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Characteristics of Urinary Tract Infections in Patients with Spinal Cord Injuries Hospitalized at a Rehabilitation Centre

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BACKGROUND
The aims of this study were to determine the prevalence of urinary tract infections (UTIs), identify the most frequently isolated pathogens associated with UTIs, and evaluate the antimicrobial susceptibility of these pathogens in spinal cord injury (SCI) patients.

MATERIAL and METHODS
A total of 91 patient charts were retrospectively evaluated in this study. The demographic data of these patients, length of hospital stay, SCI data, mode of bladder emptying, number of UTI episodes, microorganisms isolated by urine culture, and antimicrobial susceptibility tests were recorded.

RESULTS
Of the 91 SCI patients, 53 were males and 38 were females, with a mean age of 45.29 (±17.87) years. A total of 47 UTI episodes were recorded in 38 SCI patients, nine of whom had experienced two episodes. The prevalence of UTI was 41.7% (38/91). The most frequently isolated pathogen was Escherichia coli (57.4%). The antimicrobial agents were most frequently susceptible were gentamicin (72.3%), piperacillin/tazobactam (57.4%), and meropenem (48.9%).

CONCLUSION
The UTI prevalence in patients with SCI was considerably high. E. coli was the most common uropathogen, and gentamicin was the most frequently used antimicrobial agent.

Keywords: Spinal cord injury, urinary tract infection, epidemiology

INTRODUCTION

The risk of urinary tract infections (UTIs) is higher in patients with a spinal cord injury (SCI) because of a lack of normal physiological urination resulting from neurogenic bladder in most patients. UTIs are considerably more frequent because of urinary catheter use, residual urine in the bladder due to incomplete emptying, renal stones, obstructed urinary outflow, dysregulation of the autonomic nervous system, and an unbalanced bladder evacuation. These are significant causes of morbidity and mortality (1, 2). Although UTIs occur in 22% of patients with acute SCI in the first 50 days, the UTI prevalence is approximately 20% in patients with chronic SCI (3). UTIs were detected in 60% of SCI patients in a rehabilitation center study in Thailand (4). A mortality rate of nearly 34% is reported in patients with SCI due to urinary sepsis, and this is the second most frequent cause of death in patients with SCI (5, 6).

Pannek and Nehiba (7) found that the incidence of UTIs was 9.7% in SCI patients after urodynamic studies. Because the UTI risk is high after invasive interventions of the urinary system, as with urodynamic assessments, prophylactic antimicrobial treatments are recommended by the American Urological Association and the European Association of Urology. Specifically, these recommendations are for patients with risk factors that include old age, low immunity, diabetes mellitus, smoking, poor alimentation, urinary system anatomical abnormalities, external catheter use, presence of bacterial colonization, and a history of recurrent UTIs and long-term hospitalization before urodynamic assessment (8, 9). Prophylactic antibiotic therapy is used if the infection occurs predictably in a certain setting and it is well known to be associated with a specific organism. Prophylactic antibiotic therapy is mandatory before invasive interventions, such as urodynamic assessments, in patients with SCI who already have most of these risk factors to decrease the risk of UTIs (10). Empirical treatment with antimicrobial agents may also be started in patients with clinical findings suggestive of UTIs until the urine culture results are obtained (11). An approach is to use broad-spectrum antimicrobial agents as initial empiric therapy with the intent to cover multiple possible pathogens commonly associated with the spe-

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cific clinical syndrome. Unfortunately, choosing appropriate prophylactics or empirical antibiotics is difficult. This difficulty is due to the presence of multiple uropathogens and variable antimicrobial sensitivities. In consideration of these difficulties, we aimed to determine the prevalence of UTIs in SCI patients, identify the most frequently isolated pathogens, and evaluate antibiotic sensitivity in patients hospitalized and followed up between 2010 and 2014 at our institution.

MATERIAL and METHODS

Ethics committee approval for this study was obtained from the local ethics committee. We retrospectively evaluated the charts of 91 patients. The sample size was determined based on another similar study (11). We evaluated the charts of patients (diagnosed with SCI) who were hospitalized and followed up in the physical medicine and rehabilitation department between January 2010 and September 2014. This study was a retrospective study, so the consent form was not taken. In patients with multiple hospitalizations, the authors selected the most recent admission for evaluation.

The patients' demographic data, presence of systemic diseases, hospitalization length, SCI duration, SCI cause, neurological level of the injury, and the injury classification according to the American Spinal Cord Injury Association Impairment Scale (12) were recorded. We also recorded the presence of complete or incomplete injuries, the SCI type (paraplegia, tetraplegia, cauda equina syndrome, or spina bifida), fecal and urinary incontinence, modes of bladder emptying, number of UTI episodes, isolated microorganisms, antibiotic sensitivity test results, and hemoglobin levels. However, the urinary ultrasonography (USG) and urodynamic evaluation results could not be obtained because of missing data in the charts.

Urine cultures were obtained using the clean-catch technique for patients able to void spontaneously or at the time of catheterization, according to the rehabilitation unit protocol. Urine specimens were sent to the Microbiology Laboratory of Selçuk University Medical School and were inoculated in eosin methylene blue agar (Becton, Dickinson, and Company, Sparks, MD) and blood agar [trypticase soy agar with 5% sheep blood (TSA IIt)] with inoculation loops calibrated with sterile 1-µl loops. The plates were incubated overnight at 37ºC (±1.5°C). The colonies were then counted and, when concluded to be significant, identified following standard microbiological techniques (13, 14). Significant bacteriuria was considered from the level of 10^5 or more colonies of colony-forming units (CFUs) per cm^3. Bacterial identification and antimicrobial susceptibility testing was performed with a VITEK 2 (bioMerieux, France) automatized system. Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853, and Staphylococcus aureus ATCC 29213 were used as quality control strains.

In the present study, UTI was defined as the presence of significant bacteriuria with signs and symptoms of UTI. These signs and symptoms included fever, discomfort, pain in the kidney or bladder, onset of urinary incontinence, increased spasticity of skeletal muscles (especially in lower extremities), sweating, or autonomic dysreflexia. Urine cultures with a bacterial colony count of 10^5 CFUs or higher were considered as significant bacteriuria (15).

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 16.0; Chicago, IL, USA). Continuous variables, such as age, length of hospital stay, and UTI episodes, were presented as the mean±standard deviation (SD). Categorical variables, such as gender, injury level, pathogens, and susceptible antibiotics, were presented as percentages. Data from the UTI and non-UTI groups showing a normal distribution were compared using Student's t-test and those not showing a normal distribution were compared using the Mann–Whitney U test. The chi-square test was used for the comparison of frequencies. The statistical significance level was set at $p<0.05$.

RESULTS

Of the 91 SCI patients, there were 53 males and 38 females with an overall mean age of 45.29 (±17.87) years (age range 16–75). The average length of hospital stay was 35.95 (±23.52) days. The neurological injury levels included 37% cervical, 47% thoracic, and 16% lumbosacral. There were 12 patients using clean intermittent catheterization (CIC); there were 11 patients (30.6%) with UTI and there was 1 patient (2.6%) without UTI. There were 47 UTI episodes in 38 of the SCI patients; several patients had recurrent UTIs on an admission. There were nine patients with two episodes. The prevalence of UTIs was 41.7% (38/91).

The vast majority of uropathogens were gram-negative bacteria. E. coli was the most frequently isolated pathogen (57.4%) followed by P. aeruginosa (14.8%) and Klebsiella pneumoniae (10.6%). The three most sensitive antibiotics were gentamicin (72.3%), piperacillin/tazobactam (57.4%), and meropenem (48.9%) (Table 1). The antimicrobial susceptibility and resistance status of E. coli strains determined after years of hospitalization are shown in Table 2.

All of the patient charts that were evaluated for this study were classified as either patients with UTIs or without UTIs. The patients' characteristics in both groups are shown in Table 3. Statistically significant differences were found between the two groups in terms of length of hospital stay, fecal incontinence, urinary incontinence, and mode of bladder emptying ($p<0.001$, $p<0.001$, $p=0.002$, and $p<0.001$, respectively).

DISCUSSION

In our assessment of SCI patients, the prevalence of UTIs was 41.7%. E. coli was the most common uropathogen, and gentamicin was the most frequently used antimicrobial agent. The length of hospital stay was longer in patients with UTIs. These patients also had higher rates of fecal and urinary incontinence and higher rates of bladder emptying with CIC.

The UTI rate in SCI patients remains high, despite advancements in treatment methods. The prevalence of UTIs was 41.7% in the present study, supporting previously reported results (3, 4). Most frequently, E. coli, P. aeruginosa, or K. pneumoniae are isolated in urine cultures after a UTI develops (11, 16-18). E. coli was the most frequently detected uropathogen in our study, followed by P. aeruginosa and K. pneumoniae, findings that concurs with previous studies (11, 16-18).

In the present study, the three most sensitive antibiotics were gentamicin, piperacillin/tazobactam, and meropenem. Interestingly,

TABLE 1. Uropathogens and their antibiotic susceptibility pattern

Uropathogens	n: 47	Number of sensitive tests/total number of available tests									
		Ampicillin	Ciprofloxacin	Ceftriaxone	Gentamicin	Tazobactam	Piperacillin/ Imipenem	Meropenem	Cefuroxime	Trimethoprim-sulfamethoxazole	Ertapenem
Escherichia coli	27	9/27	10/27	9/27	20/27	15/27	8/27	14/27	11/27	11/27	5/27
Peudomonas aeruginosa	7	0/7	6/7	0/7	6/7	6/7	3/7	4/7	0/7	0/7	0/7
Klebsiella pneumoniae	5	0/5	4/5	2/5	3/5	4/5	3/5	4/5	2/5	2/5	3/5
Acinetobacter	3	1/3	0/3	0/5	2/3	0/3	1/3	0/3	0/3	0/3	0/3
Staphylococcus epidermidis	2	0/2	0/2	0/2	2/2	0/2	0/2	0/2	0/2	2/2	0/2
Enterobacter cloacae	1	0/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1	1/1
Proteus mirabilis	1	0/1	0/1	1/1	0/1	1/1	0/1	0/1	0/1	0/1	1/1
Serratia marcescens	1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	0/1	1/1
Total sensitivity (%)*		21.28	44.6	27.6	72.3	57.4	34	48.9	29.7	34	23.4

* total sensitivity was calculated by the number of sensitive organisms/total organisms (47)

TABLE 2. Changing susceptibility and resistance status of Escherichia coli strains against antibiotics during the years of hospitalization

	2010 (n: 4) d/d'	2011 (n: 5) d/d'	2012 (n: 4) d/d'	2013 (n: 7) d/d'	2014 (n: 7) d/d'
Ampicillin	2/1	2/5	0/5	0/4	4/1
Ciprofloxacin	0/0	3/1	3/1	2/2	1/2
Ceftriaxone	3/0	2/1	1/1	2/1	0/0
Gentamicin	3/0	3/1	3/2	4/0	5/0
Piperacillin/Tazobactam	3/0	3/1	4/0	3/1	0/0
Imipenem	0/0	3/0	2/0	1/0	0/0
Meropenem	3/0	4/0	3/0	2/0	0/0
Cefuroxime	0/0	3/1	3/2	1/2	3/0
Trimethoprim-sulfamethoxazole	3/0	3/1	1/4	1/2	1/1
Ertapenem	0/0	0/0	2/0	2/0	0/0

d: susceptible; d': resistant

only 27.6% and 44.6% of the detected pathogens were susceptible to ceftriaxone and ciprofloxacin, respectively. However, these antibiotics are frequently used in the prophylaxis against UTIs and in their empirical treatment (4). This was consistent with other studies, which revealed that the prevalence of antimicrobial resistance in uropathogens is increasing worldwide (17, 18). Because the incidence of UTI in SCI patients is very high, there is a very high chance of transmission of multi-drug resistant strains among patients (19). When examining the antimicrobial susceptibility of E. coli strains in this study, there was no resistance against imipenem, meropenem, or ertapenem between 2010 and 2014; however, resistance against ampicillin and trimethoprim-sulfamethoxazole was detected in some, but not all, strains. SCI patients with symptomatic UTI should be treated with the most specific, narrowest spectrum antibiotics available for the shortest possible time (19). On the other hand, most strains were susceptible against gentamicin and piperacillin/tazobactam. According to this data, a preference for carbapenem, gentamicin, or piperacillin/tazobactam in the empirical or prophylactic antimicrobial treatment of UTIs may provide better treatment success.

Hand hygiene and staff and patient education are recognized as important aspects of care in the prevention of UTI in patients with SCI (20). Waites et al. (16) reported the absence of an association between the risk of UTIs and gender, type of injury etiology, urinary stones, co-morbidities, surgery, and previous antimicrobial treatments. Based on comparing patient groups with and without UTIs in the present study, the length of the hospital stay was longer in those patients with UTIs; furthermore, in the UTI group, the frequency of fecal and urinary incontinence was higher and there was a greater presence of bladder emptying by CIC. Unfortunately, it is difficult to determine whether the cause of the increased hospital stay was due to the presence of UTIs or the length of hospital stay were a risk factor for UTI development. However, both conditions increase the risk of nosocomial infections, which increase costs and morbidity and mortality rates (21). Therefore, the length of hospital stay of hospitalized patients, especially SCI patients, should be as short as possible.

One of the reasons E. coli is the most common uropathogen causing UTIs is because of fecal contamination due to fecal incontinence, which is present in most SCI patients (22). The frequency of fecal incontinence was higher in UTI patients in the present study, which supports previous findings (22).

The mode of bladder emptying in SCI patients is important with respect to the risk of UTI development. Oz et al. (23) found that the rate of bacteriuria was 53.3% in patients using CIC and 82.9% in those with permanent catheters in their study of 63 SCI patients. Also, the UTI frequency was higher in patients using CIC than in those with normal voiding in another study (17). In the present study, the frequency of permanent catheterization was nearly equal in patients with and without UTIs. However, CIC was more frequently used by those with UTIs, whereas spontaneous micturition was more frequent in the group without UTIs. According to these results, it seems that spontaneous voiding carries the least risk of UTIs. On the other hand, in the presence of vesico-urethral reflux, CIC is a safer and healthier mode of bladder emptying because it causes less residual urine and enables a regular and rhythmic bladder emptying mode (24, 25).

The present study has some limitations. The first limitation is that because it is a retrospective study, urinary ultrasonogra-

TABLE 3. Comparison of variables of the patients with and without UTI (n:91)

Variables	UTI (n: 38)	No UTI (n: 53)	p value
Age (years), mean (SD)	44.63 (17.63)	45.77 (18.19)	0.766
Male gender, n (%)	18 (47.4%)	35 (66%)	0.075
Systemic disease, n (%)			
Diabetes mellitus	7 (18.9%)	4 (7.5%)	0.183
Hypertension	1 (2.7%)	3 (5.7%)	
Length of hospital stay (days), mean (SD)	49.86 (16.56)	25.98 (22.79)	<0.001*
Duration of SCI (months), mean (SD)	16.24 (30.26)	31.34 (55.55)	0.132
Cause of SCI, n (%)			
Traffic accident	5 (13.2%)	8 (15.4%)	
Occupational accident	3 (7.9%)	3 (5.8%)	
Falling	14 (36.8%)	10 (19.2%)	
Fire arm wounds	0	2 (3.8%)	0.391
Cuts	0	1 (1.9%)	
Tumor	3 (7.9%)	2 (3.8%)	
Postoperative	4 (10.5%)	6 (11.5%)	
Infection	0	3 (5.8%)	
Others	9 (23.7%)	18 (32.8%)	
Neurological level, n (%)			
Cervical	11 (28.9%)	25 (46.1%)	0.245
Thoracic	24 (63.2%)	19 (35.5%)	
Lumbar	3 (7.9%)	10 (18.4%)	
ASIA classification**n (%)			
A	12 (40%)	9 (26.5%)	
B	1 (3.3%)	1 (2.9%)	0.180
C	10 (33.3%)	7 (20.6%)	
D	7 (23.3%)	17 (50%)	
E			
Complete SCI, n (%)	14 (37.8%)	13 (25.5%)	0.215
Type of SCI, n (%)			
Paraplegia	12 (31.6%)	20 (37.8%)	
Tetraplegia	24 (63.2%)	30 (56.6%)	0.901
Cauda equina syndrome	1 (2.6%)	2 (3.8%)	
Spina bifida	1 (2.6%)	1 (1.8%)	
Presence of fecal incontinence**n (%)	33 (86.8%)	21 (50%)	<0.001*
Presence of urinary incontinence**n (%)	35 (92.1%)	26 (61.9%)	0.002*
Mode of bladder emptying**n (%)			
Spontaneous micturition	5 (13.9%)	20 (52.6%)	<0.001*
Permanent urinary catheter	20 (55.6%)	17 (44.7%)	
CIC	11 (30.6%)	1 (2.6%)	
Hemoglobin level (g/dl), mean (SD)	12.64 (1.17)	12.74 (1.97)	0.788

UTI: urinary tract infection; SD: standard deviation; SCI: spinal cord injury; ASIA: American Spinal Cord Injury Association; CIC: clean intermittent catheterization

* Statistical significant at p value <0.05; ** There was missing data

phy examinations and urodynamic studies could not be found in some patient charts, which is a cause of missing data. The second limitation is the limited number of patients, although all patients from the past 4 years were reviewed. Therefore, a generalization from the results is not feasible, and the possible risk factors associated with UTIs could not be evaluated because of the insufficient sample size. Thus, there is a need to conduct further prospective studies that include a larger number of patients.

In conclusion, the UTI prevalence in SCI patients was considerably high. Close urological follow-up is crucial in ensuring that adequate bladder drainage is achieved, avoiding the use of long-term indwelling urinary catheters, if at all possible. The modes of bladder emptying, including spontaneous micturition and the use of permanent urinary catheter or CIC, are decided by the clinical characteristics of SCI patients. Gram-negative bacteria, especially E. coli, were the most frequently isolated uropathogen, and carbapenem, gentamicin, and piperacillin/tazobactam were the most frequently used antimicrobial agents. Resistance against antibiotics shows a continual increase. Therefore, the length of hospitalization should be shortened to decrease the risk of UTIs. Finally, when a UTI is detected, an antimicrobial agent with the narrowest susceptibility spectrum should be chosen and used for as short a time as possible.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Selçuk University School of Medicine.

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

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