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Trends in Multidrug Resistant Bacteria and *Clostridium difficile* in an Integrated Healthcare Network, 2008-2015

Bert K. Lopansri, MD[1,2]; Dominika Swistun, PhD[1]; Rajesh Mehta, RPh, MS[1]; Brandon Webb, MD[1]; Eddie Stenehjem, MD, MSc[1]; Michelle Keane, BS, MBA[4]; David J. Pombo, MD[3]; Kristin Dascomb, MD, PhD[1]; John P. Burke, MD[1,2]

[1]Intermountain Medical Center, Murray, UT; [2]University of Utah School of Medicine, Salt Lake City, UT; [3]Cape Cod Hospital, [4]Enterprise Analysis Corporation

Contact Information:
Bert Lopansri, MD
Bert.Lopansri@imail.org

ABSTRACT (AMENDED)

Background: Multidrug resistant bacteria (MDRO) and *Clostridium difficile* infections are threats to patient safety. The objective of our study was to describe the burden of MDROs and *Clostridium difficile* and to depict changing trends over time in an integrated healthcare network.

Methods: We abstracted electronic data from patients seen at any of Intermountain Healthcare's 22 hospitals and affiliated clinics between January 1, 2008 and December 31, 2015 who had clinical cultures positive for antibiotic resistant Gram-positive or Gram-negative bacteria and/or a laboratory tests positive for toxigenic C. *difficile*. MDRO was defined as resistance to ≥3 antibiotic classes, pan-resistance as resistance to all antibiotics tested. Carbapenem resistant *Enterobacteriaceae* (CRE) was defined according to CDC definitions. Specimens collected 48h after a hospital admission (for C. *difficile* ≥72h) were classified as hospital acquired.

Results: A total of 4,019,314 patient encounters were identified during our time period of interest. This yielded 62,573 cultures, from 39,158 patients, which met our inclusion definitions. The prevalence of all studied organisms was 15.5 MDROs per 1,000 patient encounters and incidence of 8.2 MDROs per 1,000 patient encounters. Of the 900,000 hospital admissions during the study period, 12,705 (1.4%) were from patients positive for an MDRO and/or C. *difficile*. Methicillin resistant *Staphylococcus aureus*, C. *difficile* and ESBL harboring Gram-negative rods were the most common organisms (Figure 1). We observed a 222% increase in the prevalence of C. *difficile* and a 322% increase in ESBL positive organisms from 2008 to 2015 whereas MRSA rates decreased by 32% (Figure 3). All other organisms occurred at a roughly constant rate over time. MRSA, ESBL *E. coli* and CRE *E.coli* were less frequently acquired in the hospital; however, vancomycin resistant *E. faecium*, MDRO *P. aeruginosa* and other CRE were more frequently acquired in hospitals (Figure 6).

Conclusions: While MRSA continues to be the most common antibiotic resistant bacteria, rates have been declining. In contrast, ESBL and C. *difficile* rates continue to increase. The rate of acquiring an MDRO in acute care facilities varies by bacterial species. Understanding these trends helps focus limited infection control resources.

INTRODUCTION

- Infections due to multidrug resistant organisms (MDRO) pose significant challenges to the care of patients in hospitals and other healthcare settings globally contributing to increased morbidity and mortality and increased costs of care.
- Methicillin resistant *Staphylococcus aureus* (MRSA) has long been the most common MDRO; however, over the past decade numerous antibiotic resistant gram negative rods have emerged and disseminated globally [1-3].
- As a result, the Centers for Disease Control and Prevention has highlighted the resistance threats and proposed broad solutions to combat the emergence and spread of resistance [4], which include:
  - Preventing infections and spread of resistance
  - Tracking and surveillance
  - Improving antibiotic prescribing
  - Developing new drugs and diagnostic tests

METHODS

OBJECTIVE: To describe the trends of antibiotic resistant bacteria and *Clostridium difficile* in an integrated healthcare network between January 1, 2008 and December 31, 2015.

SETTING AND SUBJECTS: Data were collected for adults aged ≥18 years old who had cultures positive for the following organisms of interest, identified in an Intermountain Healthcare Laboratory:

- Methicillin Resistant *S. aureus* (MRSA)
- Vancomycin resistant *Enterococcus faecium*
- ESBL *E. coli* and ESBL *Klebsiella* spp.
- MDRO *Enterobacter* spp., *Pseudomonas* spp. and *Acinetobacter* spp.
- Pan-resistant Gram negative rods
- Carbapenem resistant *Enterobacteriaceae* spp.
- *Clostridium difficile*

DATA COLLECTION AND ANALYSIS:

- Clinical and administrative data were collected from the Intermountain Healthcare Enterprise Data Warehouse.
- We collected data from all unique encounters (culture collected at least 30 days apart for inpatient and outpatient encounters) in which a result was positive for an organism of interest. We defined hospital acquired as cultures collected >48 hours after admission, >72 hours for C. *difficile*.
- Detailed data were collected only for those admitted to an Intermountain Healthcare facility.
- Differences in trends were measured by time series linear model trend estimation.

RESULTS: All Encounters, Inpatient and Outpatient (n=60,486)

Table 1: Overall Statistics: 8-Years of Inpatient and Outpatient Encounters

Hospitals Included	**20**
Small (<50 beds)	9 (45%)
Medium (50-200 beds)	7 (35%)
Large (>200 beds)	4 (20%)
Total Number of Encounters	**4,019,314**
Number of Outpatient Encounters	3,119,531 (78%)
Number of Hospital Admissions	899,783 (22%)
8-Year Encounters with MDRO and C. *difficile*	**60,486**
MRSA	30,630 (51%)
C. *difficile*	20,188 (33%)
ESBL *E. coli*	4,782 (8%)
ESBL *Klebsiella* spp.	639 (1%)
VRE	2,260 (4%)
MDR *P. aeruginosa*	872 (1%)
MDR *A. baumanii*	447 (1%)
MDR *Enterobacter* spp.	334 (1%)
CRE	240 (.4%)
Pan-resistant GNR	94 (.2%)
Overall Prevalence of MDRO and C. *difficile*/1,000 encounters	**15.05**
MRSA	7.62
C. *difficile*	5.02
ESBL *E. coli*	1.19
ESBL *Klebsiella* spp.	0.16
VRE	0.56
MDR *P. aeruginosa*	0.22
MDR *A. baumanii*	0.11
MDR *Enterobacter* spp.	0.08
CRE	0.06
Pan-resistant GNR	0.02
Encounters admitted to hospital with MDRO	**12,750**
Single MDRO	12,144 (95%)
Two MDROs	523 (4%)
More than Two MDROs	83 (1%)

Table 2. Unique inpatient and outpatient encounters with MDRO by bacterial species

Organism	Unique Encounters with Resistant Organism	Total Unique Encounters by Bacterial spp.	% Resistant
MRSA	30,630	83,506	37%
ESBL *E. coli*	4,782	236,114	2%
ESBL *Klebsiella* spp	639	43,714	1%
VRE	2,260	5,073	45%
MDR *P. aeruginosa*	872	19,228	5%
MDR *A. baumanii*	447	1,409	32%
MDR *Enterobacter* spp	334	14,932	2%
CRE	240	294,760	<.1%
Pan-resistant GNR	94	315,397	<.1%

Figure 2. 8-Year Compound Aggregate Growth Rate of MDROs and *C. difficile*

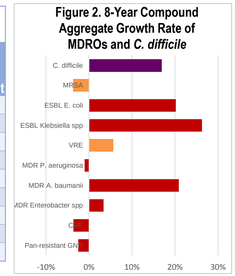


Figure 3. Incident Rate of Unique MDRO Encounters

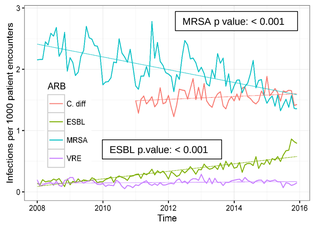


FIGURE 1. Distribution of MDROs and *C. difficile* over an 8-year period: 2008-2015

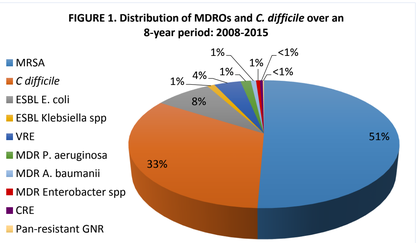
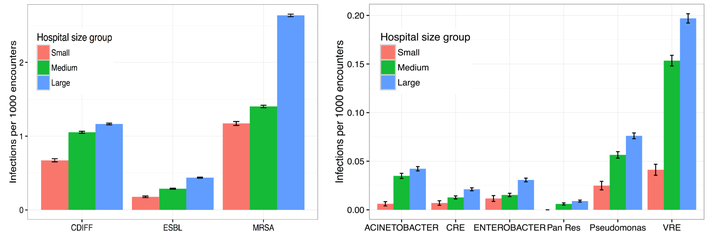


Figure 4. Distribution of MDROs and *C. difficile* by hospital size: Small (<50 beds), Medium (51-200 beds), Large (201+ beds)



CONCLUSIONS

- Patients with MDROs are more likely to be admitted from ambulatory settings and to require additional care in healthcare settings following discharge.
- MDROs are less frequently observed in patients evaluated at small community hospitals.
- 70% of MDROs identified over the past 8 years originated from an ambulatory setting. Similarly 70% of MDROs detected on admitted patients were attributed to acquisition in non-acute care settings.
- MRSA is the most common MDRO, showing higher incidence in larger hospitals, throughout our system but overall rates and hospital acquired infections continue to decline.
- *C. difficile* rates continue to increase with adoption of more sensitive tests in clinical laboratories.
- Similar to U.S. trends described in the Study for Monitoring Antimicrobial Resistance Trends [5], ESBL infections throughout our healthcare system continue to increase, growing faster than other antibiotic resistant bacteria.
- While ESBLs are more frequently encountered in ambulatory settings, the rate of HA ESBLs is steadily increasing while rate of other MDROs remain flat or are decreasing.

RESULTS: 8-Year Inpatient Admissions (n=12,750)

Figure 5: Admission Source and Discharge Disposition for Patients with MDRO

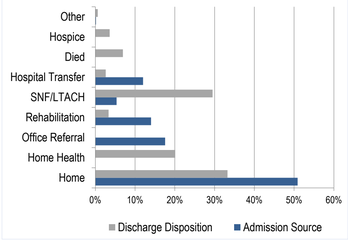


Figure 6: Location of MDRO Acquisition in Hospitalized Patients

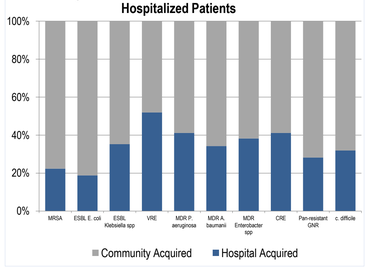


Figure 7: Hospital-acquired C. difficile, MRSA and VRE in a Healthcare System

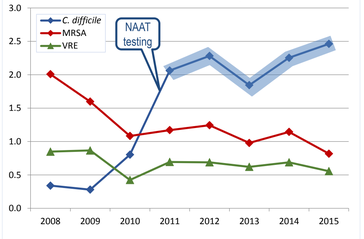
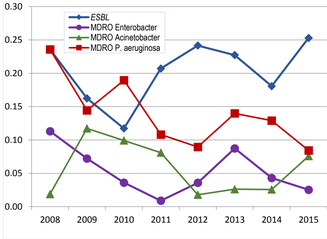


Figure 8. Hospital-acquired Gram Negative Rods in a Healthcare System



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