Original Article

Antibiogram data of urinary tract infection in spinal cord injury patients in an outpatient setting

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ABSTRACT

الأهداف: إنشاء بيانات المضادات الحيوية للمرضى الذين يعانون من إصابة النخاع الشوكي (SCI) والتي من شأنها أن تساعد في التمييز بين الجراثيم المسببة لعدوى المسالك البولية المتكررة اعتماداً على طريقة التبول وفعالية المضاد الحيوي ضدها.

المنهجية: اشتملت الدراسة على إجمالي 499 نتيجة لزراعة البول من 151 مريض من مرضى إصابات النخاع الشوكي الذين يعانون من أعراض عدوى المسالك البولية (UTI) مع بيلة جرثومية كبيرة وبيلة قيحية مع أكثر من 10 خلايا دم بيضاء لكل مجال طاقة عالي. صُنف طريقة التبول على النحو التالي: قسطرة ذاتية متقطعة (SIC)، أو قسطرة فوق العانة (SPC)، أو قسطرة فولي، أو قسطرة الواقي الذكري، أو التبول من دون قسطرة.

النتائج: البيانات الديموغرافية كانت على النحو التالي: الذكور، العدد =124 (82.2%)؛ الإناث، العدد=27 (17.8%)؛ متوسط العمر 39 سنة؛ شلل نصفي، العدد=105 (69.5%)؛ شلل رباعي، العدد=45 (29.8%). القسطرة الذاتية المتقطعة هي الأكثر استخداماً بين المرضي (العدد=64، 42.3%)، يليه قسطرة فولي (العدد=39، 25.8%). كانت الإشريكية القولونية هي أكثر جرثومة مسببة لعدوى المسالة البولية (29%) وتزداد شيوعاً في المرضى المستخدمين للقسطرة الذاتية المتقطعة. تكثر جرثومة المُتَقَلِّبَة الرَّائعَة في المرضى المستخدمين لقسطرة فوق العانة (33%)، وتكثَر جرثَومة الكَلَبْسية الرئوية لدى المرضى الذين يتبولون من دون قسطرة (30%). فعَالية المضادات الحيوية هي كالتالي: الجينتاميسين (44.1%)، النيتروفورانتوين (39.1%)، أوجمنتين (33.5%)، والسيبروفلوكساسين (31.5%).

الخلاصة: تفضيل مرضى النخاع الشوكي المحليين لقسطرة فولي كطريقة للتبول ولمعرفة سبب ذلك يحتاج إلى المزيد من الدراسة. لوحظ اختلاف الجرثومة المسببة لعدوى المسالك البولية باختلاف طريقة التبول. ازدادت مقاولة الجراثيم للمضاد الحيوي السيبروفلوكساسين في جميع طرق التبول ما عدى مستخدمين قسطرة فوق العانة. المضاد الحيوي الأكثر فعالية ويأخذ عن طريق الفم هو النيتروفورانتوين ويليه أوجمنتين ثم السيفوروكسيم.

Objectives: To establish antibiogram data for patients with spinal cord injury (SCI) that would help differentiate the organisms commonly present depending on the voiding method and antibiotic sensitivity for empirical treatment.

Methods: A total of 499 urine culture results were obtained from 151 SCI patients with symptomatic urinary tract infection (UTI) with significant bacteriuria and pyuria with more than 10 white blood cells per high power field. The voiding method was categorized as follows: self-intermittent catheterization (SIC), suprapubic catheter (SPC), Foley catheter, condom catheter, or voiding freely.

Results: The demographic data were as follows: male, n=124 (82.2%); female, n=27 (17.8%); mean age, 39; paraplegic n=105 (69.5%); and tetraplegic, n=45 (29.8%). The SIC was the most common voiding method (n=64, 42.3%), followed by Foley catheter (n=39, 25.8%). Escherichia coli was the most common organism overall (29%) and more frequent in patients using SIC as the voiding method. *Proteus mirabilis* was present more frequently in patients using SPC (33%), and *Klebsiella pneumoniae* in voiding freely cultures (30%). Antibiotic sensitivity was as follows Gentamicin (44.1%), Nitrofurantoin (39.1%), Augmentin (33.5%), and Ciprofloxacin (31.5%).

Conclusion: Increased preference of the local population to foley catheter as a voiding method which needs to be investigated more. The type of voiding methods in patients with SCI results in different common causative organisms of UTI. Ciprofloxacin resistance profile increased overall except in patients voiding with SPC. Nitrofurantoin is the most overall sensitive oral antibiotic in our sample followed by Augmentin then Cefuroxime.

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Every year, between 250,000 and 500,000 people endure a spinal cord injury (SCI).[1] Saudi Arabia has one of the highest rates of SCI worldwide.[2,3] Most cases of septicemia in these patients are attributed to the urinary tract, with a high mortality risk of 15%.[4]

Urinary tract infections (UTIs) are common in patients with SCI and have a high societal cost, as people with SCIs and neurogenic lower urinary tract dysfunction are at significant risk of morbidity from UTIs, with approximately 2 episodes of UTIs per year.[5] The problem of frequent UTIs is amplified by the high prevalence of multiple drug-resistant strains (MDR) within SCI populations, which exacerbates the clinical, social, and economic consequences of the disease, making UTIs more expensive and difficult to treat.[6–8]

A major challenge for patients with SCI and clinicians is that when patients develop a UTI, simple oral antibiotics are frequently ineffective.[9] Girard et al[10] found that in patients with SCI, the majority of hospital-acquired infections in rehabilitation units were UTIs. Clinically, a growing number of patients are colonized by potentially pathogenic organisms, and if cross-infection occurs, few known antibiotics are effective. A North American study by Thom et al[6] showed that up to 73% of inpatients with SCI became colonized with MDR during an inpatient hospital stay, while Mylotte et al[11] found that 44% of patients with SCI were colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) in surveillance cultures.

High rates of colonization have been attributed to the neurogenic lower urinary tract dysfunction and bladder management type (particularly indwelling catheterization), high rates of antibiotic use, mechanical ventilation, and pressure ulcers.[6,10–12] Some of these patients are now effectively in the post-antibiotic therapy era. This highlights the need to optimize UTI treatment and limit the unnecessary treatment of asymptomatic bacteriuria. A key method for achieving this is the use of antibiograms. Antibiograms represent the sensitivity and resistance profiles of microbial species to a group of antibiotics. North American clinician surveys found that 95% of SCI clinicians believed that improved access to antibiograms would reduce antibiotic resistance.[13]

Our goal was to develop an SCI-UTI antibiogram that would reveal the most common causative organisms for each voiding method and their antibiotic sensitivity. These data will help physicians empirically treat SCI-UTI using the most appropriate antibiotics. We believe that these antibiogram data will guide further research and help establish future SCI-UTI antibiotic therapy guidelines.

Methods. This was an observational cross-sectional study. The medical records of patients with SCI from the Prince Sultan Medical Military City (PSMMC) Rehabilitation Unit from 2008 to 2019 was gathered. A total of 350 patients had an SCI, and 199 were excluded because they met our exclusion criteria (patients with SCI but with no UTI, lack of proper documentation, insufficient urine culture results, and hospital-acquired UTI). Following the definition of urinary tract infection by The National Institute on Disability and Rehabilitation Research (NIDRR) Consensus Statement (1992)[14] for an SCI patient to be diagnosed with UTI has to meet the three points criteria (significant bacteriuria, pyuria with more than 10 white blood cells per high power field and at least one symptom or sign of UTI). Significant bacteriuria is defined by the presence of more than 10^2 colony-forming units/millimeter (CFU/ml) in patients voiding with SIC and 10^4 CFU/ml for patients using SPC, foley catheters, condom catheter and voiding freely. Symptoms and signs of UTI in SCI patients include (fever, suprapubic pain, increase in incontinence, autonomic dysreflexia, worsening of spasticity, and fatigue). The calculated sample size was 385 with a confidence interval of 95%. A total of 151 patients met the inclusion criteria (patients with SCI and with UTI, proper documentation, community-acquired UTI, and sufficient urine culture results). This study

Table 1 - Demographics data.

Demographics categories	n (%)
Gender	
Male	124 (82.2)
Female	27 (17.8)
Age	
16-30	34 (22.5)
31-50	65 (43.1)
51-70	35 (23.2)
70 and more	17 (11.2)
Level of injury	
Paraplegia	105 (69.5)
Tetraplegia	45(29.8)
Cauda Equina Syndrome	1 (0.7)
Voiding method	
Self-intermittent catheterization	64 (42.3)
Indwelling Foley catheter	39 (25.8)
Free voiding	29 (19.2)
Suprapubic catheter	15 (10)
Condom catheter	4 (2.7)

Table 2 - Comparing different organisms frequencies by voiding methods.

Organisms by voiding methods	Freely	Condom Catheter	Foley catheter	Self-intermittent catheterization	Suprapubic catheter	Total
Acinetobacter Baumanii	2 (33.4)	0	0	3 (50)	1 (16.7)	6 (1.2)
Citrobacter Koseri	0	0	0	2 (66.7)	1 (33.3)	3 (0.6)
Citrobacter Freundii	0	0	1 (16.7)	4 (66.7)	1 (16.7)	6 (1.2)
Enterobacter Cloacae	5 (35.7)	0	3 (21.4)	4 (28.6)	2 (14.3)	14 (2.8)
Enterococcus Aerogens	0	0	0	1 (100)	0	1 (0.2)
Enterococcus Faecalis	3 (12.5)	0	4 (16.7)	13 (54.2)	4 (16.7)	24 (4.8)
Enterococcus Faecium	0	0	0	1 (100)	0	1 (0.2)
Escherichia Coli	16 (11)	4 (2.7)	36 (24.7)	68 (46.6)	22 (15.1)	146 (29.3)
Escherichia Coli (ESBL)*	6 (27.3)	0	0	15 (68.2)	1 (4.5)	22 (4.4)
Klebsiella Oxytoca	0	0	0	1 (50)	1 (50)	2 (0.4)
Klebsiella Pnumoniae	21 (20.8)	0	11 (10.9)	56 (55.4)	13 (12.9)	101 (20.2)
Klebsiella Pnumoniae(ESBL)*	1 (12.5)	0	0	7 (87.5)	0	8 (1.6)
Morganella Morganii	0	0	2 (22.2)	5 (55.6)	2 (22.2)	9(1.8)
Proteus Mirabilis	11 (16.7)	0	13 (19.7)	20 (30.3)	22 (33.3)	66 (13.2)
*Proteus Mirabilis (MDR**)*	0	0	1 (25)	3 (75)	0	4 (0.8)
Providencia Stuartii	0	0	2 (15.4)	9 (69.2)	2 (15.4)	13(2.6)
*Providencia Stuartii (MDR**)*	1 (14.3)	0	6 (85.7)	0	0	7 (1.4)
Pseudomonas Aeruginosa	2 (3.4)	1 (1.7)	20 (34.5)	27 (46.6)	8 (13.8)	58 (11.6)
*Pseudomonas Aeruginosa(MDR**)*	0	0	1 (50)	1 (50)	0	2 (0.4)
Serratia Marcescens	0	0	0	1 (100)	0	1 (0.2)
Staphylococcus Aureus	0	0	1 (50)	1 (50)	0	2 (0.4)
*Staphylococcus Aureus (MRSA***)*	0	0	0	2 (66.7)	1 (33.3)	3 (0.6)
Total	68 (13.6)	5 (1)	101 (20.2)	244 (48.%)	81 (16.2)	499 (100)

*Extended-spectrum beta-lactamases, **Multiple drug resistant strain, ***Methicillin-resistant Staphylococcus aureus

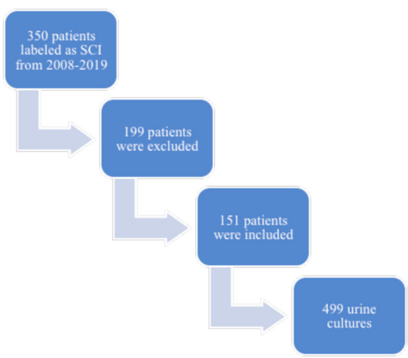

Figure 1 - Data collection process.

was approved by the Institutional Review Board (IRB) Ethics Committee of Prince Sultan Medical Military City in Riyadh, Saudi Arabia, with the approval number E-2126.We collected 499 urine culture results from these 151 patients with documented UTI (**Figure 1**).

We created a Google Form for manual entry of the urine culture results and demographic data (age, gender, level of injury, and voiding method). The voiding method was recorded as documented in the medical records and included: free voiding, self-intermittent catheterization (SIC), suprapubic catheter (SPC), indwelling Foley catheter (IDC) or condom catheter. Google Form data sheets were extracted in Excel format and analyzed using Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 29 (IBM Corp., Armonk, N.Y., USA) for a descriptive analysis of the data.

Results. In total, 499 urine culture results were collected from 151 patients with SCI, of which 124 were men (82.2%) and 27 were women (17.8%). The most frequent age group was from 31 to 50 years (43.1%). Paraplegia was the most common level of injury (n=105, 69.5%), followed by tetraplegia (n=45, 29.8%), and finally one patient with cauda equina syndrome. The SIC was the voiding method used by most patients (n=64, 42.3%), followed by IDC (n=39, 25.8%), voiding freely (n=29, 19.2%), SPC (n=15, 10%), and finally condom catheter (n=4, 2.7%). Demographic data are summarized in **Table 1**.

Table 3 - Comparing antibiotics sensitivity by voiding method.

Antibiotic by voiding methods	Freely	Condom catheter	Foley catheter	Self-intermittent catheterization	Suprapubic catheter	Total
Amikacin	11 (12.6)	0	14 (16.1)	45 (51.7)	17 (19.5)	87 (17.4)
Ampilicin	12 (15.6)	0	12 (15.6)	37 (48.1)	16 (20.8)	77 (15.4)
Augmentin	23 (13.8)	2 (1.2)	33 (19.8)	83 (49.7)	26 (15.6)	167 (33.5)
Azithromycin	1 (100)	0	0	0	0	1 (0.2)
Ciprofloxacin	12 (7.6)	2 (1.3)	33 (21)	83 (52.9)	27 (17.2)	157 (31.5)
Ceftazidime	3 (5.3)	1 (1.8)	19 (33.3)	24 (42.1)	10 (17.5)	57 (11.4)
Cefazolin	1 (100)	0	0	0	0	1 (0.2)
Cefuroxime	25 (15.8)	4 (2.5)	34 (21.5)	71 (44.9)	24 (15.2)	158 (31.7)
Cefotaxime	1 (5.6)	0	3 (16.7)	12 (66.7)	2 (11.1)	18 (3.6)
Cefipime	1 (8.3)	0	2 (16.7)	7 (58.3)	2 (16.7)	12 (2.4)
Colistin	5 (17.9)	0	6 (21.4)	13 (46.4)	4 (14.3)	28 (5.6)
Chloramphenicol	1 (100)	0	0	0	0	1 (0.2)
Clindamycin	0	0	0	1 (100)	0	1 (0.2)
Ertapanem	8 (12.5)	0	7 (10.9)	36 (56.2)	13 (20.3)	64 (12.8)
Erythromycin	0	0	0	1 (100)	0	1 (0.2)
Fosfomycin	1 (2.8)	0	4 (11.1)	24 (66.7)	7 (19.4)	36 (7.2)
Flucloxacillin	0	0	1 (33.3)	2 (66.7)	0	3 (0.6)
Imipenem	11 (13.4)	0	14 (17.1)	45 (54.9)	12 (14.6)	82 (16.4)
Gentamicin	34 (15.5)	3 (1.4)	47 (21.4)	111 (50.5)	25 (11.4)	220 (44.1)
Levofloxacin	1 (14.3)	0	2 (28.6)	2 (28.6)	2 (28.6)	7 (1.4)
Meropenem	13 (16)	0	16 (19.8)	37 (45.7)	15 (18.5)	81 (16.2)
Nalidixic Acid	1 (50)	0	1 (50)	0	0	2 (0.4)
Nitrofurantoin	25 (12.8)	4 (2.1)	36 (18.5)	103 (52.8)	27 (13.8)	195 (39.1)
Norfloxacin	14 (16.7)	3 (3.6)	17 (20.2)	37 (44)	13 (15.5)	84 (16.8)
Trimethoprim /Sulfamethoxazole	23 (14.6)	2 (1.3)	25 (15.9)	89 (56.7)	18 (11.5)	157 (31.5)
Tazocin	4 (4.9)	1 (1.2)	21 (25.6)	41 (50)	15 (18.3)	82 (16.4)
Tetracycline	1 (33.3)	0	0	1 (33.3)	1 (33.3)	3 (0.6)
Tigecycline	2 (40)	0	1 (20)	2 (40)	0	5 (1)
Tobramycin	1 (50)	0	1 (50)	0	0	2 (0.4)
Trimethoprim	4 (50)	0	1 (12.5)	3 (37.5)	0	8 (1.6)
Vancomycin	3 (20)	0	2 (13.3)	7 (46.7)	3 (20)	15 (3)
Total	68 (13.6)	5 (1)	101 (20.2)	244 (48.9)	81 (16)	499 (100)

Escherichia coli was the most common UTI-causing organism in patients using SIC (n=68, 46.6%) and IDC (n=36, 24.7%). *Proteus mirabilis* and *E. coli* had equal frequency in patients using SPC (n=22, 33.3%), while patients who voided freely experienced frequent UTIs caused by *Klebsiella pneumoniae*. Further details regarding the other organisms identified in the urine cultures are given in **Table 2**.

The results showed the greatest antibiotic sensitivity against cultures of all voiding methods with gentamicin (n=220, 44.1%), except the urine cultures of patients using SPC. Nitrofurantoin was the second most effective and best oral antibiotic in patients using all voiding methods (n=195, 39.1%). Trimethoprim-sulfamethoxazole was more effective than ciprofloxacin and augmentin in patients using SIC. Ciprofloxacin overall resistance was increased especially in patients who voided freely, however, ciprofloxacin sensitivity is better and similar to nitrofurantoin in SCI patients with SPC. Cefuroxime sensitivity profile is equal to nitrofurantoin in patients who voided freely. Further details regarding antibiotic sensitivity are presented in **Table 3**.

Discussion. Urinary tract bacterial colonization in patients with SCI is expected owing to the frequent use of catheterization and contamination from the adjacent perineum. The high frequency of yearly UTIs in these patients poses a challenge in choosing and administering an adequate treatment, which could consequently increase the overall antimicrobial resistance.

We noted an increased rate of using IDC as a voiding method in our data compared to a similar study which showed that IDC was the least used method of voiding.[15] Using IDC for long-term management of the bladder is known to cause more complications over time including a higher incidence of multidrug resistance UTI and bladder cancer.[16,17,18] This could reflect the local patients' preference for the voiding method and also emphasize the need for Physiatrists and Urologists to educate the patients and choose the safest voiding method.

E. coli was the most common causative organism in our data, especially in patients who used SIC as a voiding method. A similar finding was reported by Kyoung Ho Ryu and Min-Soo Kang;[15,19] however, the frequent causative organism in patients using SPC was found to be *Pseudomonas* in their study compared to *P. mirabilis* and *E. coli* in our study. *Pseudomonas aeruginosa* was the predominant cause of UTIs in other published studies of patients with SCI.[5,15] Vladimír Šámal reported that the most common multidrug-resistant bacteria were *Klebsiella spp*. (29%) and *Escherichia coli* (24%) compared to our findings of *Klebsiella Pnumoniae* Extended-spectrum beta-lactamases (ESBL) (1.6%) and *Escherichia Coli (ESBL)* (4.4%), this difference is due to urine culture collection from inpatients in contrast to outpatients in our study.[18] These overall variations may be attributed to the geographical nature of the antibiogram data, which suggests further investigation is needed.

Symptomatic patients presenting to the clinic require empirical oral antibiotic treatment and close follow-up to reassess their response to the medication. Ciprofloxacin is still used as a first-line therapy; however, our results showed an increase in the level of resistance to this antibiotic, especially in urine cultures from patients who voided freely. The high level of resistance to Ciprofloxacin is consistent with recent data published by Vladimír Šámal,[18] Clayton Patros[20] and the newest Saudi Ministry of Health (MOH) national antibiogram for non-SCI patients.[21]

This study showed that gentamicin was the most effective antibiotic; although, a previous study showed high sensitivity for vancomycin, meropenem, and imipenem in SCI patients with UTI.[15] However, this information is not helpful in outpatient settings because these antibiotics are administered intravenously. Nitrofurantoin was the best oral antibiotic for all patients using all voiding methods in our study, followed by Augmentin then Cefuroxime. For non-SCI patients with UTIs, the published UTI management protocol by the Saudi Ministry of Health recommends trimethoprim/sulfamethoxazole as the first-line therapy for complicated UTIs, followed by nitrofurantoin then ciprofloxacin.[21] Higher sensitivity to Augmentin been reported in SIC group (61.3%) compared our finding of (49.7%), which means that Augment can be a good first line therapy to patients using SIC.[15] Previous literature showed more resistance to Ciprofloxacin especially in the SIC group (33.9%) compared to our results of (52.9%).[15]

The limitations of our study were the small population size. Our sample could not represent all patients with SCI owing to the exclusion of a large number of patients because of the lack of proper documentation. Furthermore, the hospital laboratory does not report sensitivity to carbapenems unless the urine culture is resistant to multiple antibiotics, which explains the low number of carbapenem sensitivity reports compared to those for the other drugs.

A further multicenter studies with a larger number of cultures from patients with SCI to establish a national antibiogram for our target patients, which could result in better knowledge and management of SCI-UTIs.

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