

# Pediatric Kidney Transplantation

## Kids are Different

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**Keywords.** child, kidney  
transplantation, arteriovenous  
fistula, immunosuppression,  
lymphoproliferative disorders

The pediatric kidney transplant recipient differs from the adult recipient in many ways, including immune responsiveness, drug metabolism and clearance, perfusion of transplanted organs, and risk for posttransplant lymphoproliferative disease. Pediatric patients also have special quality of life issues such as cosmetic side effects of medications, stunted growth and sexual maturation, and separation from their peers. Congenital urological anomalies and glomerulosclerosis are the most common causes of pediatric end-stage renal disease. In the pediatric patients, consideration for preemptive transplantation should be first and arteriovenous fistula placement second. Pediatric patients should receive priority for kidneys from deceased donors to shorten the wait time for transplant. Fevers or changes in blood pressure may identify allograft dysfunction weeks before changes in creatinine occur. Thus, monitoring serum creatinine level is a poor indicator of allograft dysfunction in this setting. There is great concern about nonadherence to immunosuppressive therapy as children reach the stage of adolescence. This report highlights these and other important differences in the evaluation and management of the pediatric kidney transplant recipients compared with the adult and provides practical guidance to the practitioners involved in caring for such patients.

IJKD 2013;7:429-31  
www.ijkd.org

### INTRODUCTION

Kidney transplantation is the treatment of choice for pediatric patients with end-stage renal disease (ESRD). Advances in surgical techniques and preoperative and postoperative care, as well as immunosuppressive therapy have contributed to increase patient and graft survival for this population.<sup>1-3</sup>

There are however, important differences in the pediatric transplantation compared with adult patient.<sup>2-8</sup> First, the etiology of ESRD is different in children than it is in adults,<sup>2,3</sup> and factors such as metabolic consequences and growth, emotional and sexual maturity, and the impact on quality of life make the child with ESRD distinct.<sup>4-8</sup> Second, the pediatric kidney transplantation has become increasingly complex, particularly for children

who have multiple congenital anomalies.<sup>2,3</sup> Third, the metabolism of medications is quite different in children than in adults. Young children often require more frequent drugs dosing to avoid both very high blood peak and low trough levels, which may cause complications.<sup>9-13</sup> Fourth, monitoring serum creatinine level is a poor indicator of allograft dysfunction in the small children who are the recipients of adult kidneys. Fifth, children are at a greater risk for lymphoproliferative disorder and transplant-related infections following the kidney transplantation than adult patients.<sup>14</sup> Sixth, in pediatric patients, consideration for preemptive transplantation must be first and arteriovenous fistula placement second to avoid the complications associated with hemodialysis treatment and vascular access.<sup>15-17</sup>

### CAUSES OF KIDNEY FAILURE

Congenital genitourinary tract abnormalities and glomerulonephritis are the most common causes of pediatric ESRD. Many children with congenital urological abnormalities, including myelomeningocele, require surgical correction before or during the time of transplantation. Therefore, care of the pediatric transplant patient requires a multidisciplinary team approach consisting of a neurosurgeon, a urologist, an orthopedic surgeon, and other allied specialists to deliver optimal care and improve outcomes.<sup>2,3</sup>

### PSYCHOSOCIAL AND EMOTIONAL IMPACT

End-stage renal disease affects the physical, emotional, and sexual growth of the maturing child. These physical side effects make them to become more and more isolated and take a toll on their self-esteem.<sup>4</sup> Unfortunately, psychological disorders and psychological care are not being detected early to initiate treatment and reduce the future disability. Pediatric transplant patients are to be closely monitored and appropriately treated for the transplant-related psychological disorders.

Evidence suggests a strong inverse relationship between socioeconomic status and graft failure among children in developed countries. Children with low socioeconomic status have a higher graft failure rate than children with normal socioeconomic background.<sup>5-8</sup>

### IMMUNOSUPPRESSIVE REGIMENS

Induction therapy with daclizumab, tacrolimus, and mycophenolate mofetil has shown complete corticosteroid avoidance in the pediatric kidney transplantation. Maintenance therapy with tacrolimus and mycophenolate mofetil have also shown promise in complete corticosteroid avoidance in pediatric patients, thereby reducing physical side effects, improving quality of life, and medication adherence.<sup>9-13</sup> Calcineurin inhibitors which are given twice a day in adults, may require three times daily dosing in small children. Likewise, rapamycin which is usually given once a day in adult patients, it may require dosing every 12 hours in young children.<sup>9-13</sup>

### MORBIDITY AND MORTALITY

Children are at a higher risk for posttransplant-related infections and lymphoproliferative disorders than adult patients.<sup>2,3</sup>

### PREEMPTIVE TRANSPLANTATION

While arteriovenous fistula placement may work very effectively for adults with ESRD, to avoid the complications associated with acute or cuffed catheters, considering fistulas should be second for the pediatric kidney transplant patients, and consideration for preemptive transplantation must be first. Children with irreversible stage 4 chronic kidney disease should be pushed for preemptive transplantation unless there is a contraindication.<sup>15-18</sup>

The major criterion for preemptive transplantation is the availability of a donor. Children with congenital renal dysplasia are the best candidates to undergo transplantation preemptively. Exclusion criteria for preemptive transplantation include heavy proteinuria, high-grade vesicoureteral reflux, chronic infection, and resistant hypertension.<sup>17-19</sup> Evidence shows that patients who undergo transplantation at the time of active nephrotic syndrome have a greater chance of clotting their new allograft.

### PREOPERATIVE CARE

Renal dysplasia in children is usually associated with polyuria due to the impaired ability to concentrate urine maximally. Volume depletion during the perioperative course, if not corrected, can cause vascular thrombosis and graft failure.<sup>20,21</sup>

### MEDICATION ADHERENCE

There is great concern about poor or nonadherence to medical therapy as children reach the stage of adolescence. The use of team approach, especially one that incorporates patients, nurses, social workers, dietitians, pharmacists, and primary care physician is an effective method for improving patient adherence to the medication regimen. Pediatric nephrologists remain the cornerstone of management as well as general team direction.<sup>20</sup>

### PANEL-REACTIVE ANTIBODIES

The presence of high panel-reactive antibodies, prior to transplantation because of multiple blood transfusions, is associated with the increased rate of allograft rejection in both adults and children. Therefore, antibody-reduction protocols including the use of B-cell monoclonal antibodies (rituximab) in combination with plasmapheresis may be indicated to prevent graft failure in high-risk patients.<sup>20,21</sup> After transplantation, these patients need not only routine monitoring but surveillance

for the presence of donor-specific antibodies, which may also trigger the use of an antibody-reduction protocol prior to overt rejection.<sup>20</sup>

### TRANSPLANTATION IN SMALL CHILDREN

The size and age of children poses another special issue in pediatric transplantation, which corresponds to times of rapid growth. The use of an adult kidney in smaller children affects the ratio of the surface area of the kidney to the surface area of the child. Therefore, monitoring serum creatinine level is a poor indicator of allograft dysfunction in this setting. Conversely, fevers or changes in blood pressure may identify allograft dysfunction weeks before changes in creatinine occur.<sup>17,21-23</sup>

### CONFLICT OF INTEREST

None declared.

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Received April 2013  
Accepted May 2013