0.91 to 2.15). Total length of stay in hospital range from 8 days to 15 days with mean stay of  $10 \pm 2$  days. Over all complication in our donors was 13% with no donor mortality. **Conclusion:** Our program ensures donor safety with good short term outcomes which is attributed to strict donor selection and trained transplant team.

**Key words:** Liver transplant, Living Donor, Safety

### INTRODUCTION

The first living donor liver transplantation (LDLT) was performed in 1989<sup>1</sup> since then, LDLT has become a valid option to overcome the shortage of deceased donors, due to modified surgical techniques and patient's care improvements<sup>2</sup>. LDLT has three advantages for recipients compared with cadaver transplantation. First, short waiting list for transplant, thus the morbidity and mortality that may occur during the waiting period is prevented. Second, liver quality in living donors is better than cadaver donor livers because the living donors undergo comprehensive medical investigations and chosen after a series of investigations. Third advantage is that the cold ischemic time is

significantly shorter in LDLT<sup>3</sup>. Although LDLT is a potentially life-saving operation for the recipient, but at the same time it is a major surgical procedure applied to healthy donors and does not provide any direct medical advantage. Donor hepatectomy has reported major morbidity and mortality that leads to ethical problems<sup>4</sup>. The only advantage of this procedure for the donor is the psychological satisfaction of saving a loved one's life. So, the safety of the healthy donor should be the prime important concern and if possible the donor hepatectomy surgery should be done without any mortality or minimum morbidity. However, over time with the increase in the amount of LDLTs performed increase in donor mortality and morbidity has been seen<sup>5</sup>. To date, 23 donor mortalities have been reported and several donors have required liver

transplantation after developing liver failure after liver donation<sup>6</sup>. As a result, LDLT is only performed in situations where a reasonable result can be gained for the recipient and at the same time ensuring the donor's safety. The aim of this single-center study in Pakistan is to assess the complications linked to donor hepatectomy and to report donor outcome in our center where more than 130 transplants have been done since 2012.

## **MATERIAL AND METHODS**

Shaikh Zaid hospital performed its first transplant on August 13, 2011, till now 130 transplants have been carried out. We retrospectively collected the data of 100 patients who underwent liver transplant in our hospital from 2011 to May 2016, so that a minimum of one year follow up of the patients can be ensured.

### **Donor selection and investigation:**

All potential donors undergoing liver transplant were in good health and aged between 18 to 50 years, with blood group compatibility, willing to donate and blood relative of the recipient. Evaluation of the donors started with detailed history and examinations and after that Donors underwent a series of investigations before transplant so that the safety of both recipient and donor could be ensured (Table-1). C.T scan along with liver volumetry carried out to delineate the anatomy including the arterial, portal vein and hepatic veins and to identify any variants in anatomy. Graft recipient weight ratio (GRWR) calculated and remnant liver volume also calculated. Liver attenuation index calculated (LAI), all patients having LAI more than 15% or less than 5% had liver biopsies. More than 30% remnant liver volume was kept for all donors. MRCP was done to delineate biliary anatomy. After completion of investigations, evaluation by independent physician and informed consent of the donor. Approval sought from ethical committee of hospital and Punjab Human Organ Transplant Authority (PHOTA).

### **Operative procedure:**

Donor surgery was aided by central venous line and arterial line for hemodynamic control. Donor hepatectomy was performed under low central venous pressure. A reverse L shaped incision is given, Thompson retractor use for exposure, liver

was mobilized, retrograde cholecystectomy was done and cystic duct used to perform the cholangiogram to delineate the biliary anatomy, porta hepatis dissected out, zone of ischemia identified and liver resection done using CUSA and liver hanging manoeuvre, graft of right lobe taken out after transaction of right portal vein, right hepatic artery and right hepatic duct and their stumps were closed. After procurement, graft was weighed and flushed with university of Wisconsin solution. Bile leak or biliary stenosis was checked by injecting methylene blue from cystic duct and then performing cholangiogram. Residual donor liver was fixed to anterior abdominal wall with falciform ligament Hemostasis was secured and drain placed in right sub phrenic space, abdominal wall closed in layers and skin approximated using staplers.

### **Postoperative Management:**

After the operation donors were shifted to the intensive care unit (ICU). Central venous pressure was kept between 5 and 10 cm of water. A Doppler ultrasound was performed to ensure patency of arterial, portal inflow and hepatic venous outflow. Donors were advised to refrain from right lateral position in the early postoperative period. Drains were removed as soon as the output decreased. They were generally shifted to floor on the second or third postoperative day.

### **Statistical Analysis:**

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<sup>1</sup> were included as morbidity. Data analysis was performed on SPSS version 20.

<b>Step 01</b>	<b>Blood test</b>	Grouping, complete blood count, prothrombin time/international normalized ratio, liver function tests, urea, creatinine, electrolytes, urine R/E, HCV antibody, hepatitis B profile (hepatitis B surface antigen), human immunodeficiency virus 1 and 2 screen
	<b>Radiology</b>	Ultrasound abdomen with liver donor protocol, if donor is female than ultrasound abdomen and pelvis, chest x-ray PA view
	<b>Consultation</b>	Transplant surgeon
<b>Step 02</b>	<b>Radiology</b>	Triphasic CT scan of liver with volumetry
<b>Step 03</b>	<b>Blood test</b>	Albumin, G6PD deficiency, reticulocyte count, hemoglobin A1c, thyroid function tests, serum ferritin, ceruloplasmin, fasting lipid profile, calcium, phosphate, , hepatitis B core antibody, hepatitis B surface antibody, arterial blood gases
	<b>Immunology</b>	Anti-nuclear antibody, cytomegalovirus IgG, toxoplasma IgG, IgM
	<b>Radiology</b>	MRCP, Doppler ultrasound abdomen, echocardiography, pulmonary function test
	<b>Urine</b>	Complete report, culture and sensitivity
	<b>Consultation</b>	Cardiologist, pulmonologist, dentist, ophthalmologist, Psychiatrist, anesthetist, hepatologist, gynecologist if female, independent assessor

**Table-1:** Donor Evaluation/Investigations

**RESULTS**

Of the 100 donors 76(76%) were male and 24 (24%) were female, Male to female ratio was 3.1:1. mean age of the donors was 25.78 ranging from 18 years to 47 years. Mostly donors were in their twenties and thirties, only 4 donors were more than 40 years of age. Mean age of the patients was 45.61 ± 9.57 years. 65 patients had decompensated cirrhosis due to chronic HCV infection, 16 patients had decompensated cirrhosis due to chronic HBV infection. One patient had both HBV and HCV infection while 5 patients had both HBV and HDV infection. Ten patients had HCC, one patient had cryptogenic cirrhosis of liver, while 2 patients had Budd Chiari syndrome (Table-2).

<b>Causes of liver disease</b>	<b>No. of cases</b>
<b>HCV</b>	65
<b>HBV</b>	16
<b>HCC</b>	10
<b>HBV + HDV</b>	05
<b>HCV + HBV</b>	01
<b>Budd chiari</b>	02
<b>Cryptogenic liver cirrhosis</b>	01

**Table-2:** Indications of LDLT

Mean BMI of donors was 22.26 ± 2.77 kg/m<sup>2</sup> (range, 16.60-29.00 kg/m<sup>2</sup>). Of the donors, 7 (7%) had BMI <18.8 kg/m<sup>2</sup>. All donors were related to recipient. Son (28%), siblings (22%) nephew (16%) and cousins (22%) were the most common relatives.

Seventy six donors (76%) had the same blood group as recipients, whereas 24 (24%) had compatible blood groups. No ABO incompatible transplant was done in our center. All donors donated a right lobe graft. MHV was not taken with the graft in 9(9%) donors, while partial MHV was taken in 90(90%) grafts. One graft was harvested with complete MHV. Estimated GRWR from liver volumetry was 1.2 + 0.21 (ranging from 0.91 to 2.15). Mean duration of surgery 13.6 + 2.38 hours. Out of 100 donors 89 had classic portal vein anatomy; 9. Had type 2 and two patients were found to have type 3 anatomic variation. Whereas 81 (81%) patients had type 1 conventional hepatic artery anatomy, rest of the patients 19 (19%) had variable anatomy. (74%) had normal type 1 biliary anatomy. 87 donors had uneventful recovery in post-operative period whereas 13 had complications including re-exploration (4%) due to bleeding from phrenic vessel (1%), vena cava stitch surface (2%) and cut surface of CBD (1%), 2 patients had bile leakage from cut surface of the liver which was managed conservatively, 6 patients had superficial wound infection and only a single patient had decompensation which was managed with supportive care and who recovered after prolong ICU stay. There was no per-operative mortality or major bleeding in any of our donor, estimated blood loss during donor Hepatectomy was 325±50ml, and did not required any perioperative transfusion, 4 patients required blood transfusion during

exploration and 1 patient in prolong i.c.u stay. Minimum I.C.U stay was 2 days and maximum was 14 days due to hepatic decompensation, mean I.C.U stay was 4±1days, total length of stay in hospital range from 8 days to 15 days with mean stay of 10±2 days.

	Number	Percentage%
<b>Gender</b>		
male	76	76%
female	24	24%
<b>Relation</b>		
Son	28	28%
Nephew	16	16%
Brother	18	18%
Sister	04	04%
Daughter	04	04%
Wife	08	08%
Niece	16	16%
First Cousin	22	22%
		<b>Range</b>
Age	25.78	18-47
BMI	22.25	16.60-29.00
Operative Time	13.6	10.45-16.32
Blood Loss	325	290-400
ICU stay	4	2-14
Total hospital stay	10	8-15

**Table-3:** Characteristics of donors

## DISCUSSION

Due to limited cadaveric grafts, currently LDLT is performed with increasing frequency worldwide. Donor Hepatectomy is generally without problems but in literature morbidity and mortality linked to this procedure are at varying rates<sup>8,9,10,11</sup>. Right lobe Hepatectomy is associated with a higher complication rate, but the mortality related to this procedure has reduced from 2% to 0.4-0.5% in last 20 years<sup>12,13,14</sup> hence making this procedure further safe for the donor.

The current study highlights outcomes of voluntary donors who underwent donor hepatectomy in our liver transplant program from 2012 to 2016. No donor mortality was observed during this period and morbidity comparable with other centers was achieved. Major indication for liver transplantation turned out to be end stage liver disease due to chronic hepatitis C infection (60%) and hepatitis B infection (16%) followed by HCC (12.7%) thus indicating the huge burden caused by chronic HCV in our population<sup>15</sup>.

Clavien- Dindo grading system is an effective and commonly employed method for grading postoperative complications. A grade-2 and above complication rate of 10 - 40% has been previously reported in LDLT donors. A complication rate of 13% was observed in these donors, which falls well within the range of previous reports<sup>9-12</sup>. Decreased complication rate in our donors can be attributed to mostly young donors, strict selection criteria, meticulous surgery and perioperative and postoperative care provided to our donors.

Most common complication in our donors was superficial wound infection among which 4 were smokers. Postoperative intra-abdominal hemorrhage is an important complication that may occur after donor Hepatectomy with a rate of 1.4% reported by a recent study<sup>16</sup>. 2<sup>nd</sup> common complication was re-exploration due to post-operative bleeding, rate of re-exploration in our donors have significantly decreased over the time, and none of the donor had re-exploration in 2016. None of the patients had transfusion during donor Hepatectomy, transfusion was done during re-exploration surgery.

Biliary complications can be the most frequent complications in live donors,<sup>17</sup> however in our study only 2 patients had post-operative bile leakage which was seen on 3<sup>rd</sup> and 4<sup>th</sup> post-operative day, one patient bile leakage resolved after 5 days without any intervention whereas 2<sup>nd</sup> donor had an ercp + stenting for bile leakage and during one year follow up none of the donors had biliary stricture.

Since it has been shown that a donor remnant liver volume < 30 - 35% is associated with higher rate of complications<sup>18,19</sup>, the minimum donor residual volume at the study center was 30% and ranged between 30-45% with an exception of a single donor in which we operated with a residual volume of 28%. We paid the price of not following the safety margin as this donor had post-operative hepatic decompensation, prolong I.C.U and hospital stay, and needed post-operative transfusion and supportive care.

For any transplant center, ensuring donor safety is of paramount importance as it is a decisive factor in future success of the program. Good donor outcomes in our center with limited resources were possible because of ample training of members of transplant team in high volume centers along with stringent donor selection criteria to ensure inclusion

of healthy and fit individuals with no underlying comorbid conditions and relatively younger age (18-50) which is lower than many other centers that perform LDLT<sup>20</sup> as our result support the concept that Younger age is associated with better regenerative ability of remnant liver with better outcomes<sup>21</sup>. The limitation of our study was its retrospective nature with relatively shorter follow up, thus it is difficult to comment on long term complications but still our program ensures donor safety with good outcomes.

### CONCLUSION

Donor safety is of paramount importance and is only possible with appropriate donor selection requiring very detailed studies, a problem-free hepatectomy process, and close postoperative donor monitoring. Our study shows that good donor outcomes can be achieved in a new transplant center of a developing country and thus proves itself to be a safe transplant program. We emphasize the highest degree of precision during donor hepatectomy to avoid mortality and reduce morbidity as far as possible.

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