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Point Prevalence of *Klebsiella pneumoniae* Carbapenemase-Producing *Enterobacteriaceae* in Maryland

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Carbapenem-resistant *Enterobacteriaceae* (CRE) have emerged as significant healthcare-associated multidrug-resistant pathogens across the United States.¹ *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae* (KPCs) are the primary organisms of antibiotic resistance for this type of infection in the US.² Bacterial strains that harbor carbapenem resistance genes have shown resistance to all known first line therapeutic options and the threat of the spread of these organisms is of great concern to the US healthcare system.³ Colonization and infection with KPCs have been associated with several healthcare-associated factors, and an increase in associated morbidity and mortality has been documented.⁴

Despite its notoriety, the true burden of KPCs is unknown. The colonized patient is an important reservoir of CREs and represents a key to understanding the spread and control of these organisms. In this study, we determined the colonization prevalence of KPCs in a cohort of mechanically ventilated patients residing in all healthcare settings (acute and long term care) by performing a statewide prospective cross-sectional prevalence survey to determine the burden of KPCs in Maryland.

All healthcare facilities that provide care to mechanically ventilated patients in Maryland were invited to participate; participation was voluntary. The prevalence survey was performed during a 12-day period from July-August 2010. Each facility collected peri-anal and sputum samples from eligible patients. The survey was performed as a public health initiative and no patient identifying information was collected. Peri-anal cultures were obtained using Staplex II cotton swabs (Staplex) and sputum cultures were collected during routine respiratory care. All samples were analyzed for a previous study and frozen at -70°C .⁵ The samples were thawed and the detection of KPCs was performed following the

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CDC method.⁶ Susceptibility testing and amplification and sequencing of *bla*_{KPC} was performed on all isolates.^{7,8} Multi-locus sequence typing was performed on KPC-producing *Klebsiella pneumoniae* and *Escherichia coli* isolates to determine strain relatedness.

Forty (70%) of the 57 eligible healthcare facilities within 5 regions of Maryland participated in the survey (Figure 1); 30 (67%) of the eligible acute care facilities and 10 (83%) of the eligible LTC facilities. Among the 40 facilities that participated, five facilities (four acute care and one LTC) did not have an eligible/ventilated patient during the study period and therefore no specimens were collected. Characteristics of participating facilities were published previously.⁵

Among participating facilities, there were 390 patients eligible to be enrolled and surveillance cultures were obtained from 358 (92%). KPC-producing genes were detected in 22 bacterial isolates from 20 (6%) patients (5 sputa and 17 peri-anal; Table 1). Two patients had KPCs detected in both the sputum and peri-anal specimen. KPCs were isolated from patients in 9 (23%) healthcare facilities, 4 acute care and 5 LTC facilities. Eleven (55%) of the 20 patients resided in a LTC facility. KPCs were found in two regions of Maryland. Culture detected 15 *K. pneumoniae*, 6 *E. coli*, and 1 *Enterobacter cloacae*. Of these isolates, 19 harbored the *bla*_{KPC-2} and 3 harbored the *bla*_{KPC-3}. Molecular typing revealed three different *K. pneumoniae* strains found in 4 acute care and 3 LTC facilities. Of the *K. pneumoniae* isolates, 60% (9/15) were ST 258 found in 6 healthcare facilities (3 acute care and 3 LTC). There were four different *E. coli* strains detected in 4 facilities (1 acute care and 3 LTC). Of the *E. coli* 50% (3/6) were ST 131 found in 1 acute care and 2 LTC facilities. One facility had KPC producing *K. pneumoniae*, *E. coli*, and *E. cloacae* detected harboring either the KPC-2 or KPC-3 gene.

We found that mechanically ventilated patients have a high prevalence of KPCs within a variety of healthcare facilities in Maryland. We showed that 6% of patients from 40 acute care and LTC facilities in Maryland were colonized with KPC-producing *Enterobacteriaceae*. 55% of the KPCs were found in LTC facilities. KPCs were found primarily in peri-anal swabs but in three patients, KPCs were only found in the sputum. These CREs were detected exclusively in the central and national capital regions in Maryland, which are more populated areas with a higher number of healthcare facilities. Molecular typing data showed transmission of organisms within and between healthcare facilities.

KPCs are emerging as a serious threat within the US, yet the true burden is unknown. In 2012, the CDC reported that 4.6% of acute care hospitals reported at least one CRE from clinical cultures.⁹ However, previous to this study, no statewide active surveillance of the true burden of CREs has been reported anywhere in the nation. Thibodeau et al performed a voluntary, statewide, paper-based survey on clinical cultures in Massachusetts hospitals and found that nearly half of all Massachusetts hospitals detected a CRE in 2010 and that these CREs were more often detected in teaching hospitals than non-teaching hospitals.¹⁰ However, the use of clinical cultures only as well as the use of differing definitions of CREs make it difficult to interpret the Massachusetts results. In our study we collected surveillance peri-anal and sputum cultures and used enrichment techniques to determine the prevalence

of KPCs utilizing identical laboratory methods and definitions for each facility. We also performed molecular typing on bacterial strains harboring KPCs and revealed a dominant strain type for both *K. pneumoniae* and *E. coli*.

This study has several limitations. We could not rule out response bias since only 70% of the healthcare facilities participated in survey. At the time of this study, the importance of urine as a specimen to detect CREs was unknown therefore we might have missed patients colonized with KPCs. In addition, this point prevalence was limited to patients receiving mechanical ventilation, who are known to have higher rates of colonization, and therefore the KPC prevalence cannot be generalized to other patients populations.

In conclusion, this is the first study to our knowledge to examine the colonization rate of KPCs in a cohort of mechanically ventilated patients residing in both acute and long term care healthcare facilities in one state within the United States.

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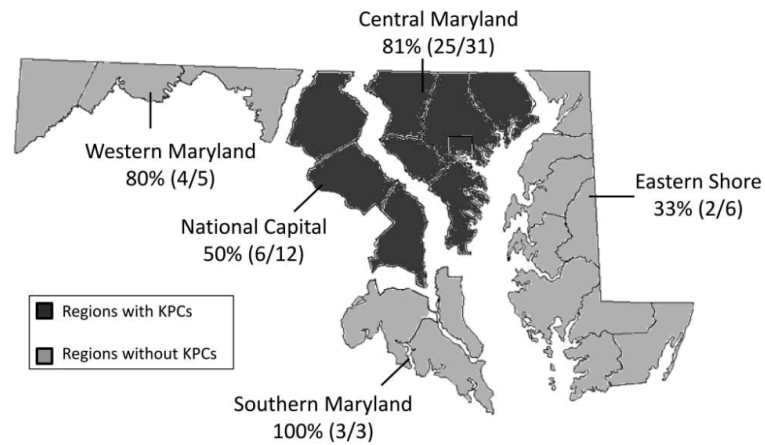


Figure 1. Seventy (70%) of Maryland Healthcare centers with mechanically ventilated patients participated in the study. KPC-producing *Enterobacteriaceae* were found in 23% of facilities, which were located in 2 major regions of Maryland.

Table 1Characterization of *Enterobacteriaceae*-producing *Klebsiella pneumoniae* carbapenemase.

Patient	Facility	Facility Type	Region	Specimen	Organism	Sequence Type	blaKPC
1	1	LTC	Central Maryland	sputum	<i>K. pneumoniae</i>	15	KPC-3
2	1	LTC	Central Maryland	peri-anal	<i>E. coli</i>	167	KPC-2
3	2	LTC	Central Maryland	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
4	3	Acute	Central Maryland	sputum	<i>K. pneumoniae</i>	258	KPC-2
5	3	Acute	Central Maryland	peri-anal	<i>E. coli</i>	95	KPC-3
6	3	Acute	Central Maryland	peri-anal	<i>E. coli</i>	131	KPC-2
7	3	Acute	Central Maryland	peri-anal	<i>E. cloacae</i>	NT*	KPC-2
8	4	LTC	Central Maryland	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
9	4	LTC	Central Maryland	peri-anal	<i>E. coli</i>	131	KPC-2
10	4	LTC	Central Maryland	peri-anal	<i>E. coli</i>	167	KPC-2
11	5	LTC	Central Maryland	peri-anal	<i>E. coli</i>	131	KPC-2
12	6	Acute	National Capital	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
13	7	Acute	Central Maryland	peri-anal	<i>K. pneumoniae</i>	15	KPC-3
14-1	8	LTC	National Capital	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
14-2	8	LTC	National Capital	sputum	<i>K. pneumoniae</i>	258	KPC-2
15	8	LTC	National Capital	peri-anal	<i>K. pneumoniae</i>	340	KPC-2
16	8	LTC	National Capital	peri-anal	<i>K. pneumoniae</i>	340	KPC-2
17	8	LTC	National Capital	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
18	9	Acute	National Capital	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
19-1	9	Acute	National Capital	peri-anal	<i>K. pneumoniae</i>	258	KPC-2
19-2	9	Acute	National Capital	sputum	<i>K. pneumoniae</i>	258	KPC-2
20	9	Acute	National Capital	sputum	<i>K. pneumoniae</i>	258	KPC-2

* NT: not tested