

Incidence and risk factors for urinary tract infection in the first year after kidney transplantation at 108 Military Central Hospital, Vietnam

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Summary

Objective: To determine the incidence of urinary tract infections in kidney transplant patients in our hospital, to identify the microbial pathogens, risk factors for urinary tract infection. **Subject and method:** Primary kidney transplant patients at 108 Military Central Hospital with full follow-up records in the first year were included in the study. Age, sex, cause of kidney failure, pre-transplantation treatment measures, post-transplantation immunosuppressive regimen were collected. Patient was followed and midstream urine was cultured monthly. **Result:** There were 94 kidney transplant patients included in our study. Seventy patients (74.5%) were male and 24 (25.5%) were female. One hundred and two episodes of urinary tract infections in 37 patients (39.4%) were reported. Sex (female) ($p=0.003$; 95% CI: 1.716-14.021), urologic complications ($p=0.006$, 95% CI: 0.001-0.320) were found as risk factors for UTI in the first year of transplantation. *Escherichia coli* and *Klebsiella pneumoniae* were the most frequently isolated pathogens. UTI had no negative impact on short-term graft survival. **Conclusion:** The results of our study showed a high incidence of UTI in kidney transplant recipients. Infection control methods should be used regularly during post-transplant therapy.

Keywords: Urinary tract infection, kidney transplantation, gram-negative bacteria, 108 Military Central Hospital, Vietnam.

1. Background

In kidney transplant recipients, the risk of infection is increased compared to the general population due to intensive immunosuppressive drug use, surgical procedures and environmental factors. The most common infections in renal transplant patients are urinary tract infections (UTI). The reported frequency of UTI following renal transplantation ranged from 35% to 79% [1].

The increasing prevalence of UTI caused by multidrug-resistant microorganism is one of the

major challenges in transplant patients [2]. The common types of bacteria that cause UTI are gram-negative bacteria such as *Escherichia coli* (30-80%), *Klebsiella pneumoniae* (10%), *Proteus* (5%) and *Pseudomonas* (5%), and gram-positive bacteria such as *Enterococcus* sp. and *Staphylococcus aureus* [3].

The frequency of urinary tract infections may also vary between countries and centers with different environmental, social and economic characteristics. Therefore, determining the frequency and risk factors of urinary tract infections in each transplantation population is very important for determining prevention and treatment strategies.

The aim of our study was to determine the prevalence of urinary tract infection in kidney transplant recipients during the first year of kidney

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transplantation, to identify the causative organism as well as the underlying risk factors.

2. Subject and method

2.1. Subject

Study was performed at the Department of Nephrology and Dialysis, 108 Military Central Hospital, Vietnam. Patients who underwent renal transplantation between December 2016 and July 2022 were included in the study. Patients younger than 18 years of age and patients with primary non-functioning kidney were excluded from the study. Several episodes of urinary tract infections that develop during the first year after transplantation have been examined retrospectively. Basiliximab was used as the standard inducer, while anti-thymocyte globulin (ATG) was administered to patients receiving from brain-dead donors. The patients were started on a triple-drug immunosuppressive regimen typically consisting of calcineurin inhibitors (tacrolimus or cyclosporine), mycophenolate mofetil (MMF), and prednisone. Corticosteroids were progressively tapered to 5mg/day over three months after kidney transplant surgery. Induction regimens and maintenance immunosuppressive drugs at follow-up were also recorded.

Antibiotic prophylaxis with a single dose of ceftriaxon of 2g/day for 7-10 days was used in all patients after surgery. The ureteral stents placed during the transplant operation were removed 4 weeks after transplantation. Posttransplant urologic complications were defined as a need for intermittent catheterization, infection while catheterization, infection when patient is inpatient after kidney transplant surgery, bladder atony, need for surgical reconstruction of the urinary tract including ureteral necrosis, and ureteral and/or urethral strictures [1].

UTI was defined as the presence of urine culture positivity with more than 10^5 colony forming units

(> 10^5 CFU/mL) of bacteria per mL with UTIs symptoms. A positive urine culture without any clinical symptoms was considered as asymptomatic bacteriuria. All UTI patients were treated.

Demographic data, immunosuppressive drug regimens and transplant-related clinical features of the patients were compared regarding the presence of at least one episode of UTI. UTI characteristics including related microorganisms and antibiotic resistant patterns were also further analyzed. Risk factors associated with UTI were explored.

2.2. Method

The characteristics of the study patients were expressed as mean or median, as appropriate for categorical variables, percentages and variables with continuity. Independent samples T-test and one-way ANOVA tests were used for comparing parametric variables. For comparing categorical data, Chi-square test was used. Cox regression analysis was used to investigate the risk factors for the development of urinary tract infection. For all statistical analysis, p value <0.05 was considered significant. All data are analyzed with SPSS (version 26.0; SPSS Inc, Chicago, IL) statistical package.

3. Result

Characteristics of study subjects

Clinical characteristics and transplant-related data were illustrated in Table 1. There were 39/94 patients experienced at least one UTI over the study period and the incidence rate for a UTI was 41.4% across the whole cohort. A total of 102 UTI episodes were analyzed in the UTI group and the mean number of UTIs per person in this group was 3.02 ± 1.8 , with no difference in age, sex, duration of dialysis, source of organ donation, induction therapy, or anti-inflammatory therapy, immunosuppression, as well as kidney transplant function between the group of patients with UTI and the group without UTI ($p > 0.05$).

Table 1. Demographic and clinical data in patients with or without urinary tract infections (UTI)

Demographic and clinical	UTI (+) n = 37	UTI (-) n = 57	p-value
Age (years)	42.11 ± 13.1	45.75 ± 12.5	0.181
Sex, n (%)			0.085
Female	16 (43.2%)	8 (14%)	
Male	21 (56.8%)	49 (86%)	
Dialysis vintage (median, months)	34	27	0.497
Living, n (%)	35 (94.6%)	55 (96.5%)	0.656
Donor sex (Male), n (%)	29 (78.4%)	39 (66.4%)	0.292
Donor age (years)	31.8 ± 10.9	45 ± 11.3	0.325
Induction, n (%)			0.844
ATG	3 (8.1%)	4 (7.0%)	
Basiliximab	34 (91.9%)	53 (93.0%)	
Maintenance immunosuppressive drugs			0.756
Tacrolimus	36 (97.3%)	56 (98.2%)	
Cyclosporine	1 (2.7%)	1 (1.8%)	
mTor inhibitors	1 (2.7%)	6 (10.5%)	
Immunosuppressive drug			
Trough levels (ng/mL)			
Tacrolimus	8.8 ± 3.5	8.22 ± 3.6	0.062
Cyclosporin	125 ± 0.1	123 ± 9.8	0.903
mTor inhibitor	1.41 ± 1.5	3.32 ± 14.1	0.744
Creatinine at 1 st month (mg/dL)	129.58 ± 57.6	137.57 ± 87.4	0.272
Creatinine at 1 st year (mg/dL)	117 ± 0.1	103.38 ± 33.0	0.682
eGFR at 1 st month (mL/min/1.73m ²)	63.29 ± 30.6	63.17 ± 24.8	0.972
eGFR at 1 st year (mL/min/1.73m ²)	58.90 ± 0.1	79.17 ± 19.5	0.303

Note: ATG: Anti-thymocyte globulin; mTor: Mammalian target of rapamycin; eGFR: estimated glomerular filtration rate; $p < 0.05$: Statistically significant.

There were seventy-six urine cultures sample (74.5%) $> 10^5$ CFU/mL for up to 1 month after kidney transplantation ($p < 0.05$). This was the period of the patients highest infection in the first year after transplantation (22 patients, 59.4%). The lowest number of infected urine samples was at 12 months with only 4 sample (1 patient, 2.7%) infected. The frequency of urinary tract infections of patients after kidney transplant is shown in Table 2.

Table 2. Urinary tract infection in the first year

Time after transplant	Urine infection sample (n, %)	Patient with infection (n, %)	p
After transplantation - 1 month	76 (74.5)	22 (59.4)	<0,05
1 month - 3 months	11 (10.7)	9 (24.3)	
3 months - 6 months	6 (5.8)	3 (8.1)	
6 months - 9 months	5 (4.9)	2 (5.4)	
9 months - 12 months	4 (3.7)	1 (2.7)	
Total	102	37	

In multivariate analysis sex (female) (p=0.003), and urologic complications (p=0.006) were found as the main independent risk factors for UTI development in the first year of transplantation (Table 3).

Table 3. Independent risk factors for urinary tract infections in the first year after transplantation

Parameters	OR (95% CI)	p-value
Age	1.031 (0.994-1.070)	0.097
Sex (female)	4.905 (1.716-14.021)	0.003*
Dialysis vintage	2.718 (0.601-12.289)	0.194
Peritoneal dialysis	1.297 (1.013-1.661)	0.868
Hypertension	0.286 (0.049-1.671)	0.165
BMI > 25	0.765 (0.292-2.001)	0.584
Urologic complications after transplantation	0.190 (0.001-0.320)	0.006*

Note: BMI: Body mass Index; *p<0.05: Statistically significant.

The most common pathogen was *Escherichia coli*, isolated in 47 episodes (46%), followed by *Klebsiella pneumoniae* in 16 episodes (12.6%) and *Enterococcus faecalis* in 19 episodes (18.6%); Other bacteria accounted for 20 episodes (19.6%) in the UTI episodes. In total, 102 microorganisms were isolated in all patients. Including 47 *Escherichia coli* isolates, 16 *Klebsiella pneumoniae* isolates, 19 *Enterococcus faecalis* isolates, 20 Other bacteria isolates. A detailed description of UTI attacks, including the pathogens, groups of antibiotics sensitive to bacteria based on antibiogram, and antimicrobial susceptibility profiles used against the most common bacteria is summarized in Table 4.

Table 4. Causative agents and treatment choices for UTI during the first year of transplantation (102 agents in total 67 UTI attack)

Microorganisms	n, (%)
<i>Escherichia coli</i>	47 (46)
<i>Klebsiella pneumoniae</i>	16 (15.6)
<i>Enterococcus faecalis</i>	19 (18.6)
Other bacteria	20 (19.6)
Treatments	UTI attack n, (%)
Penicillins	19 (28.3)
Cephalosporins	5 (7.4)
Ciprofloxacin	7 (10.4)
Aminnoglycoside	7 (10.4)
Ureido penicillin	4 (5.9)
Tetracyclin	2 (2.9)
Glycopeptid	10 (14.9)
Polymyxin	13 (19.4)

There were 21 male patients (56.7%), 16 female patients (43.2%) with bacterial UTI. Notably, male patients had fewer episodes of UTI than female patients (34/68 episodes) (Table 5).

Table 5. Comparison of male and female patients with UTI

	Male (n = 21)	Female (n = 16)	p-value
Age (years)	39.7 ± 12	45.1 ± 14,2	0.219
Dialysis vintage (n) (%)	17 (81%)	14 (87.5%)	0.592
Living/Deceased (n) (%)	20 (95.2%)	15 (93.8%)	0.843
Induction (ATG) (n) (%)	3 (14.3%)	-	0.115
DM or PTDM (n) (%)	2 (9.5%)	1 (6.25%)	0.346
Urologic complication (n) (%)	3 (42.8%)	3 (21.4%)	0.354
Total UTI episodes (n)	34	68	0.003*
Mean UTI episodes (n)	1.6	4.25	0.002*
Bacteria	34	68	0.003*

Note: DM: Diabetes mellitus; PTDM: Post-transplant diabetes mellitus; ATG: Anti-thymocyte globulin; *p<0.05: Statistically significant.

In regard to immunosuppressive regimes, induction regimens were not different between the patients with UTI and those without UTI. Maintenance immunosuppressive drugs and the trough levels of the drugs were similar. There were no significant differences between the groups. Immunosuppressive drugs and drug levels were also similar in males and females.

4. Discussion

Post-transplant UTI in kidney transplant patients have become common. Increased morbidity and re-hospitalization are the consequences of UTI in kidney transplant recipients. Therefore understanding and exploring the UTI details is etiology crucial in transplant practice. In our study we found that UTI incidence in the first year after transplantation was 39.4%. Although the incidence of UTI in kidney transplant recipients has been reported ranging between 7%-80% depending on the diagnostic criteria used, our UTI rate is relatively lower than reported elsewhere [4]. In our study, the frequency of urinary tract infections was highest in the period after surgery to 1 month after kidney transplant, because during this time the patient still used a drain, urinary catheter as well as a sonder JJ and immunosuppressive doses are the highest during this time to prevent acute rejection, making

the patient more susceptible to infection than at other times. The rate of asymptomatic UTI was quite high. One possible explanation for this could be that we used routine screening with midstream urine culture at all follow-up visits, and detected UTIs in the urine in time before they were symptomatic proof. The relatively mild course of UTI attacks might result from early detection and immediate antibiotic treatment in our cohort. So none of our UTI cases progressed to sepsis. Factors such as gender and the presence of urinary complications stand out as important risk factors in our patient. Therefore, we recommend that patients with risk factors receive adequate screening and care during the first year after kidney transplantation.

According to a recently published study from Australia, The authors isolated the microorganism causing UTI in only 3.9% of urine cultures [5]. Bodro et al. demonstrated that 37% of bacteria are the cause of UTIs in kidney transplant recipients [6]. However, there are some studies showing that the rate of UTI is similar to our study [7]. According to a recently published meta-analysis, more than 50% of isolates causing UTI in kidney transplant recipients were shown to be resistant to more than 50% of the antibiotics used in Middle East countries [8]. Thus we can conclude that the increasing rate of UTI in

transplant recipients may be a major concern worldwide in the coming years.

There are many studies showing that urinary tract infections are more common in female recipients [1], This is also similar to our study, the rate of UTI in female patients is higher than in male patients. The explanation for this difference may be that the structure of the female genitals is complicated, more susceptible to infections than men, and because the length of the female urethra is shorter, it is easier to get bacteria that cause UTI episodes female. Brakemeir et al. also reported that the prevalence of bacterial infections causing UTIs was different between men and women, with women having a higher risk of UTI than men [9]. Our findings were also consistent with this previously published data.

These results should be interpreted with caution due to the single-center and retrospective nature of the study and the relatively small number of patients. The low number of events limits further statistical analysis for exploring the exact effect of female gender on UTI.

5. Conclusion

The results of our study indicate that gender factor, and urinary complications are risk factors for UTI in the first year after kidney transplantation ($p < 0.05$). The rate of UTI in our study was relatively low (39.4%), and UTI occurs mainly in the first month after kidney transplantation (74.5%). Infection control methods should be applied more vigorously, especially routine midstream urine culture, to be able to detect UTI early and prompt treatment in kidney transplant patients, especially female kidney transplant patients.

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