Results from a Carbapenem-Resistant Enterobacteriaceae (CRE) Point Prevalence Study Conducted at a University Hospital

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ABSTRACT

Background: Multi-drug resistant (MDR) Gram-negative pathogens account for hospital-associated infections, increased morbidity, mortality and outbreaks. Some patients are colonized asymptomatically. These patients serve as carriers for potential transmission of highly-resistant pathogens to the environment, healthcare workers, and other patients resulting in poor outcomes. The objective of this point-prevalence study was to determine how many patients harbored genes coding for MDR pathogens in the institution.
Methods: The Infection Prevention & Control Department and the Division of Infectious Diseases at the University of Louisville organized a performance improvement activity from November 17-20, 2014. Patients were informed of the need for the hospital to know how many patients had a "resistant germ". They were offered a peri-anal swab while clarifying that their declination would not influence their care. Swab collection was performed by designated personnel. The in-patient psychiatry and neonatal units were excluded. The swab was used to check for carbapenem-resistant Enterobacteriaceae (CRE)-associated genes (KPC, NDM, IMP, VIM, and OXA-48), carbapenemase producer-associated genes (OXA-23 and OXA-51), an extended spectrum β-lactamase (ESBL)-associated gene (CTX-M) and a vancomycin-resistant Enterococci-associated gene (*van*A) using the Acuitas® MDRO Gene Test (OpGen).
Results: Among 250 eligible patients, 214 (89%) agreed to be swabbed while 26 declined, and 10 were unavailable. We found 24 patients with a *van*A gene and nine patients with a resistant Gram-negative gene (an IMP, an OXA-51, seven CTX-M). Three patients were identified to carry CRE that were gene test negative (two *Enterobacter cloacae* complex and one *Klebsiella pneumoniae*).
Conclusions: MDR pathogens were identified among patients who were swabbed. Admission surveillance should be considered moving forward because contact isolation could be instituted to prevent spread among hospitalized patients as soon as patients are found to be positive.

INTRODUCTION

Multidrug-resistant organisms (MDRO) affect approximately 5% of inpatients annually, and are estimated to cost the US healthcare system 35 to 45 billion dollars annually. [1] MDRO rates are rising in the US. A recent publication reports a 5-fold increase in CRE incidence over 5 years in the Southeast region, which includes the state of Kentucky. [2]

MDROs are associated with enormous morbidity and mortality, infecting two million patients annually and resulting in more than 23,000 deaths each year in the US. [3] Patients with CRE bloodstream infections have a 50% mortality rate. [3]
The University of Louisville (UofL) Hospital has a history of having multidrug-resistant bacteria – *Acinetobacter baumanii* and *Klebsiella pneumoniae* (a CRE) [4,5].

CRE and ESBL are multi-drug resistant Gram-negative pathogens often responsible for the infections:
- Central Line Bloodstream-Associated (CLABSI)
- Catheter-Associated Urinary Tract (CAUTI)
- Ventilator Associated Event (VAE)/Pneumonia

Colonized, asymptomatic carriers silently transmit MDROs to others. [6]
High colonization (asymptomatic carriers) leads to higher infection rates. [7]
A total of 7% of CRE colonized patients develop infection. [8]

INTRODUCTION, CONTINUED

The CDC rates the CRE threat in the US as urgent and the ESBL threat as serious. [4] Risks are compounded because hospitals transfer unscreened patients and antibiotics are overused.

Reducing MDRO rates and the impact they have on patients and hospitals requires a bundled infection control strategy which includes:

- hand hygiene
- education
- isolation precautions
- cohorting
- antibiotic stewardship
- outbreak detection and management
- patient screening and surveillance

UofL has instituted all of the the strategies except the last one – patient screening and surveillance. Before dedicating resources to determine patients' status at admission, the prevalence of CRE needs to be determined at a hospital.

MATERIALS AND METHODS

Design and Population

This was a point prevalence study initiated by the Infection Prevention and Control (IP&C) Department of the University of Louisville Hospital. The hospital is licensed for 400 beds, but typically accommodates between 200 and 250 beds. It is the only Level 1 trauma center in the region and has a bone marrow transplant unit, burn unit, and an OB/gynecologic floor as well as general medical and surgical services. All patients were candidates of the performance improvement project except for patients in the emergency department, out-patient surgery, psychiatry unit and neonatal ICU.

Process for Participation

Representatives of the IP&C Department introduced themselves to patients (or powers of attorney) and discussed the following message in plain language:

- The IP&C department was responsible for keeping the facility free from bacteria resistant to antibiotics.
- The only way to know for sure if MDRO was present in patients in the hospital was to check everyone.
- If infected, people can become carriers around their rectal area.

So each patient who was approached was invited to have their peri-anal area swabbed for specific genes that cause resistance. If a patient was not in their room, an effort was made to return to have the discussion and obtain the sample. It was made clear that participating or not would not affect their care during their hospitalization.

A total of 10 genes were checked using the Acuitas® MDRO Gene Test (OpGen, Inc., Gaithersburg, MD). **Table 1**

The performance improvement project was reviewed by the hospital institute for research and innovation, and the university office of clinical research services and support.

RESULTS

A total of 250 patients were in the hospital as candidates to be provided the information regarding MDR bacteria in hospitals. Among those approached, 214 (89%) patients permitted a swab to be taken, 26 declined and 10 were not available. (see **Figure 1**) The genes evaluated for each patient are in **Table 1**. The subgroups of patients in each ICU with the number of positive results for genotype and phenotype tests is in **Table 2**.

Figure 1: The process of determining the evaluable patients from the total in the hospital

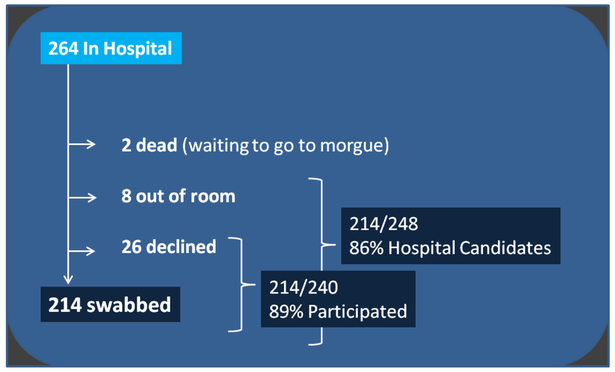

Table 1: Genes checked in each patient and the number positive of each.

MDRO Genes per Swab		Results
CRE Associated	KPC	0
	NDM	0
	IMP	1
	OXA-48	0
Carbapenemase producer Associated	OXA-23	0
	OXA-51	1
ESBL Associated	CTX-M-1	6
	CTX-M-2	1
VRE Associated	Van A	24

RESULTS, CONTINUED

Table 2: Genotype and phenotype results for patients in each unit.

Location	Denominator	Gram (-) gene*	Phenotype†	VanA on VRE
Med Floor (9E)	20	2	0	1
Surgery ICU (9W)	8	2	0	2
Stroke (9 Center)	6	0	0	0
Surgery Floor (9S)	19	1	0	1
Surgery Floor (8E)	13	0	0	1
Surgery ICU (8W)	9	0	0	0
Surgery Floor (8S)	11	1	0	1
Med Floor (7E)	17	0	0	2
CCU (7W)	4	0	0	1
Med Floor (7S)	15	0	0	1
Bone Marrow XU (6E)	18	0	1	9
MICU (6W)	10	1	0	2
Heme/Onc Floor (6S)	15	1	0	1
Burn (5 Center)	4	0	0	0
Med/Surg Floor (5S)	10	1	2	1
Neurosurg ICU (5W)	9	0	0	0
Labor & Delivery (3E)	11	0	0	0
Post-partum (3S)	15	0	0	1

* AcuitasMDRO Gene Test † Acuitas CR Elite Test

CONCLUSIONS

- Three CRE were identified by their resistant phenotype among patients who were swabbed.
- Two more non-CRE, but potentially carbapenem resistant organisms were noted by their genotype; potentially a *Pseudomonas* and an *Acinetobacter.*
- MDRO admission surveillance detects asymptomatic colonized patients that serve as an important reservoir for transmission and infection among hospitalized patients.
- MDRO admission surveillance should be considered moving forward because it guides contact isolation to prevent MDRO spread and endemicity within an institution.

REFERENCES

1. Magill, S., Edwards, J.E., Bamberg, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med*, 2014;370:1198-1208. http://dx.doi.org/10.1056/MEJMoa1306801
2. Thaden JT, Lewis SS, Hazen KC, et al. Rising Rates of Carbapenem-Resistant Enterobacteriaceae in Community Hospitals…Southeastern United States. *Inf Control Hosp Epi*. 2014:35:978-983.
3. Antibiotic Resistant Threats in the United States. CDC. Retrieved from http://www.cdc.gov/drugresistance/threat-report-2013/
4. Beavers SF, Blossom DB and Wiemken TL, et al. Comparison of risk factors for recovery of Acinetobacter baumanii during outbreaks at two Kentucky hospitals, 2006. *Public Health Reports*. 2009;124:868-74.
5. Arnold FW, Heishman C, Wardlow LC. A case of a metallo-β-lactamase producing *Klebsiella pneumoniae* Louisville, Kentucky. *Ky Med J* 2014;112:23-9.
6. 6 Snitkin ES, Zelazny AM, Thomas PJ, et al. Tracking a Hospital Outbreak of Carbapenem-Resistant Klebsiella pneumoniae with Whole-Genome Sequencing. *Science Trans Med* 2012;148: 1-9.
7. 7 Hayden M., Lin M., Lolans K et al. Prevention of Colonization and Infection by Klebsiella pneumonia Carbapenemase-Producing Enterobacteriaceae in Long-term Acute-Care Hospitals. *Clin Infect Dis*. 2014.
8. 8 Borer A, Eskira S, Nativ R, et al. A Multifaceted Intervention Strategy for Eradication of a Hospital-Wide Outbreak Caused by Carbapenem-Resistant *Klebsiella pneumoniae* in Southern Israel. *Inf Control Hosp Epi.* 2011;32:1158-1165.