

## Common Pathogens and their Antimicrobial Susceptibility Pattern in Urinary Tract Infection Among Spinal Cord Injury Cohort

Waqas Khalil, Omer Jamshed, Hina Kanwal, Talha Liaquat\*, Syed Tameem Ul Hassan, Fahad Hasnain\*

Department of Medicine, Armed Forces Institute of Rehabilitation Medicine/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

\*Department of Anesthesia, Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

### ABSTRACT

**Objective:** To determine the frequency of nosocomial urinary tract infections in patients admitted for spinal cord injury rehabilitation, identify the organisms responsible, and determine their susceptibility to systemic antimicrobials.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Armed Forces Institute of Rehabilitation Medicine, Rawalpindi Pakistan, from Sep 2022 to Apr 2023.

**Methodology:** Samples for urine culture and sensitivity were taken from 47 individuals; 25 of these were excluded due to the growth of mixed organisms. Both male and female patients were included with Spinal Cord injury and admitted to the Inpatient Department for rehabilitation. Spinal cord injuries were classified as acute (<6 months) and chronic (>six months), depending upon the time elapsed since the injury. Symptoms of urinary tract infections were documented.

**Results:** The sample showed a male preponderance, with 18(81.80%) males and 4(18.20%) females. Twelve individuals (54.5%) had symptoms of urinary tract infection. The urine sample yielded microbial growth in 19(86.40%) samples, confirming the diagnosis of UTI. Out of the participants, 9(40.90%) had acute SCI, while 13(59.10%) had chronic SCI. The mean duration since the SCI was 8.04±5.84 months.

**Conclusion:** In patients with urinary tract infections associated with spinal cord injury, *Klebsiella* and *Escherichia coli* were found to be the major causative organisms. Meropenem, Fosfomycin, and Gentamicin were found to be the most effective initial choice of antibiotics, exhibiting increased sensitivity against the alleged microorganisms.

**Keywords:** Antimicrobial susceptibility, Nosocomial infections, Rehabilitation medicine, Spinal cord injury.

**How to Cite This Article:** Khalil W, Jamshed O, Kanwal H, Liaquat T, Hassan STU, Hasnain F. Common Pathogens and their Antimicrobial Susceptibility Pattern in Urinary Tract Infection among Spinal Cord Injury Cohort. Pak Armed Forces Med J 2024; 74(4): 931-935. DOI: <https://doi.org/10.51253/pafmj.v74i4.10376>

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### INTRODUCTION

Hospital-acquired infections, also known as nosocomial infections, are a significant public health issue due to not only the additional financial burden but also due to an associated increase in morbidity in patients who are already suffering from an underlying illness. One of the injuries associated with hospital-acquired infections is spinal cord injury, which can often present with neurogenic bladder, leading to an increased tendency to develop urinary tract infections (UTIs). UTIs are by far the most common infection in spinal cord injury patients, occurring at a rate of 2.5 events per patient per year<sup>1</sup>.

Spinal cord injury patients have an increased tendency to develop UTIs due to factors such as overdistension of the urinary bladder, vesicoureteral reflux, high-pressure voiding and large post-void residual volumes. In addition, these patients often have urinary catheters inserted, which also increases

the risk of UTI development<sup>2</sup>. Approximately 20% of patients with an acute onset spinal cord injury develop UTIs within the first 50 days, and the annual incidence of UTI associated with spinal cord injury is 20%, according to results from multiple studies<sup>3-6</sup>.

Recognising nosocomial UTIs as a problem in spinal cord injury patients is essential as, with the appropriate interventions, it can be managed, and its incidence can be significantly lowered. In 1996, a nationwide survey in France revealed a UTI rate of 5.2% in long-term healthcare and rehabilitation facilities<sup>7</sup>. An active intervention policy led to UTIs dropping to 4% by 2001. Mortality in patients with spinal cord injury is due to a variety of causes, with respiratory distress and cardiovascular being the two most common. Infections are the third most significant cause, with a mortality rate of 9.4%<sup>8</sup>.

While a variety of organisms cause UTIs, the most commonly found are *E. Coli*, *Klebsiella*, *Proteus* and *Enterococcus*. According to a meta-analysis conducted on the epidemiology of pathogens responsible for UTIs in China, before 2012, the most common causative

**Correspondence:** Dr Waqas Khalil, Department of Medicine, Armed Forces Institute of Rehabilitation Medicine, Rawalpindi Pakistan  
Received: 18 May 2023; revision received: 05 Jul 2023; accepted: 10 Jul 2023

organism was *E. coli*, followed by *Klebsiella* and *Enterococcus*. After 2012, the third most common organism was *Proteus* <sup>9</sup>. The purpose of this study is to determine the frequency of nosocomial urinary tract infections in patients admitted for rehabilitation of spinal cord injuries, identify the organisms responsible, and determine their susceptibility to systemic antimicrobials.

**METHODOLOGY**

The cross-sectional study was carried out at the Armed Forces Institute of Rehabilitation Medicine, Rawalpindi Pakistan, from September 2022 to April 2023. Approval from the Hospital Ethical Review Committee was sought (ERC # 02/2022 dated 24 August 2022). The sample size was calculated using the OpenEpi sample size calculator, keeping the reference prevalence for nosocomial UTI to be 0.7%.<sup>8</sup>

**Inclusion Criteria:** Patients of either gender with spinal cord injuries (symptomatic and asymptomatic) admitted to the Inpatient Department for rehabilitation (for more than 48 hours), aged 18 to 60, were included.

**Exclusion Criteria:** The study excluded patients with a history of urinary tract trauma, pelvic fractures, immunosuppressive therapy, and a known immunocompromised state. The urinary sample yielding poly-microbial growth was also excluded.

The study used a non-probability consecutive sampling technique, and we included all the patients fulfilling the inclusion-exclusion criteria during our study duration. Excel sheet was used to compile data regarding variables like age, gender, duration of spinal cord injury, duration of hospital stay, symptoms of UTI, culture and sensitivity report of urine samples. Care was taken to collect urine from the clamped catheter to avoid contamination of the collected sample. Collected urine samples were sent to the Armed Forces Institute of Pathology, Rawalpindi for culture and sensitivity. Spinal cord injuries were classified as acute (<6 months) and chronic (> six months), depending upon the time elapsed since the injury. Symptoms of UTI like Urinary frequency, urinary urgency, burning micturition and or associated fever were documented.

Statistical Package for Social Sciences (SPSS) version 22.0 was used for the data analysis. Quantitative variables with normal distribution were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics.

The *p*-value lower than or up to 0.05 was considered as significant.

**RESULTS**

Samples for urine culture and sensitivity were taken from 47 individuals. Out of these 47 samples, 25 urine samples yielded growth of mixed organisms and thus were excluded from the study. Of the remaining 22 individuals, the mean age was 38.54±6.55 years and ranged from 23 to 49 years. The sample showed male preponderance as 18(81.80%) individuals were male while 4(18.20%) were females. Twelve individuals (54.5%) had symptoms of urinary tract infection, while the rest of the participants were asymptomatic (n=10, 45.40%). The urine sample yielded microbial growth in 19(86.40%) samples, confirming the diagnosis of UTI. Frequency of yielded microbial growth on urine culture is shown in Table-I. Out of the participants, 9(40.90%) had acute SCI, while 13(59.10%) had chronic SCI. The mean duration since the SCI was 8.04±5.84 months. The mean duration since the current date of admission was 4.81±4.37 weeks, ranging from 1 to 20 weeks. Antibiotic susceptibility of yielded organisms is described in Table-II. Association of nosocomial urinary tract infection with different parameters is shown in Table-III.

**Table I: Frequency of Yielded Microbial Growth on Urine Culture (n=22)**

| Organisms              | n (%)     |
|------------------------|-----------|
| Klebsiella species     | 11(50%)   |
| Escheria coli          | 4(18.20%) |
| Enterococcus faecalis  | 2(9.10%)  |
| Candida species        | 1(4.50%)  |
| Pseudomonas aeruginosa | 1(4.50%)  |
| No Organisms           | 3(13.60%) |

**Table III: Association of Nosocomial Urinary Tract Infection with Different Parameters (n=22)**

| Parameters                | Nosocomial UTI (n=22)                |             | <i>p</i> -value |
|---------------------------|--------------------------------------|-------------|-----------------|
| Age                       | 18 to 35 years (n=7)                 | 7(31.81%)   | 0.53            |
|                           | 36 to 60 years (n=15)                | 12((54.54%) |                 |
| Gender                    | Male (n=18)                          | 16(72.72%)  | 0.47            |
|                           | Female (n=4)                         | 3(13.63%)   |                 |
| Duration of Injury        | Acute (n=9)                          | 9(40.90%)   | 0.24            |
|                           | Chronic (n=13)                       | 10(45.45%)  |                 |
| Duration of Hospital Stay | Less than or equal to 4 weeks (n=15) | 13(59.09%)  | 0.95            |
|                           | Greater than 4 weeks (n=7)           | 6(27.27%)   |                 |

## Common Pathogens and their Antimicrobial Susceptibility

**Table-II: Antibiotic susceptibility of yielded Organisms (n=22)**

| Organisms              | Sensitivity  |           |            |           |           |           |           |           |
|------------------------|--------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|
|                        | Co-amoxiclav |           | Gentamicin |           | Imipenem  |           | Meropenem |           |
|                        | Yes          | No        | Yes        | No        | Yes       | No        | Yes       | No        |
| Klebsiela species      | 2(18.18%)    | 9(81.81%) | 8(72.72%)  | 3(27.27%) | 3(27.27%) | 8(72.72%) | 8(72.72%) | 3(27.27%) |
| Escheria coli          | Nil (0%)     | 4(100%)   | Nil (0%)   | 4(100%)   | 2(50%)    | 2(50%)    | Nil (0%)  | 4(100%)   |
| Enterococcus fecalis   | Nil (0%)     | 2(100%)   | Nil (0%)   | 2(100%)   | Nil (0%)  | 2(100%)   | 2(100%)   | Nil (0%)  |
| Candida species        | Nil (0%)     | 1(100%)   | Nil (0%)   | 1(100%)   | Nil (0%)  | 1(100%)   | Nil (0%)  | 1(100%)   |
| Pseudomonas aeruginosa | Nil (0%)     | 1(100%)   | Nil (0%)   | 1(100%)   | Nil (0%)  | 1(100%)   | Nil (0%)  | 1(100%)   |

| Organisms              | Sensitivity   |          |                |         |            |         |                |         |                        |         |
|------------------------|---------------|----------|----------------|---------|------------|---------|----------------|---------|------------------------|---------|
|                        | Ciprofloxacin |          | Nitrofurantoin |         | Fosfomycin |         | Co-trimoxazole |         | Pipracilin +Tazobectum |         |
|                        | Yes           | No       | Yes            | No      | Yes        | No      | Yes            | No      | Yes                    | No      |
| Klebsiela species      | Nil (0%)      | 4(100%)  | 4(100%)        | 0(0%)   | 3(75%)     | 1(25%)  | Nil (0%)       | 4(100%) | Nil (0%)               | 4(100%) |
| Escheria coli          | Nil (0%)      | 2(100%)  | Nil (0%)       | 2(100%) | Nil (0%)   | 2(100%) | Nil (0%)       | 2(100%) | 2(100%)                | 0(0%)   |
| Enterococcus fecalis   | Nil (0%)      | 2(100%)  | Nil (0%)       | 1(100%) | Nil (0%)   | 1(100%) | Nil (0%)       | 1(100%) | Nil (0%)               | 1(100%) |
| Candida species        | Nil (0%)      | 1(100%)  | Nil (0%)       | 1(100%) | Nil (0%)   | 1(100%) | Nil (0%)       | 1(100%) | Nil (0%)               | 1(100%) |
| Pseudomonas aeruginosa | 1(100%)       | Nil (0%) | Nil (0%)       | 1(100%) | Nil (0%)   | 1(100%) | Nil (0%)       | 1(100%) | Nil (0%)               | 1(100%) |

**Table III: Association of Nosocomial Urinary Tract Infection with Different Parameters (n=22)**

| Parameters                | Nosocomial UTI (n=22)                |            |           | p-value |
|---------------------------|--------------------------------------|------------|-----------|---------|
| Age                       | 18 to 35 years (n=7)                 | 7(31.81%)  | Nil       | 0.53    |
|                           | 36 to 60 years (n=15)                | 12(54.54%) | 3(13.63%) |         |
| Gender                    | Male (n=18)                          | 16(72.72%) | 2(9.09%)  | 0.47    |
|                           | Female (n=4)                         | 3(13.63%)  | 1(4.54%)  |         |
| Duration of Injury        | Acute (n=9)                          | 9(40.90%)  | Nil       | 0.24    |
|                           | Chronic (n=13)                       | 10(45.45%) | 3(13.63%) |         |
| Duration of Hospital Stay | Less than or equal to 4 weeks (n=15) | 13(59.09%) | 2(9.09%)  | 0.95    |
|                           | Greater than 4 weeks (n=7)           | 6(27.27%)  | 1(4.54%)  |         |

## DISCUSSION

Urinary tract infections (UTIs) due to spinal cord injuries represent a significant cause of mortality and morbidity among patients, and as such, identifying the problem and appropriately managing it is important. In settings where adequate management guidelines are implemented, urosepsis mortality rates experience a significant reduction of 10-15%<sup>10</sup>. Our study shows that 53% of the patients had bacteriuria that consisted of mixed organisms. These mixed cultures were excluded from the study as they represented contaminated samples. A study at the Armed Forces Institute of Pathology showed a nosocomial urinary tract infection rate of 69.17%<sup>11</sup>. Catheterisation in SCI patients presents as a significant risk factor for increased incidence of UTIs in SCI patients, with UTIs accounting for up to 40% of nosocomial infections, most of these being due to catheterisation<sup>12</sup>. An epidemiological study assessing the incidence of UTIs in SCI showed an incidence of 2.72 per 100 persons, while for individuals with normal voiding, the incidence was only 0.06 per 100 individuals<sup>13</sup>. A retrospective analysis of UTIs in SCI patients showed that out of 276 SCI patients, both acute and chronic, symptomatic UTIs were found in 39% of patients<sup>14</sup>.

The most common organism found in urine cultures is usually *E. coli*<sup>9</sup>, while in our study, the most common organism was *Klebsiella*, with *E. coli* being the second most common. However, our sample size is only 22, so significant conclusions cannot be drawn regarding the percentage of bacterial pathogens. Another study also showed *E.coli* as the most prevalent causative agent for UTIs, accounting for up to 69.6%<sup>15</sup>. Regarding drug resistance, *E. coli* was found to be resistant to  $\beta$ -lactamase inhibitors after 2012<sup>9</sup>. *K. pneumoniae* was resistant to Aztreonam and Amikacin before 2012. Our study showed both *E. coli* and *Klebsiella* being sensitive to Fosfomycin, Gentamicin and Meropenem, thus presenting these drugs as suitable empirical drugs of choice for management.

In all SCI patients, catheterisation is the most significantly associated with UTI development. An epidemiological study showed the incidence of UTIs in patients with male indwelling catheters to be 2.72 per 100 persons, female suprapubic catheterisation to be 0.34 per 100 persons and 0.06 for normal individuals<sup>12</sup>. Clean intermittent self-catheterisation (CISC) is one of the methods to control UTI incidence. Other methods that have been attempted to control UTIs include systemic antimicrobials, sealed tubing and catheter

junctions and silver ion-coated catheters with varying levels of success <sup>16</sup>.

The easiest method is to prevent bacterial entry into the urinary tract. For that purpose, hospitals have implemented clean intermittent self-catheterisation (CISC) training programs so patients can perform the procedure themselves without increasing infection risk <sup>17</sup>. The best strategy to manage UTIs in SCI patients seems to be prevention. However, once infection has developed, the primary treatment method is antibiotics. Asymptomatic bacteriuria need not be treated with antibiotics, while symptomatic infections warrant treatment in all patients <sup>12</sup>. Polymicrobial infections are more common in catheterised patients, and repeated antibiotic exposure increases the risk of infection with drug-resistant variants. Thus, catheterised patients should have catheters regularly replaced, and the results of sensitivity tests should guide antibiotic treatment choices. Waites *et al.* showed that of all the isolates from SCI patients with UTIs, 33% tend to be multi-drug resistant organisms <sup>18</sup>.

#### LIMITATIONS OF STUDY

It has been seen that antibiotic resistance trends tend to change over time, so extending this study over a wide period of time can allow observation of these trends to see which antibiotics are becoming less effective. Fosfomycin, Meropenem and Gentamicin have exhibited adequate effectiveness for various organisms. These were suitable candidates for initial antibiotic treatment. However, sensitivity cultures should always determine prolonged antibiotic treatment to prevent future development of drug resistance.

#### ACKNOWLEDGEMENT

We would like to thank Dr Taimoor Ashraf Khan for assisting in data analysis and critical manuscript review.

#### CONCLUSIONS

In patients with UTI associated with spinal cord injury, *Klebsiella* and *E. coli* were found to be major causative organisms. Meropenem, Fosfomycin and Gentamicin were found to be the most effective initial choice of antibiotics, exhibiting increased sensitivity against the alleged microorganisms.

**Conflict of Interest:** None.

#### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WK & OJ: Conception, study design, drafting the manuscript, approval of the final version to be published.

HK & TL: Data acquisition, data analysis, critical review, approval of the final version to be published.

TUH & FH: Data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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