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Major Article

Multidrug-resistant *Acinetobacter*: Risk factors and outcomes in veterans with spinal cord injuries and disorders

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Background: Multidrug-resistant (MDR) *Acinetobacter* is a growing concern and has been identified as a serious threat by the Centers for Disease Control and Prevention. However, there is little information on MDR *Acinetobacter* in individuals with spinal cord injuries and disorders (SCI/Ds). Therefore, the objective of this study was to identify risk factors for, and assess outcomes of, MDR *Acinetobacter* in veterans with SCI/Ds.
Methods: This was a retrospective cohort study from January 1, 2012-December 31, 2013, using national Veterans Affairs medical encounter and microbiology data.
Results: A total of 773 *Acinetobacter* cultures were identified in 571 patients, of which 58.9% were MDR. Inpatient culture, sputum and other specimen type, receipt of antibiotics within 90 days before culture date, and pressure ulcers were identified as independent predictors of MDR *Acinetobacter*. Highest odds of MDR *Acinetobacter* were seen with previous antibiotic use (odds ratio, 7.27; 95% confidence interval, 2.59-20.54). Thirty-day mortality was 5.3% in this study. Multidrug resistance, previous mechanical ventilation 90 days before the culture, and cancer were all independent risk factors for 30-day mortality.
Conclusions: There should be increased efforts to highlight the importance of antimicrobial stewardship to improve infection control to help limit spread of *Acinetobacter* in health care settings.

BACKGROUND

Multidrug-resistant gram-negative organisms (MDRGNOs) have been an increasing concern in both health care and community settings.[1] Infections with MDRGNOs are associated with increased mortality, prolonged hospital length of stay, and higher health care costs.[2] The Centers for Disease Control and Prevention (CDC) estimate that at least 23,000 people die each year as a direct result of an antibiotic-resistant infection.[1] Among MDRGNOs, multidrug-resistant (MDR) *Acinetobacter* is of particular concern because of this organism's frequent role in severe hospital-acquired infections and nosocomial outbreaks.[3,4] Approximately 63% of all *Acinetobacter* infections are considered MDR, and MDR *Acinetobacter* has been highlighted as a serious threat by the CDC.[1] Furthermore, approximately 2% of all health care–associated infections reported to the National Healthcare Safety Network in 2009-2010 were caused by *Acinetobacter baumannii*; of these, 68% of *A baumannii* central line–associated bloodstream infections and 78% of *A baumannii* catheter-associated urinary tract infections were reported to be MDR.[4]

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Individuals with spinal cord injuries and disorders (SCI/Ds) are at increased risk for infections because of frequent contact with the health care system and use of invasive devises such as vascular and urinary catheters.[5,6] The increased and repeated use of antibiotics to treat infections in SCI/Ds may also increase the risk for MDR infections.[6] MDR infections were at approximately 60% in 2012-2013 in those with SCI/Ds.[7] Risk factors for MDR organisms in persons with SCI/Ds include catheterization, pressure ulcers, and previous antibiotic exposure.[5,6,8,9] *Acinetobacter* infections ranged from 0.7%-12.6% in persons with SCI/Ds[9,10] between 2008 and 2014, and *A baumannii* has been found to be more frequent in those with SCI/Ds versus those without SCI/Ds.[7] Existing literature on *Acinetobacter* infections in patients with SCI/Ds is scarce and are limited to urine cultures and urinary tract infections,[9,10] are embedded within studies focusing on multiple organisms,[5,7-10] and do not focus on outcomes.[5,7-10]

Although several studies have focused on risk factors and outcomes for MDR *Acinetobacter* infections, no studies have specifically evaluated this organism in SCI/Ds. Similar to other MDRGNOs, previous antibiotic use and specifically broad-spectrum antibiotics, such as carbapenems and fluoroquinolones, are risk factors for MDR *Acinetobacter* in the general population.[11,12] Other notable risk factors are mechanical ventilation,[13,14] pressure ulcers,[11,15] and male sex.[16] MDR *Acinetobacter* infections are also associated with higher rates of mortality and longer hospital stays.[16,17] Therefore the objective of this study was to describe the burden of, identify risk factors for, and assess outcomes of MDR *Acinetobacter* in veterans with SCI/Ds.

METHODS

Study design, setting, and population

This was a retrospective cohort study from January 1, 2012-December 31, 2013, using national Veterans Affairs (VA) medical encounter and microbiology data. Data were included for 110 VA facilities. The sample included all veterans with SCI/Ds seen at a VA medical center during the study period. We excluded veterans with multiple sclerosis and amyotrophic lateral sclerosis because these diseases are not usually associated with stable nonprogressive spinal cord neurologic deficits and therefore are not the focus of the VA SCI/D system of care. Veterans with SCI/Ds were included in the sample if they had a positive culture for *Acinetobacter* spp within the study period.

Because national VA data were included in this study, specific methods for bacterial identification and susceptibility testing may have varied slightly by facility or by specimen type; however, all VA microbiology laboratories follow the Clinical and Laboratory Standards Institute guidelines for bacterial identification and susceptibility testing. Only those cultures with associated antibiotic sensitivity testing performed were included in this study. Cultures were identified as MDR if they were resistant to at least 1 agent in at least ≥3 antimicrobial categories tested, as defined by Magiorakos et al.[3] These antimicrobial categories were aminoglycosides, antipseudomonal carbapenems, antipseudomonal fluoroquinolones, antipseudomonal penicillins + β-lactamase inhibitors, extended-spectrum cephalosporins, folate pathway inhibitors, penicillins + β-lactamase inhibitors, polymyxins, and tetracyclines.[5] All isolates not meeting the MDR criteria were categorized as non-MDR. Duplicate cultures, defined as *Acinetobacter* cultures with the same antibiotic susceptibility profile, were excluded if the duplicate culture occurred within 30 days of a previous culture.[18] This study was approved by the Edward Hines Jr VA Hospital Institutional Review Board.

Data sources and definitions

Patient demographics, health care utilization, facility characteristics, microbiology, and pharmacy data were collected from the VA Corporate Data Warehouse. The VA Corporate Data Warehouse is a national repository that includes clinical and administrative data from the Veterans Health Administration and is updated daily. Mortality data were obtained from the VA Vital Status File, which contains dates of death combined from the Veterans Benefits Administration Beneficiary Identification and Records Locator System Death file, the VA Medicare Vital Status File, and the Social Security Administration Death Master File. SCI/D characteristics, such as duration and level of injury, were obtained from the VA spinal cord dysfunction (SCD) Registry, a national database containing information on spinal cord characteristics derived from patient registries.

Demographic data, such as age, sex, race-ethnicity, and comorbidities, were identified 365 days prior to and during the visit or admission where the culture was identified. Specimen type was categorized into 4 categories including urine, blood, sputum, and other. Other specimen types included wound, tissue, body fluid, and bone cultures. Comorbidities were identified using ICD-9 codes of conditions from the Deyo-Charlson comorbidity index, including pressure ulcer, which is a common condition in patients with SCI/Ds.[19] Thirty-day and 1-year mortality were defined as death of the patient within 30 days and 1 year from the date of the culture collected, respectively. Thirty-day hospital readmission was defined as patient readmission within 30 days of the positive culture date and was only applicable for those patients with an initial culture collected in an inpatient setting.

The VA SCI/D system of care includes 24 regional SCI centers, called hubs, which provide comprehensive care delivered by interdisciplinary teams. These hub SCI/D centers are connected to spoke facilities that provide community-based care for SCI/D patients. Data were analyzed to assess whether there were differences in MDR *Acinetobacter* in hub versus spoke facilities. Region was defined using the U.S. Census Bureau regions. San Juan, Puerto Rico, and Manilla were grouped into the South region.[20]

Statistical analysis

Bivariate analysis using χ^2 tests was conducted, and unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to identify potential risk factors and outcomes of MDR *Acinetobacter*. A multivariable regression model, cluster adjusted by patient to account for multiple cultures per patient, was used to identify independent predictors. Variables that were significant in the unadjusted results were included in the multivariable model. Bivariate analysis was also used to identify risk factors related to 30-day mortality. Only the first culture of *Acinetobacter* per patient during the study period was included for mortality analysis, and analysis was conducted on person level. Poisson regression was used to identify independent risk factors for 30-day mortality, and the most parsimonious model was selected. Incidence rate ratios (IRRs) and 95% CIs were reported for the Poisson regression. $P \leq .05$ was considered statically significant. All statistical analyses were performed using STATA software version 14.1 (StataCorp, College Station, TX).

RESULTS

There were a total of 978 *Acinetobacter* cultures identified during the study time frame. After excluding duplicates (n = 205) there were 773 *Acinetobacter* cultures identified in 571 individuals with SCI/Ds. Overall, of a total 27,904 MDRGNO cultures among 8,691 patients were identified, of which 2.8% of cultures were *Acinetobacter*