The Era of Pediatric Liver Transplantation in India

Liver transplantation is well established as a viable treatment for children with end-stage liver disease (ESLD). As surgical techniques have become more standard and related specialties have kept pace with developments in this field, the success rates have improved to 95% at 1 year and to about 70% at 5 years. Since the first pediatric liver transplantation in 1998 by our group, there are now a number of liver transplant centers in the country offering pediatric liver transplant. The absence of a national registry makes it difficult to assess the actual number. It is estimated that India will need about 4000 transplants per year, and we are presently nowhere near meeting this demand.

The story of the development of pediatric liver transplantation in India mirrors that of many countries with limited resources (CLR). The first liver transplant in children in India was performed in 1998 by our group with the assistance of a team of surgeons from St. Christopher’s Hospital, Philadelphia, led by our mentor Dr. Stephen Dunn. The experience in CLR is developing programs in one of the three ways. The first is of a “greenfield” project involving local talent assisted by a team from abroad. This is how we started our program. Yet another is to have a returning specialist after a period of training abroad start a program often only to be disappointed with the available assistance and infrastructure.[1] The last is to have whole teams of surgeons and supporting specialists spend a sufficient period abroad with a well-established center and develop a program on their return. This last route is often not practical and can be very expensive to any institution.[2]

The early experience in most centers, however established, is one of a steep learning curve marked by many early failures and eventual success. The Kaplan–Meier curve [Figure 1] shows our early experience illustrating this observation.[3] In time, early survival of 90% at time to discharge can be achieved consistently. The problem in countries like ours is to sustain good long-term survival. We notice an intermediate-term and long-term loss of patients to infections, posttransplant lymphoproliferative disorder, inadequate medical assistance in remote areas, and noncompliance with immunosuppression. This is unique to CLR an observation also reported from Africa and Egypt.

The Search for a Suitable Donor

The slow development of deceased donor transplantation (DDTx) and organ-sharing networks in India and the rarity of deceased pediatric donors led to the need for live donors. These were usually parents of the child. Early in our experience, the mother was often the “preferred” choice by the extended family – a strong cultural influence in India. However, as the program became more successful, an encouraging change was that more fathers were willing to donate. Even among related live donors, notwithstanding the proven benefits, anatomical variations such as multiple hepatic arteries or the predilection for fatty change in Indian subjects made the identification of a suitable donor difficult.

Other factors that strongly influenced the availability of suitable donors were a reluctance to split livers to share the left lateral segments with a child on the waiting list. Participating centres in the organ sharing network would prefer to have the whole liver for their adult recipients. Also, the lack of technical ability and resources to perform the split in donor centre has limited the progress of split liver transplants.

Complications

Reliance on living donor organs and technical variant grafts results in greater technical challenges due to small graft vessels and bile ducts. For these reasons, vascular and bile duct complications are more frequently
The loss of a graft from such complications possesses a special problem in our country. The inability to rescue by emergency listing and prioritizing to a cadaver in many cases leads to the loss of the patient.

**Infections**

The incidence of posttransplant infections varies. In a relatively well-developed country like Korea, a study from the Asan Medical Center reported an incidence of 70% in a cohort of 95 children who underwent LDLT.[6] In a more pertinent study from Egypt representing an emerging country,[7] 26 patients developed 62 infections either bacterial, viral, fungal, or mixed during the follow-up period of 1.5 years. Fifty percent occurred in the 1st month after transplant. Our own experience, detailed later, confirms this high incidence of infections in the posttransplant period and its impact on morbidity and mortality.

Finally, financial constraints would always be a major hurdle in the absence of any form of organized insurance or state-sponsored support for pediatric liver transplantation. With improving results and more centers starting programs, philanthropic and some state-based support is now emerging.

**Opinion**

The future of pediatric liver transplantation in India will eventually be determined by our ability to sustain the initial success over the life of the child. The early experience available to us is not very encouraging. Significant early complications still plague the initial outcome of the operation. Our inability to rescue failed grafts due to the scarce availability of deceased donor or split-liver grafts places a practical and ethical burden on the family and the team. It is not easy to approach another member of the family, just after failure and great expense, to find another donor and relive the whole experience of the procedure. The very concept of live donor transplantation of asking a healthy parent to part with a portion of the liver to save the child’s life at personal risk, however justified, begs the question – why are we not promoting and developing a more robust deceased donor network.

**Very late outcomes (10–20 years): Dunn S. personal communication**

Half of asymptomatic liver transplant recipients in the WithDraw study had Ishak Level 2 fibrosis, 53% of allografts had failed by 20 years, and 69% of patients were alive at 20 years. One author predicts that the current half-life of hepatic allograft in the USA is 13 years. Only 32% of pediatric recipients achieved ideal survival defined as excellent graft function, single-drug immunosuppression, good quality of life, and minimal comorbidity.

Recent long-term reports place the need for retransplantation in over 10% of children. In our experience, we have had successful retransplants in 2 of 88 children, both reduced grafts from deceased donors.

Despite successful adoption of monotherapy with tacrolimus in a majority of recipients, the risks of long term immunosuppression on renal function is a concern. One child in our series needs a renal transplant 10 years after the liver transplant, and at least four others have developed renal insufficiency requiring modifications in immunotherapy.

In conclusion, 20 years ago, if primary attempts at treatment had failed, the outcome for children with biliary atresia, acute liver failure, or metabolic disease was hopeless. Since the advent of pediatric liver transplantation, remarkable successes have been achieved, with almost 90% of children with ESLD now having a new lease on life. This has been possible due to the pioneering efforts of the medical and surgical fraternity in the country, mainly in the private sector, starting and sustaining programs as also close cooperation in sharing knowledge and resources. The government needs to do more to support the
immediate- and long-term cost of this complex but essential procedure or else it will always remain the privilege of a few who can afford it.

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REFERENCES
1. Rela M, Reddy MS. Ethics of transplantation in countries with limited resources. In: Dunn SP, Horslen S, editors. Solid Organ Transplantation in Infants and Children. Cham: Springer International Publishing; 2017. p. 1-6.
2. Quak SH. Liver transplantation in the developing world. Curr Opin Organ Transplant. 2009;14:540-3.
3. Rao S, D’Cruz AL. Experience in India. In: Dunn SP, Horslen S, editors. Solid Organ Transplantation in Infants and Children. Cham: Springer International Publishing; 2017. p. 1-2.
4. Neto JS, Carone E, Pugliese V, Salzedas A, Fonseca EA, Teng H, et al. Living donor liver transplantation for children in Brazil weighing less than 10 kilograms. Liver Transplant 2007;13:1153-8.
5. Shibasaki S, Taniguchi M, Shimamura T, Suzuki T, Yamashita K, Wakayama K, et al. Risk factors for portal vein complications in pediatric living donor liver transplantation. Clin Transplant 2010;24:550-6.
6. Kim JM, Kim KM, Yi NJ, Choe YH, Kim MS, Suh KS, et al. Pediatric liver transplantation outcomes in Korea. J Korean Med Sci 2013;28:42-7.
7. Behairy BES, Konsowa HAS, Zakaria HM, Elsalam OHA, Sira MM. Infection after pediatric living related liver transplantation. Int J Transplant Res Med 2015;1:12-5.