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Review Article

Renal transplantation in children: Current status and challenges

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ABSTRACT

Renal transplantation is the treatment of choice for children with end-stage renal disease (ESRD) since it decreases morbidity and mortality and improves quality of life. Potent immunosuppressive medications have significantly improved the short and medium-term outcomes while long-term outcomes continue to remain a challenge. This article reviews the current practices involved in the care of pediatric renal transplant recipients and challenges faced by them. Here, we provide a brief overview of various aspects of care for pediatric renal transplant recipients that include indications and contraindications, immunologic workup, pre-transplant evaluation, currently used immunosuppressive therapies, long-term complications and graft survival.

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Renal transplantation is the treatment of choice for children with end-stage renal disease (ESRD) since it decreases morbidity and mortality, improves nutrition, growth and quality of life in comparison to chronic dialysis.¹ A lot of progress has been made since first successful transplant was performed in identical twins in December 1954. Successful transplantation has brought forth new challenges which must be dealt with to make further progress in this field. Young children face unique challenges due to their small size, immature immune system, viral naïve status and unique bladder issues in those with ESRD due to congenital anomalies of kidneys and urinary tract (CAKUT). In addition, impact of changing growth parameters, hormonal milieu, metabolism, psychosocial and behavior development during adolescence

and early adulthood on transplant is not well characterized as many young children with successful transplant develop allograft failure upon reaching adolescence.² Addressing these challenges would help improve long-term graft survival.

1. Indications and contraindications to transplantation

Children are usually excellent candidates for kidney transplantation due to absence of co-morbidities. However with increasing survival of extremely premature and those with genetic syndromes, many children with significant co-morbidities are developing ESRD. Renal transplantation in these

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Table 1 – Contraindications to renal transplantation in children.

Absolute contraindications	Relative contraindications
<ul style="list-style-type: none"> • Acute infection • Untreated malignancy • Oxalosis, methylmalonic aciduria and other genetic syndromes that might benefit from a combined liver-kidney transplant • Life-limiting co-existing medical conditions: advanced cardiac, pulmonary, neurologic or other systemic disease • Multi-organ failure • Progressive neurologic illness • Persistent vegetative state • Pregnancy 	<ul style="list-style-type: none"> • Uncontrolled HIV, hepatitis B or C infection • BKV and other infections • Recurrent FSGS in previous transplant • Active immune mediated glomerulonephritis (SLE, anti-GBM and ANCA associated GN) • Extreme obesity and malnutrition • Psychosocial concerns including poor adherence with medical regimen

HIV: human immunodeficiency virus; BKV: BK virus; FSGS: focal segmental glomerulosclerosis; SLE: systemic lupus erythematosus; GBM: glomerular basement membrane; ANCA: anti-neutrophil cytoplasmic antibody; GN: glomerulonephritis.

children is surgically, medically and ethically challenging and needs thoughtful multidisciplinary approach to help families make decision for their children.³

While there is no clear agreement on the contraindications to renal transplantation in children, general contraindications to renal transplantation in children are listed in Table 1.⁴⁻⁶

Psychosocial concerns, poor adherence to medical therapies including ability to afford long-term medications and medical monitoring remains one of the biggest challenges facing successful renal transplant in children and needs to be carefully addressed prior to and on ongoing bases.

2. Pre-transplant evaluation of the recipient

Pre-transplant evaluation aims to optimize the outcome of transplant so that adequate preparations can be made prior to these patients receiving transplant (Table 2).^{4,6}

Congenital abnormalities of the kidney and urinary tract (CAKUT) are a leading cause for CKD and ESRD. Some of these abnormalities, especially those affecting the lower urinary tract may have to be addressed prior to the renal transplantation with the aim of achieving normal/high capacity and compliant urinary bladder. Poor graft function or graft loss can be a direct consequence of a poorly compliant bladder which may transmit the high intravesical pressure to the upper urinary tract and newly transplanted kidney.⁷ Pre-transplant urologic evaluation by vesicocystourethrogram (VCUG), uroflow and urodynamics and surgery if required for bladder augmentation, obstructive uropathy or reflux should be performed prior to transplant. Some children with obstructive uropathy may require creation of Mitrofanoff for clean intermittent catheterization and some may require incontinent urinary diversion depending upon each child and family's unique circumstances. Some children with chronically infected kidneys may require native nephrectomies prior to transplant.

3. Donor source

While children can receive allografts from deceased donors, living donor allografts have a distinct advantage of providing longer half-life¹ due to healthier organs and decrease in cold

ischemia time (CIT). Increased CIT increases risk of acute rejection (AR) by enhancing the expression of HLA antigens and adhesion molecules on the surface of endothelial and renal tubular cells.⁸ Fig. 1 demonstrates the patient and allograft survival over time after living vs deceased donor renal transplants.⁹ Living donors also offer the advantage of scheduling a pre-emptive transplant which saves the need and costs associated with initiation of dialysis. Such

Table 2 – Pre-transplant evaluation of children.

1. *Detailed history:* Establish the cause of ESRD to evaluate risk of primary disease recurrence post-transplant, e.g. in FSGS and atypical HUS
Identify need for native nephrectomies prior to transplant (chronic infections or congenital nephrotic syndrome, large polycystic kidneys, intractable hypertension)
Nutrition evaluation and optimization
2. Complete physical examination with special focus on GU, lower spine, perineum and neurologic examination
3. *Immunization:* Ensure up to date immunizations including pneumovax-23 and meningitis since live viral vaccines are contraindicated after transplant
3. *Psychosocial evaluation/counseling of the child and family:* Important for transplant success since non-adherence to therapy is the most important cause of late graft failure
3. *Immunologic evaluation:* ABO and HLA typing, screening for anti-HLA antibodies, cross match
4. *Exposure to infections:* Antibodies to viral infections (CMV, EBV, HSV, HIV, Varicella Zoster virus, hepatitis B and C), hepatitis B surface antigen, serologic tests for syphilis, chest X-ray and tuberculin testing.
5. *Urologic evaluation:* Important since UTIs or high bladder pressure can adversely affect graft survival. Urinalysis and urine culture, ultrasonography including post-void images of the bladder, VCUG. Voiding diary, uroflow, urodynamics and rarely cystoscopy in patients with complicated urologic problems.
6. *Optional:* Neurocognitive evaluation, hematologic evaluation if suspected to be at risk for thrombosis, cardiac, pulmonary, dental and ophthalmologic as indicated.

FSGS: focal segmental glomerular sclerosis; HUS: hemolytic uremic syndrome; GU: genitourinary; HLA: human leukocyte antigen; CMV: cytomegalovirus; EBV: Epstein-Barr virus; HSV: herpes simplex virus; HIV: human immunodeficiency virus; VCUG: voiding cystourethrogram.

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