ORIGINAL ARTICLE

Bacterial susceptibility patterns in patients with spinal cord injury and disorder (SCI/D): an opportunity for customized stewardship tools

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Study design: Retrospective observational study of bacterial susceptibilities in Veterans with SCI/D as compared to a general patient population.

Objectives: The purpose of this project was to evaluate the prevalence and susceptibility of bacteria isolated from spinal cord injury and disorder (SCI/D) patients as compared with a general patient population and determine whether a SCI/D-specific antibiogram, a report of bacterial susceptibilities used to guide empiric antibiotic selection, would be a useful stewardship tool.

Setting: Veterans Affairs Medical Center located in Cook county, IL, USA.

Methods: Microbiology reports from 1 October 2012 to 30 September 2013 were compiled into a SCI/D-specific antibiogram and compared to a non-SCI/D antibiogram.

Results: Persons with positive cultures and SCI/D were younger and had a higher Charlson Index as compared to non-SCI/D patients ($P < 0.0001$ for both). Five thousand one hundred and thirty-one unique isolate cultures were evaluated (SCI/D = 23.0%). Frequencies of pathogens isolated in SCI/D and non-SCI/D differed. Methicillin-resistant *Staphylococcus aureus* occurred more frequently in SCI/D (27.8% vs 55.4%; $P < 0.0001$). Gram-negatives had generally lower susceptibilities in SCI/D and a higher frequency of organisms producing extended-spectrum Beta-lactamases (17.6% vs 5.0%; $P < 0.0001$), carbapenem-resistant *Enterobacteriaceae* (2.4% vs 0.5%; $P < 0.0001$), carbapenem resistance (7.6% vs 2.4%; $P < 0.0001$) and isolates resistant to ≥ 3 antibiotic classes (60.7% vs 28.0%; $P = 0.0001$).

Conclusion: Different pathogens with poorer susceptibilities are isolated in SCI/D. Thus an SCI/D-specific antibiogram reflective of resistance patterns in these patients may increase the appropriateness of empiric antibiotic selection. The frequency of multi-drug resistant organisms in cultures obtained from patients with SCI/D is worrisome.

Spinal Cord (2016) **54**, 1001–1009; doi:10.1038/sc.2016.38; published online 22 March 2016

INTRODUCTION

Antibiotic resistance increases the likelihood of initial inadequate therapy, which corresponds to an increased mortality, length of stay and health-care costs.^{1–14} Antibiograms are facility-specific aggregated reports of bacterial susceptibilities and are recommended as a component of antimicrobial stewardship programs.¹⁵ Clinically, the antibiogram is used as a tool to aid providers in making evidence-based decisions when choosing the most appropriate agent for initial empiric antibiotic treatment because they are reflective of the susceptibility of organisms isolated at that facility.¹⁶ Thus antibiograms specific to certain patient care areas may allow for identification of resistance issues specific to that population and allow for focused antimicrobial stewardship and infection-control efforts.^{15,17,18} However, less than half of academic medical centers have unit-specific antibiograms.¹⁹ As inappropriate initial empiric

antibiotic treatment is associated with increased morbidity and mortality, the lack of unit-specific antibiograms may negatively affect clinical outcomes because clinicians have less information available to guide treatment selection.¹⁵ Further, previous studies comparing unit-specific antibiograms to hospital-wide antibiograms found significant differences in the susceptibility rates across different units,^{20,21} suggesting that use of unit-specific or population-stratified antibiograms might be appropriate.²²

Individuals with spinal cord injury or disorder (SCI/D) are at high risk for infections and antimicrobial resistance compared to the general patient population secondary to factors, such as frequent hospitalization, previous antibiotic use, frequent and chronic use of invasive devices and development of pressure ulcers.^{23,24} However, data on bacterial resistance in the SCI/D population is scarce and use of antibiograms in hospital units caring for these patients is limited.²⁵

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This project was presented, in part, as a poster at the Infectious Disease Society of America Annual Meeting in Philadelphia, PA, USA, October 2014.

Received 8 November 2015; revised 8 February 2016; accepted 13 February 2016; published online 22 March 2016

The lack of SCI-specific antimicrobial susceptibility data poses a significant limitation to the optimal management of infectious diseases in SCI/D patients, because resistance patterns differ based on patient history, care area and past exposure to health-care services and antimicrobials.^{26,27} This leads to potential significant bias in using hospital antibiograms to guide treatment decisions, particularly for complicated patients with SCI/D. Thus the purpose of this project was to evaluate the prevalence and resistance patterns of bacteria isolated from patients with SCI/D as compared to a general patient population and determine whether an SCI/D-specific antibiogram would be valuable for facilities treating these patients.

MATERIALS AND METHODS

Study design, setting and population

A retrospective cross-sectional analysis of microbiology laboratory reports from 1 October 2012 to 30 September 2013 for all cultures (inpatient and outpatient) obtained at a 471-bed Midwestern VA facility were evaluated. The SCI/D cohort at the study facility was identified using an ongoing registry of Veterans with SCI/D maintained by the VA Allocation Resource Center (ARC), which is used to allocate resources to VA medical centers.²⁸ The SCI/D group was compared with the remaining non-SCI/D patients with cultures during the study period. Patient location (inpatient vs outpatient) was defined as the patient location when the culture was taken. This study was reviewed and approved by the local institutional review board.

Microbiology data and definitions

Microbiology data were obtained from the VA's Corporate Data Warehouse, which includes data on medical encounters occurring in the VA health-care system. Microbiology records were queried to extract all cultures for aerobic and anaerobic bacteria, regardless of the source (for example, blood, urine, sputum). Only the first isolate cultured from a single patient was included unless the susceptibility pattern changed. Consistent with current recommendations for comparing susceptibility results, only those bacteria isolated in ≥ 30 non-surveillance cultures were included in this evaluation.²⁹ Extended spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae* and *Klebsiella*-producing carbapenemases (KPC) were conducted using broth microdilution and the modified Hodge test, respectively, using standardized Clinical and Laboratory Standards Institute methodology.³⁰

Multi-drug resistant Gram-negatives were defined as isolates with intermediate or resistant susceptibilities to ≥ 3 of the following classes/agents: aminoglycosides, ampicillin, aztreonam, antipseudomonal penicillins in combination with a Beta-lactamase inhibitor, carbapenems, cephalosporins, cephamycins, chloramphenicol, colistin, fluoroquinolones, fosfomycin, penicillins in combination with a Beta-lactamase inhibitor, sulfamethoxazole/trimethoprim, tetracyclines, and tigecycline.³⁰ Carbapenem resistance was evaluated for all organisms based on testing resistant to any agent in the carbapenem class. Carbapenem-resistant *Enterobacteriaceae* (CRE) was based on agent minimum inhibitory concentrations and organism isolated according to definitions by the Clinical and Laboratory Standards Institute.³¹ For *Escherichia* sp., *Klebsiella* sp., *Enterobacter* sp., *Salmonella* sp., *Shigella* sp., *Serratia* sp. or *Citrobacter* sp., CRE was defined as intermediate or resistant minimum inhibitory concentrations for the carbapenem class (exception ertapenem = resistant only) and resistant to all tested third-generation cephalosporins. *Proteus* sp., *Providencia* sp. and *Morganella* sp. were similarly defined with the exception of displaying nonsusceptible minimum inhibitory concentrations to at least two of the following: imipenem, meropenem, and/or doripenem.

Statistical analysis

Antimicrobial susceptibility results of individual isolates were compiled into a standardized SCI/D-specific antibiogram and compared to a compiled non-SCI/D antibiogram using Chi-square tests and Fisher's Exact test as appropriate. Comparison of susceptibilities by location were similarly conducted within each group. Demographics of persons were compared using Student's *t*-test or Chi-square. SAS 9.3 (SAS, Inc, Cary, NC, USA) was used for data and statistical analyses. A *P*-value < 0.05 was considered significant.

RESULTS

During the study period, there were a total of 5131 unique cultures for 3135 unique patients. Veterans with SCI/D had 23.0% ($n = 1179$) of unique cultures for 249 unique patients. There was a higher mean number of cultures per patient with SCI/D as compared to the overall hospital population (SCI/D = 4.7 cultures/patient, overall = 1.4 cultures/patient, P -value < 0.0001). Overall, those with SCI/D were younger and more likely to be male than those without SCI/D (Table 1). Compared to those without SCI/D, Veterans with SCI/D had a higher Charlson Index (a measure of severity of illness) but were less likely to have cerebrovascular disease, chronic pulmonary disease, heart failure or renal disease ($P \leq 0.0423$ for all). Although those with SCI/D were more likely to be hospitalized within the past 30 and 90 days ($P \leq 0.0001$), the frequency of surgical

Table 1 Demographics of patients with positive cultures

	SCI number, (%) N = 249	Non-SCI, number (%) N = 2886	P-value
<i>Age (years)</i>			
Mean $\pm$ s.d. (range)	61.3 $\pm$ 13.0 (24–91)	66.8 $\pm$ 14.8 (19–112)	< 0.0001
< 50	37 (14.9%)	302 (10.5%)	< 0.0001
50–64	105 (42.2%)	846 (29.3%)	
> 65	107 (43.0%)	1738 (60.2%)	
Sex, % male	240 (96.4%)	2613 (90.5%)	0.0020
<i>SCI characteristics</i>			
Traumatic injury	151 (60.6%)	0	—
Tetraplegia	44 (17.7%)	0	—
Paraplegia	205 (82.3%)	0	—
<i>Duration of injury (years) (n = 201)</i>			
Mean $\pm$ s.d. (range)	23.2 $\pm$ 15.2 (2.2–62.6)	0	—
< 10	57 (28.4%)	0	—
10–19	38 (18.9%)	0	—
≥ 20	106 (52.7%)	0	—
<i>Charlson Index comorbidity score</i>			
Mean $\pm$ s.d. (range)	3.1 $\pm$ 1.9 (0–10)	2.0 $\pm$ 2.3 (0–18)	< 0.0001
<i>Past medical history^a</i>			
Congestive heart failure	17 (6.8%)	369 (12.8%)	0.0060
Cerebrovascular disease	19 (7.6%)	256 (8.9%)	< 0.0001
Chronic pulmonary disease	31 (12.5%)	505 (17.5%)	0.0423
Renal disease	28 (11.2%)	480 (16.6%)	0.0269
<i>Health-care utilization</i>			
Hospitalization in the prior 30 days	157 (63.1%)	1126 (39.0%)	< 0.0001
Hospitalization in the prior 90 days	191 (76.7%)	1270 (44.0%)	< 0.0001
Surgery in the prior 30 days	20 (8.0%)	222 (7.7%)	0.8471
Surgery in the prior 90 days	26 (10.4%)	267 (9.3%)	0.5359

Abbreviation: SCI, spinal cord injury.

^aNo difference in the frequency of myocardial infarction and diabetes.

procedures within the past 30 and 90 days did not differ between groups ($P=NS$).

Frequencies of pathogens isolated in the two groups differed. The most frequent pathogens identified in Veterans with SCI/D were *Enterococcus* sp. (15.2%), *Escherichia coli* (14.5%), *Pseudomonas aeruginosa* (12.2%), *Enterococcus faecalis* (11.0%), *Klebsiella pneumoniae* (9.3%) and *Proteus mirabilis* (9.0%) (Table 2). All of these organisms, except for *E. coli*, were significantly more likely to be isolated in those with SCI/D compared to those without SCI/D. Compared to those without SCI/D, *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Streptococcus agalactiae* and viridans *Streptococcus* were less likely to be isolated in those with SCI/D.

Key antimicrobial agents and their susceptibilities are reported for select organisms in Table 3. Susceptibilities were generally poorer in those with SCI/D. *S. aureus* isolates in patients with SCI/D were less susceptible to oxacillin, clindamycin, erythromycin and tetracycline than in isolates from non-SCI/D patients. *E. faecalis* was less susceptible to gentamicin (for synergy) in SCI/D patients, but there were no differences when stratified by vancomycin susceptibility. As compared to non-SCI/D, methicillin-susceptible *S. aureus* (MSSA) was less susceptible to clindamycin and erythromycin in SCI/D ($P\leq 0.04$ for both). Although SCI/D isolates of methicillin-resistant *S. aureus* (MRSA) were less susceptible to clindamycin, they were more susceptible to tetracyclines ($P\leq 0.04$ for both). For every antibiotic tested, *K. pneumoniae* was significantly less susceptible in patients with SCI/D ($P<0.05$; Table 3). Similarly, *E. coli* had lower susceptibilities for all agents tested except for carbapenems. *P. mirabilis* also demonstrated lower susceptibilities in SCI/D for Beta-lactams, quinolones, gentamicin and tobramycin ($P<0.05$). The *P. aeruginosa* isolates from SCI/D were less

susceptible to cefepime, ciprofloxacin, gentamicin, imipenem and tobramycin as compared to the isolates in those without SCI/D ($P\leq 0.02$ for all).

Over half (57.1%; $n=2928$) of the unique cultures were associated with the inpatient setting; 27.1% ($n=794$) were for Veterans with SCI/D. In all, 42.9% ($n=2203$) of cultures were taken in the outpatient setting; 17.5% ($n=385$) in Veterans with SCI/D. In both groups, coagulase-negative *Staphylococcus*, *S. aureus*, *Enterococcus* sp., *P. aeruginosa*, *K. pneumoniae*, *P. mirabilis*, *Providencia stuartii* and *Acinetobacter baumannii* were more frequently isolated in the inpatient setting (Table 4). As compared to isolates in those with SCI/D in the inpatient setting, non-SCI/D outpatient cultures had higher frequencies of *E. coli*. *Enterobacter cloacae* was isolated more frequently in outpatients with SCI/D, whereas this organism was more frequent in the inpatient setting in those without SCI/D.

Differences were identified in the susceptibility of organisms isolated by location (Table 5). Although there was no difference in the frequency of MRSA or methicillin-resistant coagulase-negative *Staphylococcus* in inpatient and outpatients, there was a greater frequency of vancomycin resistant Enterococci (VRE) isolates cultured in the inpatient setting, although this difference was not significant in those with SCI/D (SCI/D group: inpatient = 11.1%, outpatient = 5.0%, P = not significant; non-SCI/D group: inpatient = 10.1%, outpatient = 2.1%, $P<0.01$). For both groups, inpatient *E. coli* isolates were significantly less susceptible for aztreonam, cefepime, ceftriaxone, ciprofloxacin and piperacillin/tazobactam ($P\leq 0.04$). For patients without SCI/D, *E. coli* inpatient isolates were less susceptible to cefazolin, ampicillin/sulbactam, gentamicin and tobramycin ($P\leq 0.03$). Interestingly, there were no common differences in susceptibilities by culture location for *K. pneumoniae*. For

Table 2 Distribution and frequency of bacteria identified in SCI vs facility-wide antibiograms

	Number (%) of cultures				
	Overall, N = 5131	SCI cultures, number (%), N = 1179	Non-SCI cultures, number (%), N = 3952	OR (95% CI)	P-value
<i>Gram-positive bacteria</i>					
<i>Staphylococcus aureus</i>	507 (9.9%)	90 (7.6%)	417 (10.6%)	0.70 (0.55–0.89)	0.0032
Coagulase-negative <i>Staphylococcus</i>	589 (11.5%)	65 (5.5%)	524 (13.3%)	0.38 (0.29–0.50)	<0.0001
<i>Streptococcus viridans</i>	261 (5.1%)	22 (1.9%)	239 (6.1%)	0.30 (0.19–0.46)	<0.0001
<i>Streptococcus agalactiae</i>	98 (1.7%)	11 (0.93%)	76 (1.9%)	0.48 (0.25–0.91)	0.0208
<i>Enterococcus faecalis</i>	429 (8.4%)	130 (11.0%)	299 (7.6%)	1.5 (1.2–1.9)	0.0002
<i>Enterococcus faecium</i>	89 (1.7%)	25 (2.1%)	64 (1.6%)	1.3 (0.83–2.1)	0.2475
<i>Enterococcus</i> sp.	459 (7.7%)	136 (15.2%)	323 (6.4%)	0.38 (0.31–0.47)	<0.0001
<i>Gram-negative bacteria</i>					
<i>Escherichia coli</i>	796 (15.5%)	171 (14.5%)	625 (15.8%)	0.90 (0.75–1.08)	0.2752
<i>Klebsiella pneumoniae</i>	340 (6.6%)	110 (9.3%)	230 (5.8%)	1.7 (1.3–2.1)	<0.0001
<i>Proteus mirabilis</i>	275 (5.4%)	106 (9.0%)	169 (4.3%)	2.2 (1.7–2.8)	<0.0001
<i>Serratia marcescens</i>	73 (1.4%)	26 (2.2%)	47 (1.2%)	1.9 (1.2–3.0)	0.0097
<i>Pseudomonas aeruginosa</i>	438 (12.2%)	144 (12.2%)	294 (7.4%)	1.7 (1.4–2.1)	<0.0001
<i>Enterobacter cloacae</i>	104 (2.0%)	18 (1.5%)	86 (2.2%)	0.70 (0.42–1.2)	0.1649
<i>Morganella morganii</i>	87 (1.7%)	49 (4.2%)	38 (1.0%)	4.7 (2.9–6.9)	<0.0001
<i>Citrobacter koseri</i>	65 (1.3%)	31 (2.6%)	34 (0.86%)	3.1 (1.9–5.1)	<0.0001
<i>Acinetobacter baumannii</i>	40 (0.78%)	19 (1.6%)	21 (0.53%)	3.1 (1.6–5.7)	0.0002
<i>Providencia stuartii</i>	41 (0.80%)	26 (2.2%)	15 (0.38%)	5.9 (3.1–11.2)	<0.0001

Abbreviations: CI, confidence interval; OR, odds ratio; SCI, spinal cord injury.

Table 3 Differences in antimicrobial susceptibility for select organisms

Organism and antimicrobial	Number of cultures susceptible (% susceptible)			P-value
	SCI cultures, number (%), N = 1179	Non-SCI cultures, number (%), N = 3952	Unadjusted OR (95% CI)	
Gram-positive bacteria				
Staphylococcus aureus ^{a,b,c,d}				
Oxacillin	25 (27.8%)	219 (55.4%)	0.31 (0.19–0.51)	<0.0001
Clindamycin	13 (36.1%)	230 (71.2%)	0.23 (0.11–0.47)	<0.0001
Erythromycin	8 (21.6%)	148 (44.7%)	0.34 (0.15–0.77)	0.0070
SMX/TMP	89 (98.9%)	391 (99.0%)	0.91 (0.10–8.2)	0.9335
Tetracycline	89 (98.9%)	346 (87.6%)	12.6 (1.7–92.5)	0.0015
Rifampin	88 (100%)	377 (99.2%)	1.64 (0.08–32.1) ^e	0.4030
Coagulase negative				
Staphylococcus aureus ^{a,b,c}				
Oxacillin	29 (44.6%)	247 (50.1%)	0.80 (0.48–1.35)	0.4057
Clindamycin	35 (66.0%)	158 (60.3%)	1.28 (0.69–2.38)	0.4346
Erythromycin	25 (47.2%)	104 (39.3%)	1.38 (0.76–2.50)	0.2835
SMX/TMP	38 (59.4%)	351 (71.5%)	0.58 (0.34–1.00)	0.0465
Tetracycline	56 (86.2%)	437 (88.6%)	0.80 (0.37–1.70)	0.5569
Quinupristin/dalfopristin	63 (96.9%)	492 (99.8%)	0.06 (0.01–0.72)	0.0029
Enterococcus faecalis ^{b,c}				
Ampicillin	129 (100%)	299 (100%)	—	—
Gentamicin	9 (42.9%)	50 (70.4%)	0.32 (0.12–0.86)	0.0207
Streptomycin	17 (81.0%)	52 (71.2%)	1.7 (0.52–5.7)	0.3744
Rifampin	98 (76.0%)	216 (72.2%)	1.2 (0.75–2.0)	0.4233
Vancomycin	118 (81.5%)	280 (93.7%)	0.73 (0.34–1.6)	0.4192
Gram-negative bacteria				
Escherichia coli				
Amikacin	165 (97.1%)	620 (99.4%)	0.21 (0.6–0.80)	0.0120
Ampicillin/Sulbactam	58 (33.9%)	309 (49.5%)	0.52 (0.37–0.75)	0.0003
Aztreonam	135 (79.4%)	570 (91.4%)	0.37 (0.23–0.58)	<0.0001
Cefazolin	109 (63.7%)	494 (79.2%)	0.46 (0.32–0.67)	<0.0001
Cefepime ^f	136 (79.5%)	573 (91.8%)	0.35 (0.22–0.55)	<0.0001
Ceftriaxone	135 (79.0%)	571 (91.5%)	0.35 (0.22–0.55)	<0.0001
Ciprofloxacin	76 (44.4%)	430 (68.9%)	0.36 (0.26–0.51)	<0.0001
Ertapenem	169 (98.8%)	618 (99.0%)	0.82 (0.16–4.10)	0.8092
Gentamicin	127 (74.3%)	555 (88.9%)	0.36 (0.23–0.55)	<0.0001
Imipenem	170 (99.4%)	622 (99.8%)	0.27 (0.02–4.39)	0.3269
Piperacillin/tazobactam	158 (92.4%)	600 (96.2%)	0.49 (0.24–0.98)	0.0388
SMX/TMP	93 (54.4%)	462 (74.0%)	0.42 (0.29–0.59)	<0.0001
Tobramycin	125 (73.1%)	537 (86.2%)	0.44 (0.29–0.65)	<0.0001
Amikacin	10 (100%)	41 (100%)	—	—
Klebsiella pneumoniae				
Amikacin	95 (86.4%)	223 (97.4%)	0.17 (0.06–0.45)	<0.0001
Ampicillin/sulbactam	54 (49.1%)	171 (74.4%)	0.33 (0.21–0.54)	<0.0001
Aztreonam	74 (67.3%)	220 (95.7%)	0.09 (0.04–0.20)	<0.0001
Cefazolin	70 (63.6%)	210 (91.3%)	0.17 (0.09–0.30)	<0.0001
Cefepime ^f	74 (67.3%)	220 (95.7%)	0.09 (0.04–0.20)	<0.0001
Ceftriaxone	74 (67.3%)	220 (95.7%)	0.09 (0.04–0.20)	<0.0001
Ciprofloxacin	78 (70.9%)	210 (91.3%)	0.23 (0.13–0.43)	<0.0001
Ertapenem	95 (86.4%)	225 (97.8%)	0.14 (0.05–0.40)	<0.0001
Gentamicin	92 (83.6%)	221 (96.1%)	0.21 (0.09–0.48)	<0.0001
Imipenem	97 (88.2%)	226 (98.3%)	0.13 (0.04–0.42)	<0.0001
Piperacillin/tazobactam	87 (79.1%)	221 (96.1%)	0.15 (0.07–0.35)	<0.0001
SMX/TMP	75 (68.2%)	204 (88.7%)	0.27 (0.15–0.48)	<0.0001
Tobramycin	81 (73.6%)	216 (93.9%)	0.18 (0.09–0.36)	<0.0001
Proteus mirabilis				
Amikacin	103 (97.2%)	167 (99.4%)	0.21 (0.02–2.0)	0.1330
Ampicillin	44 (41.9%)	129 (76.8%)	0.22 (0.13–0.37)	<0.0001
Ampicillin/sulbactam	67 (63.2%)	147 (87.5%)	0.25 (0.13–0.45)	<0.0001
Aztreonam	65 (61.3%)	150 (89.3%)	0.19 (0.10–0.36)	<0.0001
Cefazolin	49 (46.7%)	136 (81.4%)	0.20 (0.12–0.34)	<0.0001
Cefepime ^f	66 (62.3%)	153 (91.1%)	0.16 (0.08–0.31)	<0.0001
Ceftriaxone	65 (61.3%)	152 (90.5%)	0.17 (0.09–0.32)	<0.0001

Table 3 (Continued)

Organism and antimicrobial	Number of cultures susceptible (% susceptible)			P-value
	SCI cultures, number (%), N = 1179	Non-SCI cultures, number (%), N = 3952	Unadjusted OR (95% CI)	
Ciprofloxacin	44 (40.6%)	119 (71.3%)	0.28 (0.16–0.46)	<0.0001
Ertapenem	104 (99.1%)	167 (99.4%)	0.62 (0.04–10.1)	0.7364
Gentamicin	76 (71.7%)	147 (87.5%)	0.36 (0.19–0.67)	0.0011
Imipenem	104 (98.1%)	167 (99.4%)	0.31 (0.03–3.5)	0.3170
Meropenem	61 (100%)	93 (100%)	—	—
Piperacillin/tazobactam	101 (95.3%)	168 (100%)	0.05 (0.003–1.0)	0.0045
SMX/TMP	68 (64.8%)	133 (79.2%)	0.48 (0.28–0.84)	0.0086
Tobramycin	76 (71.7%)	147 (87.5%)	0.36 (0.19–0.67)	0.0011
<i>Pseudomonas aeruginosa</i>				
Amikacin	115 (79.9%)	251 (86.6%)	0.62 (0.36–0.05)	0.0710
Aztreonam	83 (57.6%)	196 (67.6%)	0.65 (0.43–0.99)	0.0417
Cefepime	88 (61.1%)	211 (72.8%)	0.59 (0.39–0.90)	0.0136
Ceftazidime	112 (77.8%)	240 (82.8%)	0.73 (0.44–1.2)	0.2120
Ceftriaxone	13 (9.0%)	57 (19.7%)	0.41 (0.21–0.77)	0.0046
Ciprofloxacin	67 (46.5%)	186 (64.4%)	0.48 (0.32–0.72)	0.0004
Gentamicin	76 (52.8%)	209 (72.1%)	0.43 (0.29–0.66)	<0.0001
Imipenem	87 (60.4%)	209 (72.1%)	0.59 (0.39–0.90)	0.0141
Piperacillin/tazobactam	116 (80.6%)	243 (83.8%)	0.80 (0.48–1.3)	0.4009
Tobramycin	106 (73.6%)	247 (85.2%)	0.49 (0.30–0.79)	0.0036
Colistin	23 (95.8%)	32 (84.2%)	4.3 (0.49–32.3)	0.1590

Abbreviations: CI, confidence interval; OR, odds ratio; SCI, spinal cord injury; SMX/TMP, sulfamethoxazole/trimethoprim.

^aVancomycin ≥ 99% susceptible.^bLinezolid ≥ 99% susceptible.^cDaptomycin ≥ 99% susceptible.^dQuinupristin/dalfopristin ≥ 99% susceptible.^eEquivalent susceptibilities to ceftazidime.^fLogit OR.Table 4 Distribution and frequency of isolates by culture location^a stratified by SCI/D and non-SCI/D

Organism	SCI			Non-SCI/D		
	Inpatient isolates, number (%), N = 794	Outpatient isolates, number (%), N = 385	P-value	Inpatient isolates, number (%), N = 2134	Outpatient isolates, number (%), N = 1818	P-value
<i>Gram-positive bacteria</i>						
<i>S. aureus</i>	67 (74.4)	16 (17.8)	<0.0001	232 (55.6)	181 (43.4)	<0.0001
Coagulase-negative	49 (75.4)	11 (16.9)	<0.0001	303 (57.8)	217 (41.4)	<0.0001
<i>Staphylococcus</i>						
<i>S. viridans</i>	13 (59.1)	9 (40.9)	0.3938	92 (38.5)	145 (60.7)	<0.0001
<i>S. agalactiae</i>	8 (72.7)	3 (27.3)	0.1317	35 (46.1)	41 (53.9)	0.4913
<i>E. faecalis</i>	82 (63.1)	40 (30.8)	<0.0001	159 (53.2)	140 (46.8)	0.2719
<i>E. faecium</i>	22 (88)	3 (12)	0.0001	47 (73.4)	17 (26.6)	0.0002
<i>Enterococcus</i> sp.	9 (81.8)	2 (18.2)	0.0348	15 (88.2)	2 (11.8)	0.0016
<i>Gram-negative bacteria</i>						
<i>E. coli</i>	110 (64.3)	50 (29.2)	<0.0001	253 (40.5)	366 (58.6)	<0.0001
<i>K. pneumoniae</i>	72 (65.5)	29 (26.4)	<0.0001	128 (55.7)	97 (42.2)	<0.0001
<i>P. mirabilis</i>	67 (63.2)	23 (21.7)	<0.0001	94 (55.6)	72 (42.6)	<0.0001
<i>P. aeruginosa</i>	109 (75.7)	31 (21.5)	<0.0001	207 (70.4)	86 (29.3)	<0.0001
<i>E. cloacae</i>	7 (38.9)	10 (55.6)	0.0302	44 (51.2)	41 (47.7)	<0.0001
<i>M. Morganii</i>	31 (63.3)	13 (26.5)	<0.0001	19 (50)	19 (50)	1.0
<i>S. marcescens</i>	14 (53.8)	9 (34.6)	0.0302	28 (59.6)	19 (40.4)	0.1893
<i>C. koseri</i>	19 (61.3)	7 (22.6)	0.0039	21 (61.8)	13 (38.2)	0.1701
<i>P. stuartii</i>	20 (76.9)	6 (23.1)	0.0060	12 (80)	1 (6.7)	0.0006
<i>A. baumannii</i>	16 (84.2)	3 (15.8)	0.0029	17 (81)	4 (19)	0.0046

Abbreviation: SCI/D, spinal cord injury and disorder.

^aSome isolates were unable to be linked to a culture location. Therefore, inpatient and outpatient isolates may not sum to 100%.

Table 5 Differences in select antimicrobial susceptibilities for select organisms by culture location^a stratified by SCI/D and non-SCI/D

Organism and antimicrobial	SCI cultures, number (% susceptible)			Non-SCI cultures, number (% susceptible)		
	Inpatient N = 794	Outpatient N = 385	P value	Inpatient N = 2134	Outpatient N = 1818	P value
<i>Gram-positive bacteria</i>						
<i>Staphylococcus aureus</i>						
Oxacillin	17 (25.4%)	6 (37.5%)	0.6221	116 (54.5%)	101 (56.7%)	0.8813
Clindamycin	12 (38.7%)	1 (33.3%)	0.7801	120 (67.4%)	108 (76.1%)	0.2238
SMX/TMP	66 (98.5%)	16 (100%)	0.8407	210 (98.6%)	177 (99.4%)	0.6925
<i>Coagulase-negative</i>						
<i>Staphylococcus</i>						
Oxacillin	24 (49.0%)	4 (36.4%)	0.4707	136 (47.4%)	108 (53.2%)	0.0995
<i>Enterococcus faecalis</i>						
Vancomycin	72 (88.9%)	38 (95.0%)	0.3540	143 (89.9%)	137 (97.9%)	0.0051
<i>Gram-negative bacteria</i>						
<i>Escherichia coli</i>						
Ampicillin/Sulbactam	42 (38.2%)	13 (26.0%)	0.2854	110 (41.3%)	185 (50.8%)	0.0219
Aztreonam	85 (77.3%)	45 (90.0%)	0.0110	226 (89.7%)	341 (93.2%)	0.0005
Cefazolin	69 (62.7%)	36 (72.0%)	0.0784	189 (75%)	303 (82.8%)	0.0014
Cefepime	85 (77.3%)	45 (90.0%)	0.0190	228 (90.5%)	342 (93.4%)	0.0004
Ceftriaxone	85 (77.3%)	45 (90.0%)	0.0035	226 (89.7%)	342 (93.4%)	0.0003
Ciprofloxacin	49 (44.5%)	26 (52.0%)	0.0347	163 (64.7%)	265 (72.4%)	0.0209
Gentamicin	84 (76.4%)	38 (76.0%)	0.0777	226 (89.7%)	327 (89.3%)	0.0001
Piperacillin/tazobactam	102 (92.7%)	48 (96.0%)	0.0302	237 (94.0%)	359 (98.1%)	<0.0001
Tobramycin	79 (71.8%)	40 (80.0%)	0.1991	212 (84.5%)	324 (88.5%)	<0.0001
<i>Klebsiella pneumoniae</i>						
Cefazolin	41 (56.9%)	23 (79.3%)	0.1050	112 (87.5%)	94 (96.9%)	0.0306
Ciprofloxacin	45 (62.5%)	27 (93.1%)	0.0088	117 (91.4%)	89 (91.8%)	0.1027
Gentamicin	60 (83.3%)	26 (89.7%)	0.2637	126 (98.4%)	91 (93.8%)	0.0359
Piperacillin/tazobactam	53 (73.6%)	28 (96.6%)	0.0236	121 (94.5%)	95 (97.9%)	0.3845
Tobramycin	50 (69.4%)	26 (89.7%)	0.0498	121 (94.5%)	91 (93.8%)	0.4106
Amikacin	60 (83.3%)	29 (100%)	0.0174	122 (95.3%)	96 (100%)	0.0880
<i>Pseudomonas aeruginosa</i>						
Cefepime	66 (60.6%)	19 (61.3%)	0.8439	140 (68.3%)	70 (83.3%)	0.0276
Imipenem	62 (56.9%)	23 (74.2%)	0.2007	130 (63.4%)	78 (92.9%)	<0.0001
Piperacillin/tazobactam	83 (76.1%)	30 (96.8%)	0.0362	161 (78.5%)	81 (96.4%)	0.0008
Tobramycin	78 (71.6%)	26 (83.9%)	0.2161	167 (81.5%)	79 (94.0%)	0.0219

Abbreviations: SCI/D, spinal cord injury and disorder; SMX/TMP, sulfamethoxazole/trimethoprim.

^aSome isolates were unable to be linked to a culture location. Therefore, inpatient and outpatient isolates may not sum to 100%. In addition, not all cultures went sent for susceptibilities.

inpatient SCI/D patients, *K. pneumoniae* isolates, ciprofloxacin, piperacillin/tazobactam, tobramycin and amikacin were significantly less susceptible ($P<0.05$). In patients without SCI/D, *K. pneumoniae* was less susceptible to cefazolin and gentamicin. *P. aeruginosa* isolates cultured in the inpatient setting were less susceptible to piperacillin/tazobactam for both groups ($P<0.04$). Additionally, non-SCI/D inpatient isolates were less susceptible to cefepime, imipenem and tobramycin for *P. aeruginosa* ($P<0.03$).

Significantly more ESBL-producing organisms were isolated in patients with SCI/D ($P<0.0001$). *E. coli* produced ESBLs most frequently overall and occurred significantly more frequently in the non-SCI/D group ($P<0.001$; Table 6). Conversely, *P. mirabilis* and *K. pneumoniae* were more frequently ESBL-producers in Veterans with SCI/D. Resistance to at least one agent in the carbapenem class occurred in 3.6% of unique isolates. The SCI/D patients had significantly more isolates with carbapenem resistance (7.6% of all SCI/D isolates) as compared to those without SCI/D (2.4% of all non-SCI/D isolates, $P<0.0001$). Although there were

few isolates meeting the definition of CRE ($n=21$), CREs were more common in the SCI/D group (2.4% vs 0.5%; $P<0.0001$). Multi-drug resistance occurred in 36.6% of all Gram-negative isolates in the sample: 60.7% of SCI/D and 28.0% of non-SCI/D cultures ($P=0.0001$). For multi-drug resistance isolates, susceptibilities exceeded 80% only for amikacin, ertapenem and imipenem. With the exception of ampicillin/sulbactam, susceptibilities for multi-drug resistant isolates were generally poorer in Veterans with SCI/D (Table 6).

DISCUSSION

Increasing antimicrobial resistance in complex infections can result in inadequate empiric prescribing. Antibigrams are commonly used tools to guide empiric selection of antimicrobial agents based on bacterial susceptibility patterns at a specific hospital. The lack of rapid and accurate diagnostic tests for pathogen identification and antimicrobial susceptibility is a challenge for all providers, especially for those who care for populations such as SCI/D, with high rates of bacterial resistance. Although the use of an antibiogram to guide

Table 6 Gram-negative resistance

Resistance mechanism	Overall, number (%), N = 2026	SCI cultures, number (%), N = 586	Non-SCI cultures, number (%), N = 1440	Unadjusted OR (95% CI)	P-value
<i>Extended spectrum beta-lactamase (ESBL)</i>					
ESBL	175	103 (17.6%)	72 (5.0%)	2.0 (1.3–3.1)	<0.0001
<i>Escherichia coli</i>	79 (45.1%)	31 (39.2%)	48 (60.8%)	0.22 (0.11–0.41)	<0.0001
<i>Proteus mirabilis</i>	53 (30.3%)	39 (73.6%)	14 (26.4%)	2.5 (1.2–5.1)	<0.0001
<i>Klebsiella pneumoniae</i>	43 (24.6%)	33 (76.7%)	10 (23.3%)	2.9 (1.3–6.4)	<0.0001
Imipenem susceptible	156 (89.1%)	89 (86.4%)	67 (94.4%)	0.47 (0.16–1.4)	0.0902
Ertapenem susceptible	157 (89.7%)	91 (88.4%)	66 (93.0%)	0.69 (0.25–1.9)	0.3143
<i>Carbapenem resistant</i>					
Overall	184	90 (7.6%)	94 (2.4%)	3.4 (2.5–4.6)	<0.0001
<i>Carbapenem-resistant Enterobacteriaceae</i>					
Overall	21	14 (2.4%)	7 (0.5%)	6.8 (2.7–16.8)	<0.0001
<i>Multi-drug resistance</i>					
Overall	1017	447 (60.7%)	570 (28.0%)	3.9 (3.3–4.7)	0.0001
Amikacin susceptible	1017	382 (85.5%)	518 (90.9%)	0.59 (0.40–0.87)	0.0072
Ampicillin/sulbactam susceptible	814	68 (18.9%)	42 (9.2%)	2.3 (1.5–3.5)	<0.0001
Aztreonam susceptible	995	217 (50.2%)	327 (58.1%)	0.73 (0.57–0.94)	0.0137
Cefazolin susceptible	792	74 (21.5%)	154 (34.4%)	0.52 (0.38–0.72)	<0.0001
Cefepime susceptible	1016	239 (53.6%)	393 (69.0%)	0.52 (0.40–0.67)	<0.0001
Ceftazidime susceptible	1017	224 (50.1%)	367 (64.4%)	0.56 (0.43–0.72)	<0.0001
Ceftriaxone susceptible	1017	196 (43.9%)	323 (56.7%)	0.60 (0.47–0.77)	<0.0001
Ciprofloxacin susceptible	1016	103 (23.0%)	221 (38.8%)	0.47 (0.36–0.62)	<0.0001
Ertapenem susceptible	792	325 (94.5%)	432 (96.4%)	0.63 (0.32–1.25)	0.1852
Gentamicin susceptible	1017	236 (52.8%)	392 (68.8%)	0.51 (0.39–0.66)	<0.0001
Imipenem susceptible	1017	360 (80.5%)	491 (86.1%)	0.67 (0.48–0.93)	0.0164
Piperacillin/tazobactam susceptible	995	337 (78.0%)	436 (77.4%)	1.03 (0.76–1.40)	0.8314
SMX/TMP susceptible	820	118 (32.7%)	237 (51.6%)	0.45 (0.34–0.61)	<0.0001
Tobramycin susceptible	1017	261 (58.4%)	390 (68.4%)	0.65 (0.50–0.84)	0.0009
Colistin susceptible	59	23 (95.8%)	32 (91.4%)	2.2 (0.21–22.1)	0.5085

Abbreviations: CI, confidence interval; OR, odds ratio; SCI, spinal cord injury.

empirical antimicrobial treatment has been well documented in the hospital setting,³² the applicability of an antibiogram to SCI/D patients has previously not been explored. As our results demonstrate, not only were the organisms isolated different, but susceptibilities were also generally poorer in Veterans with SCI/D. This difference was especially meaningful in Gram-negative organisms. In addition, inpatient isolates in patients without SCI/D were generally less susceptible where few differences were identified by culture location within the SCI/D group. Patients with SCI/D have multiple risk factors for resistant organisms,^{23,24} and our data reflect this increased risk. Carbapenem resistance, MRSA, ESBLs, CREs and multi-drug resistant Gram-negatives were significantly more frequent in Veterans with SCI/D.

Antibiograms are a resource to trend bacterial susceptibility over time, assist with formulary decisions, identify antimicrobial overuse and detect outbreaks and lapse of infection-prevention strategies. Use of local susceptibility data, which is contained in an antibiogram, is also recommended to be used when formulating an antimicrobial stewardship program.^{15,32} Although antibiograms are a valuable tool, it has been reported that half of SCI/D providers do not use the facility antibiogram to guide empiric treatment regimens.²⁵ The reasons for this lack of use have not been explored, but it is possible that SCI/D

providers are aware that bacterial susceptibility patterns in the overall facility-wide antibiogram do not reflect those observed in patients with SCI/D. Providing a customized antibiogram composed of only SCI/D isolates may improve empiric antibiotic prescribing as the information contained in the antibiogram better reflects those pathogens causing infection.

Comparison of bacterial susceptibilities patterns to develop an SCI-specific antibiogram is not without limitations. The microbiology laboratory reports that were collected and analyzed in this study represent all non-surveillance cultures from all sources obtained from patients regardless of the hospital location. Cultures from different sources may have differing susceptibilities, and consideration of the source of the infection is critical to therapy selection (for example, urine vs blood). Our definition of multi-drug resistance did not account for intrinsic resistance and thus may be an overestimate of high-level resistance for each Gram-negative organism. In addition, the cultures and susceptibilities represented in an antibiogram are highly dependent on the geographic location and the population served. Therefore, our results of bacterial susceptibilities may not apply to the entire SCI/D population. Although the results presented herein are representative of the Veteran population at our facility, they may not be generalizable to other patients seen in other facilities.

General limitations of antibiograms include inability to differentiate colonization from infection and lack of patient-specific characteristics and isolate source.

To our knowledge, this is the first report comparing the results of an antibiogram prepared specifically from cultures obtained from patients with SCI/D to cultures obtained from a non-SCI/D population. Although previous studies have described patterns in susceptibility of urinary pathogens in the SCI/D setting,^{33–35} the overall prevalence of bacteria responsible for causing disease and the corresponding susceptibilities in this patient population are still largely unknown. In addition, the changing epidemiology of infection and bacterial resistance requires more recent data. In the results presented herein, the frequency of isolation and corresponding susceptibilities of several of the most commonly isolated bacteria from SCI/D patients revealed significant differences compared with the non-SCI/D antibiogram, for which susceptibilities were generally decreased. Thus, reliance on the hospital antibiogram for selecting initial antimicrobial therapy for SCI/D patients could potentially lead to inadequate empiric treatment. It has been found in previous studies that over one-third of patients with SCI/D received inadequate empiric treatment with an antibiotic.^{36,37} The availability of more representative data from patients with SCI/D, in the form of an SCI-specific antibiogram, would not only be highly useful in guiding selection of an empiric antimicrobial agent, but may also result in the preservation of antimicrobials through prudent and judicious selection. In addition, the availability of antibiograms specific to certain care areas could offer an avenue for expansion of antimicrobial stewardship efforts customized to the population, including education and improved empirical antimicrobial prescribing.

Different pathogens with poorer susceptibilities are causing infections in patients with SCI/D. However, in a population known to be colonized with multi-drug resistant organisms, future work should be conducted to determine the frequency of colonization vs infection. Thus antimicrobial stewardship is important in this population. Developing stewardship resources, such as unit-specific antibiograms, may be useful in increasing appropriateness of empiric antibiotic treatment.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs, the Health Services Research and Development Service or the United States government. This work was supported by the US Department of Veterans Affairs as a QUERI center grant (SCI 98-001) and QUERI LIP (QLP 97-009).

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