Epidemiologic Surveillance of Carbapenem-resistant Enterobacteriaceae in a Large Academic Teaching Hospital in Houston, Texas

Contact Information:
Travis Carlson
University of Houston
Phone: (713) 743-9878
Email: tjcarlson@uh.edu

Carlson TJ [1], Gonzales-Luna AJ [1], Endres BT [1], Kuo J [1], Lancaster C [1], Miranda J [1], Bassères E [1], Begum K [1], Alam MJ [1], Garey KW [1]

[1]Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

ABSTRACT

Background: Carbapenem-resistant Enterobacteriaceae (CRE) have been classified as an urgent threat by the Centers for Disease Control and Prevention (CDC) since 2013. This study sought to understand the current epidemiological trends and characteristics of CRE at our institution.

Methods: Clinical CRE isolates were collected from a single hospital in the Texas Medical Center (TMC) between February 2017 and December 2018. They were identified daily by TheraDoc (Premier Inc., Charlotte, NC) and defined using the CDC definition found in their 2012 CRE Toolkit. Organism identification and MIC determinations were performed using the Vitek 2 system (bioMérieux, Marcy l'Étoile, France), and minimum inhibitory concentrations (MICs) were interpreted using the 29th edition of the Clinical Laboratory Standards Institute M100 document or product package insert. The Xpert Carba-R (Cepheid, Sunnyvale, CA) aided in the detection and differentiation of the bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} gene sequences from pure colonies. The Wilcoxon rank-sum test was used to compare MIC distributions between carbapenemase and non-carbapenemase producers.

Results: A total of 92 CRE isolates were identified during the study period. The most common culture sites were urine (42.4%), lung (19.6%), wound (14.1%), and blood (13.0%). Nine species were identified, the most prevalent of which were *Klebsiella pneumoniae* (50.0%), *Escherichia coli* (17.4%), and *Enterobacter cloacae* complex (10.9%). Polymerase chain reaction identified only bla_{KPC}, which was present in 50.0% of tested isolates. Overall, the MIC_{50}/MIC_{90} values for meropenem and ertapenem were 16/16 µg/mL (range 0.25-16 µg/mL) and 8/8 µg/mL (range 1-16 µg/mL), respectively. The MIC_{90} values for amikacin, gentamicin, tobramycin, and tigecycline were intermediate or resistant, but all tested isolates (n = 26) were susceptible to ceftazidime/avibactam. Meropenem, ertapenem, levofloxacin, and ceftazidime/avibactam MICs were higher in those isolates harboring a bla_{KPC} gene ($P < .05$).

Conclusions: Carbapenemase production was limited to bla_{KPC} and was present in 50.0% of clinical CRE isolates, which is similar to previous epidemiological observations in the United States. Carbapenemase production affected the MICs of carbapenems, ceftazidime/avibactam, and levofloxacin suggesting the presence of other antimicrobial resistance genes. This will have to be confirmed by whole genome sequencing.

BACKGROUND

- CRE have been classified as an urgent threat by the CDC since 2013
- *Klebsiella pneumoniae* carbapenemase (KPC) is almost exclusively the only carbapenemase expressed by CRE isolates collected in the United States
- Approximately 50% of CRE isolates do not harbor any known β-lactamase genes
- Many institutions do not have the capability to prospectively detect antimicrobial resistance genes, and clinicians are forced to make treatment decisions based on phenotypic or epidemiologic data alone

SPECIFIC AIMS

1. To better understand the epidemiology of CRE in Houston, Texas
2. To describe the mechanisms of resistance expressed by CRE isolates in Houston, Texas

METHODS

Study design / Inclusion

- Clinical CRE isolates were collected from a single hospital in the TMC between February 2017 and December 2018
- CRE were identified daily via TheraDoc (Premier Inc., Charlotte, NC)

2012 CDC Definition of CRE

Nonsusceptible (intermediate or resistant) to:

- imipenem, OR
- meropenem, OR
- doripenem

AND resistant to all third-generation cephalosporins tested

- Organism identification and MIC determinations were performed by the Vitek 2 system (bioMérieux, Marcy l'Étoile, France)
- MICs were interpreted using the 29th edition of the CLSI M100 document or product package insert
- The Xpert Carba-R (Cepheid, Sunnyvale, CA) aided in the detection and differentiation of the bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{OXA-48}, and bla_{IMP} gene sequences

Statistical analysis

- All statistical analyses were performed using Stata, version 15.1 (StataCorp LLC, College Station, Texas)
- Descriptive statistics, including MIC_{50} and MIC_{90} values, were determined
- The Wilcoxon rank-sum test was used to compare MIC distributions between carbapenemase and non-carbapenemase producing isolates
- All tests were two-tailed, and *P*-values less than 0.05 were considered statistically significant

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RESULTS

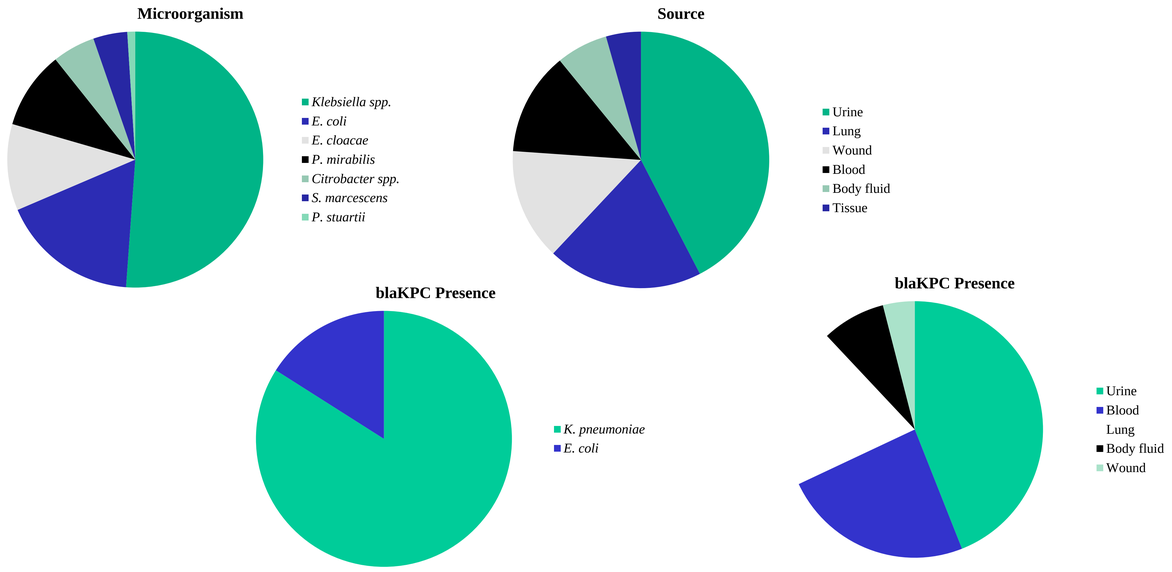

Table 1. Relevant MIC distributions stratified by microorganism and resistance mechanism

	Klebsiella spp. MIC_{50}/MIC_{90} (range)	*E. coli* MIC_{50}/MIC_{90} (range)	*E. cloacae* MIC_{50}/MIC_{90} (range)	*P. mirabilis* MIC_{50}/MIC_{90} (range)	*Citrobacter* spp. MIC_{50}/MIC_{90} (range)	*S. marcescens* MIC_{50}/MIC_{90} (range)	All species MIC_{50}/MIC_{90} (range)	Percent susceptible	*P*-value
Meropenem	KPC: 16/16 (1-16) Non-KPC: 4/16 (1-16)	KPC: 16/16 (16-16) Non-KPC: 1/16 (1-16)	8/8 (0.25-8)	1/4 (0.5-4)	16/16 (1-16)	8/8 (8-8)	KPC: 16/16 (16-16) Non-KPC: 4/16 (0.25-16)	KPC: 0% Non-KPC:45%	<.001
Ertapenem	KPC: 8/8 (2-8) Non-KPC: 4/16 (1-16)	KPC: 8/8 (4-8) Non-KPC: 4/8 (4-8)	4/8 (1-8)	1/4 (1-4)	16/16 (8-16)	4/8 (1-8)	KPC: 8/8 (2-8) Non-KPC: 4/8 (1-8)	KPC: 0% Non-KPC: 0%	.033
Tobramycin	KPC: 16/16 (1-16) Non-KPC: 8/16 (1-16)	KPC: 4/16 (1-16) Non-KPC: 16/16 (2-16)	1/8 (1-8)	1/1 (1-1)	8/16 (1-16)	2/8 (1-8)	KPC: 8/16 (1-16) Non-KPC: 1/16 (1-16)	KPC: 40% Non-KPC: 56%	.167
Gentamicin	KPC: 4/16 (1-16) Non-KPC: 8/16 (1-16)	KPC: 1/16 (1-16) Non-KPC: 1/16 (1-16)	1/16 (1-16)	1/1 (1-1)	8/16 (1-16)	2/4 (1-4)	KPC: 4/16 (1-16) Non-KPC: 1/16 (1-16)	KPC: 74% Non-KPC: 60%	.928
Amikacin	KPC: 4/64 (2-64) Non-KPC: 2/8 (2-64)	KPC: 4/8 (2-8) Non-KPC: 16/32 (4-32)	2/2 (2-2)	2/2 (2-2)	2/8 (2-8)	8/16 (2-16)	KPC: 4/64 (2-64) Non-KPC: 2/16 (2-64)	KPC: 76% Non-KPC: 92%	.157
Levofloxacin	KPC: 8/8 (0.125-8) Non-KPC: 8/8 (4-8)	KPC: 8/8 (8-8) Non-KPC: 8/8 (0.125-8)	0.5/8 (0.125-8)	0.125/4 (0.125-4)	4/8 (1-8)	1/2 (0.125-2)	KPC: 8/8 (0.125-8) Non-KPC: 8/8 (0.125-8)	KPC: 8% Non-KPC: 28%	.025
Tetracycline	KPC: 4/16 (1-16) Non-KPC: 16/16 (2-16)	KPC: 16/16 (1-16) Non-KPC: 16/16 (16-16)	16/16 (2-16)	16/16 (16-16)	4/16 (4-16)	16/16 (4-16)	KPC: 4/16 (1-16) Non-KPC: 16/16 (2-16)	KPC: 64% Non-KPC: 24%	.009
Tigecycline	KPC: 2/4 (2-4) Non-KPC: 4/4 (2-4)	---	---	---	---	---	KPC: 2/4 (1-4) Non-KPC: 4/4 (2-4)	KPC: 75% Non-KPC: 33%	.354
Trimethoprim-sulfamethoxazole	KPC: 40/320 (20-320) Non-KPC: 320/320 (20-640)	KPC: 320/320 (320-320) Non-KPC: 320/320 (20-320)	20/320 (20-320)	20/320 (20-320)	320/320 (20-320)	80/160 (20-160)	KPC: 320/320 (20-320) Non-KPC: 40/320 (20-640)	KPC: 44% Non-KPC: 52%	.643
Ceftazidime-avibactam	KPC: 2/8 (1-8) Non-KPC: 1/2 (1-2)	1/8 (0.125-8)	---	---	---	---	KPC: 2/8 (1-8) Non-KPC: 1/2 (1-2)	KPC: 100% Non-KPC: 100%	.046

CONCLUSIONS

- Carbapenemase production was limited to bla_{KPC} and was present in 50.0% of clinical CRE isolates
- Meropenem, ertapenem, levofloxacin, and ceftazidime/avibactam MICs were higher in those isolates harboring a bla_{KPC} gene