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RESEARCH ARTICLE

PEDIATRIC KIDNEY TRANSPLANT RECIPIENT EVALUATION: UNIQUE CONSIDERATIONS AND MANAGEMENT STRATEGIES

Abdulrahman Ishag[1], Dr. Mohammed Abbas[2], Mujtaba Abdelrahem Ahmed Abdelrahem[3], Mohammed Mahmmoud Fadelallah Eljack[4] and Umalhassan Alawad Abdallah Elamin[5]

[1]University of Sinnar, Sennar, Sudan, Internal Medicine; [2]University of the Holy Quran and Islamic Sciences, Omdurman, Sudan [3]University of Sinnar, Sennar, Sudan, Faculty of Medicine; [4]University of Bakhtalruda, Ad Douiem, Sudan, Medicine and Health Sciences; [5]University of Khartoum, Khartoum, Sudan, Clinical Pharmacy

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Corresponding author:
Abdulrahman Ishag

ABSTRACT

Background: Pediatric kidney transplantation requires distinct clinical and immunological strategies compared to adult recipients, due to developmental physiology, growth implications, and unique disease etiologies leading to end-stage renal disease. This review synthesizes the critical, age-specific considerations necessary to optimize evaluation, management, and long-term outcomes in this vulnerable population. Methods: A comprehensive review of contemporary literature and clinical guidelines was conducted. Key subjects were analyzed, including pre-transplant multidisciplinary assessment (encompassing urological, cardiovascular, and psychosocial evaluation), surgical challenges in tiny recipients, immunogenetic factors, immunosuppression protocols, and adherence strategies. Results from relevant studies were integrated to provide management strategies. Results: The management of pediatric kidney transplant recipients needs a personalized, multidisciplinary approach. The main findings highlight the importance of detailed urological assessment and reconstruction, the significant impact of Human Leukocyte Antigen (HLA) matching on graft survival and retransplantation wait times, and the efficacy of certain immunosuppression protocols. Moreover, medication non-adherence, particularly during adolescence, was identified as a major risk factor for graft loss. A structured transition process from pediatric to adult care is essential for maintaining long-term allograft function. Conclusions: Successful pediatric kidney transplantation depends on addressing the specific anatomical, developmental, and immunological characteristics of children. Integrating rigorous pre-transplant preparation, individualized immunosuppression, and strong planning for transition can significantly improve graft and patient outcomes. Future research should focus on longitudinal data and interventions to improve adolescent adherence.

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INTRODUCTION

Dialysis significantly impacts childhood activities, disrupting schooling and psychological development. It is linked to poor linear growth, inadequate weight gain, anemia, bone disease, hypertension, myocardial dyfunction, and family psychological problems. Transplantation enables normalization of childhood, supports better growth, enhances psychomotor skills, and reduces mortality. Kidney transplants have been performed in children of all ages, with adolescents making up the largest group of pediatric transplant recipients. Most transplant centers recommend a minimum infant weight of at least 10 kg before considering transplantation. An eGFR of <15 ml/min/1.73 m² is ideal for listing for deceased donor transplant (1,2). The primary kidney diseases leading to end-stage kidney disease (ESKD) in children differ from those in adults (3,4).

While most issues related to pre- and post-transplant care are similar across all age groups, there are specific concerns in pediatric recipients. These unique considerations include Primary Diseases, the impact of ESKD on neurological development, age-related differences in immune function and viral infection, age-related behavioral issues, and transplant timing within the life course (5,6).

Pre-Transplant Evaluation: A Multidisciplinary Approachl The pre-transplant evaluation should be conducted by a multidisciplinary team, including a social worker and psychologist, especially for young recipients and their families.

Initial Screening and Psychosocial Assessment: About 10% of children will require tests to rule out specific conditions, including glomerulonephritis (C3, C4, ANA, ANCA, and

GBM), cystinosis (white blood cell cysteine), hyperoxaluria (urine and plasma oxalate), and genetic testing (7-9). The psychological assessment is critical and includes compliance evaluation, as non-compliance is a significant issue among adolescents. It also covers body image concerns, adherence to CKD medications or dialysis, family support, and the patient's understanding of their illness and treatment (10-12). Young kidney transplant recipients may need referrals to mental health care, and psychological support is essential throughout the transition period. Specific needs include mental health screenings, financial counseling (13), and sexual health and fertility counseling (14).

Medical Optimization

Cardiovascular Disease Assessment: Left ventricular hypertrophy (LVH) is widespread in ESKD due to fluid retention, hypertension, and bone disease. Annual echocardiography is required in ESKD.

Nutrition Assessment: Poor feeding is a common problem in advanced CKD. Early gastrostomy or nasogastric (NG) feeding may help with fluid and medication administration after transplant.

Hematology Assessment: Graft loss due to venous and arterial thrombosis occurs in 1-5% of cases. Children require hematological evaluation if they have a history of hypercoagulability, such as recurrent dialysis line clotting, previous stroke, or a family history of thrombosis.

Vascular Access for Transplant: Children under 20 kg, those with a history of previous abdominal surgery, multiple central lines, and known vascular anomalies should undergo detailed arterial and venous anatomy assessment. Preoperative magnetic resonance (MR) or computed tomography (CT) angiography is recommended to assess the size, morphology, and patency of vessels (5,6).

Urological Assessment and Management: The pre-transplant urological assessment should be tailored to the age and presentation, as the evaluation needs of a young child differ from those of an adolescent. The etiology of ESKD, the child's age, and susceptibility to complications should be considered by the assessment team.

Urological Workup: The goals of urological evaluation are to identify the etiology of ESKD (congenital or acquired or both), assess the urinary bladder compliance and volume adequacy, determine the indications for nephrectomy, evaluate the susceptibility to urological complications and their risk factors, and plan the surgical approach to placing a large graft into a small recipient (15,16). The urological evaluation should include assessment of bladder capacity, bladder morphology, bladder pressure, bladder compliance, and voiding pressures (15,17). The preoperative assessment includes a history of native renal disease, a clinical examination with particular attention to the stoma, abdominal scar, and catheter. Investigations should include urine examination and culture, abdominal ultrasound, micturating cystourethrogram (MCUG), urodynamic studies, and uroflow studies. In candidates who maintain urine output, a voiding diary that records urinary continence, voiding times, and voided volumes helps determine the indication for urodynamic studies (15,16). Non-invasive urodynamic studies should measure and confirm urinary bladder function. They are invaluable when combined with voiding history, uroflowmetry, bladder diary, and post-void bladder volume (18). Fluoroscopic urodynamic studies (FUDS) are used to evaluate children with lower urinary tract dysfunction, with the main goals of confirming, characterizing, and improving the management of difficult urinary bladders before kidney transplantation (15,17). MCUG is used to identify anatomical abnormalities of the urinary tract and is recommended for recipients with more urological malformations or a history of lower urinary tract symptoms. However, there is no consensus on the routine use of MCUG in the pre-transplant assessment of children (18,19).

Management of Bladder Dysfunction: Lower urinary tract management approaches include urotherapy, pharmacological therapy, intermittent catheterization, and surgical reconstruction. Conservative treatment should be considered as the initial option before considering reconstructive surgery (20,21).

Reconstructive surgeries are categorized by their function

Bladder Drainage Facilitation: The Mitrofanoff channel is a standard method for enabling bladder drainage. It allows patients to empty their bladders through a stoma without a urostomy pouch, typically using the appendix to create a conduit between the stoma and the bladder (22,23). The Mitrofanoff procedure is indicated for refractory idiopathic bladder dysfunction, posterior urethral valves, severe urethral stricture disease, Prune belly syndrome, refractory neurogenic bladder, and epispadias (22,23).

Urinary Bladder Storage Improvement: Bladder augmentation is used to treat patients with poor bladder compliance and decreased bladder capacity. This is indicated in cases of upper urinary tract abnormalities caused by increased detrusor pressures at low urinary bladder capacity and incontinence related to idiopathic detrusor instability. Decreased urinary bladder capacity may be observed in cases of spinal cord diseases (cord injury, multiple sclerosis, and spina bifida) or congenital conditions such as urinary bladder exstrophy and its variants. Less common causes include radiation or chronic interstitial cystitis (19-21). Bladder augmentation is associated with increased morbidity; therefore, precise patient selection and counseling are necessary (24).

Urinary Diversion: This includes continent urinary diversion, usually performed by creating a Mitrofanoff channel, and incontinent urinary diversion. Vesicostomy creation is a temporary solution for lower urinary tract dysfunction, enabling transplantation in infants, with definitive reconstructive surgery possible once the child's size is adequate (25,26).

Bladder Outlet Procedures: This includes bladder neck sling (increasing the fixed outlet), insertion of an artificial urinary sphincter (creating a variable outlet resistance), and closure of the bladder neck with a reciprocal bladder drainage solution (27).

Pre-Transplant Nephrectomy: The potential advantages of retaining the native kidneys include erythropoietin production, calcium and vitamin D homeostasis, solute excretion, and

residual urine output (19). However, the typical indications for nephrectomy include chronic kidney parenchymal infection, proteinuria with hypoalbuminemia (such as congenital nephrotic syndrome or Denys–Drash syndrome), medically uncontrolled hypertension, large polycystic kidneys, and cancer (20). Nephrectomies can be staged, with the left nephrectomy performed before the transplant and the right nephrectomy performed during transplantation. Congenital nephrotic syndrome predisposes children to infections and thrombosis due to loss of immunoglobulins and complement, and pre-transplant nephrectomy improves immune and nutritional status. Bilateral nephrectomy improves respiratory symptoms, allows for gastrostomy and peritoneal placement in severe cases of autosomal recessive polycystic kidney disease, and can be performed early in life (21). To reduce the burden of primary disease, some centers perform bilateral nephrectomy for focal segmental glomerulosclerosis (24,28,29).

Surgical and Immunological Considerations

Challenges in Transplanting an Adult Organ into a Small Child

Transplanting an adult allograft into a small child presents several unique challenges:

Space and Compartment Syndrome: The space created for the kidney may still be small for the large adult organ, requiring partial closure and monitoring for compartment syndrome.

Vascular Issues: Positioning of the kidney relative to vessels carries the risk of tortuous vessels, graft thrombosis, suboptimal function, and artery stenosis.

Vessel Size Mismatch: This necessitates a more proximal anastomosis site.

Cardiac Output Mismatch: Adult allografts can absorb a significant percentage of their cardiac output. The kidneys receive 20% of the adult cardiac output. For a 70 kg adult with a blood volume of 5 liters, the kidneys are perfused with approximately 500 ml of blood per minute each. If one kidney is transplanted into a small child weighing 10 kg and with an estimated blood volume of 1 liter, maintaining the same perfusion would require directing half of the child's cardiac output to the transplanted kidney. This scenario is clearly unsustainable. It results in graft hypoperfusion and a significantly lower resting blood pressure than in the adult, in whom the donated kidney was initially adapted (30). Appropriate fluid resuscitation is necessary to avoid states that could induce vascular thrombosis or acute tubular necrosis (ATN) in the allograft, requiring careful attention to blood flow, blood pressure, and blood volume (31).

The Importance of HLA Match and Retransplantation: Human Leukocyte Antigen (HLA) matching is critical for graft survival and future retransplantation. The effect of HLA mismatches on recipient survival is demonstrated in the **Table (1)** (32):

Table 1. Median of survival years by HLA mismatches

HLA mismatches	Median survival (years)
0 MM	20 years
1 MM	18 years
2 MM	15 years
3 MM	12 years

The effect of HLA mismatches becomes more pronounced over time (32). In the first transplant, recipients with four to six HLA mismatches fared worse than those with zero to one or two to three mismatches, but this effect became more pronounced ten years after the transplant. This was significant for HLA class I and class II mismatches. Increasing mismatches in the first transplant are associated with longer waiting times for subsequent transplants (33). Even with modern immunosuppressants, the risk of rejection remains increased, particularly antibody-mediated rejection (ABMR) (31). Fifty percent of allograft loss is mainly caused by chronic immune injury (32). Furthermore, HLA-DR mismatches were found to increase the risk of post-transplant lymphoproliferative disorder (PTLD) (33). The ideal immunosuppression approach should be based on HLA matching and clinical biomarkers. The waiting time for retransplantation is affected by allograft failure. The rate of HLA sensitization increased after allograft failure in correlation with the level of HLA mismatches. The effect of HLA mismatches on retransplantation waiting time is shown on **Table (2)** below (32,33):

Table (2): Effect of HLA mismatches on transplantation waiting time

HLA mismatches	Waiting time for transplantation
0-1 HLA mismatches	2 years
2-3 mismatches	3 years
4-6 mismatches	5 years
One- HLA -DR mismatche	19 months
Two- HLA DR mismatche	23 months

The HLA-DR mismatches in the first transplant were found to be associated with decreased survival in the second transplant. However, HLA-DR mismatches caused by a living donor at the first transplant did not affect the outcomes of the second transplant (32).

V)Immunosuppression Management in Pediatric Kidney Transplant

Immunosuppression protocols are generally defined as

TWIST (Early steroid withdrawal): Includes a short course of steroids, basiliximab, tacrolimus, and Mycophenolate Mofetil (MMF).

PAT-B (Steroid maintenance): Involves prednisolone, azathioprine, tacrolimus, and basiliximab.

Early Steroid Withdrawal Regimen (TWIST)

The guidelines recommend the following for TWIST (1D):

Basiliximab: The dose is 20 mg for recipients weighing 35 kg or more and 10 mg for those weighing less than 35 kg. It should be administered 2 hours before the procedure and again after 4 days (D4).

Prednisolone: The dose is mg/m² per day, prescribed on **Table (3)**:

Table 3. Prednisolone withdrawal regimen after transplant (TWIST protocol)

Day of transplant	The dose of prednisolone(maximum dose)
Day0	Methyl prednisolone 600 mg/m² (maximum dose 500 mg)
Day1	60 mg (max dose)
Day2	40 mg (max dose)
Day3	30 mg (the max dose)
Day4	20 mg (the max dose)
Day5	Zero

Tacrolimus: The initial dose should be 0.15 mg/kg twice daily, and the maximum dose should not exceed 5 mg twice daily.

Mycophenolate Mofetil (MMF): During the first 14 days, the dose should be prescribed as 600 mg/m² twice per day, and the maximum dose should not exceed 1 gram. From day 15 onward, the dose should be 300 mg/m² twice per day.

Steroids Maintenance Regimen (PAT-B)

Basiliximab: The dose is 20 mg for recipients who weigh 35 kg or more, and 10 mg for those who weigh less than 35 kg. It should be administered 2 hours before the procedure and after 4 days (D4).

Prednisolone: The dose is mg/m² per day, prescribed on **Table(4)**:

Table 4. Methylprednisolone tapering regimen (PAT-B protocol)

Day of Transplant	Dose of Methylpredinsolone (maximum dose)
Day0	**600mg/m^2 (max 500mg)**
Day 1-2	The maximum dose is 60mg.
Day 3-7	The maximum dose is 40 mg.
Day 8-14	The maximum dose is 30 mg.
Day 15-21	The maximum dose is 20 mg.
Day 22-28	The maximum dose is 10 mg.
Day 29-90	The maximum dose is 10 mg on alternate days.
Day 91 post-transplant	The maximum dose is 5 mg on alternate days.

Azathioprine: The prescribed dose should be 2 mg/kg daily starting from the first day of transplant onward.

Tacrolimus: The initial dose should be 0.15 mg/kg twice daily, and the maximum dose should not exceed 5 mg twice daily.

Induction Therapy and Drug Monitoring: The guidelines recommend that Methylprednisolone 600 mg/m² (maximum dose 500 mg) be administered as induction therapy on the first day of transplant for children and young recipients receiving either the TWIST or PAT-B protocol (1D).

For drug dose monitoring, the guidelines recommend that, for children receiving either the TWIST or PAT-B protocol, target ranges for tacrolimus trough levels should be explained on **Table(5)**:

Table (5): Recommended tacrolimus trough levels after transplant

Days Post-transplant	Recommended Tacrolimus Level (ng/mL)
First 2 months	8-12
3-12 months	5-8
Beyond the first year	Should be individualized.

Adherence and Transition to Adult Care: The long-term success of pediatric kidney transplantation depends heavily on two critical factors: adherence and the transition from pediatric to adult healthcare services.

The Adherence Crisis: Non-adherence is a significant problem, occurring in over 60% of adolescents. It is linked to 7 out of 20 cases of unexpected graft loss within 3 years of transfer to adult care.

Risk factors for non-adherence include healthy teenagers struggling toward independence, complex medication regimens (6-8 dosing of medications), being female, and a history of previous graft loss due to adherence issues. Adherence can be improved through education and planning the medication regimen.

Transitional Care Best Practices: The transition process must be carefully managed. Best practices include:

Do not transfer during a crisis (medical or family). Consider treatment plans of other medical teams. Time transfers after major educational and social milestones (ideally after completing school and puberty). Have a written transfer policy approved by all parties, including a process for consultation with patients, parents, and families. Complete a written transition plan by age 14. Appoint clinical leaders for transition in both pediatric and adult services.

CONCLUSION

Pediatric kidney transplantation is complicated by differences in anatomical size, developmental physiology, disease aetiology and psychosocial issues. Successful outcomes require a multidisciplinary approach including full urological assessment, meticulous vascular and surgical planning, optimization of HLA matching to improve graft survival and reduce retransplantation waiting times and tailored immunosuppression protocols (early steroid withdrawal or steroid maintenance). Medication adherence, particularly in adolescence, is a key determinant of long-term success and requires structured transition programs from paediatric to adult care. Future research should be focused on interventions to improve adherence and longitudinal outcomes in this vulnerable population.

Declarations

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