



Pediatric transplantation: An international perspective



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ABSTRACT

Abdominal solid-organ transplantation has revolutionized the life of children with end-stage organ failure. The international practice of transplant in the pediatric population is heterogeneous. Global trends in pediatric transplant activity are increasing, with diffusion of transplant activities into developing and emerging economies. The organization of deceased donor programs varies internationally (with strong association to a country's gross domestic product (GDP) per capita and health spending). While deceased donor programs are well established in advanced economies, emerging and developing countries rely heavily on living donor programs. There are efforts underway to increase availability of pediatric and neonatal donor organs. Prioritization of organs for children exists in different forms throughout the world. Pediatric transplantation as a subspecialty is young but growing around the world with a need to train surgeons and physicians in this discipline. Outreach efforts with multinational and multi-institutional partnerships have enabled resource poor countries to establish new transplant programs for children. Further international collaboration, good quality data collection and audit, prospective research and ongoing mentorship, and education are needed to further improve outcomes of all children receiving solid-organ transplants.

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Introduction

Organ transplantation for children remains one of the most complex and challenging areas within current medical practice and it is understandable that different challenges, practices, and opportunities exist across the international community. Although solid-organ transplant for children is both resource and labor intensive, its cost effectiveness and impact on their lives and quality of life is well established.^{1,2} Local and regional factors around the world impact transplant programs, and this review will endeavor to address the differences in practice seen and to highlight the problems of access for children living in resource poor environments. We will confine discussion to abdominal solid-organ transplantation and where available, present pediatric-specific data as most available data incorporates both children and adults published together and is not always differentiated by age.

Trends in transplant activity and issues of access to solid-organ transplant for children across the world

While the justification for transplantation programs is clear, the worldwide availability and access to transplant services varies

widely. The Global Observatory on Donation and Transplantation (GODT) is an arm of the World Health Organization (WHO) and has been prospectively collecting data from the 194 member states of the WHO, with data provided by national health authorities whenever transplantation programs exist. In 2011, 62% of the 112,239 solid-organ transplantations that were reported occurred in high-income countries with only 9% and 1%, respectively, being performed in lower-middle and lower income countries. Of the reporting Member States of the WHO, 57% had some sort of transplantation program and 36% had deceased donor programs.³ There is a significant association between transplantation activity and country GDP per capita and percentage of GDP spent on health care. Until 2011 most of the increase in transplant activity had been observed in advanced economies.³ More recently, however, transplant activity in China⁴ and India⁵ have shown an exponential growth in activity due to the changing socioeconomic factors and development of pediatric transplant programs in these countries.

Reliable worldwide pediatric-specific data is difficult to find with known deficiencies and inconsistencies in reporting. It is likely that pediatric solid-organ transplant activity would follow the same trends as the published data, which combines adult and pediatric transplants. Pediatric transplant rates will most likely be disproportionately lower in developing nations when compared to the data published from advanced economies.

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Worldwide pediatric renal transplant activity

The burden of End Stage Renal Disease (ESRD) for children has been estimated to be around 200–300 per million age related population (pmarp) using robust registry data from high-income countries. Several worldwide registries systematically report prevalence rates of ESRD below 100 pmarp, an indication that these registries fail to capture the true burden of disease.⁶ Renal Replacement Therapy (RRT) rates are estimated to be around 83 pmarp in the US,⁷ 63 pmarp in Canada,⁸ 64 pmarp in Australia and New Zealand,⁹ 55 pmarp in Europe,¹⁰ and 22 pmarp in Japan.¹¹

Kidney transplant is the most common form of RRT in high-income countries and the transplant incidence rates reported are 10 pmarp in the US (2010 data)⁷ and 6 pmarp in Europe (2008 data), with a range in Europe from 0 to 13 pmarp strongly associated with country income.¹² In the developing world, pediatric transplant rates ranged from 1 to 2 pmarp in countries like Pakistan, Arab countries, and South Africa and less than 4 pmarp in Brazil.^{13–16} Within countries, access to transplantation varied depending on ethnicity and income.^{17–19} Regional discrepancies within developing nations have affected recipient access to transplantation. A recent Brazilian publication detailed a regional discrepancy of 3–4 fold decrease in access to a deceased donor transplant between children from the North/Midwest of the country compared to those from the South/South East.²⁰

Harmbat et al. (2016) estimate that less than 10% of children with kidney failure needing renal replacement therapy actually receive it.⁶ The unmet need is considerable in large parts of the world (especially in China, India and Pakistan, South Asia, Sub Saharan Africa, and Oceania), and as a result, thousands of children in these regions die due to ESRD without access to dialysis or transplant.^{6,21}

Worldwide pediatric liver transplant activity

Several liver transplant registries around the world collect data on activity and outcomes of liver transplants including pediatric liver transplants. In North America, 7% of all liver transplants are in children, 11% in Europe and 17% in Australia Organ Procurement and Transplant Network (OPTN) in North America,²² European Liver Transplant Registry²³ and Australia and New Zealand Liver Transplant Registry (ANZLTR).²⁴ Most of these transplants are from deceased donors, with 89% from OPTN data²² and 91% from ANZLTR data.²⁴

In contrast to this, in Japan, 35% of all liver transplants are done in children with the vast majority being living donor liver transplants (99.5%).²⁵ By 2013, the Japanese liver transplant society registry had recorded 2224 pediatric living donor liver transplants (1989–2013) with only 13 children having received deceased donor organs in that period. In South Korea, 85% of all pediatric liver transplants were from living donors.²⁵

In Latin America, pediatric liver transplant activity across the different countries varies. In 1980, the Latin American transplantation society was formed and it began collecting data into the Latin American transplant registry in 1989. Data collection has not however been consistent. As of 2016, a total of 4593 pediatric liver transplants were recorded.²⁶ A large proportion of pediatric liver transplants were done in Brazil followed by Argentina, Mexico, Chile, and Columbia. Due to the varying success with deceased donor organs, in Brazil 54% of all the liver transplants were from living donors.²⁶

In China, the China Liver transplant registry was set up in 2005. In 2007, Regulation of Human Organ Transplantation Legislation was passed and only certified centers could perform liver

transplants. By 2009, only 319 liver transplants in children had been performed due to cultural and economic reasons.²⁷ From 2011 onwards, there was a sharp rise in pediatric liver transplant activity with 25 centers able to perform these transplants. The improvements were driven by socioeconomic changes, increased availability of deceased organs, changing social attitudes, and increasing confidence in surgical outcomes.²⁸ In India, almost all pediatric liver transplants are done in private hospitals. With an expanding middle class increasingly able to afford out of pocket expenses for the transplant, this activity has shown an exponential rise in the last few years.^{5,29}

The reality in most developing countries with regard to access to liver transplant is illustrated in a Vietnamese report that reviews 280 children from 2009 to 2014 with chronic liver disease managed by a regional transplant center in Vietnam.³⁰ They identified 67 patients satisfying criteria for transplantation and of these, only 28.4% of parents consented to the procedure and only one transplant occurred in the time period.³⁰ Postulated reasons for the low consent and transplant rates included financial costs, distance from home, the reality of lifelong treatment and follow-up, and treatment and shortage of donors.

Worldwide intestinal transplant activity

In 2015, the Intestinal Transplant Registry (ITR) recorded a total of 2699 patients who had received intestinal transplants from 1985 onwards, of which, 697 (62%) were children. From 2007, the number of intestinal transplants has progressively declined due to better success with overall management of intestinal failure and due to persistent concerns about long-term outcomes in intestinal transplant recipients.³¹

The vast majority of intestinal transplants have been done in North America, particularly the United States. Europe does about one third of this volume, with small volumes in South America and even smaller volumes in Asia and Australia.³¹ So far, only two pediatric intestinal transplants have been performed in Australia.

In Asia, due to the issues with deceased donor organ availability, around 34% of their grafts come from living donors, compared to 1% in the rest of the world.³¹ In Japan, 10 out of 14 (71%) intestinal transplants for children had come from living donors.³²

Issues of organ availability and organization of transplant services across the world

In general, countries with greater access to medical care and high levels of gross national income per capita have better organized deceased donor programs allowing greater organ availability. The WHO consultation in 2010 classified five hierarchical levels of capacity with respect to provision of organ donation and transplant services in a given country.³ Level 1 being no local transplant activity to Level 5, a well-established multi-organ deceased donor transplant program with a government recognized authority responsible for oversight of donation and transplant activities. Although this is a generalization, several countries in the last decade have made important changes to the legislation and organization of organ donation that have resulted in significant increases in transplant activity. Notable are Turkey (2001), Korea (2006), Australia (2008), Brazil (2005), and Croatia (2011). Croatia's changes resulted in a tenfold increase in transplant activity. In China, Philippines, and Pakistan, there was an initial decline in activity after stricter regulations were put into place.³

The most successful model of organization of organ donation is the “Spanish model.” Spain has a presumed consent or opt out

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