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Burden and Risk Factors of Multi-drug Resistant Gram-negative Organisms in Veterans with Spinal Cord Injury

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Background

- Multi-drug resistant gram-negative organisms (MDRGNOs) account for a steadily increasing rate of infections in healthcare settings every year.[1,2]
- Persons with spinal cord injury (SCI) are at high risk for infections compared to the general patient population due to frequent hospitalization or contact with the health care system and chronic use of invasive medical devices.[3,4]
- Limited data are available on the prevalence and factors associated with MDRGNOs in a large at-risk population, such as patients with SCI.
- Early single site studies in rehabilitation/SCI units in the 1990's suggested 22-33% of gram-negatives were MDR; defined as resistant to 2 or more antimicrobial classes.[5,6]
- A more recent study from a Department of Veterans Affairs (VA) facility found that 60% of gram-negatives were MDR defined as resistant to 3 or more antimicrobial classes.[7]
- Therefore, we assessed clinical cultures in a large sample of Veterans with SCI across the nation to determine the burden of MDRGNOs.

Objectives

To describe the prevalence of and risk factors (including antimicrobial exposure) for MDR gram-negative organisms in Veterans with SCI.

Methods

- **Study Design and Setting:** Retrospective cohort study including 142 VA Medical Care facilities and affiliated clinics
- **Study Population and Timeframe:** 19,657 Veterans with SCI receiving care January 1, 2012-December 31, 2013
- **Data collection:** National VA clinical and microbiology data were used to collect demographics and medical characteristics
- **Outcome definition:** MDRGNO = Culture with at least 1 MDR gram-negative organism (yes/no)
  - Resistant/intermediate to ≥ 1 antibiotic in ≥ 3 antibiotic classes[8]
  - Did not include intrinsic resistance
- **Statistical Analyses:** Bivariate statistics and multivariable cluster adjusted models were fit to identify factors associated with MDRGNO; unadjusted and adjusted ORs and 95% CIs are presented.

Study Sample

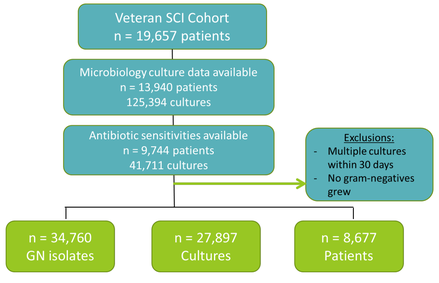


Figure 1. Most Frequent Gram-Negative Isolates (>5%)

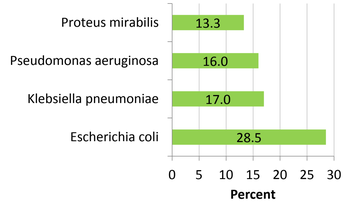


Figure 2. Most Frequent Gram-Negative Isolates: Percentage MDR

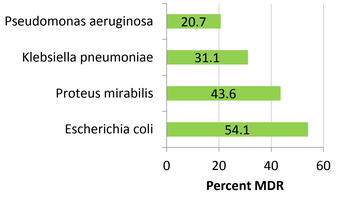
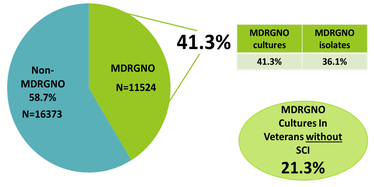


Figure 3. Overall Percentage of MDR Gram-Negative Cultures



Demographics and unadjusted association with MDRGNOs

- Male gender (97%)
- Age 50-64 years (41.5%), 65+ (42.4%)
  - Older age associated with MDRGNOs
- Level and Completeness of Injury: Tetraplegia (45.4%), Complete (43.9%)
  - Tetraplegia and Completeness associated with MDRGNOs
- Duration of injury: 0-10 years (36.7%)
  - Shorter duration of injury associated with MDRGNOs

Figure 4a. Frequency of MDRGNO by Facility

(Bubble size corresponds to isolate frequency)

Red = SCI Center, Yellow= non-SCI Center

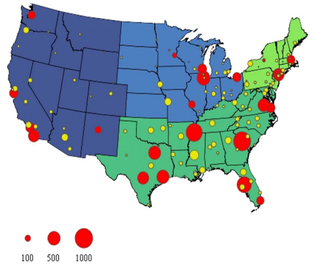


Figure 4b. Percent of SCI Patients with MDRGNO by Facility

(Bubble size corresponds to percent of all SCI patients)

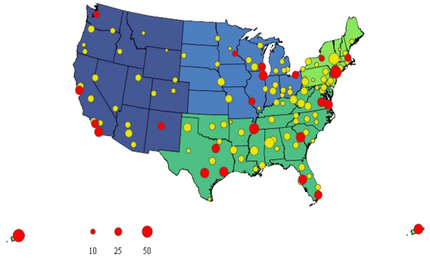


Table 1. Association between Facility, Medical, and Healthcare Exposures, and an MDRGNO Culture

Facility Characteristics	MDR N=11524 (%)	Non-MDR N=16373 (%)	Unadjusted OR (95%CI)
SCI Center			
No	3970 (34.4)	6263 (38.3)	Reference
Yes	7554 (65.6)	10110 (61.7)	**118 (1.12-1.24)**
U.S. Region			
Northeast	1169 (10.1)	1470 (9.0)	Reference
Midwest	1766 (15.3)	3362 (20.5)	**0.66 (0.60-0.73)**
South	6289 (54.6)	7988(48.8)	0.99 (0.91-1.08)
West	1911 (16.6)	3281 (20.0)	**0.73 (0.67-0.81)**
Medical Characteristics			
Source			
Outpatient	5031 (43.7)	8886 (54.3)	Reference
Inpatient	5808 (50.4)	6775 (41.4)	**1.51 (1.44-1.59)**
Long-term care	685 (5.9)	712 (4.3)	**1.70 (1.52-1.90)**
Specimen type			
Urine	9952 (86.4)	14211 (86.8)	Reference
Blood	224 (1.9)	309 (1.9)	1.04 (0.87-1.23)
Other	1348 (11.7)	1853 (11.3)	1.04 (0.96-1.12)
Polymicrobial culture	3301 (28.6)	2658 (16.2)	**2.07 (1.95-2.19)**
Pressure ulcer	3796 (32.9)	3823 (23.3)	**1.61 (1.53-1.70)**
Mean Charlson score (sd)	2.0 (1.8)	1.7 (1.8)	<0.0001
Healthcare Exposures			
Long-Term Care Facility in past 90 days	360 (3.1)	352 (2.1)	**1.47 (1.26-1.70)**
ICU stay in past 90 days	1076 (9.3)	953 (5.8)	**1.67 (1.52-1.82)**
Previous Hospitalization in past 90 days	3611 (31.3)	3827 (23.4)	**1.50 (1.42-1.58)**
Mechanical ventilator in past 90 days	584 (5.1)	535 (3.3)	**1.58 (1.40-1.78)**
Antibiotics in past 90 days	8109 (70.4)	10027 (61.2)	**1.50 (1.43-1.58)**

Bolded items are significant at 0.05 level.

Figure 5. Factors Associated with MDRGNO Compared to non-MDRGNO Cultures in Multivariable Analyses

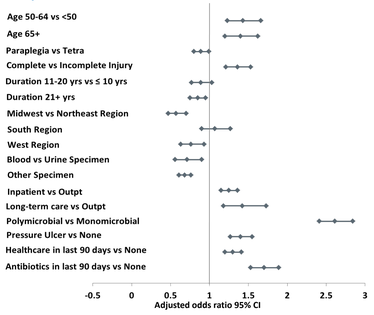


Table 2. Antibiotic exposures and association with MDRGNOs in Multivariable Analyses*

Antibiotics	MDR N=11524	Non-MDR N=16373	Adjusted OR and 95% CI
Sulfonamides	16.5%	14.9%	**1.28 (1.11-1.49)**
Nitrofurantoins	10.7%	9.3%	**1.41 (1.17-1.68)**
Fluoroquinolones	29.6%	24.1%	**1.48 (1.31-1.67)**
3rd & 4th Gen Cephalosporins	12.7%	8.2%	**1.48 (1.23-1.79)**
Carbapenems	5.0%	2.0%	**2.65 (1.93-3.64)**
Colistin	0.6%	0.1%	3.50 (0.99-12.43)

Bolded items are significant at 0.05 level.
*** Model adjusted for all variables in Figure 5.**

Conclusions

- This is the largest study describing the prevalence and factors associated with MDRGNOs in the SCI population.
- MDRGNOs were much higher than in previous studies of Veterans with SCI and much higher than in non-SCI Veterans (41.3% vs 21.3%).[5,6]
- Older age and more severe injury characteristics were associated with MDRGNOs
  - Longer duration of injury was protective: Is the immunity of SCI patients against bacterial invasion stronger over time after repeated infections?[3,9,10]
- There was significant variation in MDRGNOs across regions and facilities.
  - This is consistent with general acute care studies showing differences across patient populations, antimicrobial use patterns, and infection control practices.[11]
  - It is important for health care facilities/systems to benchmark and assess local rates so that prevention and control can be focused.
- Polymicrobial cultures were a strong factor associated with MDRGNOs, independent of urine cultures which are often polymicrobial.[5,12]
  - Polymicrobial cultures have been shown to be a factor in inadequate antibiotic treatment.
  - Suggests opportunity for spread of resistance between organisms.
- Health care exposures, including being in long-term care, were important factors emphasizing the needed for continued infection control and improving environmental exposures.
- Specific antibiotic exposures, including those commonly used for urinary tract infection, were important factors associated with MDRGNOs.
  - Emphasizes the ongoing need for antimicrobial stewardship; improving appropriate use and decreasing inappropriate use.

Limitations

- Limited information on invasive devices.
- Did not distinguish between infection and colonization or account for treatment.
- Lack of medical information on encounters outside the VA healthcare system. However, this is the largest system of care for people with SCI with an extensive electronic health record data warehouse.

Acknowledgements/Disclaimer

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- The views expressed in this presentation are the presenters and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government.

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