Original Article

Initial experience of pediatric liver transplantation – An Indian prospective

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\textbf{A B S T R A C T}

Background: Liver transplantation is well established treatment modality worldwide as an effective treatment for end-stage liver disease with only chance of long-term survival. Over the years survival following liver transplantation in pediatric group of patients has improved significantly because of improved diagnostic tools, technical refinements at operation and improved perioperative intensive care management.

Aim: To assess feasibility and outcome of pediatric liver transplant in India.

Materials and methods: From Apr 2007 to June 2011, total 15 children underwent liver transplant at our institution and 11 were died while on work up, 6 had Acute Liver Failure (ALF) and rest 5 had Chronic liver disease (CLD).

Results: Biliary atresia was the commonest indication ($n = 8$). Twelve children had living donor transplants, mothers being the donors in a majority of these. Common surgical complications were vascular problems ($n = 3$) and bowel perforation ($n = 2$). Common medical complications included pulmonary sepsis. Overall 1-year survival was 73.4%. All survivors are doing well, have caught up with physical and developmental milestones and are engaged in age appropriate activities.

Conclusions: Optimization of patients, nutritional improvement and control of sepsis with early transplant is important predictor of outcome in pediatric population.

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1. Introduction

Liver transplantation is well established worldwide as an effective treatment for end-stage liver disease in children. Acceptance in India has been slow because of considerations of cost, infections, inability to support long-term care.\textsuperscript{1} In India, the first pediatric liver transplants were performed in 1998 and since then many centers have established successful programs.\textsuperscript{2} However not much of the progress happens in pediatric liver transplant in India. Early western short series of pediatric liver transplantation described patient survival rates of between 11% and 39%.\textsuperscript{2,3} In the last 10 years, further developments have taken place in the field of pediatric liver transplantation, e.g. improvements in preoperative nutritional supplementation, immunosuppression and perioperative intensive care management, technical refinements, routine intraoperative Doppler-ultrasound, and better patient selection, thus improving the early patient outcome in large
pediatric transplant centers to more than 90%. Barring 1 or 2 centers in India pediatric liver transplant has not been widely practiced. The present study analyzes our initial experience with pediatric liver transplants.

2. Patients and methods

Total 62 transplants (15 pediatric + 47 adult) were performed from Apr 2007 to Feb 2012 at our institution. A total 26 pediatric patients were worked up for liver transplantation, 6 with acute liver failure (ALF) and 20 due to chronic liver disease (CLD). Of these 15 underwent liver transplant with age ranging from 5 months–12 years. All patients with ALF (4 acute viral hepatitis, 2 cryptogenic) and 5 patients with CLD (3 biliary atresia, 1 Wilson disease, 1 cryptogenic) were died while work up. Demographic data are summarized in [Table 1]. The indications for liver transplantation are listed in [Fig. 1].

3 patients underwent Kasai procedure for biliary atresia earlier; rest does not have any previous intra abdominal surgery. All except 3 patients underwent living donor liver transplant (LDLT). 3 patients received liver grafts from deceased donors; one patient received an “in situ” split left lateral segment and the other 2 received a whole liver graft from pediatric donor. “In situ” splitting of deceased donor liver an attractive option as it allows for perfect hemostasis as well ensuring control of bile leaks from the cut surface by performing methylene blue dye test. In addition the cold ischemia time can be kept to the minimum for the two split grafts. However for “in situ” splitting necessitates a stable donor.

7 out of 15 patients were provided preoperative nutritional support (5 with enteral feed with nasogastric tube and 2 with parental nutrition) to improve their nutrition status. A total 7 patients were less than 6 kg of weight and they received reduced left lateral segments from living donors to ensure that the grafts were within 3% of their body weight and to avoid compression, hypo perfusion of the graft and intra abdominal compartment syndrome after abdominal wall closure all of which is critical to the survival of the graft. One patient required Gore-Tex mesh closure of the abdominal wall followed by delayed closure 3 days later.

Implantation technique — of 15 liver grafts, 4 were left lobe, 9 were left lateral reduced grafts [Figs. 2 and 3]. The left hepatic vein of these grafts was anastomosed to the left middle hepatic vein or the entire hepatic venous stump of the recipient using the triangulation technique to ensure unimpeded outflow. Two patients received whole liver grafts from pediatric donors. Reperfusion was done via the portal vein in 12 cases and in rest 3 patients portal venous anastomosis was done with collateral. One patient requires extra anatomic hepatic artery reconstruction due to intimal injury with iliac artery graft of donor with conduit was anastomized with infra renal aorta.

Biliary anastomosis was done under magnification using interrupted 6 ‘0’ PDS sutures. No biliary stents were used. 12 recipients underwent Roux-en-Y hepaticojunostomy and duct-to-duct anastomosis was done in 3 patients.

3. Results

11 patients died while on work up (6 ALF, SCLD). However among the patient who could successfully underwent liver transplant overall 1 year survival is 73.3%. A total of 4 patients who died, 2 died in the perioperative (within 28 days after surgery) period; one due to HAT and the other due to sepsis. A 6-month-old baby died 8 months after transplant due to pulmonary sepsis. Another 5-year old recipient who was transplanted for PIFC died 11 months later. Most common morbidity was pulmonary sepsis which occurred in 5 patients. Two patients developed HAT, in one revascularization was successfully carried out with reexploration and thrombectomy. However other patient could not salvaged. One 5-month old with biliary atresia (Kasai done) had PVT; urgent revascularization of the graft was carried out with stored deceased donor iliac vein to create a venous conduit from the recipient SMV to graft portal vein.

Table 1 – Demographic details of patients being worked up for liver transplantation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N = 15/26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>5 months–12 years</td>
</tr>
<tr>
<td>Sex M:F</td>
<td>6:9 (11:15)</td>
</tr>
<tr>
<td>Weight kg</td>
<td>5.4–30 (5–32) kg</td>
</tr>
</tbody>
</table>
Two patients required relaparotomy for bowel perforation in the immediate postoperative period one of which was due to pigtail drain induced small bowel injury. Other had injury while abdominal closure. Two patients had prolonged ascites requiring prolonged drainage; one due to chyloous leak which subsided following Inj Octreotide and TPN. One patient who had received a whole liver graft developed ischemic necrosis of the right lobe due to hypo perfusion. She underwent emergency reexploration and right hepatectomy on the 4th postoperative day followed by an uncomplicated recovery. There were no biliary complications.

4. Discussion

Pediatric patients with ESLD have very little reserve and require intensive monitoring and prompt management. Even the slightest delay may lead to fatal outcome. In our series all 6 patients with ALF died, 2 due to active sepsis could not be transplanted while 4 died during work up of donors. As the transplant work up for donor requires minimum 2–3 days in Indian set up. Most children require only a left lateral segment graft; the morbidity and risks to the donor are much less than adult-to-adult living donor liver transplantation. Left lateral segment is a near optimal size graft for the child, reduces the risk for the donor, and the incidence of rejection is reduced. Bare minimum investigation should be done for donors and authorization should be avoided especially if parents are donors to avoid unnecessary delay in transplant.1

On the other hand 4 patients with CLD died while work up due to repeated cholangitis and nutritional insufficiency. Nutritional status impacts perioperative outcome as majority of patients have cholestatic liver disease that leads to recurrent cholangitis as well as protein caloric malnutrition and superimposed CLD also cause further deterioration in general health. The optimization of nutritional status in pediatric patients has translated into improved survival after transplantation, fewer infections, and a reduction of surgical complications. Biliary atresia is the commonest indication for the pediatric liver transplantation in most of the series as in ours.6 Eight patients underwent transplant for biliary atresia with 3 had underwent earlier Kasai procedure but developed secondary biliary cirrhosis. Perioperative morbidity after pediatric liver transplantation mainly includes vascular, biliary complications, intestinal perforation, and sepsis.1 Warnaar et al reported a HAT incidence of 13.7%, about a third of who were recanalized successfully.7 In our series 2 patients had HAT; one was successfully salvaged with reexploration with thrombectomy. Various risk factors and the etiology of hepatic artery thrombosis have been discussed in the literature and especially small children less than 3 years old weighing less than 15 kg have been reported to have a high incidence of arterial thrombosis.8 In the literature incidence of portal vein thrombosis is reported as 4%.8 In our series we had one portal vein thrombosis. The portal vein in children, especially after a Kasai procedure is often narrow, fibrotic and often encased in inflammatory lymph nodes. A high risk of portal vein thrombosis exists in these children.1 For early detection and prevention of complication associated with vascular thrombosis we routinely get Doppler-ultrasound examination performed by the same highly experienced radiologist during operation, before and immediately after closure of the abdominal wall, as well as in the ICU for twice a day for first 7 days.

Biliary complications including bile leaks and anastomotic strictures have historically been a major problem of partial liver grafts. An initial series of SLT in the early 1990s had a biliary complication rate of 20%–25%.5,10 The bile ducts on the graft are often very small and multiple. A Roux-en-Y drainage of all these ducts is the procedure of choice. Occasionally, a duct-to-duct anastomosis is possible, but care need to be taken to preserve vascularity of the recipient duct during the explantation procedure. In this series in 12 patients we did Roux-en-Y hepaticojejunostomy and in rest 3 primary duct-to-duct anastomosis were done with no biliary complication. Other common cause of morbidity is sepsis and iatrogenic enteric perforation. We had two iatrogenic enteric perforations one while closure of abdomen and in other due to pigtail drainage for clinically significant ascites due to portal vein thrombosis.

Acute rejection was seen in 20% (n = 3). All responded to pulse steroid and intensification of immune suppression. There have been no long-term adverse effects in these patients and their course has been similar to those who did not have acute rejection. In the LDLT scenario, acute rejection is less common and usually completely reverses with adequate therapy. Incidence of acute rejection has been reported to be between 40% and 70%.8

5. Conclusion

Prognosis of pediatric patients with ALF can be bettered with intensive monitoring, control of sepsis and early transplant with bare minimum investigations to decrease the delay. The early survival and complication rates are at par with other centers as well as with adult population in the same center. Most of the child can achieve the normal physical and mental growth post transplant. However intense counseling regarding hygiene, drug level monitoring and optimal medical review needs to emphasize to the patients parents to avoid late
and infectious complications which can be lethal to the transplanted patient. This study shows the feasibility of the pediatric liver transplant with good early outcome in India. However long-term studies are required to assess delayed outcome and to address probable logistic support in Indian scenario.

**Conflicts of interest**

All authors have none to declare.

**References**

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