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# Clinico-microbiological profile of urinary tract infections in hospitalized spinal cord injury patients

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**Abstract:**

**BACKGROUND:** Hospitalized spinal cord injury (SCI) patients are predisposed to develop nosocomial infections owing to a variety of risk factors, and treatment of such infections is usually suboptimal.

**AIMS:** We aimed to evaluate the prevalence of urinary tract infection (UTI) in hospitalized SCI patients along with their clinical profile, prevailing uropathogens, and their antibiotic sensitivity patterns.

**SETTING AND DESIGN:** This is a cross-sectional, analytical study carried out at a tertiary military center specialized in management of SCI.

**MATERIALS AND METHODS:** Fifty-two admitted patients of SCI were selected, whose clinical profiles including times since injury and since present admission, level of spinal injury, American Spinal Injury Association scale, urinary or fecal incontinence, and mode of bladder emptying were assessed, and sterile midstream urine samples were subjected to cytological and microbiological examination inclusive of antibiotic sensitivity testing using VITEK 2 (bioMerieux®, France) automated system.

**STATISTICAL ANALYSIS USED:** Comparisons were made for each variable using Chi-square test.

**RESULTS:** The prevalence of UTIs in our cohort was 67.31% (35/52 patients). Statistically significant differences were found in development of UTI in the presence of a neurogenic bladder, fecal incontinence, usage of clean intermittent catheterization as mode of bladder emptying, pyuria, and increased length of hospital stay ($P < 0.05$). The most common uropathogen isolated was *Klebsiella pneumoniae*. Antibiotics to which the isolated uropathogens were most sensitive were colistin (97.1%), tigecycline (82.9%), and ertapenem (74.3%).

**CONCLUSION:** UTI in SCI patients is often mismanaged owing to unnecessary or faulty empirical antibiotic institution. We have tried to provide a systematic antibiotic protocol for management of this oft encountered entity.

**Keywords:**

Antibiotic sensitivity, spinal cord injury, urinary tract infection, uropathogens

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## Introduction

Patients with a spinal cord injury (SCI) are at a high risk of developing nosocomial and community-acquired infections due to prolonged hospital stays, either for acute or chronic rehabilitation, post-SCI complications such as deep vein thrombosis, decubitus ulcers, or pneumonia, and frequent use of invasive medical devices such as intravascular and urinary catheters.[1] Urinary tract infections (UTIs) are a common occurrence, especially in late or subsequent hospitalizations, with an incidence of almost 34%.[2] Multiple risk factors exist for development of UTI in SCI patients which include altered voiding dynamics, increased intravesical pressures, increased postvoiding residual volumes, indwelling or intermittent urinary catheterization, and prolonged antibiotic exposure.[3]

This cohort of patients is prone to significant morbidity and mortality. Catheter-associated bacteremia is the most common source of Gram-negative bacteremia in hospitalized patients which predisposes them to an



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increased risk of mortality.[3] UTIs can have serious consequences, most notably, acute kidney damage via inflammation and parenchymal destruction, and may in turn progress to chronic kidney disease, septicemia, or renal failure.[4] Despite improved methods of treatment, urinary tract morbidity ranks as the second leading cause of death in the SCI patient.[5]

Patients of SCI are particularly susceptible to misdiagnosis and inadequate empirical therapy of UTI primarily due to delayed diagnosis in these patients, as distinguishing active infection from asymptomatic bacteriuria is a challenge since there is an absence of classic symptomatology, there exists a high frequency of other foci of infection, and there are increased rates of asymptomatic colonization of the urinary tract. It is critical to understand the clinical profile of UTIs in SCI patients, to successfully tailor treatment and develop prevention strategies for avoiding potentially catastrophic complications.[1]

This study was aimed at evaluating the clinical profile of hospitalized SCI patients in a military hospital, whose random urine samples were collected to identify the prevalence of UTI in this subset, describe factors associated with occurrence of UTI, and evaluate prevailing microorganisms in the hospital setting and the antibiotic sensitivity pattern obtained in this population.

## Materials and Methods

This study is a cross-sectional, analytical study which was aimed at evaluating the prevalence of UTI in hospitalized SCI patients along with the prevailing uropathogen profile and their antibiotic sensitivity patterns. The present study was conducted in a spinal cord injury center (SCIC) at a tertiary care military hospital affiliated to a medical college in Pune, India, between March 2020 and September 2020. Ethical clearance was obtained from the institutional ethics committee prior to the start of the study. The inclusion criteria for our study were all adult patients admitted to the SCIC wards irrespective of their diagnoses, comorbidities, and length of stay. We did not exclude any admitted case of SCI. None of the subjects were admitted to intensive care at the time of the present study. A written, informed consent was obtained from all the study participants.

All demographic data were noted on an Excel® sheet which included age, sex, time since injury, time since present admission, level of spinal injury, American Spinal Injury Association (ASIA) impairment scale, comorbidities if any, urinary incontinence, fecal incontinence, mode of bladder emptying (indwelling catheter, clean intermittent catheterization [CIC], and condom drainage), and any other post-SCI complications.

Urine samples were collected in two sterile containers by collecting midstream sample for the patients who could spontaneously void the urine and by aseptic, nontouch technique for catheter specimens of urine. The urine sample for catheterized patients was taken from sampling port over tubing of catheter drainage bag after applying a clamp below the port and after disinfecting the sample port site with alcohol-impregnated swab. A total of 20-ml urine was collected from each patient, of which 10 ml was put in the first sterile container for urine culture and antibiotic sensitivity test. The remaining sample was put in the second urine container for routine urine examination. The samples were taken in two separate containers to avoid any cross-contamination in the laboratory while handling during sample analysis for routine examination. The samples were properly labeled and immediately sent for investigation.

Both the samples were given a unique identification number and immediately processed for microbiological examination and cytological studies. In microbiological studies, all samples were inoculated in CLED agar (HiMedia) and in blood agar (HiMedia) using calibrated 1-µl sterile inoculation loops. Backsides of the plates were labeled with the patient's name with the unique ID initially allotted to the specimens. The plates were then allowed to incubate overnight at 37°C in the incubator. The growth obtained after incubation period was observed regarding type of colonies, color, and number of colonies. Samples showing number of colonies to be significant ($10^5$ or more colonies of colony-forming units [CFUs] per $cm^3$) were further processed for bacterial identification and antibiotic sensitivity testing using VITEK 2 (bioMerieux®, France) automated system.

Samples processed for cytological studies were evaluated for various physical and microscopic examinations as per the protocol of the laboratory. All slides prepared for cytological examinations were evaluated by a single pathologist.

In the current study, UTI was defined as the presence of significant bacteriuria with signs or symptoms of UTI. These included fever, discomfort or pain in the flanks, increased spasticity of skeletal muscles (especially in lower extremities), excessive sweating, or autonomic dysreflexia. Significant bacteriuria was defined as urine cultures with a bacterial colony count of $10^5$ CFUs or higher.[6] Pyuria was defined as white blood cells in the urine sample found to be more than 10 cells/high-power field.[7]

### Statistical analysis

STROBE guidelines for cross-sectional studies were followed for reporting our study. Chi-square test was applied to analyze the categorical variables, and

the Statistical Package for the Social Sciences (SPSS) version 21© (SPSS Inc., Chicago, IL, USA) software was used to conduct data analysis.

## Results

We analyzed 52 patients admitted in the SCI ward of our hospital, of which all were males with an average age of 29.38 ± 8.19 years. The mean duration of SCI was 747.77 days, and the mean length of hospital stay was 378.13 days. Fifteen (28.85%) patients had a cervical cord injury, 27 (51.92%) had a thoracic spine injury, while 10 (19.23%) had an injury at the level of lumbar spine. Using ASIA impairment scale, 26 (50%) subjects had an A type, 15 (28.84%) had a B type, and 11 (21.15%) had a C type of lesion. None of our patients had an indwelling urine catheter, but 37 (71.15%) patients had to use (CIC) while 7 (13.46%) used a condom drainage for bladder emptying; the rest of our patients voided urine spontaneously. The prevalence of UTIs in our study group was 67.31% (35/52 patients).

For analysis of different variables, we divided our study group into two groups, namely patients with UTI and patients without UTI. Comparisons were made for each variable using Chi-square test, and the results are described in Table 1.

Based on this analysis, statistically significant differences were found in development of UTI in the presence of a neurogenic bladder, presence of fecal incontinence, usage of CIC as mode of bladder emptying, presence of pyuria on laboratory evaluation, and the length of hospital stay ($P < 0.05$).

The most common uropathogen isolated from the urine samples was *Klebsiella pneumoniae*. The details of other uropathogens cultured from our study group are expressed in Table 2.

Following the isolation of the uropathogens, antibiotic sensitivity testing was done using a panel of most prescribed antibiotics, relative to the broad category of organism (e.g. Gram-negative bacilli, Gram-negative cocci, etc.). The percentage of total sensitivity was calculated using the formula:

$$\text{Total sensitivity } (\%) = \frac{\text{Number of sensitive organisms isolated } (n)}{\text{Total number of organisms isolated } (35)}$$

The different antibiotics commonly used and their sensitivities are elaborated in Table 3.

The three antibiotics to which the isolated uropathogens were most sensitive were found to be colistin (97.1%), tigecycline (82.9%), and ertapenem (74.3%).

## Discussion

The prevalence of UTIs in SCI patients in our evaluation was 67.31% (35/52 patients). *K. pneumoniae* was the most frequently isolated organism, and colistin was

**Table 1: Comparison of variables in patients with and without urinary tract infections**

| Variable | UTI present (*n*=35), *n* (%) | UTI absent (*n*=17), *n* (%) | *P* |
|---|---|---|---|
| Age (years), mean±SD | 30.057±8.68 | 28±7.11 | 0.180 |
| Duration of SCI (days), mean±SD | 850.90±407.91 | 535.44±222.83 | 0.093 |
| Length of hospital stay (days), mean±SD | 524.51±237.72 | 385.52±217.70 | <0.001** |
| Systemic disease (hypertension and diabetes mellitus) | 4 (11.42) | 0 | 0.147 |
| Level of lesion | | | |
| Cervical | 10 (28.57) | 5 (29.41) | 0.629 |
| Dorsal | 20 (57.14) | 7 (41.17) | 0.950 |
| Lumbar | 5 (14.28) | 5 (29.41) | 0.813 |
| ASIA scale | | | |
| A | 18 (51.43) | 8 (47.06) | 0.834 |
| B | 10 (28.57) | 5 (29.41) | 0.957 |
| C | 7 (20) | 4 (23.53) | 0.795 |
| Presence of urinary incontinence | 28 (80) | 11 (64.71) | 0.232 |
| Presence of fecal incontinence | 22 (62.86) | 4 (23.53) | 0.008** |
| Presence of neurogenic bladder | 33 (94.29) | 11 (64.71) | 0.006** |
| Mode of bladder emptying | | | |
| Spontaneous | 2 (5.71) | 6 (35.29) | 0.284 |
| CIC | 28 (80) | 9 (52.94) | 0.043** |
| Condom drainage | 5 (14.29) | 2 (11.76) | 0.803 |
| Presence of pyuria | 21 (60) | 0 | <0.001** |

**Statistically significant difference with *P*<0.05. UTI: Urinary tract infection, CIC: Clean intermittent catheterization, ASIA: American Spinal Injury Association, SD: Standard deviation, SCI: Spinal cord injury

the antibiotic most sensitive to maximum number of isolates.

The prevalence of UTI remains historically high in SCI patients.[8,9] Risk factors for the same are structural, such as altered voiding dynamics, bladder overdistension, presence of vesicoureteric reflux, increased voiding pressures, increased postvoid residual volume, frequent presence of urolithiasis, and routine use of urinary catheters (either indwelling or [CIC]). Furthermore, behavioral factors such as adjustment to the disability, patients' knowledge and self-hygiene, existing support systems, and access to medical services play a crucial role in development of UTIs.[3] Our prevalence rate of 67.31% is not in consonance with world literature, which reflects the fact that the risk factor profile in our set of patients is unlike the existing situation across the world. Our patient population is primarily a serving, male military population and the average age is usually below 30 years with minimal to no preexisting comorbidities, and the average hospital stay postinjury and subsequent management is very high, as these soldiers are discharged only after a complete and satisfactory rehabilitation is achieved, unlike populations studied previously which are a mix of male and female patients with associated comorbidities, a wide age range, and a restricted hospital stay owing to cost concerns.

**Table 2: Uropathogens isolated in the urine samples of our study population**

| Organism cultured | Number of patients, *n* (%) |
|---|---|
| *Klebsiella pneumoniae* | 22 (62.86) |
| *Escherichia coli* | 7 (20.00) |
| *Pseudomonas aeruginosa* | 2 (5.71) |
| *Klebsiella oxytoca* | 1 (2.86) |
| *Enterobacter cloacae* | 1 (2.86) |
| *Acinetobacter baumannii* complex | 1 (2.86) |
| *Serratia marcescens* | 1 (2.86) |
| Total | 35 (100.00) |

The presence of *K. pneumoniae* as the most frequently isolated organism in our set of patients indicates the peculiarity of this specimen found in our health-care setup, which is different from those found in other parts of the world. Most of the literature has found *Escherichia coli* as the most frequently isolated organism in UTIs in SCI patients.[10,11] One reason why *E. coli* is the most grown uropathogen in SCI patients is because of fecal incontinence leading to fecal contamination, which is present in most SCI patients.[12] However, Waites *et al*.[10] reported that persons on intermittent catheterization had polymicrobial bacteriuria, a fact which could be explained by diverse Gram-negative bacteria from the bowel, perineum, and urethra gaining access to the bladder, helped by a contaminated instrument. Hence, owing to the unique microbial profile of our SCIC and the fact that most of our patients used intermittent catheterization as the primary mode of bladder management, the increased isolation of *K. pneumoniae* could be explained.

We have also studied various known risk factors associated with development of UTI in SCI patients. In our study, we found that length of hospital stay was a statistically significant factor in development of UTI in our patient population, which is in consonance with the data from the study of Albayrak *et al*.[13] As length of hospitalization increases, risk of cross-contamination due to caregivers or health-care workers increases and predisposes these patients to develop newer microbial variants of UTI. Our SCI patients who used CIC as the primary mode of bladder management had an increased incidence of UTI versus the patients who used condom drainage, which has been shown to happen in a study conducted by Cullen *et al*.[11] Despite all precautions, the Foley's catheter used for intermittent catheterization is usually contaminated either during storage or while handling. We could not establish any association between development of UTI and level of SCI.

**Table 3: Antibiotic sensitivity pattern of various antibiotics**

| Antibiotic | Total number of sensitive organisms (*n*) | Total number of resistant organisms (*n*) | Total sensitivity (%) |
|---|---|---|---|
| Amoxycillin | 6 | 29 | 17.1 |
| Cefuroxime | 12 | 23 | 34.3 |
| Ceftriaxone | 12 | 23 | 34.3 |
| Cefoperazone/sulbactam | 15 | 20 | 57.1 |
| Piperacillin/tazobactam | 19 | 16 | 54.3 |
| Imipenem | 21 | 14 | 60.0 |
| Meropenem | 24 | 11 | 68.6 |
| Ertapenem | 26 | 9 | 74.3 |
| Amikacin | 25 | 10 | 71.4 |
| Gentamicin | 24 | 11 | 68.6 |
| Ciprofloxacin | 10 | 25 | 28.6 |
| Colistin | 34 | 1 | 97.1 |
| Nitrofurantoin | 19 | 16 | 54.3 |
| Tigecycline | 29 | 6 | 82.9 |

Prophylactic antibiotics for prevention of UTI in SCI patients remain controversial till date. Many studies have tried to justify their routine use, while others have rejected their clinical value expressing concern over development of antibiotic resistance. However, certain at-risk individuals including immunocompromised individuals, individuals with a vesicoureteric reflux, presence of urease-producing organisms like *Proteus mirabilis* which predispose to stone formation, and subsequent bladder outlet obstruction have been recommended prophylactic antibiotics.[3] We follow the above guidelines in instituting prophylactic antibiotics to our at-risk SCI patients and do not, as a general measure, prescribe them to all our patients.

Empirical antibiotic therapy is very often prescribed in SCI patients demonstrating signs or symptoms of UTI, after urine samples have been sent for examination and culture and sensitivity. Ampicillin plus gentamicin, ciprofloxacin, ceftriaxone, amikacin,[8] and nitrofurantoin are some of the most frequently used antibiotics used for this purpose. Most patients with SCI in the acute setting receive systemic, broad-spectrum antibiotics to treat or prevent infectious complications related to trauma, not restricted to UTI. This antibiotic pressure further enables colonization by resistant bacteria.[14] Research has revealed an increasing amount of multidrug resistance to these first-line antibiotics across the world, especially in SCI patients.[11,15] As the incidence of UTI in SCI patients is high, there is an increased risk of transmission of such multidrug-resistant strains among hospitalized patients.[5] Hospital infection control committees (HICCs) have been established in all health-care facilities across India as mandated by the National Accreditation Board for Hospitals and Healthcare Providers which maintains a surveillance of most isolated organisms and the antibiograms of commonly used antimicrobial agents, to assist the clinicians in instituting appropriate first-line empirical antibiotics based on existing antibiograms. Based on our data, we found that drugs such as ceftriaxone, nitrofurantoin, ciprofloxacin, and piperacillin/tazobactam, which are commonly used in hospitals as first-line agents, are not useful owing to widespread resistance across the microbial spectrum. In consultation with our HICC, we have made certain recommendations as regards different echelons of antimicrobial usage in SCI patients exhibiting symptoms of UTI.

There remain, however, a few limitations of our study, namely it being a cross-sectional study and no radiological assessment of associated renal disorders (e.g. Ultrasonography or urodynamic flow studies) being done, primarily owing to a relative scarcity of resources.

### Recommendations at our center

Based on the results of our study, the HICC of our hospital has formulated the following guidelines for antibiotic usage in SCI patients who are suspected to have a UTI.

a. No routine prescription of antibiotics for asymptomatic patients despite evidence of bacteriuria, except in cases where the patient is immunocompromised, has an established vesicoureteric reflux, or there is evidence of the presence of urease producing organisms like *P. mirabilis*
b. In patients who have symptoms of fever, discomfort or pain in the flanks, increased spasticity of skeletal muscles (especially in lower extremities), excessive sweating, or autonomic dysreflexia or laboratory evidence of pyuria, a sterile urine sample should be collected and sent for analysis, followed by institution of first-line antibiotic which is given empirically. That antibiotic as on date is injection ertapenem 1 g intravenous (IV)/day
c. In case of an associated renal dysfunction, injection tigecycline 100 mg IV infusion followed by 50 mg IV infusion q12 h should be used instead
d. Specific antibiotic should then be prescribed after culture and sensitivity reports of urine sample are obtained. Although injection colistin is sensitive to almost all uropathogens, a routine use is discouraged since frequent use can cause widespread resistance to the same.

## Conclusion

UTI in SCI patients remains a very real and common pathology encountered on a very regular basis and is often mismanaged owing to unnecessary or faulty empirical antibiotic institution. A scientific evaluation of the clinical and microbiological profile at SCICs will enable the HICCs of these centers to institute a well-planned and systematic antibiotic protocol for management of this oft encountered entity. We have noted that the presence of a neurogenic bladder, fecal incontinence, usage of CIC as mode of bladder emptying, pyuria, and increased length of hospital stay are significant risk factors for development of UTI in SCI patients, and considering the evolving pattern of antimicrobial resistance, routine prescription of antibiotics for asymptomatic bacteriuria is not advisable and injectable drugs should be wisely instituted only after clinico-microbiological evidence of UTI.

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### Conflicts of interest

There are no conflicts of interest.

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