Leading Article

Paediatric liver transplantation in Sri Lanka; From an impossible dream to a lifesaving reality

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Introduction

Organ transplantation for children is evolving in Sri Lanka (SL)[1-5]. Paediatric kidney and bone marrow transplants emerged within the country in 2004 and 2021, respectively[4,5]. In 2020, the first successful paediatric liver transplantation (PLT) was reported in SL[1]. Liver transplantation (LT) is the cure for children with medically refractory acute liver failure, end stage liver disease and unresectable liver tumuors[2]. PLT is particularly challenging due to the small body size and sensitive haemodynamics of children. It requires demanding clinical expertise and commitment, along with state-of-the-art infrastructure, to achieve successful outcomes[2,6,7]. Till recently, due to lack of PLT facilities in SL, most children with liver failure died, only a handful being able to afford treatment overseas. In 2016, Shanmugam NP, *et al*[8] reported the non-availability of PLT facilities in SL and Wickramasekera N, *et al*[9] stated that the low survival of Sri Lankan children with biliary atresia (BA) was due to limited access to LT. Since the first PLT in 2020, the PLT programme in SL has been evolving steadily amidst challenging circumstances[1-3]. This article examines the current state of the PLT programme in SL, describing the challenges encountered and the proposed solutions.

Spectrum of liver disease in children and Sri Lankan experience

Children are susceptible to a distinct array of liver diseases, among which BA is the leading indication necessitating LT[2,8]. Genetic and metabolic disorders frequently manifest during childhood including progressive familial intrahepatic cholestasis (PFIC), Wilson disease (WD), Alagille syndrome, and tyrosinaemia[2,6,7]. Autoimmune liver diseases (AILD) and non-alcoholic fatty liver disease (NAFLD) are being increasingly observed in adolescents[10]. Malignant conditions such as hepatoblastoma, hepatocellular carcinoma, and Langerhans cell histiocytosis may also necessitate LT in specific circumstances[2,6].

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Limited data are available on liver diseases among Sri Lankan children. Infaq M, *et al*[11] reported on 60 infants with cholestasis, revealing that a significant portion suffered from BA (26%) and neonatal hepatitis syndrome (26%). Wickramasekera N, *et al*[9] documented a nine-year experience and outcomes of Kasai portoenterostomy in 79 patients with BA. Increasing incidence of NAFLD is reported among adolescents, predicting a future epidemic of cirrhosis in young adults[10]. Fernando M, *et al*[2] reported on the initial experience of PLT in SL stating that WD, AILD, BA and PFIC type 3 were the underlying aetiologies.

Paediatric LT programme in Sri Lanka

Following the first PLT in the world in 1963, PLT programmes have undergone significant evolution. In SL, a milestone was reached with the first successful PLT in 2020, performed on a 9-year-old child with PFIC type 3 by Colombo North Centre for Liver Diseases (CNCLD)[1,2]. It raised the standard of the Sri Lankan healthcare system towards the international benchmark. Since then, from June 2020 to May 2023, the paediatric LT programme by CNCLD has made substantial progress, completing a total of 14 paediatric liver transplants amidst the crisis situations of COVID-19 and the economic crisis[1,2,3,12]. Living donation predominated, most of the donors being parents[2]. Interestingly, a substantial proportion of donors comprised Buddhist Priests[2].

Despite this success, the number of PLTs being performed falls significantly below the country's demand[2]. Fernando M, *et al*[2] reported that of approximately 70 children being listed for LT over three years, only 14 were able to have a LT due to many reasons. Out of the left-out young children, many may have succumbed to the illness with a handful travelling abroad for treatment[1-3]. The limitation of resources with operating theatre and intensive care facilities, inadequate trained health staff and lack of uninterrupted medical supplies are among the reasons for not being able to cater to the national need for PLT at present[2]. This situation emphasizes the pressing need for further enhancement of the PLT programme by allocating more health resources and providing specialized training for healthcare staff. This will increase the capacity to do more in-house PLT to satisfy the country's need, and to also save money spent travelling overseas for such treatment.

The challenges identified in the establishment of the paediatric LT programme in SL with proposed solutions

1. Not being able to cater for all children requiring LT

In the Sri Lankan cohort of 70 children listed for LT over three years, the majority were young infants with BA and failed Kasai[2]. These are difficult cases for LT and are not the ideal cases for a PLT programme at its initiation[2,13]. In addition, these infants often present with additional complications such as portal vein thrombosis, portal vein hypoplasia, prior portoenterostomy, cholangitis and malnutrition[8,9]. Managing transplantation and recovery in these patients poses significant challenges[13]. Particularly in the early phases of a transplant programme, when the team was navigating the learning curve, these cases became the most demanding. Failures during this initial learning phase can have a profound impact on the team's confidence and the overall progress of the programme. Hence, we had to accept the challenge of not being able to cater to all those who walked into the programme and be selective when choosing transplant candidates. This challenge is expected to be overcome with the development of expertise within the country with more and more clinical experience.

2. Lack of state-of-the-art infrastructure, health care facilities and medical supplies.

PLT demands sophisticated infrastructure and medical equipment to achieve good outcomes. Instalment of the infrastructure is costly with a requirement for substantial initial capital investment and there will be ongoing expenses for consumables and for maintenance of the equipment. In a country like SL, which was subjected to the dual strain on the economy with COVID -19 and the economic crisis, it was hard to divert health funds for this kind of an endeavour[12].

Successful models of LT programmes in Europe and North America are typically supported by state or insurance-funded initiatives, with similar financial structures observed in East Asia as well. In India, a country with cultural and social similarities to SL, PLT is well-established within privately funded institutions that have invested in state-of-the-art infrastructure, resulting in positive outcomes[14]. However, the establishment of a private-sector PLT programme raises concerns about equitable access to care, a fundamental cornerstone principle in Sri Lanka's health system, which aims to continue providing free healthcare in the state sector. It also raises ethical issues related to health disparities for children from economically disadvantaged backgrounds.

In order to overcome the challenges, CNCLD established a dedicated institute for paediatric and adult liver disease and transplantation in January 2024 as a public private partnership. Setting a good example, the corporate sector largely supported the initial establishment of the PLT programme in SL. This support was extended to the extent of constructing a dedicated liver transplant institute by a single donor which was completed and equipped in January 2024. Once fully operational, the new centre of CNCLD will be able to cater for PLTs within the country.

The subsequent challenge for the PLT programme in SL is the sustainability of such dedicated centres with uninterrupted services. This requires a pragmatic and practical model which includes funds from the state, corporate sector, charitable organisations, and patient generated incomes within a well-regulated framework. Furthermore, centralization of PLT services to a few centres would enable the maximum utilization of the capital investment while allowing the team to be trained to their maximum potential. A good example of this is the United Kingdom, a large country having only three PLT centres. The work of Shanmugam NP, *et al*[8] underscores the benefits of service centralization in enhancing surgical skills, for less complex procedures like the Kasai procedure for BA to improve outcomes in keeping with this theory.

3. Lack of trained health care staff

A trained multidisciplinary team is crucial to achieve good outcomes following PLT. This includes hepatobiliary transplant surgeons, anaesthetists, paediatric hepatologists, intensivists, interventional radiologists, pathologists and trained nursing and technical staff. In addition, specialities such as nutrition, transfusion medicine and microbiology play a pivotal role in overall outcomes following PLT. The ongoing economic crisis has also intensified the migration of trained medical consultants from the country and the majority of postgraduates has chosen not to return following their mandatory overseas training, prior to specialization. This would only further hinder the provision of PLT services in the country.

LT is a physically demanding and psychologically stressful speciality management process. Though the initial specialists selected the field, driven by passion and the desire for pioneering, this motivation alone is inadequate to attract the next generation of clinicians to pursue PLT as a career. Having a dedicated and well-equipped centre, with a pleasant working environment to practise what they have learnt would be a good method of retaining the trained staff.

4. Limitation of suitable donors

LT necessitates a suitably ABO matched donor, while HLA matching is not required. ABO-incompatible LT can be performed in young infants[3]. Living donation is prevalent in the Asian region due to cultural factors and due to lack of established deceased donor programmes[15]. Conversely, cadaveric donation is more widespread in the Western world[15,16]. In paediatric patients, living donation is a more viable option compared to adults. This is attributed to the relatively young and healthy parents, who are often willing to donate[2,3,15,16]. Fernando M, *et al*[2] reported that the median age and BMI of the living donors was 33 (range 25-43) years and 22 (range 19-24) years respectively during the initial three years of PLT in SL. However, in this cohort, there were 15 children who did not have suitable living donors in the family due to blood group incompatibility or presence of fatty liver disease[2]. On such occasions, Buddhist priests have come forward to donate due to altruistic reasons[2]. Overcoming the challenges related to living donors, it is important to educate the parents of children with diagnosed chronic liver disease, to lose weight in advance and to maintain a healthy lifestyle. Lifestyle change counselling of parents of children especially with BA, immediately following Kasai is helpful, as this group of children would require LT at a later stage in life[8,9].

The alternative in the absence of a living donor is obtaining graft from a deceased donor (DD). Of the 14 PLTs performed so far in SL by CNCLD, two had

deceased donor liver transplant (DDLT). Both these patients had poor outcomes due to primary non-function[2]. Hence, in the current PLT programme in SL, DDLTs are not encouraged. The poor outcome may be attributed to suboptimal graft quality resulting from substandard management of donors, failures in organ preservation, and eventual graft quality deterioration during the ex-situ split. To improve the DD pool and the quality, it is crucial to have increased awareness among the public regarding organ donation and to have a client friendly, less cumbersome donation programme. Securing the services of trained intensive care staff for donor management is important to improve graft quality. Establishment of a well-coordinated national DD management system is also important for prompt and fair distribution of grafts. This will fill the gap for the required grafts which are not fulfilled by living donors for children requiring LT.

5. Inadequate public awareness and motivation for LT

PLT is still in its budding stage in SL. The previously accepted fate for most of these children was the death sentence when they required LT, unless they were able to afford the costly treatment overseas. A similar mindset might influence professionals due to lack of awareness and trust on local PLT services. Hence, awareness programmes are required to ensure that families seek help from PLT services locally and that professionals make the appropriate referrals in a timely manner. Success stories regarding life after LT should be shared to develop more confidence among families and professionals who have the option of choosing between LT and the conservative approach. This would improve the motivation and trust towards this lifesaving PLT service.

6. Lack of community services and government funding to maintain post-LT medical requirements.

LT will not provide a simple solution for liver failure, as it would need adherence to lifelong immunosuppression[2,7]. Continuous maintenance of adherence to medications would require a good network of follow-up. This would require satisfactory community services and shared care with local healthcare teams. Further, local paediatric teams can be trained through professional colleges and by formulating written guidelines on post-LT care and instances to seek expert help.

Maintenance of the transplanted liver graft requires an uninterrupted supply of immunosuppressants which might be challenging in the economic crisis[2]. A case that exemplifies this emerged in the context of a 14-year-old child from an economically disadvantaged background[2]. Despite earnest reminders, the child's mother ceased attending scheduled clinic visits, ultimately resulting in a terminal rejection[2]. Post-LT care could be supported by the state, assisted by the corporate sector, together with charitable organisations. As a good initiative, the President's Fund has recently increased the financial allowance given to paediatric LT patients at CNCLD, up to 1 million Sri Lankan rupees (LKR) in January 2024, which was just 0.3 million LKR previously[17]. Hopefully, once these LT recipients grow and become productive citizens of the country, one would be able to recover the health costs involved, and it will be a sum saved by preventing money migrating overseas for such services.

7. Post-operative infections

Post-operative infections have posed significant challenges to the SL cohort of PLT recipients resulting in significant morbidity and mortality[2]. Fernando M, *et al*[2] reported that all post-LT children sustained post-operative infections. Children afflicted by chronic liver disease are frequently hospitalized, relying on antibiotics and this leaves them colonized by various organisms[2,18]. LT recipients require central lines and regular venous access, in addition to enduring lengthy surgical procedures and ventilation[18]. The combination of diminished chest capacity and shallow breathing caused by both abdominal surgery-induced pain and underlying medical conditions substantially heightens the risk of chest infections. Compounded with these factors is the initiation of immunosuppressive therapy, administered during surgery to minimize re-perfusion injury[2,18]. Furthermore, sharing of the same infrastructure with non-LT patients increases the risk of cross-infections[2]. To mitigate the threat of sepsis, several strategies may prove beneficial. Adhering to standard precautions, eradicating colonization before LT, and minimizing the duration of both ventilation and central venous access can all play a significant role in reducing the infection risk. Most of all, having a dedicated infrastructure facility for LT will have a profound impact on outcomes.

Conclusion

Though the necessity for establishing a PLT programme in Sri Lanka is indisputable, initial phase of establishing a PLT programme in state health sector, within the current economic context faces many unique challenges. However, the current PLT programme by CNCLD being a free service, equal access will be provided to all children across the country in alignment with the Sri Lankan health policy. While the initial expenses associated with a PLT are substantial, LT proves to be cost-effective over the long-term by preventing mortality. LT in children not only contributes to the nation's productivity, but also boosts the country's health system to modern standards. Thus, the PLT programme in the country, should be supported to reach its potential heights.

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