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Urinary Tract Infection in Kidney Transplant Recipients: The predictors and two-year outcomes

Enver Yüksel [iD] [1], Hasan Akkoç [iD] [2]

1 Department of nephrology: University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Diyarbakir, Turkey

2 Department of Pharmacology, Dicle University Education and Research Hospital, Dicle University Medical Faculty, Diyarbakir, Turkey

Abstract

Background: Urinary tract infection (UTI) is the most common infection in kidney transplant recipients (KTR). Our aim in this study is to determine the prevalence, risk factors, and causative microorganisms of UTI. In addition, to compare the kidney functions of the patients in the 2nd year who developed and did not develop UTI after transplantation.

Method: Two hundred sixteen patients underwent kidney transplantation in our center between July 2012 and March 2020. A total of 206 patients with 267 episodes of UTI were included in the study. The impacts of catheterization, hemodialysis duration, gender, posttransplant prolonged hospital stay on UTI development, and UTI on two-year allograft functions, were evaluated.

Results: The mean age of the study patients was 34.5±12.7, and 43.7% of them were women. At least one UTI attack developed in 38.8% (80/206) of the KTR. Thirty-one KTR developed recurrent UTI (R-UTI). UTI incidence was found 38.8% in our cohort. Female gender, posttransplant prolonged hospital stay, presence of prolonged double-j stent and foley catheter durations were found associated with UTI development. (p<0.001, p<0.001, p<0.001, p<0.001, respectively). The mean estimated glomerular filtration rate eGFR in KTR with UTI at 2-year post-transplant was significantly lower than KTR without UTI (71.2±29.2 vs 82.4±23.9; p=0.006). Low eGFR was more prominent among the KTR with R-UTI (69.9±31.6). Escherichia coli and Klebsiella pneumonia were the most frequently isolated microorganisms in our cohort.

Conclusions: This study demonstrated UTI may have an adverse impact on allograft function in KTR, especially in KTR with R-UTI.

Keywords: Kidney transplantation, recurrent urinary tract infections, urinary tract infections.

Böbrek Nakli Alıcılarında İdrar Yolu Enfeksiyonu: Öngörücüleri ve iki yıllık sonuçları

Öz

Amaç: Üriner sistem enfeksiyonu (ÜSE), böbrek nakil alıcılarındaki (BNA) enfeksiyonların içinde en sık görülenidir. Bu çalışmadaki amacımız ÜSE' lerin prevalansını, risk faktörlerini ve etken mikroorganizmaları belirlemektir. Ayrıca nakil sonrası ÜSE gelişen ve gelişmeyen hastaların 2. yıldaki böbrek fonksiyonlarını karşılaştırmaktır.

Yöntemler: Temmuz 2012-Mart 2020 tarihleri arasında merkezimizde 216 hastaya böbrek nakli yapıldı. Çalışmaya 267 ÜSE atağı olan toplam 206 hasta dahil edildi. Kateterizasyon, hemodiyaliz süresi, cinsiyetin, nakil sonrası hastanede kalış süresinin ÜSE gelişimi üzerindeki etkileri ve ÜSE 'nin iki yıllık allogreft fonksiyonları üzerindeki etkileri değerlendirildi.

Bulgular: Çalışma hastalarının ortalama yaşı 34.5±12.7 olup, 43.7%' si kadındı. Böbrek nakli alıcılarının 38.8% (80)' ninde en az bir ÜSE atağı gelişti. Üriner sistem enfeksiyonu olan BNA' ların 31' inde tekrarlayan ÜSE (T-ÜSE) gelişti. Kadın cinsiyet, nakil sonrası hastanede kalış süresinin uzaması, double-j stent ve foley kateter sürelerinin uzamasının ÜSE gelişimi ile ilişkili olduğu bulundu (sırasıyla p<0.001, p<0.001, p<0.001, p<0.001). Transplantasyondan 2 yıl sonra ÜSE' li BNA' larda ortalama tahmini glomerüler filtrasyon hızı eGFR, ÜSE' siz BNA' lardan önemli ölçüde düşük bulundu (71.2±29.2'ye karşı 82.4±23.9; p=0.006). Düşük eGFR, T-ÜSE (69.9±31.6) olan BNA' larda daha belirgindi. Kohortumuzda en sık izole edilen mikroorganizmalar Escherichiacoli ve Klebsiellapneumonia idi.

Sonuç: Bu çalışma, ÜSE ' nin BNA' larda, özellikle T-ÜSE' li BNA 'larda allogreft fonksiyonu üzerinde olumsuz bir etkisi olabileceğini göstermiştir.

Anahtar kelimeler: Böbrek nakli, idrar yolu enfeksiyonları, tekrarlayan idrar yolu enfeksiyonları.

INTRODUCTION

Kidney transplantation (KT) is the most successful treatment method in patients with end-stage renal disease (ESRD). Surgical procedures, immunosuppressive medicine, dialysis duration, and environmental factors increase the risk of infection in kidney transplant recipients (KTR) compared to the general population. Urinary tract infection (UTI) is the most common infection in KTRs and is especially common in the first year post-transplant in which immunosuppressive treatment is administered more intense[1,2]. UTI is also the leading cause of hospitalization in KTRs[3]. Previous studies indicated that diabetes mellitus, female gender, anatomical abnormalities, cadaveric donors, prolonged postoperative hospitalization, ureteral stents, and bladder catheterization are the main risk factors for UTI development[4]. Conflicting results have been reported in studies examining the effects of UTI and recurrent UTI (R-UTI) on allograft functions in the long-term in KTR[5-7].

Gram-negative bacteria are the most common cause of UTI in both KTR and the non-transplanted population[8]. Escherichia coli (30-80%) is the most common uropathogen, followed by Klebsiella pneumoniae (10%), Proteus spp (5%) and Pseudomonas aeuroginosa (5%) species[9]. The increasing number of drug-resistant microorganisms in the etiology of UTI among KTR has become a challenge for clinicians. This leads to a longer length of hospitalization and increased cost. It was also been shown that UTI are associated with acute allograft dysfunction in this population[10].

Our primary goal in kidney transplant recipients is to prevent infections whenever possible and to protect allograft function with rational approaches. The impact of UTI on short-term outcomes of allograft in KTR has been studied previously and controversial results were published which needs to be interpreted cautiously. However, the long-term outcomes regarding the issue need to be more clarified.[2] In this study, we aimed to determine

the prevalence of UTI, risk factors for UTI, the microorganisms that lead to UTI in KTR, the relationship between those factors, and their impact on two-year allograft function.

METHOD

Study design and participants

This single-center, retrospective, and observational cohort study that includes all kidney transplantations performed between July 2012 and March 2020. The study complies with the principles of the Declaration of Helsinki and is approved by the Institutional Research Ethics Committee of our hospital (proof; 24/03/2022, no; 56). The ethics committee waived the requirement for informed consent due to the retrospective nature of the study. The KTRs over the age of 18 and with a history of at least one urinary tract infection and who were followed up regularly posttransplant two-year in our center were considered for data evaluation.

Exclusion criteria

The patients;

•Age under 18 years

•With primary non-functioning allograft kidney

•Transferred to other centers for various reasons within two years after transplantation

•Died in the early period (within 30 days after KT)

• Had missing data were excluded from the study.

In our center, routine screening for asymptomatic bacteriuria is not performed in patients within posttransplant 3 months. However, a detailed investigation had been performed on patients with symptoms or clinical suspicion of UTI.

Data collection

Kidney transplant recipients who met the inclusion criteria were evaluated. The clinical features of the patients with symptomatic UTI were recorded. All study data were obtained by means of our hospital's electronic health system (nucleus), patient files, and the national electronic health system (NEHS) of Turkey. The Median follow-up duration was 24 months. Information related to demographic characteristics of patients, comorbidities, medical history, drugs used for induction, laboratory and microbiological data, immunosuppression treatments, donor status (living, deceased), type of transplantation (preemptive-hemodialysis-peritoneal dialysis), type of renal replacement treatment (RRT) and RRT duration, urinary catheter and ureteral stent durations, CKD etiology, development of rejection and date of death were recorded. In addition, causative microorganisms and antibiotic resistances were recorded.

Kidney transplant recipients were divided into two groups; Group 1 (KTRs with posttransplant UTI history) and Groups 2 (KTRs without posttransplant UTI history). All UTIs were categorized depending on the first diagnosing time postoperatively; within the first month, between 1-12 months, and between 13-24 months. The complete blood count, whole urine test, urine culture, and routine biochemistry tests were considered in evaluating the KTRs.

Immunosuppression Regimens

Induction therapy consisted of basiliximab or anti-thymocyte globulin with tacrolimus, mycophenolatemofetil/sodium, and intravenous methylprednisolone. All KTRs received an induction protocol that consists of methylprednisolone plus anti-thymocyte globulin (ATG) or basiliximab according to risk stratification. A triple immunosuppressive regimen principally consisting of calcineurin inhibitors (tacrolimus or cyclosporine), mycophenolatemofetil/mycophenolate sodium, and prednisone is preferred for maintenance immune suppressive therapy. Maintenance immunosuppression therapy was adjusted over

time considering the patients' immunological risk status. Corticosteroids were progressively tapered to 5 mg/day over 3 months. Mycophenolatemofetil/mycophenolate sodium was used at a dose of 1 g / 720 mg twice a day, unless there were side effects that required dose reduction.

Prophylactic Approaches

A single dose of 2 g cefuroxime was administered to all patients for prophylaxis before the transplant surgery. Trimethoprim/sulfamethoxazole (TMP / SMX) was administered on the 7th day after transplantation and continued at a dose of 400/80 mg/day for 6 months in the prophylaxis of Pneumocystis jirovecii[12].

Urinary Catheter and Double-J Stent

A bladder catheter was inserted in all KTRs during transplantation and removed at the discharge. Ureteral stents were placed during transplantation and were removed 4-6 weeks after transplantation in a period of the absence of active UTIs. Urological complications after transplantation were defined as the need for surgical reconstruction of the urinary tract, including the need for intermittent catheterization, bladder atony, ureteral necrosis, and ureteral and/or urethral strictures.

Definitions

UTI was accepted as the detection of >105 colony forming units (CFU/mL) of microorganism per urine milliliter and positive urine culture in patients with clinical symptoms of UTI[5,13]. A positive urine culture results detected in patients without clinical symptoms were accepted as asymptomatic bacteriuria (ABU)[5,14]. Recurrent urinary tract infection (R-UTI) was defined as a urinary tract infection that progressed with three or more symptomatic episodes in at least a 12-months period or two or more in any 6-months period[5,14]. Delayed graft function (DGF) was defined as the need for dialysis within seven days after transplantation[15].

Outcomes

In this study, we aimed to investigate the risk factors that facilitate the development of UTI and the effects of UTIs on graft functions in the long term. In addition, we described the bacterial species that caused UTIs and their resistance patterns in our cohort.

RESULTS

Demographic and clinical characteristics

In our center, 216 patients underwent kidney transplantation between 07.01.2012 and 03.02.2020. A total of 10 KTRs were excluded, 8 of those were under 18-year-old, one died within posttransplant month 1, and one had a primary non-functioning allograft kidney. UTI was developed in 80 of the remaining 206 patients. 267 UTI episodes were experienced in Group 1 (Figure 1). All of the KTRs included in this study had received an allograft for the first time. The mean age of KTRS was 34.5±12.7 and 43.7% of those were female. 83.5% of kidney transplants were performed from living donation and the remains were from the cadaveric donation. 35.9% of transplants were performed in preemptive cases whereas 60.7% of from the cases of hemodialysis and 3.4% of from peritoneal dialysis (Table 1). Hypertension (32.0%) was the most common comorbidity in the recipients, followed by diabetes mellitus (13.1%), neurogenic bladder (4.9%; 10/206), and VUR (2.9%; 6/206). The demographic and clinical characteristics of the two groups were summarized in table 1. Female patients had more frequent UTIs episodes than male recipients (p<0.001) and recurrent UTIs were more common in female recipients. Frequent recurrent UTIs were also developed in patients with neurogenic bladder and VUR in transplant kidney (p=0.001, p=0.002, respectively) (Table1).

Table I: Demographic and Clinical Characteristics of all kidney transplant recipients

Characteristic	All patients, n=206	No UTI (n:126)	UTI (n:80)	Recurrent UTI (n :31)	P-value
Age in years (mean)	34.5±12.7	34.4±12.2	34.7±13.6	34.1±15.8	0.923
Gender female, %(n)	43.7% (90)	31.7%(40)	62.5%(50)	67.7% (21)	**<0.001**
Hypertension, %(n)	32.0% (66)	31.% (40)	32.5% (26)	35.5% (11)	0.91
DM or PTDM, %(n)	13.1% (27)	10.3%(13)	17.5%(14)	22.6% (7)	0.202
Neurogenic bladder, %(n)	4.9% (10)	0.8% (1)	11.2% (9)	25.8% (8)	**0.001**
VUR, %(n)	2.9% (6)	0% (0)	7.5% (6)	16.1% (5)	**0.002**
Sexual activity, %(n)	70.9% (146)	65.9% (83)	78.8% (63)	77.4% (24)	0.068
Dialysis vintage, months (mean±SD)	27.7±43.7	25.3±41.1	31.6±47.6	27.2±43.1	0.263
Dialysis dependence, % (n)					
Preemptive transplantation,	35.9% (74)	48 (38.1)	26 (32.5)	38.7% (12)	0.713
Hemodialysis	60.7% (125)	74 (58.7)	51 (63.8)	58.1% (18)	
Peritoneal dialysis	3.4% (7)	4 (3.2)	3 (3.8)	3.2 %(1)	
Double J stent, days (mean±SD)	26.0±6.67	23.1±4.0	30.5±7.4	33.3±8.2	**<0.001**
Foley catheter removal time (days)	9.0±6.63	6.8±3.9	12.6±8.3	15.1±8.8	**<0.001**
Duration ofhospitalization, days (mean±SD)	11.1±7.9	9.2±5.1	14.4±10.2	16.7±11.1	**<0.001**
Donor status , % (n)					
Living	83.5%(172)	87.3% (110)	77.5%(62)	80.6% (25)	0.098
Deceased	16.5%(34)	12.7%(16)	22.5%(18)	19.4% (6)	
Induction therapy, % (n)					0.336
ATG, %(n)	66.0%(136)	63.5% (80)	70% (56)	71% (22)	
Basiliximab, %(n)	34%(70)	36.5% (46)	30%(24)	29% (9)	
DGF, n (%)	6.8%(14)	2.4% (3)	13.8%(11)	25.8%(8)	**0.004**
Rejection within 2 years, %(n)	9.7% (20)	7.5% (12)	10%(8)	16.1% (5)	**1.000**
Pretransplantation UTIs, %(n)	5.8% (12)	1.6%(2)	12.5%(10)	22.6% (7)	**0.002**
Maintenance immunosuppressive drugs, %(n) Calcineurin Inhibitors					
mTOR inhibitor	98.4% (203)	98.4% (124)	98.8% (79)	%100 (31)	1.000
MMF/ MPA	2.4% (5)	0.8% (1)	5% (4)	6.5% (2)	0.076
	99.0%(204)	100.0% (126)	97.5% (78)	96.8% (30)	0.150
Discharge creatine, mg/dL,%(n)	1.19±0.47	1.19±0.43	1.18±0.53	1.14±0.41	0.18
Discharge eGFR, %(n)	79.9±26.9	79.6±24.8	79.6±30.0	82±31.8	0.92
Creatinine at 1st month (mg/dL), %(n)	1.17±0.60	1.18±0.56	1.16±0.66	1.07±0.30	0.079
Creatinine at 1st year (mg/dL), %(n)	1.22±0.83	1.21±0.92	1.24±0.68	1.26±0.66	0.79
Creatinine at 2st year (mg/dL), %(n)	1.28±1.04	1.20±0.94	1.43±1.18	1.54±1.52	0.36
eGFR at 1st month (ml/min), %(n)	80.6±24.3	80.8±21.8	80.2±27.9	82.7±28.1	0.81
eGFR at 1st year (ml/min), %(n)	79.3±24.7	81.9±22.4	75.6±27.9	75.5±30.8	0.09
eGFR at 2st year (ml/min), %(n)	79.2±26.4	82.4±23.9	71.2±29.2	69.9±31.6	**0.006**

ATG: anti-timosit globulin, DGF: Delayed graft function, eGFR: estimated glomerular filtration rate, mTOR: Mammalian target of rapamycin, MFA; mycophenolate sodium, MMF; mycophenolatemofetil, UTI: urinary tract infection, VUR: Vesicoureteral reflux.
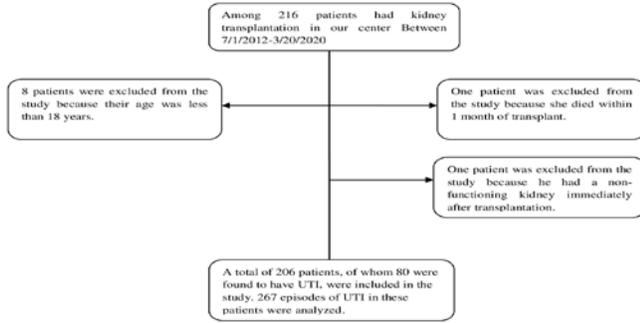
Figure 1: Flowchart of the enrollment process

Clinical outcome

The patients were divided into two groups according to whether they developed UTI (group-1) or not (group-2). At least one UTI episode was developed in 38.8% (80/206) of the patients in our study population. Recurrent UTI (R-UTI) was developed in 38.8% (31/80) of the patients who were developed urinary tract infections. In the subgroup of patients who were developed UTI, 3.3 (267/80) UTI attacks were developed per person. Thirty-nine (48.8%) of patients were developed their first UTI attack within the first month after kidney transplantation, 33 (41.2%) of patients within 1 month-12 months, and 8 (10%) of patients within 13-24 months (Table 1). UTIs were developed predominantly in the 1st year (90%, 72), and relapses were experienced mostly in this period.

The mean bladder catheter time of patients was 9.0±6.63 days. Bladder catheter times of group-1 patients (12.6±8.3) were higher than those of group-2 patients (6.8±3.9) (p=<0.001). Patients with R-UTI had the longest bladder catheter duration (15.1±8.8). In our study, urinary stents were removed cystoscopically 26.0±6.67 days after transplantation. The mean stent duration of group-1 patients (30.5±7.4) was higher than that of group-2 patients (23.1±4.0), and this was found to be directly related to increased urinary tract infection risk (p=<0.001). Again, urinary stents were removed after a longer time in R-UTIs (33.3±8.2).

The rate of patients with female gender, neurogenic bladder, VUR, development of UTI in the last 3 months before transplantation, and delayed renal function after transplantation were higher in the group that developed UTI than in the group that did not develop UTI (p<0.001, p=0.001, p=0.002, p=0.002, p=0.004, respectively). Age, dialysis duration, donor status (Living, Deceased), applied induction treatments and rejection rates were similar in both groups (p=0.92, p=0.26, p=0.09, p=0.33, p=1.00, respectively). Concomitant diseases and immunosuppressive treatment protocols were similar in both groups.

In order to determine the changes in kidney function of patients in group-1, group-2 and patients with R-UTI, 1st month, 1st year and 2nd year eGFRs were recorded and summarized in Table 1. In the 2nd year of their follow-up, the mean eGFR of group-1 patients (71.2±29.2) was lower than that of group-2 patients (82.4±23.9) (p=0.006). The eGFRs (69.9±31.6) in the 2nd year of the patients who developed recurrent UTI were also found to be lower than that of the group-1 patients. In other words, as the number of UTI attacks were increased, the eGFR value in the 2nd year was decreased. Graft loss developed in 5 (2.4%) of the patients during their two-year follow-up. Of the patients with graft loss, 3 (60%) were patients who were developed UTI.

While 66.0% (136) of the patients in our study were received intravenous ATG as induction therapy, 34% (70) were received basiliximab. Calcineurin inhibitors, mycophenolatemofetil/sodium and prednisolone combinations were mostly preferred in patients for the maintenance immunosuppressive therapy. Calcineurin inhibitors were used in 98.4% (203) of the patients, mycophenolatemofetil/sodium in 99.0% (204) and mammalian target of rapamycin (mTor) inhibitors in 2.4% (5) of the patients. While mTOR inhibitors were used instead of calcineurin inhibitors in three of our patients, mTOR inhibitors were also used instead of mycophenolatemofetil/sodium in 2 of our patients.

Microbiological Data

In our study, the most common UTI agent was Escherichia coli (43.3%) among gram negative bacilli. This was followed by Klebsiellaspp (31.8%), Enterococcus spp (8.3%) and Staphylococcus spp. (6.0%) respectively (table 2). Of these organisms, 51.7% (138) had extended spectrum beta lactamase (ESBL) positivity and 6.7% (18) had carbapenem resistance (table 2). During these UTI episodes, 123 (46.1%) of the patients were treated in hospital and

144 (53.9%) were treated as outpatients. The most commonly used antibiotic group in the treatment of patients was carbapenem, followed by phosphomycin and quinolone groups, respectively (table 2).

Table II: Causative agents andtreatment choices for UTI during the second year of transplantation

Bacteria	Number (%)
Escherichia coli	43.3% (116)
Klebsiellapneumoniae	31.8% (85)
Enterococcus faecalis	8.3% (22)
Staphylococcus spp.	6.0% (16)
Proteus mirabilis	2.7% (7)
Candida	3.0% (8)
Pseudomonas aeruginosa	1.9% (5)
Other	3% (8)
ESBL (+) Yes No	51.7% (138) 48.3% (129)
Carbapenems resistant Yes No	6.7% (18) 93.3% (249)
Class of antibiotics used	
Penicillins	7.1% (19)
Cephalosporins	11.2% (30)
Fluoroquinolones	16.1% (43)
Carbapenems	32.3%(86)
Fosfomycin	25.1% (67)
Nitrofurantoin	6.0% (16)
Antifungals	2.2% (6)
Total	(267)

ESBL; extended spectrum beta lactamase

Risk factors for UTI and its effect on graft functions

In order to determine the risk factors that facilitate the development of UTI in patients who were underwent to kidney transplantation and to determine the eGFR changes in group-1 and group-2 patients in the 2nd year after transplantation, two-group comparisons were performed. As a result, we detected female gender, long-term hospitalization after transplantation, presence of double-j stent and long foley catheter durations were important risk factors facilitating the development of UTI (p<0.001, p<0.001, p<0.001, p<0.001, respectively) (Table 3). However, neurogenic bladder, vesicoureteral reflux (VUR), experienced pre-transplantation UTI and presence of post-transplant delayed kidney function were not found to be significantly associated with post-transplant UTI development in univariate analysis. While there was no significant difference between the eGFRs of group-1 and group-2 patients in the 1st year, the mean eGFR of group-1 patients was found to be significantly lower than that of group-2 patients in the 2nd year (P=0.006).This shows that UTIs, especially recurrent UTIs, cause long-term eGFR reduction in the transplanted kidney.

Table III: Traditional univariate andmultivariate logistic regression analysis for kidney transplant recipients with and without UTI

	Univariate			Multivariate		
	Unadjusted	95 % CI	p value	Unadjusted	95 % CI	p value
Gender female, %(n)	0.27	0.15-0.50	**<0.001**	0.25	0.10-0.60	**<0.01**
Neurogenic bladder	15.8	1.96-127.6	**0.009**	24.7	0.0+-63.2	0.25
VUR in the transplant kidney	0	0.00-0.00	0.99			
Double J stent (days)	1.27	1.18-1.36	**<0.001**	1.37	1.22-1.54	**<0.001**
Foley catheter removal time (days)	1.20	1.12-1.29	**<0.001**	2.46	1.68-3.59	**<0.001**
Hospitalization duration at transplantation (days)	1.10	1.05-1.15	**<0.001**	0.48	0.36-0.65	**<0.001**
DGF, n (%)	6.53	1.76-24.2	**0.005**	1.37	0.78-24.1	0.82
Pretransplantation UTIs	8.85	1.88-41.5	**0.006**	3.03	0.32-28.32	0.32

DGF: Delayed graft function, eGFR: estimated glomerular filtration rate, UTI: urinary tract infection, VUR: Vesicoureteral reflux.

Statistical Analysis

All statistical analyses were performed using IBM SPSS software 24.0 (Armonk, NY: IBM Corp.). If the parametric and nonparametric continuous variables were normal, they were presented as mean and standard deviation (P >.05 in Kolmogorov-Smirnov test or Shapiro-Wilks [n < 30]); if the continuous variables were not normal, they were described as median. The

Categorical variables were expressed aspercentages and numbers. Parametric and nonparametric continuous variables were analyzed using Student's t-test, Mann-Whitney U test, Chi-square or Fisher's exact tests as appropriate. Relative risk with 95% confidence interval was used to assess the link between individual risk factors and the development of infections during the post-transplant period. A univariate logistic regression analysis was performed on the variables found to be statistically significant (p<0.05) in the pairwise comparison. Subsequently, all significant variables with a p value < 0.05 in the univariate analysis were considered for a multivariate logistic regression analysis.

DISCUSSION

Early diagnosis and treatment of UTIs and determination of underlying risk factors are very important in kidney transplant recipients. Because UTIs are associated with increased mortality, morbidity and hospitalization rates, they are also one of the important causes of acute graft dysfunction. For these reasons, it is important to examine UTI risk factors in more detail and to examine changes in kidney function in patients with and without UTI in the longer term. To the best of our knowledge, our study is one of the rare studies in which data with the duration of longer than one year after kidney transplantation were examined.[4] In our study, we detected female gender, long-term hospitalization after transplantation, presence of double-j stent and long foley catheter durations as risk factors facilitating the development of UTI. In addition, we found that the mean eGFR of group-1 patients (71.2±29.2) was significantly lower than that of group-2 patients (82.4±23.9) at 2nd year (p=0.006). This difference was more pronounced in those with R-UTI (69.9±31.6).

In previous studies, the frequency of UTI in KTR was reported to be between 7% and 80%[5,13,16]. These differences in the prevalence of UTI may probably be due to the lack of standardization in diagnostic criteria, antibiotics used in prophylaxis and changes in follow-up periods[5,13,17]. In our study, the frequency of UTI was found to be 38.8%. This result was in a similar rate to other studies. UTI may occur at any time after transplantation. However, studies have reported that it often develops in the first 6 months. [18] While Abbott et al. found that 84% of symptomatic UTI cases were occurred in the first 6 months after transplantation, Wu et al. was reported the incidence of UTI in the first 6 months after transplantation as 17%[19]. In our study, 90% of UTIs were occurred in the first year.

There are different results in studies regarding the distribution of post-transplant UTIs by gender. In addition to studies showing that UTIs are more common in women, there are also studies reporting that they are more common in men or that there is no difference according to gender[5,13,20]. In our study, UTI was found to be higher in women (p=<0.001) and female gender was found to be a risk factor for UTI (p=<0.001). This may be related to the short distance between the urethra and anus in women and the vaginal colonization of uropathogenic agents[21].

It was shown in previous studies that patients whose ureteral stent (Double J stent) was dropped or removed in the early period (<3 weeks) had lower post-transplant UTI rates[22,23]. Liu et al. were found that ureteral stent removal at week 1 was statistically associated with less UTI than stent removal at week 4[24]. In our center, if there are no contraindications, we try to remove the stent at 4th-6th weeks. In our study, ureteral stent duration of group-1 patients was significantly longer than that of group-2 patients (P<0.001). This was found to be associated with statistically higher UTI (P<0.001). We found that the long-term hospitalization duration after transplantation was associated with the development of UTI. Long-term hospitalization after transplantation

operation is created a risk in terms of nosocomial infections[25]. The prolongation of this period increases the possibility of endovascular and urological intervention (the bladder after, the ureter), which is resulted in increase of the risk of infection. Again, in our study, prolongation of urinary catheter time was found to be associated with the development of post-transplant UTI, similar to previous studies.

In previous studies, no consistent relationship was found between the induction agent and the development of post-transplant UTI.[1] In our study, although the rate of use of ATG (70%) was high in patients who developed UTI, this was not statistically significant (p=0.33). In other words, in our study, no relationship was found between the induction agent and UTIs after kidney transplantation. Similarly, no relationship was found between maintenance immunosuppression therapy and UTI. Probably, this may be because similar protocols are applied to the patients in our center. Thus, we may not have been able to reveal the clear difference between different medicines. Again, no relationship was found between acute rejection attacks and UTI.

Although there are studies showing that diabetic nephropathy, which is one of the causes of ESRD, is a risk factor for recurrent UTIs, no relationship was found between diabetic nephropathy and UTI in our study[26]. However, the rate of DM was high both in patients who were developed UTI and who were experienced recurrent UTI episodes, compared to patients who were not developed UTI (10.3%, 17.5%, 22.6%, respectively). Similarly, existence of UTI attacks before transplantation, advanced age, and donor type were not found to be risk factors for post-transplant UTI. Since postoperative complications were few in our patients, the relationship between urological complications and UTI could not be clearly evaluated.

In previous studies, it was reported that kidney functions returned to normal over time after an attack of UTI.[14, 26] Olenski et al. reported that patients with renal dysfunction during an UTI attack were improved their kidney function in the 2nd week after infection, and there was no difference in kidney functions 2 years later when compared to patients who did not develop UTI[4]. In our study, the 2nd year eGFR of patients who were developed UTI was found to be significantly lower when compared to patients who did not develop UTI. Especially in those with R-UTI, the decrease in this eGFR was more pronounced. Briit et al. reported in their previous study that R-UTIs were associated with weaker kidney function and higher graft failure[6]. It was shown that severe UTIs can cause graft dysfunction in the long-term in transplant patients[10]. In our study, patients with symptoms were included. Patients with asymptomatic bacteriuria were excluded. Therefore, our patients were moderate to severe UTI patients. Since both the severity of these infections and their recurrence damage the kidney over time, eGFR losses at 2nd year may have occurred in patients who developed UTI.

Carbapenem-resistant microorganism infections emerge as an important problem in kidney transplant recipients[27]. These infections result in more severe infection setting than infections that are not resistant to carbapenem and are more mortal. In our study, the rate of microorganisms resistant to carbapenem was 6.7%. Another problem that will result in difficulties in treatment in transplant recipients is ESBL-producing microorganisms. In our study population, ESBL positivity was 51.7%. Increasing ESBL positivity and carbapenem resistance in transplant recipients cause serious concerns for the future.

Our study had some limitations. Our study was retrospective and single-center. We included patients who were symptomatic and

administered therapy. This may have resulted in obtaining a lower prevalence than the true UTI in transplant recipients.

CONCLUSION

The prevalence of UTI is very high in kidney transplant recipients, in the first year after transplantation. Although many previous studies were reported that UTI episodes do not affect graft functions in the long term, we found the opposite of these results in our study. In our study, we found that patients who were developed UTI had significantly lower eGFR at 2nd year than patients who did not develop UTI. This difference was more pronounced especially in those who were developed recurrent UTI. We identified prolonged hospitalization, female gender, long-term bladder catheter and ureteral stent as facilitating factors for UTI. It is very important that transplant recipients with risk factors for UTI should be kept under regular surveillance and followed closely after transplantation. Etiological factor should be investigated studiously, especially in patients with recurrent UTI. We recommend that each transplant center to examine their own UTI risk factors, to determine the causative microorganisms and their antibiotic resistance profiles, and to review the antibiotic prophylaxis to be used.

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Ethics Committee Approval: The study complies with the principles of the Declaration of Helsinki and is approved by the Institutional Research Ethics Committee of our hospital (proof; 24/03/2022, no; 56).11 The ethics committee waived the requirement for informed consent due to the retrospective nature of the study.

Conflict of Interest: The author declares no conflict of interest.

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