

Outcome of Live Donor Liver Transplantation in Indian Children with Bodyweight <7.5 kg

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This case-series analyzed the outcome of live donor liver transplantation (LT) performed in children <7.5kg from January 2008 to June 2009 at our center. Five patients (3 males, 2 females, mean age, $8.2 \pm .4$ months; mean weight 6.8 ± 0.4 kg) underwent LT. The indications of LT included biliary atresia (3) and idiopathic neonatal hepatitis (2). Postoperative complications included acute rejection (1), portal venous thrombosis (1), bile leak (1), severe hypertension (1) and bacterial sepsis (4). There were no donor related complications. The median follow-up duration is 11 months with patient and graft survival rates of 100% each, respectively.

Key words: *Child, India, Live-related liver transplantation, Outcome.*

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In the current era, 10-year patient and graft survival rates of pediatric liver transplantation (LT) are 88 and 81%, respectively [1]. LT in small children still poses a surgical and medical challenge. Greater than 80% survival in young recipients has also been reported recently [2,3]. In this series, we describe our experience of live donor LT performed in children weighing less than 7.5 kg.

METHODS

A retrospective analysis of case-records of children <7.5kg with indications for LT enrolled sequentially from January 2008 to June 2009 was undertaken. Pre transplant assessment included blood cultures, viral serologies (HIV, HBV, HCV, HAV, CMV, HSV, VZV), ultrasound doppler, CT angiography of abdomen, dental and cardiac evaluation in addition to liver function tests, hemogram and serum biochemistry.

Parents/blood relatives were evaluated after

informed consent. A psychiatric assessment was performed in every donor. A CT angiography of liver for volumetry was obtained to assess available graft size. All grafts were obtained from left lateral segments (II,III) of living related donors. All transplants at our hospital are approved by an authorization committee.

Postoperative immunosuppression was instituted with triple-drug therapy regime, which consisted of steroids, cyclosporin and mycophenolate. Steroids were given as an intraoperative bolus of methylprednisolone (30 mg/kg) tapered over 5 days. Thereafter, prednisolone was started at a dose of 8 mg/kg tapered to 2 mg/kg over a period of five days. It was slowly tapered over next three months. Pulse methylprednisolone therapy was given at a dose of 30 mg/kg for three days in patients with suspicion/evidence of acute rejection. Cyclosporin was used in an oral dose of 2 mg/kg/dose every 12 hourly. The target trough level was 150-250 ng/mL. It was

changed to tacrolimus in a patient in whom rejection was confirmed with the target trough level of 5-10 ng/mL. Mycophenolate was administered in a dose of 600mg/m² in two divided doses.

RESULTS

Five children <7.5kg (3 males) underwent live-related LT (**Table I**). According to the Indian Academy of Pediatrics classification of malnutrition, two children each had grade II and I malnutrition, respectively. Of three patients with biliary atresia, two had prior portoenterostomy and one had cholecystojejunostomy done at another centre. Living donors were the father in three cases and a maternal uncle and an aunt in one case each. The mean age and weight of donors were 31 ± 6.3 years (range 21-41) and 64.2 ± 9.1 kg (range 51-75), respectively.

One patient had an inferior vena cava (IVC) stenosis below the right hepatic vein (HV) insertion and required a venoplasty. This patient had a large left hepatic artery (HA), atrophy of right lobe along with hypertrophy of left lobe. All patients with prior biliary surgery had dense adhesions at porta. Adhesionolysis required meticulous dissection. Dissection was performed through the sub capsular plane of liver to avoid injury to the bowel. Another difficulty during hepatectomy was thin small hepatic veins draining directly into IVC. Portal venous (PV) reconstruction in these patients is known to be

technically demanding. Two patients had a standard graft PV to the main PV anastomosis. We mobilized main PV up to the confluence of superior mesenteric vein and splenic vein and performed the anastomosis near the confluence. One patient required a PV interposition graft obtained from the internal jugular vein. One patient had a small main PV with a large coronary vein draining near the confluence. The graft PV was implanted to the common channel of main PV and coronary vein. Wedge shaped slit of lateral angles of PV were useful in case of size mismatch. Arterial reconstruction was performed between the graft artery and right HA. Biliary reconstruction was performed by Roux-en-Y hepaticojejunostomy [4,5].

Postoperative early complications: Post-operative complications are listed in **Table II**. Acute rejection was identified in one patient on postoperative day (POD) 7. The diagnosis was confirmed with a liver biopsy. The patient required change of immunosuppressive therapy from CYC to TAC along with methylprednisolone bolus therapy.

PV thrombosis was identified in one child on second POD. Immediate thrombectomy was performed but the patient had recurrent thrombosis and the graft was salvaged by a retrohepatic cavoportal anastomosis [6]. A non-anastomotic bile leak was observed in a solitary patient on 20th POD. He responded successfully to a percutaneous drain insertion.

TABLE I CLINICAL PROFILE OF THE FIVE PATIENTS

Mean age (mo)	8.2 ± 2.4 (6-12)
Mean weight (kg)	6.8 ± 0.4 (6.2-7.4)
Diagnosis	
Extrahepatic biliary atresia	3
Idiopathic neonatal hepatitis	2
Mean Total serum bilirubin (mg/dL)	27.7 ± 14.0 (12-48.3)
Mean International normalized ratio	2.1 ± 1.2 (1.3-4.6)
Mean graft to recipient weight ratio	4.2 % (3.3-5)
Mean duration of surgery (h)	12
Mean Cold ischemic time (min)	101 (40-160)
Mean Warm ischemic time (min)	34.2 (25-45)

TABLE II POSTOPERATIVE COURSE AND EARLY COMPLICATIONS

Complications	Frequency
Surgical	
bile leak	1
acute rejection	1
portal venous thrombosis	1
Medical complications	
severe hypertension	1
bacterial sepsis	4
Mean post LT stay (d)	21.6 ± 4.5
Median follow up (mo)	11
Survival	100%

WHAT THIS STUDY ADDS?

- Outcome of small pediatric recipients (<7.5 kg) undergoing living related liver transplant is excellent in the short term.

Severe hypertension was observed in one child, which responded to medical management. Infectious complications were observed in 4 (80%) patients. These included blood stream sepsis, pneumonia and urinary tract infection. The organisms isolated included *E.coli*, Acinetobacter, Pseudomonas and Klebsiella in one child each. No fungal or viral infections were observed. No deaths were recorded.

The mean duration of post LT hospital stay was 21.6 ± 4.5 days (range 17-30) with intensive care stay of 3-5 days. There was no donor related mortality or complications. All the donors were discharged on 7-10 POD.

Late complications and outcome: Abscess formation was seen at the site of BCG vaccination in a solitary patient 4 month following transplant at 9 months of age, which resolved with oral antibiotics. There were no other immunosuppression related complications. No late vascular occlusions have been documented. All patients are well with no evidence of chronic graft rejection or dysfunction and mean AST, ALT and TSB levels are 30.0 ± 4.7 U/L, 36.6 ± 5.1 U/L, 0.32 ± 0.11 mg/dL, respectively. At a median follow-up of 11 months (range, 6.7-15), our patient and graft survival rates are 100% each, respectively.

DISCUSSION

LT still remains a significant challenge with financial, follow up and survival implications especially, in small children. Data from developing countries addressing these concerns is scant. While it has been ten years since the first successful pediatric LT was performed in India in our unit [7], the outcome of LT in small children has not been reported from Indian subcontinent. In concordance with what has been reported previously, extrahepatic biliary atresia with failed Kasai procedure was the commonest indication [8,9]. In

the absence of availability of cadaveric donors, living related liver donation is the only realistic option in our country.

Literature suggests that infections are the principal complications in pediatric LT candidates, occurring in 60-70% of cases [10]. Significant bacterial infections that required therapy in the perioperative period despite antibacterial prophylaxis were seen in 4 (80%) patients. The post-transplantation hospital stay was similar to other pediatric reports, where the mean stay varied from 17-24 days [11]. With improvement in perioperative care, the length of post LT hospital stay has been reduced over the last 10 years from a maximum of 68 days to 30 days. We report 100% survival in children <7.5 kg.

In our institute, the estimated cost of LT is Rs.12-15 Lakhs (including medical and surgical management of recipient and donor), which is significantly lower than the average expenditure incurred in developed countries. Still poor financial status, lack of awareness, delayed referral, a poorly developed cadaveric program, and limited social-support groups are major hindrances, which need to be overcome to promote LT in India [12].

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