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ORIGINAL RESEARCH

Epidemiology, Infectious Agents and Treatment Profiles of Urinary Tract Infections in Kidney Transplant Recipients: A Retrospective Analysis

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ABSTRACT

Urinary tract infections (UTIs) are common complications after kidney transplantation, significantly affecting patient and graft outcomes. This study presents a thorough examination of the epidemiological features, causative pathogens, and antibiotic treatment patterns among kidney transplant recipients. A retrospective review was conducted involving 550 kidney transplant patients at a single transplant center, between January 2006 and May 2019. Patient demographics, clinical data, microbiological findings, and antibiotic susceptibility results were systematically analyzed. Among 550 transplant patients, at least one episode of UTI was observed in 200. Out of 633 UTI episodes identified, *Escherichia coli* was the most common causative microorganism, representing 64.9%. Among these, ESBL (Extended-Spectrum Beta-Lactamase) positivity was found in 51.6%. UTIs continue to be a common and challenging complication among kidney transplant recipients. Implementing specific preventive strategies and maintaining careful antibiotic policies are essential to minimize risks and enhance patient outcomes. The notably higher rate of ESBL positivity in UTI cases, which exceeds typical levels, aligns with the rising trend of antibiotic resistance observed both locally and globally in recent years. This finding serves as a crucial warning, prompting a review of antibiotic selection practices.

Keywords: Kidney transplantation. Urinary tract infections. Epidemiology. *Escherichia coli.* Antibiotic resistance.

Böbrek Nakli Alıcılarında İdrar Yolu Enfeksiyonlarının Epidemiyolojisi, Enfeksiyon Etkenleri ve Tedavi Profilleri: Retrospektif Tanımlayıcı Kohort Çalışması

ÖZET

Böbrek transplantasyonu sonrası sık görülen komplikasyonlardan olan idrar yolu enfeksiyonları (İYE), hasta ve greft sağkalımını önemli ölçüde etkilemektedir. Bu çalışmada, böbrek nakli alıcılarındaki İYE'lerin epidemiyolojik özellikleri, etken patojenleri ve antibiyotik tedavi uygulamaları detaylı olarak incelenmiştir. Ocak 2006 - Mayıs 2019 tarihleri arasında tek bir transplant merkezinde böbrek nakli yapılan 550 hasta, retrospektif olarak incelendi. Hastaların demografik ve klinik verileri ile mikrobiyolojik bulguları ve antibiyotik duyarlılık sonuçları sistematik olarak analiz edildi. İncelenen 550 hastanın 200'ünde en az bir İYE atağı gözlendi. Tanımlanan toplam 633 İYE atağında en sık saptanan etken, %64,9 oranıyla *Escherichia coli* idi. Bu izolatların %51,6'sında GSBL (Genişlemiş Spektrumlu Beta-Laktamaz) pozitifliği tespit edildi. İYE, böbrek nakli alıcıları arasında yaygın ve yönetimi zor bir komplikasyon olmaya devam etmektedir. Riskleri en aza indirmek ve hasta sağkalımını iyileştirmek için spesifik önleyici stratejilerin uygulanması ve dikkatli antibiyotik politikalarının sürdürülmesi şarttır. İYE vakalarındaki GSBL pozitiflik oranının dikkat çekici yüksekliği, son yıllarda hem yerel hem de küresel olarak gözlenen artan antibiyotik direnci eğilimiyle paralellik göstermektedir. Bu bulgu, mevcut antibiyotik seçim protokollerinin gözden geçirilmesi için kritik bir uyarı niteliğindedir.

Anahtar Kelimeler: Böbrek transplantasyonu. İdrar yolu enfeksiyonları. Epidemiyoloji. *Escherichia coli.* Antibiyotik direnci.

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Kidney transplantation is a well-established therapeutic option for patients with end-stage renal disease[1]. A successful transplant not only improves quality of life but also reduces long-term mortality risk in most patients who otherwise remain dependent on dialysis[2,3]. Among adult kidney transplant recipients, urinary tract infection (UTI) is the most common and clinically significant infection, occurring at a markedly higher incidence compared with the general population[4–6].

UTIs are reported in approximately 25% of patients within the first year after transplantation. Of these episodes, 44% present as asymptomatic bacteriuria, 32% as uncomplicated UTIs, and 24% as complicated UTIs[7–9]. Although the prevalence of UTIs in this population has been reported to vary widely, ranging from 23% to 75% in different studies[6,10], there is general agreement that the risk is greatest during the early post-transplant period, particularly within the first year[11].

Infections constitute the leading cause of emergency department visits in the early post-transplant period, with UTIs representing the primary source of sepsis [12]. While mild UTIs generally have little impact on graft function, acute pyelonephritis in the post-transplant setting can result in graft dysfunction and increased mortality[13]. Consequently, the traditional perception of UTIs as relatively benign has shifted, with growing evidence suggesting that they pose a significant threat to both graft and patient survival[14].

Despite the clinical importance of UTIs, published data on their incidence, epidemiological features, and antibiotic resistance patterns in kidney transplant recipients remain limited, often originating from single-center studies. The present study, therefore, aims to provide a comprehensive analysis of our center's experience. Specifically, we sought to characterize the clinical features of UTIs, the distribution of causative pathogens, and their antimicrobial susceptibility and resistance profiles, given their direct implications for patient and graft survival.

Material and Method

Patients and Clinical Evaluation

This study was designed as a retrospective descriptive cohort study to analyze the incidence, microbiological patterns, and risk factors of UTIs in a large cohort of kidney transplant recipients. A total of 705 patients who underwent kidney transplantation from either living or deceased donors at Bursa Uludag University Faculty of Medicine Hospital between January 2006 and May 2019 were initially screened for eligibility. Patients younger than 18 years of age and those with incomplete medical records were excluded from the analysis. The final study cohort consisted of 550 patients. Patient data were retrieved and evaluated through the institutional electronic medical record system.

In this study, UTI episode was defined as the presence of more than 10^5 colony-forming units (CFU) of bacteria per milliliter in a urine culture. Episodes without any accompanying local or systemic signs or symptoms were classified as asymptomatic bacteriuria. Episodes accompanied by clinical findings such as fever, dysuria, graft tenderness, hypotension, abdominal pain, diarrhea, or suprapubic tenderness were defined as symptomatic UTIs. Recurrent UTI was defined as the occurrence of three or more UTI episodes within one year.

Ethical statement

This retrospective study was approved by the Ethics Committee of Bursa Uludag University Faculty of Medicine (approval number: 2019-6/21, dated March 25, 2019) and conducted in accordance with the principles outlined in the Declaration of Helsinki.

Statistical Analyses

The normality of distribution for continuous variables was assessed using the Shapiro–Wilk test. Continuous variables were expressed as median (interquartile range: IQR), while categorical variables were presented as counts and percentages. Comparisons of continuous variables between patients with and without UTI were performed using the Mann–Whitney U test. Comparisons of categorical variables between these groups were conducted using the chi-square test or Fisher's exact chi-square test, as appropriate.

All statistical analyses were performed using SPSS software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). A type I error rate of 5% was accepted for statistical comparisons, and a p-value <0.05 was considered statistically significant.

Results

In our analysis of infection characteristics, at least one episode of UTI was identified in 200 out of 550 kidney transplant recipients (36.4%). Among these, 74 patients experienced recurrent UTIs. The comparison of demographic and clinical characteristics between patients with and without UTI was presented in Table I.

Female gender was strongly associated with a higher incidence of UTI (56.6% vs 21.3%, $p<0.001$). Patients in the UTI group were significantly older at the time of transplantation [45.68 (17.97) vs 41.01 (17.94) years, $p=0.002$] and received organs from older

donors [50 (18) vs 45 (18) years, p=0.002]. Anatomical and structural factors played a critical role in UTI development. A history of vesicoureteral reflux (VUR) (14.5% vs. 4.0%, p<0.001) and neurogenic bladder (4.5% vs. 0%, p<0.001) were significantly more prevalent in the UTI group. Additionally, the duration of post-transplant catheterization [12.30 (6.97) vs 10.20 (5.21) days, p=0.001] and the length of hospital stay [17 (17) vs 14 (11) days, p=0.001] were notably longer in patients who experienced at least one UTI episode. A history of CMV infection was also found to be a significant factor (26% vs 18%, p=0.026). However, factors such as donor type (p = 0.093), dialysis modality (p=0.215), and the presence of diabetes mellitus (p=0.438) did not show a statistically significant difference between the two groups.

Table I. Comparison of Demographic and Clinical Characteristics Between Patients With and Without UTI

	UTI (n=200)	Non-UTI (n=350)	p-value
Donor Type			
• Living (n=218)	70(%32.1)	148(%67.9)	0.093[a]
• Deceased (n=332)	130(%39.2)	202(%60.8)	
Sex			
• Female (n=235)	133(%56.6)	102(%43.4)	**<0.001**[a]
• Male (n=315)	67(%21.3)	248(%78.7)	
Age at Transplantation (years)	45.68(17.97)	41.01(17.94)	**0.002**[b]
Donor Age (years)	50(18)	45(18)	**0.002**[b]
Dialysis Type			
• Preemptive (n=80)	23(%28.7)	57(%71.3)	
• Hemodialysis (HD) (n=346)	132(%38.2)	214(%61.8)	0.215[a]
• Peritoneal Dialysis (PD) (n=64)	27(%42.2)	37(%57.8)	
• HD + PD (n=60)	18(%30)	42(%70)	
Dialysis Duration (months)*	73(94.50)	58(87.50)	**0.038**[b]
Postoperative (days)			
• Catheterization Duration	12.30±6.97	10.20±5.21	**0.001**[b]
• Length of Hospital Stay	17(17)	14(11)	**0.001**[b]
• Double-J Stent Duration	49.5(23)	48(15)	0.216[b]
Cold Ischemia Time (hours)	11(13)	10(13)	0.062[b]
History of Vesicoureteral Reflux			
• Present (n=43)	29(%67.4)	14(%32.6)	**<0.001**[a]
• Absent (n=507)	171(%33.7)	336(%66.3)	
Neurogenic Bladder			
• Present (n=9)	9(%100)	0	**<0.001**[c]
• Absent (n=541)	191(%35.3)	350(%64.7)	
History of CMV Infection			
• Present (n=115)	52(%45.2)	63(%64.8)	**0.026**[a]
• Absent (n=435)	148(%34)	287(%66)	
History of Diabetes Mellitus			
• Present (n=114)	45(%39.5)	69(%60.5)	0.438[a]
• Absent (n=436)	155(%35.6)	281(%64.4)	

Data were expressed as n (%), median (interquartile range: IQR). *: Calculated for patients who underwent dialysis in both groups (n=470).
a: Chi-square test, b: Mann–Whitney U test, c: Fisher's exact chi-square test.

A total of 633 UTI episodes were detected in the 200 affected patients. Among these, 74 patients (37%) experienced recurrent UTIs (defined as three or more episodes within one year). A striking subset of 35 patients (17.5% of the UTI group) experienced extreme recurrence, characterized by seven or more episodes.

When analyzed separately, of the 633 UTI episodes, 306 (48.34%) were classified as asymptomatic bacteriuria, and 327 (51.66%) were identified as symptomatic UTIs. The most common symptoms reported were pollakiuria/dysuria (79.8%) and fever (50.5%). The distribution of clinical symptoms observed in symptomatic episodes is presented in Table II.

Table II. Distribution of clinical symptoms observed in UTI episodes (n=327), n (%)

Symptoms	n	%
• Pollakiuria/Dysuria	261/327	79.8
• Fever	165/327	50.5
• Suprapubic Pain	67/327	20.5
• Diarrhea/Abdominal Pain	40/327	12.3
• Graft Pain	8/327	2.5
• Hypotension	2/327	0.6

The most frequently isolated pathogen was *Escherichia coli* (n=411), accounting for 64.9% of all isolates. Among these, extended-spectrum beta-lactamase (ESBL) production was detected in 51.6% (n=212) of the samples. The second most common pathogen was *Klebsiella pneumoniae*, identified in 19.9% of cases (n=126), of which 67.5% (n=85) were ESBL-positive. Consistent with these high resistance rates, carbapenems (Meropenem, 32.2%, and Ertapenem, 17.8%) were the most frequently administered antibiotics, accounting for 50% of all treatments.

In our study, the isolated UTI pathogens and their frequencies were presented in Table III, while the main antibiotics administered during UTI episodes were summarized in Table IV.

A detailed comparison was conducted between patients with recurrent UTIs (n=74) and those with non-recurrent UTI episodes (n=126). The duration of double-J stent placement was significantly longer in the recurrent UTI group compared to the non-recurrent group (p = 0.016). Interestingly, the frequency of recurrent UTI was significantly higher in patients receiving nitrofurantoin prophylaxis compared to those who did not (p=0.002), likely reflecting the clinical management of patients perceived to be at higher baseline risk. Regarding primary renal diseases, the highest rates of recurrence were observed in patients with VUR (50%), followed by idiopathic causes (39.4%), hypertension (38.1%), polycystic

kidney disease (30%), and glomerulonephritis (20%). While the recurrence rate was numerically higher in patients with a history of VUR (51.7% vs. 34.5%) and neurogenic bladder (66.7% vs. 35.6%), these differences did not reach statistical significance (p = 0.076 and p = 0.079, respectively).

Table III. Frequency and Proportion of Isolated Pathogens

Isolated Pathogens	n	%
Gram-Positive Bacteria		
• *Enterococcus faecalis*	27	4.3
• *Streptococcus agalactiae*	13	2.0
• *Staphylococcus epidermidis*	8	1.3
• *Enterococcus faecium*	6	0.9
• *Staphylococcus haemolyticus*	4	0.6
• *Staphylococcus saprophyticus*	2	0.3
• *Staphylococcus aureus*	1	0.2
• *Streptococcus acidominimus*	1	0.2
Gram-Negative Bacteria		
• *Escherichia coli* / ESBL +	212	33.5
• *Escherichia coli* / ESBL -	199	31.4
• *Klebsiella pneumoniae* / ESBL +	85	13.4
• *Klebsiella pneumoniae* / ESBL -	41	6.5
• *Pseudomonas aeruginosa*	7	1.1
• *Proteus mirabilis*	6	0.9
• *Enterobacter cloacae*	5	0.8
• *Acinetobacter baumanii*	4	0.6
• *Klebsiella oxytoca*	4	0.6
• *Salmonella enteritidis*	2	0.3
• *Serratia marcescens*	2	0.3
• *Enterobacter aerogenes*	1	0.2
• *Morganella morganii*	1	0.2
• *Proteus vulgaris*	1	0.2
• *Providencia stuartii*	1	0.2

Table IV. Distribution of Administered Antibiotics During UTI Episodes

Antibiotics	n	%
• Meropenem	204	32.2
• Ertapenem	113	17.8
• Ciprofloxacin	103	16.3
• Fosfomycin	47	7.4
• Ceftriaxone	40	6.3
• Cefuroxime	26	4.1
• Amoxicillin/Clavulanate	25	3.9
• Nitrofurantoin	22	3.5
• Levofloxacin	13	2.1
• Teicoplanin	9	1.4
• Cefepime	7	1.1
• Ampicillin	5	0.8
• Imipenem	5	0.8
• Piperacillin/Tazobactam	4	0.6
• Trimethoprim/Sulfamethoxazole	4	0.6

Discussion and Conclusion

The current investigation represents one of the largest single-center studies in the literature dedicated to analyzing this highly prevalent entity following kidney transplantation. Although UTIs may initially appear to be a readily manageable complication, our data and accumulating global evidence demonstrate that the issue is significantly complicated by the emergence of antibiotic resistance on a considerable scale.

The prevalence of UTIs in kidney transplant recipients varies widely across international studies, ranging from approximately 23% to 75%. However, they consistently account for approximately 40% to 50% of all infectious complications in this patient group[6,10,11]. In our cohort of 550 patients, we observed a comparable prevalence, with 36.4% of recipients experiencing at least one episode of UTI.

In recent literature, Gram-negative microorganisms remain the predominant causative agents, similar to the general population. Escherichia *coli* is the most frequently isolated pathogen, followed by *Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis*, and *Morganella morganii*[13,15]. The widespread use of prophylactic antibiotics and the treatment of asymptomatic bacteriuria in kidney transplant recipients have significantly contributed to the rise of antibiotic resistance. This has led to infections caused by multidrug-resistant organisms such as *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii*, and *Enterobacter species*, which are associated with adverse clinical outcomes[16–18].

A critical finding of our analysis was the microbiological profile across the 633 episodes of UTI documented. *Escherichia coli* was the most frequently isolated pathogen, accounting for 64.9% (n = 411) of all infections. Alarmingly, 51.6% (n=212) of these *Escherichia coli* isolates were identified as Extended-Spectrum Beta-Lactamase (ESBL) positive. The second most common causative agent was *Klebsiella pneumoniae*, isolated in 19.9% (n=126) of the attacks, with a very high rate of ESBL positivity at 67.5% (n = 85). Consistent with this resistance profile, the empirical antibiotic choice in over half of the attacks required the initiation of carbapenem-group drugs (Table IV). While our overall spectrum of microorganisms is similar to international reports, the dramatically high rate of ESBL positivity observed in our UTI episodes significantly exceeds established averages [19,20]. While these rates are substantially higher than those typically reported in worldwide studies (which often stay below 20-25%), they are in close agreement with other Turkish studies. For instance, Ak et al. reported a combined ESBL rate of 52.8% for E. coli and Klebsiella species in a similar

transplant population[21]. This regional trend of high resistance directly influenced our empirical treatment patterns, where carbapenems (Meropenem and Ertapenem) were required in 50% of all episodes to ensure clinical stability. This finding represents a significant point of distinction for Türkiye, highlighting a particularly challenging regional issue of antibiotic resistance. This observation served as a significant alert, prompting the urgent reevaluation of our current empirical antibiotic selection preferences.

The subgroup analysis of recurrent UTIs provided further clarity on the mechanisms of persistent infection. We found that the duration of double-J stent placement was significantly longer in patients with recurrent episodes (p=0.016). This finding is supported by the literature on prolonged stent and catheter duration as critical predictors of recurrent UTI and subsequent allograft dysfunction[22]. This emphasizes the clinical necessity of early stent removal (ideally within 2-4 weeks) to disrupt biofilm formation. An intriguing finding was the significantly higher recurrence rate among patients receiving nitrofurantoin prophylaxis (p=0.002). This observation likely represents an "indication bias" or "selection bias," where clinicians initiated prophylaxis specifically in patients who already exhibited high-risk features or had a history of frequent episodes. Finally, although primary diseases, such as VUR (51.7% recurrence) and neurogenic bladder (66.7% recurrence), showed higher numerical recurrence rates compared to idiopathic causes, they did not reach statistical significance (p=0.076 and p=0.079). This lack of significance, despite a strong clinical correlation, may be attributed to the limited number of patients in these specific anatomical subgroups, resulting in a loss of statistical power—a limitation also noted in other single-center descriptive cohort studies.

Despite the inherent limitations of our study, namely its single-center and retrospective design, we emphasize that UTIs are a critical complication that requires careful consideration of risk factors, effective and sufficient treatment control, and close follow-up to ensure a high quality of life for kidney transplant recipients. A refined, appropriate treatment approach will not only improve patient satisfaction but also contribute to reduced hospitalization rates and healthcare costs.

In conclusion, UTI in the post-transplant period is a highly prevalent complication with significant clinical implications. In this study, we evaluated the typical characteristics of our kidney transplant recipients who experienced UTI episodes and analyzed the features of the infections encountered in our center. The high rate of extended-spectrum beta-lactamase (ESBL) resistance observed in our study should be emphasized as a major alert for the management of antimicrobial therapy. Further multicenter studies are warranted to aid in the development of optimized strategies for complication management and treatment algorithms.

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