

# Revisiting the Management of Pediatric Kidney Transplants, A Multicenter Analysis

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The newest Kidney Disease Improving Global Outcomes (KDIGO) guideline recommendations were investigated mainly for the care of adult kidney transplant recipients, but no guideline exists for the management of pediatric transplant recipients. This review provides update recommendations in the management of pediatric kidney transplantation.

Four electronic databases, PubMed, EMBASE, Google Scholar, and Web of Science were searched systematically for the last two decades, using Mesh terms in English language. The Grades of Recommendation Assessment, Development, and Evaluation (GRADE) approach was used for grading the quality of the overall evidence and the strength of recommendations for each outcome across the studies. The overall quality of evidence categorized as high (A), moderate (B), low (C), or poor (D). The strength of a recommendation was determined as level 1 (recommended) or level 2 (suggested). The ungraded statements were determined on the basis of common sense to provide general advice.

Of the 317 citations which were screened for the evidence review, 62 were included in data extraction. The included studies were randomized controlled trials, prospective cohorts and cross-sectional, descriptive, and review studies. Of the 115 statements, 56 (48.6%) were graded 1 (we recommend), 34 (29.5%) were graded 2 (we suggest), and 25 (21.7%) were ungraded statements. Altogether, only 22 (19.1%) of recommendations reached the "A" or "B" levels of quality of evidence.

The pediatric kidney transplant recipients are different from adult recipients regarding the primary kidney diseases, surgical techniques, drug metabolism, adherence to medications, growth and neurocognitive development and immunization needs prior to transplantation.

**Keywords.** clinical practice guideline, evidence-based recommendation, graft outcome, kidney transplantation, pediatric

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## INTRODUCTION

Kidney transplantation has become the treatment of choice for children with end-stage-kidney disease (ESKD). The survival rates of pediatric kidney-

graft either from a living or deceased donor, have improved substantially over the last two decades.<sup>1-3</sup> Such advances are attributed to multiple factors including improved surgical techniques, newer

potent immunosuppressive medications, better donor selection, and more accurate understanding of pediatric-specific immune mechanisms.<sup>4,5</sup>

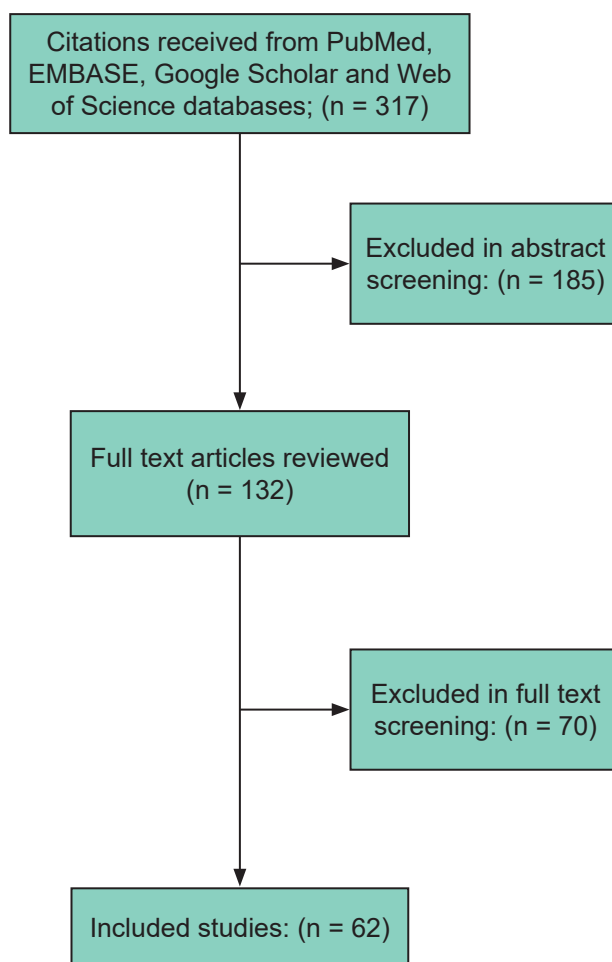
The pediatric recipients of kidney transplant are different from adult recipients regarding their primary kidney diseases, which are often associated with congenital anomalies of the kidney and urinary tract, hereditary kidney diseases such as nephronophthisis, drug metabolism, and the need of immunization prior to transplantation.<sup>6-8</sup> Furthermore, children with ESKD often have growth retardation and delayed neurocognitive development.<sup>9,10</sup> Adult-size allografts, transplanted into infants and small children may lead to a higher glomerular filtration rate; this can make the interpretation of serum creatinine results more challenging, in the case of acute rejection.<sup>11-16</sup> Childhood immunization should be completed before transplantation.<sup>17,18</sup> In addition, adolescents are shown to have the worst long-term graft survival compared to adult patients, mainly due to poor adherence to medical therapy.<sup>19</sup> The risk of graft failure associated with the early transition from pediatric to adult-oriented care is also a serious medical problem and requires a team work approach to optimize this transition.<sup>14,15,19</sup>

Because the latest Kidney Disease Improving Global Outcomes (KDIGO) guideline has mainly focused on the care of adult kidney transplant recipients,<sup>20</sup> and due to a relative paucity of data in the pediatric kidney transplantation,<sup>4,21-31</sup> we aimed to revisit and update the management of kidney allograft recipients in children.

In this article, we concentrate mainly on those recommendations that focus on: 1) evaluation and management of pediatric kidney transplantation, 2) integrates the best clinical practice from well-designed studies and patient care data, and 3) combines the best personalized practice with health care provider expertise.

### MATERIALS AND METHODS

We searched literature in PubMed, EMBASE, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews. A total of 317 citations were extracted for evidence review, out of which, 132 papers were selected for consideration. After revising, 70 papers were excluded because of repeated contents, and finally 62 studies were included in analysis (Figure 1).



Search Results Flow Chart

Grading of each study was done by one of the authors and then all papers were reviewed by co-workers to eliminate the risk of selection bias and confirm accuracy, after which revisions to the recommendations were made, where appropriate.

A systemic approach, based on Grades of recommendation, assessment, Development, and Evaluation (GRADE) was used to classify the quality of the overall evidence and the strength of recommendations for each outcome across the studies.<sup>32</sup>

According to GRADE, the overall quality of evidence categorized on the basis of study design and all intervention outcomes of interest are as follow: A, B, C, or D translating to high, moderate, low and very low, respectively. The strength of a recommendation was determined by considering both the quality of evidence and also by the potential medical risks vs. benefits and graded as level 1 (we recommend) or level 2 (we suggest).

The ungraded statements provide general advice based on common sense and they are not based on systematic evidence review.

## RESULTS

Out of 115 statements, 56 (48.6%) were graded 1 (we recommend), 34 (29.5%) were graded 2 (we suggest), and 25 (21.7%) were ungraded statements. Altogether, only 22 (19.1%) of the recommendations achieved the “A” or “B” levels of quality of evidence.

## DISCUSSION

### Access to Transplantation<sup>1,2,5,20, 33</sup>

We recommend:

- Pre-emptive transplantation with a living donor as the preferred treatment for end-stage kidney disease (1A)
- Pre-emptive transplantation (living or deceased donor) when estimated glomerular filtration rate (eGFR) is < 15 mL/min /1.73m<sup>2</sup> (1D)

We suggest:

- Candidates with primary hyperoxaluria type 1 be considered for combined or sequential liver-kidney transplantations (2C)

### Contraindication of Kidney Transplantation<sup>34</sup>

We recommend:

- Not transplanting pediatric patients with psychiatric disorders, or with ongoing substance abuse (1C)
- Kidney transplantation be delayed until active bacterial, viral, fungal or parasitic infections are treated (1C)
- Complete treatment of active tuberculosis prior to kidney transplantation (2C)
- Transplantation not done in children with active malignancy (1B)
- Excluding patients with severe obstructive lung disease (1C)

We suggest:

- Complete treatment of active tuberculosis prior to kidney transplantation (2C)

### Pre-transplant Recipient Workup<sup>1,18,19, 26, 35-41</sup>

We recommend:

- All kidney transplant recipients should be vaccinated against tetanus, hepatitis B, meningococcal, pneumococcal, hemophilus influenza, poliomyelitis, influenza, mumps,

measles, rubella (MMR), and varicella, prior to transplantation (1A)

- Vaccination should be completed for all live attenuated vaccines at least 4 weeks prior to transplantation (1B)
- Postpone kidney transplantation for at least 4 weeks, if a live vaccine should be administered (1B)
- Determine the primary cause of ESKD in candidates, in order to assess risks and management after transplantation (1A)

We suggest:

- Lifestyle modification be offered to candidates with obesity (2B)
- Screening for diabetes by oral glucose tolerance test in candidates who are not known to have diabetes (2A)
- Genetic assessment for podicin and nephrin gene mutations in candidates with the diagnosis of focal segmental glomerulosclerosis (FSGS) to inform the risk of recurrent disease (2D)
- Genetic testing to identify primary hyperoxaluria and determine treatment decisions (2C)
- Performing chest radiograph, electrocardiogram, echocardiography, abdominal ultrasound, Diethylenetriamine Pentaacetate Acid (Tc-99m DTPA) diuretic renal scan, CT angiography with excretory intravenous pyelogram (IVP) as clinically indicated (Not graded)

We recommend:

- Screening for latent tuberculosis (TB) prior to transplantation with a chest radiograph along with a purified protein derivative (PPD) skin test or interferon-gamma release assay (1C)

We suggest:

- Treating latent TB prior to or immediately after kidney transplantation as screened by a chest radiograph together with a purified protein derivative (PPD) skin test or interferon-gamma release assay (2C)
- Dental evaluation for all patients prior to kidney transplantation (2C)

We recommend:

- Screening patients for human immunodeficiency virus (HIV) infection with HIV serology tests (1A)
- Screening all patients for hepatitis B (HBV) infection with hepatitis-B surface antigen

(HBsAg), hepatitis-B surface antibody (anti-HBs), and Hepatitis B core antibody (anti-HBc) (1A)

- Screening with HBV DNA for patients with a positive HBsAg or anti-HBc (1A)
- Screening for cytomegalovirus (CMV) with CMV IgG and IgM (1C)
- Screening for Epstein-Barr virus (EBV) with EBV viral capsid antigen IgG and/or EBV nuclear antigen IgG (1C)

We suggest:

- Screening for herpes simplex virus (HSV) with HSV IgG and IgM (2C)

We recommend:

- Screening for varicella-zoster virus (VZC) with VZV IgG (1C)
- Varicella zoster virus (VZV) immunization for VZV seronegative candidates, at least 4 weeks prior to transplantation (1C)

We suggest:

- MMR screening using MMR IgG serology (2C)
- Screening for the human T-lymphotropic viruses (HTLV) type I and type II and toxoplasmosis with IgG and IgM in the epidemic areas such as northern Iran (Not graded).
- Performing a neurocognitive assessment in pediatric candidates who developed ESKD before the age of 5 years (2D)
- Performing an educational assessment in pediatric candidates of school age with educational problems (2D)

We recommend:

- Not screening for BK virus (BKV) (1C)
- To determine the cause of ESKD in candidates for risks assessment and management after kidney transplantation (1A)
- PCR testing for COVID-19 (Not graded)
- At least two doses of vaccinations against Covid-19 (Not graded)

### Pre-transplant Bilateral Nephrectomy<sup>5, 26-31</sup>

We suggest:

- High-grade vesicoureteral reflux complicated with recurrent urinary tract infections (Not graded)
- Autosomal dominant polycystic kidney disease with extraordinary enlarged kidneys (Not graded)

### Induction Therapy (Table 1)<sup>42-45</sup>

We recommend:

- Pre-medications with acetaminophen 15 mg/kg/dose (max 650 mg) and diphenhydramine 1mg/kg/dose (max 50 mg) (2D)
- Induction therapy with a combination of immunosuppressive medications before or at the time of kidney transplantation (1A)
- Interleukin 2 receptor antagonist (IL2-RA) (Basiliximab) for induction in patients with low immunological risk panel reactive antibody (PRA < 20% and no DSA) or intermediate risk (PRA between 20 and 80%, with no DSA) with a dose of 1.5 mg/kg or 12 mg/m<sup>2</sup> (max 20

**Table 1.** Induction Immunosuppressive Medications

Methylprednisolone	Start day (0) at the time of induction
Dose (IV)	10 mg/kg or 250 mg/m <sup>2</sup> (max: 500 mg) for 3 consecutive days
Basiliximab	Start day 0 (2 hours before surgery)
Dose (IV)	1.5 mg/kg/d or 12 mg/m <sup>2</sup> (max 20 mg) for 5 days. Give the second dose on day 4 transplant
Thymoglobulin	Start day 0 (2 hours before surgery)
Dose (IV)	1.5 mg/kg and again day 14 post-transplant
Side Effects	Hypersensitivity reaction to infusion (rare)
Tacrolimus	Can be started pre-transplant for living donors
Dose (Oral)	0.15 mg/kg (max: 5 mg) pre-transplant and again 4 to 5 days, when serum creatinine is < 2.0 mg/dL
Side Effects	Hypertension, glucose intolerance, nephrotoxicity, tremors
Mycophenolate-mofetil	Start post-transplant when the patient tolerates oral fluids
Dose (Oral)	10 mg/kg (max: 750 mg (600 mg/m <sup>2</sup> )) on the day of transplant and then twice daily on the evening of transplant
Side Effects	Leukopenia, thrombocytopenia, nausea, diarrhea
mTOR Inhibitor (Sirolimus)	It is not recommended in the first month post-transplant
Dose (Oral)	3 mg/m <sup>2</sup> once daily followed by 1 mg/m <sup>2</sup> /d in patients < 40 kg
Side Effects	Proteinuria and Dyslipidemia

mg) diluted with 50 mL 0.9% saline, injected intravenously over 20 to 30 minutes, 2 hours prior to transplantation and be repeated on third and fourth post-transplantation days (1B)

- Lymphocyte-depleting therapy (thymoglobulin, anti-thymocyte globulin) with a dose of 1.5 mg/kg for induction in kidney transplant recipients with high immunologic risk (PRA > 80%), multiple blood transfusions, and those with prior history of graft rejections within the first year following transplantation (1B)
- Intravenous methylprednisolone, 10 mg/kg or 250 mg/m<sup>2</sup> (max 500 mg) for three consecutive days, initiated at the time of induction and then gradually discontinued within the first week post-transplantation (1C)

#### Maintenance Immunosuppressive Therapy<sup>45-48</sup>

We recommend:

- Maintenance immunosuppression with a calcineurin inhibitor and mycophenolate mofetil (MMF), with or without steroid in most kidney transplant recipients (1B)
- Using the lowest doses of maintenance immunosuppressive medications by the second to fourth months after transplantation, if there is no episode of acute rejection (2C)
- None-withdrawal of calcineurin inhibitors (2B)
- Tapering prednisone dose within the first post-transplantation week in low-risk recipients (2C)
- None-withdrawal of prednisone, if prednisone has been used beyond the first week after transplantation (2C)

#### Methylprednisolone (Not graded)

- Starting intravenous methylprednisolone and switching to oral prednisolone as soon as oral fluid is tolerated (Not graded)

#### Cyclosporine (Not graded)

- Starting cyclosporine intravenously pre-transplant (2 mg/kg twice daily) and switching to oral administration as soon as tolerated.
- Cyclosporine as an alternative to tacrolimus (TAC) in patients with FSGS and those at risk of developing post-transplant diabetes mellitus
- Cyclosporine (5-7 mg/kg, max 250 mg) orally twice daily initiated on the day of transplantation

- The suggested cyclosporine trough level of 200 to 250 ng/mL in the first month and 100 to 150 ng/mL by the sixth month and thereafter
- MMF be given at a dose of 20 mg/kg twice daily, when cyclosporine is used as an alternative to TAC, due to interaction with cyclosporine

#### TAC (Not graded)

- TAC (0.15 mg/kg, max 7.5 mg) be given pre-transplant and again 4 to 5 days post-transplantation when the serum creatinine is < 2.0 mg/dL
- TAC recommended for patients with dyslipidemia, hirsutism and in those considered immunologically high risk
- The recommended trough level of TAC is 10 to 15 ng/mL during the first month and 5 to 8 ng/mL by the 12th month and thereafter

#### MMF (Not graded)

- Starting at dose of 10 mg/kg (max 750 mg) or 600 mg/m<sup>2</sup> twice daily for two weeks; its administration should be separated from TAC/cyclosporine by 2 hours
- Dose reductions might be needed (450 mg/m<sup>2</sup> twice daily), if there are low white blood cell count, hemoglobin or low platelets.

#### Mammalian Target of Rapamycin (mTOR Inhibitor) (Sirolimus) (Not Graded)

- Sirolimus (3 mg/m<sup>2</sup> loading dose, followed by 1 mg/m<sup>2</sup> daily in patients < 40 kg) may be used in low immunological risk patients
- Sirolimus may allow a reduction in CNI dose by 60% with cyclosporine and by 40% with TAC

#### Acute Rejection (Table 2)<sup>13-16, 20</sup>

We recommend:

- All transplant recipients be regularly monitored for any unexplained rise in serum creatinine level (1C)
- Allograft biopsy be performed in all kidney transplant recipient before treating acute rejection (1C)
- Treating subclinical and borderline acute rejection (2D)
- Intravenous methylprednisolone (250 mg/m<sup>2</sup> or 10 mg/kg), daily, for three consecutive days for the initial treatment of acute cellular

**Table 2.** Acute Allograft Rejection

Rising Serum Creatinine or Fever Can Be Due to:	Rejection Urinary Tract Obstruction Infections (Bacterial or Viral) Dehydration Nephrotoxicity (Tacrolimus) BK Virus Nephropathy Vascular Problems (Thrombosis)
Order	Fluid Balance Control Blood and Urine Cultures CMV, EBV, BK Virus, and Adenovirus PCR Tests Urine for BK Virus PCR if suspected According to Clinical Picture Allograft Ultrasound Tacrolimus or Cyclosporin Level Central Line Culture PD fluid culture, if PD catheter has been Inserted

Abbreviations: CRP, C-reactive protein; CMV, cytomegalovirus; PD, peritoneal dialysis; EBV, Epstein-Barr virus; PCR, polymerase chain reaction.

rejection (1D)

- Adding or restoring maintenance prednisone in patients who are not on steroids and experience an acute rejection episode (2D)
- Using lymphocyte-depleting antibody or OKT3 for acute rejections that do not responds to corticosteroids (2C)
- Treating acute antibody-mediated rejection with plasma exchange, intravenous immunoglobulin, anti-CD20 antibody or lymphocyte-depleting antibody, with or without corticosteroids (2C)
- Lymphocyte-depleting therapy in all in steroid-resistant acute T-cell mediated rejections (1C)
- Consider no response after 5 to 7 days of T-cell depleting therapy (Not graded)
- Treating antibody-mediated rejection (C4D positive and DSA-positive/ negative) with steroids, plasma exchange, IVIG, and rituximab
- Plasma exchange at 1.5 total body water volume, daily, for 3 days, then alternate day for a minimum total of 8 sessions. The exchanged volume is replaced by 5% albumin or plasma (2D)
- Adding MMF, if the patient is not receiving MMF or azathioprine or switching azathioprine to MMF (2D)

**Chronic Graft Dysfunction** <sup>20,49,50</sup>

We recommend:

- Kidney allograft biopsy for all patients with declining kidney function of unknown cause (1C)
- Replacing the CNI with an mTOR inhibitor for patients reduced kidney function (eGFR > 40 mL/min /1.73<sup>2</sup>) and urine protein

excretion < 500 mg/g creatinine (2D)

- All immunosuppressive medications, except for steroids, be stopped immediately after transplant nephrectomy, with subsequent gradual tapering of steroids (2C)
- Recipients with a history of graft loss due to non-adherence to receive adherence-based consult prior to re-transplantation (2D)

**Management of Hypertension and Cardiovascular Diseases (Not graded) (Table 3)**<sup>51-56</sup>

- Recommended antihypertensive agents for the control of hypertension pressure include calcium channel blockers (nifedipine or amlodipine) or beta-blockers (labetalol). ACE-inhibitors are contraindicated in the immediate post-transplant period

**Viral Diseases** <sup>20,57-59</sup>

We recommend:

- A booster vaccination for transplant recipients with positive HBs Ag and HBs Ab < 10 mIU/mL (1A)
- Prophylaxis for HbsAg positive kidney transplant recipients with lamivudine (100 mg once daily) for 6 to 12 months. initiated at the time of transplantation (1B)

We recommend:

- Cytomegalovirus (CMV) prophylaxis with oral ganciclovir or valganciclovir for all kidney recipients, for at least 3 months after transplantation, except when both donor and recipient have negative CMV serology (1B) or for at least 6 weeks after treatment with T-cell-depleting antibody (1C)

**Table 3.** Post-transplant Management of Hypertension

Nifedipine	Nifedipine
Oral Dose	Nifedipine 10 mg for children < 20 kg and 30 mg for children > 20 kg
Amlodipine	mg/kg to 1 mg/kg to a maximum of 10 mg/d
Oral Dose	Once daily preparation, tablets can be dissolved to allow smaller doses to be given
Hydralazine	
Oral Dose	0.25-0.50. 0.25 to 1.0 mg/kg/dose (max 25 mg/dose) every 6 to 8 hours
IV Bolus	0.1 to 0.2 mg/kg/dose every 4 hours given slowly (max 3mg/kg/d)
Infusion	25 to 30 mcg/kg/h (max 3 mg/kg/d)
Atenolol	
Oral Dose	1 to 2 mg/kg/d (max 100 mg/day)
Clonidine	
IV Dose	3 microgram/kg/dose over 5 to 10 minutes
Oral Dose	6 microgram/kg/dose
Labetalol	
Infusion	1 mg/kg/h then titrate to a max of 3 mg/kg/h

- Treating all patients with CMV disease with intravenous ganciclovir (1D)
- Continuing therapy until CMV is no longer detectable by plasma NAT (2D)
- Reducing immunosuppressive medications in life-threatening CMV disease, until CMV disease has resolved (2D)
- Monitoring graft function during treatment of CMV disease (2D)

We suggest:

- Screening all kidney transplant recipients for BKV with quantitative plasma nucleic acid testing (NAT) monthly for the first 3 to 6 months after transplantation, then every 3 months during the first post-transplant year, and also whenever there is an unexplained rise in serum creatinine level and after treatment for acute rejection (2D)
- Reducing immunosuppressive medications when BKV plasma NAT is persistently higher than 10,000 copies/mL ( $10^7$  copies/L) (2D)
- In patients with CMV disease, we suggest weekly monitoring of CMV by NAT (2D)

We suggest:

- Monitoring high-risk Epstein-Barr virus (EBV) (donor seropositive/recipient seronegative) kidney transplant recipients for EBV by NAT (2C) once in the first week after transplantation, then at least monthly for the first 3 to 6 months after transplantation, and every 3 months until

the end of the first post-transplant year and also after treatment for acute rejection (2D)

- Reducing or withdrawing the immunosuppressive medications in patients with EBV disease, including those with lymphoproliferative disorder (PTLD) (IC)
- Reducing immunosuppressive medications in EBV-seronegative patients with an increasing EBV load (2D)
- Patients with PTLD should wait for at least one year after achieving disease remission before consideration for re-transplantation (1B)
- Treatment of primary herpes simplex (HSV) infection with intravenous acyclovir until the patient has a clinical response and then switch to oral acyclovir or valacyclovir for more 2 to 3 weeks (Not graded)
- Treatment of primary VZV infection in kidney transplant recipients with either intravenous or oral acyclovir along with reduction in immunosuppressive medications (Not graded)

### Pneumocystis Jirovecii Infection (PJI)

We recommend:

- All kidney transplant recipients receive prophylaxis with daily sulfamethoxazole-trimethoprim (SMX-TMP) 5 mg/kg (trimethoprim component) to a maximum dose of 800/160 mg/d, for six months after transplantation and also for 6 weeks during and after treatment of acute rejection with lymphocyte-depleting antibodies (1B)
- Treatment of Pneumocystis jirovecii infection consists of reducing immunosuppressive drugs, prescribing SMX-TMP for 2 to 3 weeks and corticosteroids for 5 days (1C)

We recommend:

- Screening patients for HIV infection, using HIV serology (1A)
- Oral and esophageal candida prophylaxis with oral nystatin or clotrimazole for 3-6 months after transplantation<sup>60</sup> (1D)

### Recurrent Primary Kidney Disease<sup>20,44, 61</sup>

We suggest:

- Screening kidney transplant recipient with FSGS as primary kidney disease, for proteinuria, daily for 1 week, then weekly for 4 weeks, then every 3 months for the first year and every year thereafter (2D)

- Screening kidney transplant recipient with primary kidney disease caused by membranoproliferative glomerulonephritis (MPGN), anti-glomerular basement membrane (GBM) disease, lupus nephritis, or anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis for hematuria at least once in the first post-transplant month; then every 3 months during the first year, and then annually, thereafter (2D)
- Screening kidney transplant recipient with primary kidney disease caused by hemolytic uremic syndrome (HUS) for thrombotic microangiopathy including platelet count, peripheral smear for blood cell morphology, plasma haptoglobin, and serum lactate dehydrogenases during the episode of graft dysfunction (2D)
- If screening suggests possible recurrent disease, consider obtaining an allograft biopsy (2C)

#### Treatment of Recurrent Kidney Disease<sup>20,61</sup>

We suggest:

- Plasma exchange if the biopsy shows FSGS in those with primary FSGS kidney disease (2D)
- Using high-dose corticosteroids and cyclophosphamide in patients with recurrent ANCA-associated vasculitis or anti-GBM disease (2D)
- Treatment with an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker (ARB) in patients with recurrent glomerulonephritis and proteinuria (2C)
- Management of body oxalate burden with appropriate measures prior to transplantation in patients with primary hyperoxaluria, including pyridoxine, high calcium and low oxalate diet, increased fluid intake, potassium or sodium citrate for urine alkalinization, orthophosphate, magnesium oxide, or hemodialysis to prevent oxalate deposition until plasma and urine oxalate levels are normal (ID)

#### Growth Hormone Replacement Therapy (Not Graded)<sup>9,10, 62</sup>

- Growth hormone therapy may be considered for pediatric kidney transplant recipients with growth failure
- Growth failure is diagnosed when height

is below the 3<sup>rd</sup> percentile or height target standard deviation score is less than 2 and height increase velocity is less than 25% for chronological age

- Growth hormone typically is not started during the first six months following kidney transplantation
- The recommended dose of recombinant human growth hormone (rhGH) is 28 IU/m<sup>2</sup> /week (4 IU/m<sup>2</sup>/d) or 0.05 mg/kg/d subcutaneously
- Baseline evaluation of graft function, anthropometric assessment, bone age, hip x-ray, serum calcium, phosphorous, PTH, growth velocity, target height, and fundus examination are needed before growth hormone therapy

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#### AUTHORS' CONTRIBUTIONS

FA: Concept/Design, Data collection, Data analysis, Data interpretation, Drafting article, Critical revision of article and Approval of article. NK, AS, and EM: Data collection, Data interpretation, Critical revision of article and Approval of article. AAZ, BB, MMO, AAB, AS, NE, AD, HB, AE, MMZ and FG; Critical revision of article and Approval of article.

#### ABBREVIATIONS

ACE: Angiotensin-converting enzyme  
CDC: Complement-dependent cytotoxicity  
CNI: Calcineurin inhibitor  
CMV: Cytomegalovirus  
CRP: C-reactive protein  
CVP: Central venous pressure  
DSA: Donor-specific antibody  
DTPA: Diethylenetriamine-pentaacetic acid  
EBV: Epstein-Barr virus  
ESKD: End-stage kidney disease  
FSGS: Focal segmental glomerulosclerosis  
GBM: Glomerular basement membrane  
GFR: Glomerular filtration rate  
HLA: Human leukocyte antigen  
HTLV1: Human T-lymphocyte virus type1  
HIV: Human immune deficiency virus  
IVIG: intravenous immunoglobulin G



IVP: Intravenous pyelogram  
 JP: Jackson Pratt  
 CAKUT: Congenital anomalies of the kidney and urinary tract  
 LMWH: Low molecular weight heparin  
 MMF: Mycophenolate Mofetil  
 PCP: *Pneumocystis carinii*  
 PCR: Polymerase chain reaction  
 PJP: *Pneumocystis jirovecii* pneumonia  
 PD: Peritoneal dialysis  
 PRA: Panel reactive antibodies  
 PTLD: Lymphoproliferative disorder  
 TAC: Tacrolimus

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