Risk Factors for Urinary Tract Infection After Renal Transplantation and its Impact on Graft Function in Children and Young Adults

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Abbreviations and Acronyms

CIC = clean intermittent catheterization
ESRD = end-stage renal disease
FSGS = focal segmental glomerulosclerosis
GFR = glomerular filtration rate
RTX = renal transplantation
UTI = urinary tract infection
VUR = vesicoureteral reflux

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Purpose: Urinary tract infection will develop in 40% of children who undergo renal transplantation. Post-transplant urinary tract infection is associated with earlier graft loss in adults. However, the impact on graft function in the pediatric population is less well-known. Additionally the risk factors for post-transplant urinary tract infection in children have not been well elucidated. The purpose of this study was to assess the relationship between pre-transplant and post-transplant urinary tract infections on graft outcome, and the risk factors for post-transplant urinary tract infection.

Materials and Methods: A total of 87 patients underwent renal transplantation between July 2001 and July 2006. Patient demographics, cause of renal failure, graft outcome, and presence of pre-transplant and post-transplant urinary tract infections were recorded. Graft outcome was based on last creatinine and nephrological assessment.

Results: Median followup was 3.12 years. Of the patients 15% had pre-transplant and 32% had post-transplant urinary tract infections. Good graft function was seen in 60% of the patients and 21% had failed function. Graft function did not correlate with a history of pre-transplant or post-transplant urinary tract infection ($p > 0.2$). Of transplanted patients with urological causes of renal failure 57% had post-transplant urinary tract infection, compared to only 20% of those with a medical etiology of renal failure ($p < 0.001$).

Conclusions: In this study there was no correlation between a history of urinary tract infection (either before or after transplant) and decreased graft function. History of pre-transplant urinary tract infection was suggestive of urinary tract infection after transplant. Patients with urological causes of renal failure may be at increased risk for post-transplant urinary tract infection.

Key Words: child; kidney failure, chronic; kidney transplantation; urinary tract infections

URINARY tract infection is the most common bacterial infection in children who have undergone renal transplantation,[1–4] with an incidence higher than that in adults.[5] The risk factors for urinary tract infection after renal transplant have not been well-defined in the pediatric population.[6] Specifically the role of urinary tract infection before renal transplant as a risk factor for infection after transplant has not been well investigated. Similarly the impact of post-transplant urinary tract infection on graft function has not been clearly elucidated in children. The purpose of our study was to

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assess the risk factors for urinary tract infection after renal transplantation, particularly the correlation between infection before and after transplantation, and to evaluate the relationship between renal graft outcome and infection before and after transplantation.

PATIENTS AND METHODS

With institutional review board approval a retrospective chart review was performed on all patients who underwent renal transplantation between July 2001 and July 2006 at our institution. Patient demographics, clinical course, and the presence of UTI before and after RTX were evaluated. We arbitrarily established a classification for the etiology of ESRD based on whether the urinary tract anatomy was abnormal. All patients were followed in the combined urology and nephrology transplant clinic at our institution. They underwent mercaptoacetyltriglycine scan immediately postoperatively to assess vascular flow and to determine the presence of urine leakage or obstruction.

During followup voiding cystourethrogram or radionuclide cystogram was performed 1 to 6 months after transplant. Ultrasound was performed every 3 to 6 months for the first year, then yearly. If moderate or severe hydronephrosis was detected, mercaptoacetyltriglycine scan was performed to evaluate for the presence of obstruction. Electrolytes, blood urea nitrogen levels and creatinine levels were obtained twice weekly for the first 2 months (unless clinical circumstances indicated more frequent monitoring) and weekly to monthly thereafter.

UTI was defined as the presence of any urinary signs or symptoms (ie urgency, frequency, dysuria, suprapubic or flank discomfort, malodorous or turbid urine) with or without fever and a positive urine culture (greater than 10^5 cfu/ml) from a clean catch midstream voided or catheterized specimen taken at any time after RTX. All patients with neuropathic or nonneurogenic voiding dysfunction and a UTI after transplant were evaluated with a full urodynamic evaluation and treated with time voiding, anticholinergic medications or CIC depending on urodynamic findings.

Graft function was based on estimated GFR at last followup using the Schwartz equation (in patients younger than 18 years) or the Modification of Diet in Renal Disease study group equation (older than 18). We defined graft outcome as normal (GFR greater than 90 ml/minute/1.73 m^2), mildly depressed (60 to 89), depressed (15 to 59) or failed (less than 15). Patients with technical issues related to the transplantation procedure or acute rejection were excluded since we were primarily interested in risk factors for graft deterioration based on development of scars and acquired damage from infection.

A 2-tailed t test, chi-square test or Fisher's exact test was used for statistical analysis when appropriate. Multivariate analysis was performed using SAS® statistical software, version 9.2. A p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 46 male and 41 female children and young adults were included in the study. Median followup was 3.12 years (SE 1.66). Of the children 65 (75%) underwent dialysis preoperatively with an average duration of 21 months (SE 15.5). A total of 45 grafts (52%) were from deceased donors. Ureteral stents were not used in any patient.

Mean age at RTX was 15.10 years (SE 7.3). Among the 87 patients the cause of end-stage renal disease was nephrological in 59 (68%) and urological in 28 (32%, table 1). Focal segmental glomerulosclerosis was the most common cause of ESRD in the nephrological group and posterior urethral valves in the urological group. No patient had vesicoureteral reflux in the transplanted kidney based on initial voiding cystourethrogram or radionuclide cystogram performed 1 to 6 months after transplant. Immunosuppression consisted of triple therapy in 79 patients and dual therapy in 7. One patient was not on immunosuppression due to a failed transplant as a result of recurrent FSGS. All male patients were circumcised and dysfunction elimination syndrome could not be reliably assessed in this study.

UTI was diagnosed in 28 patients (32%) after RTX. Infections occurred at a median of 18 months (SE 16) after transplantation. Of the UTIs 11 (39%) were associated with fever. A total of 12 patients (43%) had recurrent UTIs (2 to 4 episodes). The most commonly isolated causative microorganisms in the urine culture were Klebsiella pneumoniae (30%) and Escherichia coli (25%). Patients who had VUR into the native kidneys had either undergone nephrectomy or reimplantation surgery before transplant. VUR into the transplanted kidney developed in 5 children (3 from the nephrological and 2 from the urological group) postoperatively. These patients were subsequently evaluated with urodynamics and treated for voiding abnormalities, with 4 undergoing redo ureteral reimplantation and 1 receiving dextranomer/hyaluronic acid injection.

Mean age and gender were not statistically different between patients who did and did not have a UTI after transplantation (table 2). However, the incidence of UTI after RTX was higher in children with a urological etiology of ESRD than in those with a nephrological etiology (57% vs 20%, $p = 0.0006$, table 3). A total of 11 patients in this study were on CIC with gentamicin irrigation 1 to 2 times weekly, and UTI developed after transplant in 8.

Following RTX all patients received antibiotic prophylaxis for Pneumocystis jiroveci infection for at least a year after transplantation, consisting of trimethoprim-sulfamethoxazole Monday, Wednesday and Friday, or atovaquone. Antibiotics targeted toward UTI were administered in 18 patients after