

Urinary Tract Infection After Kidney Transplantation in Children and Adolescents

Mohammad Kazem Fallahzadeh,¹ Mohammad Hossein Fallahzadeh,² Ali Derakhshan,² Mitra Basiratnia,² Ghamar Hoseini Al-Hashemi,² Mohammad Amin Fallahzadeh,² Donya Mahdavi,³ Seyed Ali Malek-Hosseini⁴

¹Shiraz Health Policy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

²Shiraz Nephro-Urology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

³Department of Psychology, University of British Columbia, Vancouver, Canada

⁴Shiraz Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Keywords. urinary tract infections, kidney transplantation, pediatrics, pyuria, vesico-ureteral reflux

Introduction. Urinary tract infection (UTI) is common after pediatric kidney transplantation. The purpose of this study was to evaluate the prevalence of UTI and its risk factors in children and adolescents with kidney transplantation in Shiraz Transplant Center.

Materials and Methods. All children with kidney transplantation from 1990 to 2008 who were under regular follow-up were included in this retrospective study. Confirmed episodes of UTI after the 1st month of kidney transplantation were reviewed.

Results. Of the 216 patients younger than 19 years at the time of transplantation, 138 were included. The mean age at the time of kidney transplantation was 13.6 ± 3.5 years. Urinary tract infection was documented in 24 patients (15 girls and 9 boys), of whom 12 experienced 1 episode, 4 had 2 episodes, and 8 had more than 2 episodes, during a median follow-up period of 54 months. Of the patients with UTI, 14 (58%) had urinary reflux-obstruction disorders as the primary kidney diseases, 6 (25%) had suffered hereditary diseases, 3 (12.5%) had glomerular disease, and 1 (4.5%) had a urinary calculus. Occurrence of UTI was not significantly different among children with different primary kidney diseases ($P = .22$). Despite using prophylactic antibiotics after the 1st month of kidney transplantation in all 5 patients with neurogenic bladder, they all experienced recurrent UTI.

Conclusions. Despite discontinuation of antibiotic therapy, UTI was uncommon in children after the first month of transplantation. Two significant risk factors for UTI were female gender and neurogenic bladder in this transplant population.

IJKD 2011;5:416-9
www.ijkd.org

INTRODUCTION

Urinary tract infection (UTI), as a common bacterial infection after kidney transplantation, is reported in 15% to 58% of pediatric kidney allograft recipients.¹⁻⁵ The prevalence of UTI after kidney transplantation is higher in female recipients and patients with ureteral stents,⁶ obstructive uropathy,⁷ urinary diversion or bladder augmentation,⁸ and vesico-ureteral reflux.^{1,3,6-9} In a previous report from Shiraz Transplant Center, UTI was detected in 37.1% of transplanted pediatric and adult

population with autosomal dominant polycystic kidneys, and it had no relation to the underlying kidney disease.¹⁰ The incidence of UTI in adults with kidney transplantation is reported to be from 30% to 79% and about 60% of episodes of bacteremia originated from this site.¹¹

The information available on UTI in the field of pediatric kidney transplantation is scarce and most of the studies are limited to the adult population.^{12,13} The aim of this study was to evaluate the prevalence of UTI and to find risk factors for UTI after the

first month of kidney transplantation in children, in Shiraz Transplant Center, which is a referral center for transplantation in the south of Iran.

MATERIALS AND METHODS

Of the 216 transplanted children (< 19 years old) from 1990 to 2008, patients who were under regular follow-up by pediatric nephrologists at Shiraz Transplant Center were included in this retrospective descriptive study of UTI episodes. Routine maintenance immunosuppressive regimen was triple therapy with prednisolone, cyclosporine, and azathioprine or mycophenolate mofetil. Urinalysis and urine culture were being performed for all patients monthly, every other month, or at the presence of fever or any urinary symptoms (dysuria, urinary frequency or incontinence, flank or abdominal pain, nocturia, enuresis, and changes in urine color and odor). Urine cultures were being done after confirmation of no antibiotic administration (except for the small group of patients who were on prophylactic antibiotic therapy).

Considering different rates of UTI in the first month after kidney transplantation and discontinuation of prophylactic antibiotic therapy after the first month in most of the patients, only confirmed episodes of UTI after the first month of kidney transplantation were considered in this study. Urinary tract infection was defined as 100 000 colonies or more of microorganisms per milliliter in one culture of midstream urine in symptomatic patients or in two samples from asymptomatic patients. Recurrent UTI was defined as more than 2 episodes of UTI during a 6-month period.

The SPSS software (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA) was used for data analysis. The chi-square and the Fisher exact tests were used to compare the occurrence of UTI in patients with cadaveric and living donor sources and those with different primary kidney diseases.

RESULTS

Charts of 138 patients (79 boys and 59 girls) with kidney transplantation were reviewed. The mean age of the patients at the time of kidney transplantation was 13.6 ± 3.5 years (range, 3 to 19 years). The source of kidney allograft donation was cadaver in 66 children (47.8%), living related in 51 (36.9%), and living unrelated in 21 (15.3%).

One hundred and eighteen children (85.5%) were on hemodialysis before kidney transplantation and 17 (12.1%) had preemptive kidney transplantation. Nine patients used prophylactic antibiotics after the first month of kidney transplantation. All of the patients had follow-ups of more than 6 months (median, 54 months) posttransplantation. Twelve patients had follow-up visits for 6 to 12 month, 15 had 13 to 24 months follow-ups, and 111 had follow-ups of more than 2 years.

Urinary tract infection episodes were documented in 24 patients (17.3%), including 17 girls and 7 boys (male-female ratio, 0.41). Characteristics of the patients with UTI are shown in Table 1. In the patients with UTI, 12 had only 1 episode, 4 had 2, and 8 had more than 2 episodes. The most common primary kidney diseases and the related incidence of UTI are illustrated in Table 2. Urinary tract infection occurred in 11 patients of the 55 with cadaveric donor (20%) and 13 of the 59 with living donor (22%). No difference was found in terms of occurrence of UTI in patients with different primary kidney diseases ($P = .23$) or those with cadaveric and living donor ($P > .99$).

Five patients in the reflux-obstruction group had neurogenic bladder, and despite taking prophylactic antibiotics after the first month of kidney transplantation, all of these patients experienced recurrent UTI. However, no episode of UTI was reported in the other 4 patients in this group, who were all on prophylactic antibiotics after the first month of kidney transplantation.

DISCUSSION

In our pediatric kidney transplant cohort, UTI had been documented in 17.3% of the patients after the first month of kidney transplantation during a median follow-up period of 54 months. This is a relatively low rate as compared to previous reports in children.^{3,5,6,8} This may be in part due to excluding the first 4 weeks after kidney transplantation.

Urinary tract infection has already been demonstrated to be common in hospitalized children with a frequency of 19.1% of pediatric nephrology admissions in Shiraz University Hospitals.¹⁴ In typical cases, urinalysis and urine culture is sufficient for diagnosis, but in suspicious patients, the best paraclinical investigation can be dimercaptosuccinic acid renal scintigraphy of the kidneys.¹⁵ A single-center experience in a small group of children with

Table 1. Characteristics of Kidney Transplant Children With Urinary Tract Infection (UTI)

Patient	Age, y	Gender	UTI Episodes	Follow-up, mo	Primary Kidney Disease	Last Serum Creatinine, mg/dL
1	18	Male	1	20	Hereditary-metabolic diseases	3.0
2	18	Male	1	6	Hereditary-metabolic diseases	1.0
3	13	Male	1	8	Obstructive uropathy/reflux	1.0
4	11	Male	1	72	Obstructive uropathy/reflux	0.5
5	11	Male	2	180	Obstructive uropathy/reflux	0.8
6	17	Male	2	61	Obstructive uropathy/reflux	0.8
7	4	Male	3	43	Obstructive uropathy/reflux	0.9
8	12	Male	3	46	Obstructive uropathy/reflux	1.3
9	11	Male	3	75	Obstructive uropathy/reflux	1.6
10	13	Female	1	32	Hereditary-metabolic diseases	1.2
11	16	Female	1	6	Hereditary-metabolic diseases	1.0
12	12	Female	1	119	Obstructive uropathy/reflux	6.0
13	12	Female	1	99	Hereditary-metabolic diseases	1.2
14	16	Female	1	43	Glomerular diseases	1.0
15	9	Female	1	99	Obstructive uropathy/reflux	1.3
16	9	Female	1	86	Obstructive uropathy/reflux	1.5
17	17	Female	1	18	Obstructive uropathy/reflux	1.4
18	18	Female	1	8	Glomerular diseases	1.5
19	11	Female	2	43	Glomerular diseases	1.1
20	12	Female	3	67	Obstructive uropathy/reflux	0.9
21	17	Female	3	36	Obstructive uropathy/reflux	1.2
22	15	Female	3	108	Urinary calculus	1.0
23	15	Female	3	38	Obstructive uropathy/reflux	1.3
24	7	Female	3	80	Hereditary-metabolic diseases	1.1

Table 2. Underlying Kidney Diseases by History of Urinary Tract Infection*

Primary Disease	Urinary Tract Infection	
	No	Yes
Reflux-obstruction	44 (38.6)	14 (58.0)
Hereditary and metabolic disorders	41 (36.0)	6 (25.0)
Glomerular diseases	23 (20.0)	3 (12.5)
Urinary calculus	1 (0.9)	1 (4.5)
Unknown	5 (4.5)	0

*Values are absolute frequencies (percents).

a mean follow-up duration of 6 years after kidney transplantation showed that late UTI occurred in about 30% of the patients, while early UTI was reported in nearly half of them.¹⁶

The frequency of UTI in kidney transplant recipients depends on many factors including age, gender, kidney function, anatomical abnormalities, source of donation, immunosuppressive protocol, primary kidney disease, duration of bladder catheterization, interventions leading to kidney or ureteral tissue injury during surgery, and follow-up period.¹⁷⁻¹⁹ Acute pyelonephritis can adversely affect kidney function in kidney transplant patients.²⁰ One recent retrospective study on 76 children after kidney transplantation revealed UTI in 28% of patients during the mean

follow-up of 3.3 years, in spite of consumption of prophylactic antibiotics.²¹ Despite discontinuation of antibiotic treatment in most of our patients after the first month of kidney transplantation, the rate of UTI in our report is lower as compared to the above report. In our study, UTI was more common in girls, as reported previously.^{1,3,18} The reported cumulative incidence of UTI in adult kidney transplant recipients was 75.1%,²⁰ which is significantly higher than that in our study and almost all other reports in children. The reason of this difference is not explicitly explained.^{17,21}

The study of Feber and coworkers showed that obstructive uropathy and vesico-ureteral reflux prior to kidney transplantation were two important risk factors for UTI after kidney transplantation in children.²¹ In the aforementioned study, long-term prophylactic antibiotic therapy failed to control UTI. In the present study, no difference was observed between patients with different primary kidney diseases including those in the reflux-obstruction group; however, all the 5 cases of neurogenic bladder in the reflux-obstruction group, experienced recurrent UTI after kidney transplantation despite consumption of prophylactic antibiotics.

Cadaveric donation has been reported to increase the rate of UTI, probably due to longer periods

of cold ischemia and higher rates of delayed graft loss.²² Nearly half of our patients received cadaveric kidneys. Furthermore, the patients in this study were treated with azathioprine or mycophenolate mofetil which have been reported to increase the risk of UTI.^{23,24} However, neither cadaveric donation nor immunosuppressive protocol was found to increase the risk of UTI in our study.

CONCLUSIONS

We conclude that in Shiraz Transplant Center, UTI has not been common in children after 4 weeks of kidney transplantation, in spite of no prophylactic antibiotic therapy. Neurogenic bladder and female gender were found to be risk factors for UTI after 4 weeks of pediatric kidney transplantation.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Krieger JN, Brem AS, Kaplan MR. Urinary tract infection in pediatric renal transplantation. *Urology*. 1980;15:362-9.
- Mueller T, Resinger C, Ruffingshofer D, Arbeiter K, Balzar E, Aufrecht C. Urinary tract infections beyond the early post-transplant period in pediatric renal graft recipients. *Wien Klin Wochenschr*. 2003;115:385-8.
- John U, Everding AS, Kuwertz-Broking E, et al. High prevalence of febrile urinary tract infections after paediatric renal transplantation. *Nephrol Dial Transplant*. 2006;21:3269-74.
- John U, Kemper MJ. Urinary tract infections in children after renal transplantation. *Pediatr Nephrol*. 2009;24:1129-36.
- Sharifian M, Rees L, Trompeter RS. High incidence of bacteriuria following renal transplantation in children. *Nephrol Dial Transplant*. 1998;13:432-5.
- de Souza RM, Olsburgh J. Urinary tract infection in the renal transplant patient. *Nat Clin Pract Nephrol*. 2008;4:252-64.
- Khositseth S, Askiti V, Nevins TE, et al. Increased urologic complications in children after kidney transplants for obstructive and reflux uropathy. *Am J Transplant*. 2007;7:2152-7.
- Hatch DA, Koyle MA, Baskin LS, et al. Kidney transplantation in children with urinary diversion or bladder augmentation. *J Urol*. 2001;165:2265-8.
- Ranchin B, Chapuis F, Dawhara M, et al. Vesicoureteral reflux after kidney transplantation in children. *Nephrol Dial Transplant*. 2000;15:1852-8.
- Salehipour M, Jalaeeian H, Salahi H, et al. Are large nonfunctional kidneys risk factors for posttransplantation urinary tract infection in patients with end-stage renal disease due to autosomal dominant polycystic kidney disease? *Transplant Proc*. 2007;39:887-8.
- Brayman KL, Stephanian E, Matas AJ, et al. Analysis of infectious complications occurring after solid-organ transplantation. *Arch Surg*. 1992;127:38-47.
- Khosroshahi HT, Mogaddam AN, Shoja MM. Efficacy of high-dose trimethoprim-sulfamethoxazol prophylaxis on early urinary tract infection after renal transplantation. *Transplant Proc*. 2006;38:2062-4.
- Maraha B, Bonten H, van Hooff H, Fiolet H, Buiting AG, Stobberingh EE. Infectious complications and antibiotic use in renal transplant recipients during a 1-year follow-up. *Clin Microbiol Infect*. 2001;7:619-25.
- Derakhshan A, Al Hashemi GH, Fallahzadeh MH. Spectrum of In-patient Renal Diseases in Children "A Report from Southern part Islamic Republic of Iran". *Saudi J Kidney Dis Transpl*. 2004;15:12-7.
- Mohkam M, Maham S, Rahmani A, et al. Technetium tc 99m dimercaptosuccinic Acid renal scintigraphy in children with acute pyelonephritis: correlation with other imaging tests. *Iran J Kidney Dis*. 2010;4:297-301.
- Gargah T, Labessi A, Gharbi Y, Lakhrou MR. [Urinary tract infections in children following renal transplantation: a single-center experience]. *Tunis Med*. 2010;88:638-41. French.
- Martin-Pena A, Cordero E, Fijo J, et al. Prospective study of infectious complications in a cohort of pediatric renal transplant recipients. *Pediatr Transplant*. 2009;13:457-63.
- Saemann M, Horl WH. Urinary tract infection in renal transplant recipients. *Eur J Clin Invest*. 2008;38 Suppl 2:58-65.
- Sorto R, Irizar SS, Delgadillo G, Alberu J, Correa-Rotter R, Morales-Buenrostro LE. Risk factors for urinary tract infections during the first year after kidney transplantation. *Transplant Proc*. 2010;42:280-1.
- Pelle G, Vimont S, Levy PP, et al. Acute pyelonephritis represents a risk factor impairing long-term kidney graft function. *Am J Transplant*. 2007;7:899-907.
- Feber J, Spatenka J, Seeman T, et al. Urinary tract infections in pediatric renal transplant recipients—a two center risk factors study. *Pediatr Transplant*. 2009;13:881-6.
- Alangaden GJ, Thyagarajan R, Gruber SA, et al. Infectious complications after kidney transplantation: current epidemiology and associated risk factors. *Clin Transplant*. 2006;20:401-9.
- Chuang P, Parikh CR, Langone A. Urinary tract infections after renal transplantation: a retrospective review at two US transplant centers. *Clin Transplant*. 2005;19:230-5.
- Kamath NS, John GT, Neelakantan N, Kirubakaran MG, Jacob CK. Acute graft pyelonephritis following renal transplantation. *Transpl Infect Dis*. 2006;8:140-7.

Correspondence to:

Mohammad Hossein Fallahzadeh, MD
Shiraz Nephro-urology Research Center, Faghihi Hospital,
Shiraz, Iran
Tel: +98 711 646 6976
E-mail: fallahzadeh@gmail.com

Received December 2010

Revised May 2011

Accepted May 2011