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International pediatric transplant association (IPTA) guidance on developing and/or expanding pediatric solid organ transplantation programs in low- and middle-income countries

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Abstract

Pediatric solid organ transplantation (SOT) is a preferred treatment for medically suitable children with end-stage organ failure. Still, many of them have no access to transplantation owing to socioeconomic constraints or lack of transplant facilities in low- and middle-income countries (LMIC). Establishing pediatric SOT programs in LMIC offers children the opportunities to receive transplant care in more familiar home environments as well as help curtail transplant tourism and improve transplant outcomes as pediatric transplantation would be performed ethically and legally. The International Pediatric Transplant Association (IPTA) is a professional organization aiming to promote safe, ethical, and high-quality pediatric transplantation worldwide. This society paper describes major obstacles to pediatric SOT in LMIC and provides guidance on developing and/or expanding pediatric SOT programs in such countries. We also summarize available resources from the IPTA Outreach Program to help establish and support pediatric SOT programs in LMIC.

KEYWORDS
children, solid organ transplant, transplant program

1 | INTRODUCTION

Pediatric solid organ transplantation (SOT) is a preferred therapeutic modality for medically suitable children with end-stage organ failure. Like many high-income countries (HIC), the burden of end-stage organ disease and unequivocal need for SOT in children exists in low- and middle-income countries (LMIC).[1–4] Yet, many of them have no access to transplantation owing to socioeconomic constraints or lack of transplant facilities in their countries,[2,3,5] raising concerns for transplant tourism.[5–7] Because the most common causes of childhood mortality in these countries are neonatal disorders, preventable infections, and malnutrition,[8–10] their governments and health authorities are still focusing on the essential healthcare interventions, such as perinatal and newborn care, immunization, and infection prevention.[4,9] Since transplantation demands extensive resources and is a costly procedure, developing pediatric SOT

Abbreviations: CMV, cytomegalovirus; EBV, Epstein–Barr virus; HIC, high-income countries; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; ICU, intensive care unit; IPTA, International Pediatric Transplant Association; LMIC, low- and middle-income countries; SOT, solid organ transplantation; WHO, World Health Organization.

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programs might be a low priority in the healthcare planning of such countries.[11] In some countries, despite having adult transplant programs, pediatric SOT programs have not yet been established.

The International Pediatric Transplant Association (IPTA) is a professional organization aiming to advance the science and practice of pediatric transplantation to improve the health of all pediatric transplant recipients around the world. One of its important missions is to promote safe, ethical, and high-quality pediatric transplantation worldwide. Establishing pediatric SOT services in LMIC offers children the opportunities to receive transplant care in more familiar home environments, contributing to the psychosocial aspects of child care and the family dynamics within the health systems. Moreover, the availability of pediatric SOT programs in these countries will help curtail transplant tourism and improve transplant outcomes as pediatric transplantation would be performed ethically and legally.[5] Improving children's access to pediatric SOT through successful pediatric transplant programs also helps reduce the existing disparity in global transplant activities.[12] Thus, we aim to provide guidance to help develop and/or expand pediatric SOT programs in LMIC, focusing on liver and kidney transplants because these are the most likely organ transplanted in these countries.

2 | OBSTACLES TO PEDIATRIC SOLID ORGAN TRANSPLANTATION IN LOW- AND MIDDLE-INCOME COUNTRIES

In the earliest stage, the national health authorities should review the local epidemiology and statistics to understand if the burden of end-stage organ disease and the projected annual transplants in children are sufficient to develop a pediatric SOT program. A major challenge in LMIC that might impact post-transplant outcomes is that children needing SOT are often diagnosed and referred late due to lack of access to specialty care and/or socioeconomic constraints. This late referral has been demonstrated to result in more significant morbidity and lower transplantation rates in children.[13] Additionally, the high incidence of malnutrition and increased burden of infectious diseases in LMIC may further impact post-transplant recovery and outcomes.[4]

Several key obstacles must be identified and addressed before new pediatric SOT programs can be successfully implemented in LMIC. These include but are not limited to the country's geographic characteristics,[3,5,11,14–17] socioeconomic, and cultural backgrounds,[2,5,11,16–18] resource availability,[2,3,5,11,15,18] healthcare structure,[15,19,20] and low organ donation rates (Table 1).[18,21–24] Transplant needs in LMIC should be tailored for socioeconomic peculiarities because pediatric SOT is a costly procedure and requires a lifelong commitment by patients and their families. The majority of the patients with unrecognized and/or untreated end-stage organ disease needing SOT in LMIC belong to the socioeconomically disadvantaged group, and their families cannot afford a transplant procedure.[17,25,26] The long-term costs of lifelong immunosuppression and the availability of pediatric formulations, frequent laboratory tests, long-term follow-ups, and unpredictable admissions for post-transplant complications could also be challenging, even for children in high-income families.[2,4] Moreover, socioeconomic constraints might affect patients' ability to return to the transplant centers for timely management of post-transplant complications and long-term follow-up, further impacting patient and graft outcomes.[11]

Access to health services and transplantation also depends upon the healthcare structure in each country.[19,20] Inadequate healthcare coverage remains the most important barrier to pediatric SOT in LMIC with limited government-funded coverage, in which patients and their families bear most healthcare costs.[2,15,19] Additionally, in countries where the private health systems have developed transplant programs, transplant patients are followed in private facilities, although they may have public health coverage or are in low-income households.[2,14]

The country's geographic characteristics and the central location of SOT programs may significantly limit the access of patients and their families residing in remote regions to transplant centers.[3,11,14,15,17] This also affects their access to early diagnosis and referral, ultimately reducing their chance of having a transplant. They may also experience high travel costs, which, if without financial support, results in a reduced chance of seeking medical advice or admissions for transplant-related complications. Furthermore, various sociocultural and religious reasons might also impact the success of SOT programs in LMIC (Table 1).[21,22,27] In some countries, although appropriate human and technological resources are available, SOT program activities remain limited due to issues with low donation rates and severe organ shortage (Table 1).[14,21–24]

3 | DEVELOP AND/OR EXPAND PEDIATRIC SOLID ORGAN TRANSPLANTATION PROGRAMS IN LOW- AND MIDDLE-INCOME COUNTRIES

Building a pediatric SOT program is a complex process involving all leadership and stakeholders. It requires governmental and institutional commitment for the investment of time, personnel, and resources, along with other essential aspects such as regulations and funding. Each type of organ transplant program has its specific challenges. Still, prerequisites for establishing a new pediatric SOT program include regulatory and ethical considerations, organ procurement organization, essential healthcare infrastructure, a well-coordinated and dedicated multidisciplinary transplant team, clinical protocols for pre- and post-transplant management, availability of age-appropriate pediatric formulations and drug monitoring, and funding.

3.1 | Regulatory and ethical requirements

3.1.1 | Legislation

The initial step to developing a SOT program is to establish a legal framework to define brain death (if deceased organ transplantation

TABLE 1 Major obstacles to developing pediatric SOT programs in LMIC and proposed solutions

Obstacles	Possible reasons	Proposed solutions
Geographic accessibility[3,5,11,14,15,17,55]	• Geographic characteristics of a country and central location of transplant programs may limit access of patients/families residing in remote regions to transplant centers	• Government support, financial aid program, charities to help improve access to transplant centers
Socioeconomic disparities[2,5,11,15–18]	• Limited access to transplant due to cost barriers in patients with low socioeconomic status • Lack of funding for long-term immunosuppressants	• Government support, financial aid programs, philanthropic organizations, government and community partnerships • Liaison with pharmaceutical companies for access to affordable immunosuppressants or low-cost generic medications
Resource availabilities[2,3,15,18,53]	• Lack of expertise, technological resource, essential infrastructure, and logistics • Financial constraints	• Collaboration with experienced transplant centers for training opportunities and support • Liaison with governmental and non-governmental organizations, partnerships between public and private sectors
Healthcare structure[15,19,20]	• Access to health services and transplant depends upon the model of private or public healthcare coverage in each country	• Develop local alliances and investment by local authorities • Investment from private sectors into transplant field • Partnerships between public and private sectors
Low rates of deceased organ donation and severe organ shortage[14,18,21–24]	• Lack of infrastructure to facilitate deceased organ donation • Lack of dedicated organizations to coordinate organ procurement[6,14] • Lack of institutional mechanisms to approach the families of potential deceased donors[56] • Lack of notification on potential brain-dead donors[15] • Lack of adequate donor care in the region[11,15]	• Health authorities to develop effective strategies to improve the detection and procurement of donors • Establish hospital organ procurement organization by giving an incentive to hospitals actively involved in organ procurement[33] • Increase awareness about the detection of potential donors among intensivists and emergency providers[14] • Engage medical and nursing staff in intensive care units in identifying and approaching family members of potential deceased donors[57] • Involve well-trained organ donation coordinators
	• Lack of public awareness on organ donation[3,5] • Concept of brain death and the benefit of organ transplant are not fully appreciated; lack of education and support among public and medical profession[6,11,27] • Cultural and religious beliefs[5,6,11,18,21–23,32]	• Establish an organ donor foundation to educate and increase public awareness about organ donation • Public educational campaigns to minimize refusal rate for organ donation • Public awareness campaign targeting public places (clubs, sports events, local businesses, colleges, and universities); involve religious leaders • Establish community networks (e.g., social media among patients/families) • Develop living donor transplant programs
	• Mistrust of medical professionals[5,23]	• Develop guidelines and protocols on identifying potential donors, determining brain death, and withdrawing mechanical supports • Standardize organ procurement procedures • Establish organ donor and recipient registries to promote fairness and transparency in the process of organ donation and allocation • Establish a transparent regulatory oversight system to ensure donor and recipient safety and prevent unethical transplant practices[28] • Maintain good communication between medical professionals and patients/families
	• Lack of legal framework and government support[5,11]	• Develop a legal framework to define brain death • Establish legislation on organ donation and sharing • Develop a national deceased donor identification and organ procurement system • Establish organizations for donor and recipient registries and national networks for organ sharing to assure fairness in organ allocation • Intergovernmental/international cooperation in helping develop and implement effective legislative framework[58]

is considered) and legislation on organ donation to ensure maximal fairness, safety, transparency, and efficiency in organ donation, as emphasized in the Declaration of Istanbul and the World Health Organization (WHO) guiding principles on human cell, tissue, and organ transplantation.[28,29] The national legislation supporting organ donation must indicate whether the country supports the recovery of organs from deceased donors and subsequent transplant into children (if deceased organ donation is considered) or supports the recovery of organs from living donors and subsequent transplant into children (if living organ donation is considered).[30] In countries accepting the death penalty, the national transplant law must also exclude the procurement of organs from prisoners sentenced to death. Many LMIC lack these regulations, and policies in HIC might not always be adapted due to differences in socioeconomic backgrounds and healthcare structure. Thus, LMIC should consider their healthcare structure to develop an appropriate national legal framework for organ donation and sharing.[29,31] Still, even in countries where the organ transplantation law has been established, organ donation programs' activities remain limited due to lack of government support, poor public awareness and support, and differences in cultural and religious beliefs (Table 1).[3,11,22,23,27,32] Indeed, the government plays a critical role in increasing organ donation rates and should be involved at multiple levels, from establishing a legal framework to raising public awareness.[4] Published literature has demonstrated that strong governmental support has led to increasing trends in deceased and living donation transplants.[16,22,33,34]

3.1.2 | Ethical considerations

Several ethical aspects should be considered regarding consent and equitable allocation of donated organs. In countries where deceased transplantation is considered, a written consent for deceased organ donation must be obtained from the family. If living organ donation is considered, a written protocol on the selection and management of living donors must be approved by the local Ethics Committee or the Institutional Review Board. An informed consent from living donors should include full respect of donor's autonomy, absence of financial gain, donor's awareness of the voluntary nature of the donation, and acknowledgment of the right to refuse donation at any time. Living donors should be legally competent, capable of weighing the information, and act free of any undue influence or coercion.[31] The final approval of the living organ donation should be given by an appropriately qualified, independent review committee. Health authorities should also ensure the same standard of care, including long-term follow-up, for both the living donor and the recipient.[28,31]

3.2 | Organizational structure

In countries where deceased organ transplantation is considered, the transplant center must be affiliated with an organ procurement organization. A written agreement between the transplant center and the organ procurement organization must be established. Organ procurement is a specific part of transplantation that requires effective networks for matching and sharing donated organs. The organ procurement organization is responsible for overseeing organ procurement, identifying, and coordinating the allocation of all donated organs. It is also essential to establish the national organ procurement and transplantation network with robust data systems able to protect privacy to maintain a list of patients who need organs, maintain a national system to match organs and patients, and assist in distributing donated organs across the regions.[35]

3.3 | Infrastructure requirements

Successful SOT programs demand adequate healthcare infrastructure.[28] Given the multidisciplinary nature of transplant programs, pediatric SOT programs must be established in tertiary hospitals equipped to perform complex pediatric surgeries. However, pediatric SOT programs are often integrated into existing adult SOT programs owing to a small number of pediatric transplants performed in most countries worldwide. This allows sharing of resources and skills between adult and pediatric transplant programs.[11] Thus, the availability of a regional adult SOT program providing the same organ transplant service is a prerequisite for establishing a new pediatric SOT program. The adult SOT program offers clinical support for the pediatric SOT program and accepts care of these transplant children when they transition to adult care.[30]

The transplant hospital should have a self-sustained intensive care unit (ICU), designated post-transplant care ward and outpatient clinics, onsite acute dialysis services, interventional radiology, and essential specialty services. Laboratory services include routine diagnostic biochemistry and hematology, therapeutic monitoring of immunosuppressants, microbiology, pathology, blood bank with the availability of leukocyte-reduced and irradiated blood products, and tissue immunology or human leukocyte antigen typing laboratory. These specialty services may not be available in the same institution in LMIC and can be outsourced to other regional hospitals. Additionally, in countries where deceased organ transplantation is considered, coordination between the transplant center and the donor hospital is critical to avoid prolonged cold ischemia time that may deteriorate allograft function. Moreover, the availability of histopathology services in a timely fashion is also crucial in post-transplant care and maintenance of allograft function.

3.4 | Personnel and training

A pediatric SOT program structure generally involves many disciplines contributing to patient care. It consists of a dedicated multidisciplinary team of surgical and medical expertise (including essential pediatric subspecialists), pediatric anesthesiologists, nursing staff,

clinical psychologist(s), pathologist(s) with expertise in organ transplant, diagnostic and interventional radiologists, dietician(s), clinical pharmacist(s) with expertise in transplant medications, transplant coordinator(s), transplant administrator(s), social worker(s), and financial coordinator(s). Unlike adult SOT programs, pediatric SOT programs also demand additional (but optional) services, such as child life therapy, school teachers, speech and language therapy, and neurocognitive and developmental psychology.

3.4.1 | Team leader and key medical personnel

The transplant program director can be either a transplant surgeon or a medical specialist (e.g., adult or pediatric cardiologist, gastroenterologist/hepatologist, and nephrologist) and is responsible for assembling a broad spectrum of healthcare providers. The administrative leadership is also needed to oversee all activities of the pediatric SOT program. Transplant professionals require prerequisite skills and additional training and commit a significant time to transplant activity. The surgeon(s) should be competent to perform transplant surgery in children and manage transplant-related surgical complications. Pediatric specialists (e.g., cardiologists, gastroenterologists/hepatologists, and nephrologists) are responsible for managing pre- and post-transplant medical complications and should have the necessary transplant training or experience. These key medical professionals also help develop evidence-based clinical protocols for pre- and post-transplant management in consultation with more experienced transplant centers and respective professional society guidelines. Allied health and nursing professionals also play an important role in promoting a new transplant system.

During the program's initial phase, collaboration and twinning with a well-established, high-volume transplant program can provide international training opportunities and support. Pediatric SOT programs in LMIC can also be initiated and supported by visiting transplant surgeons from international, more experienced transplant programs for skills and knowledge transfer.[3,5,11,36] Yet, a major issue in LMIC is that most skilled transplant surgeons and pediatric specialists trained abroad may face challenges with bureaucratic healthcare systems and suboptimal medical infrastructure when returning to their home countries.[4] Hence, government and health authorities should establish mechanisms to provide support and necessary professional incentives to retain them. These skilled specialists will eventually help sustain and expand the transplant program and provide further training to other regions.

An experienced ICU and nursing staff dedicated to transplant care are essential to ensure an optimal post-transplant outcome. The unpredictable working hours, increased work volume, and the urgent nature of transplant and transplant-related complications require a significant turnover of some personnel.[35] Thus, the transplant hospital should ensure adequate staffing and availability of essential hospital services, operating rooms, ICU and hospital beds.

3.4.2 | Transplant coordinator

This person is often a registered nurse and plays a crucial role in outpatient and inpatient settings. He/she helps provide patient and family education and coordinates care for the patients in all transplant phases, from the transplant evaluation to post-transplant care. He/she is also responsible for managing the transplant waitlist in coordination with other transplant team members, arranging all laboratory and follow-up appointments, and overseeing test results and medication compliance.

3.4.3 | Other ancillary staff members

Clinical pharmacist(s) with expertise in transplant medications have an essential role in providing a comprehensive assessment and education to patients and their families at transplant evaluation, during transplant admission and at discharge, and in post-transplant outpatient clinics. Given the complexity of the transplant process and post-transplant care, frequent outpatient visits, and unpredictable admissions requiring transportation, social service is also essential to provide support and help at every transplant stage. A clinical psychologist, psychosocial coordinator, or social worker can help perform psychosocial evaluation, assess, and coordinate the psychosocial needs of patients and their families. Other ancillary support specialties include transplant infectious disease, clinical nutrition, respiratory therapy, occupational and physical therapy, speech and language therapy, and neurocognitive and developmental psychology.

3.5 | Medications, consumables, laboratory tests

Table 2 summarizes essential medications, diagnostic tests, and procedures needed for pediatric SOT in LMIC, most of which are also included in the WHO model lists and recommendations of essential medicines, in vitro diagnostics, and priority medical devices for child health that have been used worldwide to prioritize resource allocation.[37–39]

3.6 | Infection control

A significant cause of death in immunosuppressed patients is infection. This is even more important in LMIC, where infections are considered a significant cause of morbidity and mortality in pediatric transplant recipients.[1,11,18,27,40] Thus, pre- and post-transplant age-appropriate immunization is of great importance, and infection control procedures must be carefully addressed. The transplant unit's design, location, size, and air control systems should be tailored to the local infrastructure, available resources, and funding.[41] An antimicrobial stewardship program coordinating interventions to improve and measure the appropriate use of

TABLE 2 Essential medications, diagnostics, and procedures for pediatric SOT in LMIC

Medications[a]	Laboratory tests and imaging[a]	Procedures
Immunosuppressants: **anti-thymocyte globulin (rabbit)**, **basiliximab**, azathioprine, cyclosporine, **tacrolimus**, **sirolimus**, **mycophenolate**, methylprednisolone, prednisone/prednisolone Other immunosuppressants used to treat post-transplant lymphoproliferative disorders: rituximab, cyclophosphamide	**Therapeutic monitoring of immunosuppressants (e.g., cyclosporine, tacrolimus, and sirolimus levels)**	• Allograft biopsy • Gastrointestinal endoscopy • Percutaneous transhepatic cholangiography (if liver transplant) • Dialysis services
Common post-transplant anti-infective agents: • Antibiotics according to local antibiograms (if available) • Antiviral: acyclovir, ganciclovir, valganciclovir, **CMV immune globulin** • Antifungal: clotrimazole, fluconazole, nystatin, voriconazole • Prevention of *Pneumocystis jiroveci* pneumonia: sulfamethoxazole-trimethoprim, pentamidine, dapsone	• Hematology: complete blood count, prothrombin time/international normalized ratio (INR), partial thromboplastin time, D-dimer, fibrinogen, iron studies, direct antiglobulin test, blood typing, crossmatch, isohemagglutinins titers • Clinical chemistry: comprehensive metabolic panel, glomerular filtration rate, lipase/amylase, C-reactive protein, procalcitonin, lactate, blood gas, pregnancy test • Immunoglobulin G level and **autoantibodies (e.g., antinuclear antibody, anti-smooth muscle antibody, anti-liver/kidney microsomal type 1 antibody)** • Tumor markers: lactate dehydrogenase, alpha-fetoprotein • Urine: urinalysis, urine chemistry, urine albumin:creatinine ratio, urine protein:creatinine ratio, pregnancy test	
Other medications: intravenous immunoglobulin, diuretics, anti-hypertensive medications, anti-ulcer medications (ranitidine, omeprazole), anti-platelet medication (acetylsalicylic acid), anticoagulants (enoxaparin, warfarin), vitamin K (phytomenadione), vitamin, and micronutrient products	Microbiology: • Essential viral serologies and/or PCR: hepatitis A/B/C, HIV 1 and 2, **CMV**, **EBV, Varicella** • Essential diagnostic tests for bacterial and fungal infections • Blood, urine, body fluid cultures • Stools: ova and parasite, cultures, ***Clostridium difficile* toxin** • Tuberculosis, endemic infectious disease screening Histopathology: assessment of tissue for infection, inflammation, neoplasia, and **diagnosis of allograft rejection** **Immunology and HLA typing (e.g., tissue typing of donor and recipients, donor/recipient crossmatch testing, pre- and post-transplant HLA antibody testing)** Imaging: X-ray, abdominal ultrasound (including Doppler), portable ultrasound, computed tomography scan/magnetic resonance imaging, **angiography**, electrocardiograms, echocardiogram	

Abbreviations: CMV, cytomegalovirus; EBV, Epstein–Barr virus; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; LMIC, low- and middle-income countries; SOT, solid organ transplantation; WHO, World Health Organization.

[a]Bolded items are not included in the WHO lists of essential medicines, in-vitro diagnostics, and priority medical devices for child health[37–39]

antimicrobials is also essential to minimize the risks of developing antibiotic-resistant organisms commonly seen in LMIC. Strict handwashing, proper personal protective equipment, safe injection practices, and skilled central venous line care are simple, inexpensive, but effective measures to control the majority of severe infectious complications.

Furthermore, cytomegalovirus (CMV) and Epstein–Barr virus (EBV) infections are prevalent in LMIC.[42,43] These infections remain particular concerns for transplant children due to an increased risk for the development of end-organ CMV disease and post-transplant lymphoproliferative disorders.[44–46] CMV infection has also been associated with allograft rejection, chronic allograft nephropathy in renal transplant children, and cardiac allograft vasculopathy disease in heart transplant patients, although the prevalence of these indirect effects varies according to the transplant type and concomitant EBV infection.[44,45,47–49] Therefore, evidence-based protocols for screening, monitoring, prevention, and management of CMV and EBV infections should be established to improve post-transplant outcomes in these pediatric SOT recipients.[44–46] These protocols should be regionally appropriate, taking into consideration the local epidemiology and cost–benefit ratios.

3.7 | Information technology

Effective communication between the transplant team and patients and their families is essential to ensure successful

post-transplant outcomes. The use of telehealth or telemedicine to deliver health care across the country, especially to remote areas, is helpful for early referral and long-term post-transplant care.[50] Yet, the challenge in low-income patients and families is that they may not be familiar with these technologies or have access to the needed equipment. There might also be poor network connectivity for those living in remote regions. In this case, modern telecommunication such as mobile phones, texting, and email can also be helpful.[11,50]

Technology is also beneficial for connecting the transplant team with international colleagues to discuss challenging cases and further training. Online data sharing and teleconferencing are cost-effective for consultations on radiology and histopathology.[50] Digital pathology image systems also offer a promising tool for convenient sharing of histopathology slides that can be reviewed remotely by multiple pathologists worldwide for diagnostics, consultation, education, and research purposes.[51] However, data security and patient confidentiality must be ensured strictly. Real-time connection with more experienced transplant teams for making intraoperative decisions is also beneficial to strengthen the transplant team's confidence during the inception phase.[50]

3.8 | Patient education

Transplantation demands intensive patient education throughout all phases of transplant care to ensure successful post-transplant outcomes. Patient education can be delivered via brochures, handouts, audiovisual and electronic materials. Group patient education days can also be a time-effective methodology. Patient educational resources are available on the IPTA website (https://tts.org/outreach/outreach-about); however, these materials should be adapted according to local sociocultural backgrounds and available in various local languages.

3.9 | Quality assessment and performance improvement

Maintaining a good quality transplant program is the most effective way to improve transplant outcomes. The administrative leadership plays an essential role in evaluating the transplant program's performance through quality assurance and improvement projects. The transplant program should establish objective metrics specific to the organ type and define benchmarks for outcome improvement and error reduction for each transplant phase. Data reporting on transplant volume and patient and graft survivals are essential. Still, databases on patient demographics, clinical information, and transplant-related variables are also helpful to advance clinical research and transplant outcomes.[15] An ultimate goal should be the national collection of this data and international sharing of deidentified outcome data to improve outcomes and ensure transparency. These projects, however, require dedicated personnel and access to specific software and statistical resources that might not always be available in LMIC.

3.10 | Funding

Pediatric transplantation requires extensive resources and, thus, demands high-cost care. The overall cost of a transplant procedure depends upon the organ type, the transplant program's geographic location, and the country's healthcare financing system. The cost of transplant care in children is even higher because pediatric SOT recipients often require a more extended ICU stay, more prolonged hospital stay following transplant, and more frequent post-transplant admissions than their adult counterparts. Other costs include routine monitoring laboratories, allograft biopsies, immunosuppression and other medications, unexpected post-transplant procedures, and unpredictable admissions.

The World Bank defines countries with low-income and lower middle-income economies as those with a gross national income per capita of US $1045 or less and between US $1046 and $4095, respectively.[52] The average cost of a transplant procedure in LMIC varies widely[3,16,53,54]; it has been estimated at least US $13000,[3,54] in addition to the yearly cost of at least US $2000 for immunosuppression, monitoring laboratories, and follow-up visits.[54] Thus, in countries with limited public and insurance health coverage, most patients and their families cannot afford the cost of a transplant and long-term immunosuppression.[3,7,11] Although a transplant procedure costs much lower in LMIC than in HIC, it may still constitute much more than an average annual household income.[3] Financial constraints not only make resource allocation and spending on healthcare a significant challenge in LMIC but also are the major reason for parental refusal of transplants.[2,3,17] Hence, pediatric SOT programs should consider exploring all available resources, such as lobbying pharmaceutical companies for cost-free immunosuppression or access to affordable immunosuppressants or low-cost generic medications,[11] and liaising with various funding agencies (e.g., government and philanthropic organizations, government and community partnerships) to provide free immunosuppression or financial support for patients and families in need.[5,18,53] A financial coordinator is crucial to coordinate financial resources and assist patients and their families in navigating this complex financial process.

3.11 | Sustainability

Once a pediatric transplant program has been started, it is crucial to ensure sustainability. Financial constraints are still the most significant factor in expanding the transplant numbers and sustaining pediatric SOT programs in most LMIC. A common obstacle to maintaining pediatric SOT programs in these countries is the availability and long-term cost of immunosuppression, which can be overcome by liaising with pharmaceutical companies to access affordable

immunosuppression.[11] There is also the need for continuing training of key personnel and nursing staff and adequate financial support and professional incentives to retain them.[53] Maintaining regular clinical meetings, morbidity and mortality rounds, and data review of quality assurance process and post-transplant outcomes is essential to improve transplant care. Continuous governmental support and international partnerships are also crucial to help sustain pediatric SOT programs in LMIC.

4 | IPTA OUTREACH PROGRAM

The success of a SOT program depends upon several important factors, such as essential medical infrastructure, trained surgical and medical professionals, and public perception and awareness of organ donation.[4] Because LMIC might not have these elements in place, the IPTA Outreach Program has support available to help establish pediatric SOT programs in these countries. The Outreach Program aims to engage with centers needing to develop new pediatric SOT programs or support existing programs seeking to expand their activity and/or improve the quality of their transplant services. Since its inception in 2007, the Outreach Program has supported 8 sister programs.

The Outreach Program takes place in three phases: (1) identification of emerging and sponsoring centers, (2) onsite or virtual visit for assessment of program needs and potential, and (3) follow-up and post-assessment. Generally, an emerging center will identify a suitable supporting transplant center (if an existing relationship has been established) to partner with (i.e., sponsoring center), but the Outreach Program can also assist in this process. Based on the specific program needs, the Outreach Program, in collaboration with the sponsoring center, can assist in (1) providing training of medical, nursing, and allied health personnel; (2) supporting the development of clinical programs, standards, and resources; and (3) advocating for the specific regional needs of children for transplantation and access. The emerging center is expected to submit an annual report on progress to the Outreach Program Committee, which will have to continue for 5 years after the approval for the center to remain active under the Outreach Program. Further information on the selection process, required documents, and application package are available on the IPTA website (https://tts.org/outreach/outreach-about). Specific questions about the application and submission can also be directed to the IPTA administration at info@iptaonline.org.

5 | CONCLUSIONS

Low- and middle-income countries face unique challenges in building and sustaining SOT programs for children. With careful planning, advocacy, effective regulations, strong governmental and institutional support, and international partnerships, safe, ethical, and high-quality pediatric SOT programs can be successfully implemented and/or expanded in LMIC, despite limited resources. Support is available from the IPTA Outreach Program in providing training, organizational support, and establishing guidelines and procedures.

AUTHORSHIP

H.D.V. conceptualized the manuscript, drafted the initial manuscript, revised the manuscript for important intellectual content, and approved the final manuscript as submitted. F.M., M.Mc., and R.R. conceptualized the manuscript, revised the manuscript for important intellectual content, and approved the final manuscript as submitted.

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