Utilization of the Modified Carbapenem Inactivation Method (mCIM) to Detect for Carbapenemase Production in Carbapenem-Resistant *Klebsiella (Enterobacter) aerogenes*, Nebraska 2023

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Background

Carbapenemase-producing Enterobacterales (CPE) have emerged as a serious threat in healthcare settings. Although multiple mechanisms exist that can result in carbapenem resistance, only about 30% is due to the presence of a carbapenemase gene located on a motile element which can easily be spread. As participants in the CDC's Antimicrobial Resistance Lab Network, public health laboratories, including Nebraska Public Health Laboratory (NPHL), have implemented multiple test methods to detect for CPE. This report describes the results of using the modified carbapenem inactivation method (mCIM) to screen carbapenem-resistant *Klebsiella aerogenes* (CRKA) for the presence of a carbapenemase gene.

Methods

- CRKA isolates were submitted to NPHL from clinical laboratories throughout Nebraska.
- Phenotypic susceptibility of isolates submitted:

Antibiotic	MIC (µg/ml)	Interpretation
Cefoxitin	>16	R
Cefazolin	>16	R
Ertapenem	2-4 or ≥8	I or R
Imipenem	2-4 or ≥8	I or R
Meropenem	≤1	S

- mCIM was performed according to CLSI (Clinical and Laboratory Standards Institute) methods. Refer to Figure 1.
- Reflex testing for inconclusive or positive isolates included:
  - Cepheid Xpert® Carba-R RT-PCR assay on the Cepheid GeneXpert system and
  - Whole genome sequencing using the Clear Labs Microbial Surveillance Kit v2.0 on the Clear Dx™ platform.

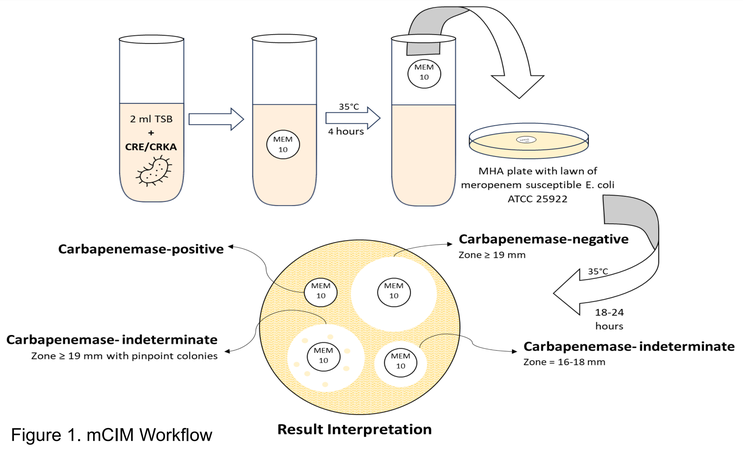

Figure 1. mCIM Workflow

Table 1. Carbapenem-resistant Enterobacterales that screened inconclusive by the mCIM assay and negative for a carbapenemase gene, Nebraska 2023[a]

Species	Number	Gene product (number)
Klebsiella aerogenes	13	*ampC* (13)
Enterobacter roggenkampii[b]	6	*bla*MIR-7 (1)
		*bla*MIR-9 (1)
		*bla*MIR-10 (1)
		*bla*MIR-15 (1)
		*bla*MIR-16 (1)
		*bla*MIR-20 (1)
Enterobacter kobei[b]	3	*bla*ACT-28 (1)
		*bla*ACT-102 (1)
		*bla*ACT-104 (1)
Enterobacter cloacae[b]	2	*bla*ACT-102 (1)
		*bla*ACT-28 (1)
Enterobacter bugandensis[b]	1	*bla*ACT-77 (1)
Enterobacter hormaechei[b]	1	*bla*ACT-15 (1)
Klebsiella pneumoniae	1	*bla*TEM-1, *bla*SHV-27 (1)
Total	27	

[a]Species and gene products were identified following bioinformatics analysis of the whole genome sequence.

[b]All phenotypically identified as *Enterobacter cloacae* complex.

Results

- 14 mCIM positive or inconclusive CRKAs
  - RT-PCR: Negative for carbapenemase gene families (KPC, NDM, VIM, IMP-1 and OXA-48)
  - WGS
    - Negative for carbapenemase gene(s)
    - Amp-C gene detected
    - SNP analysis: No relationship between isolates tested

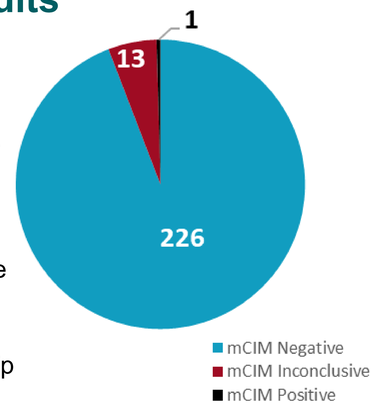

Figure 2. mCIM result interpretation of the 240 CRKA isolates screened.

Conclusion

- CRKA inconclusive or resistant to ertapenem and/or imipenem, but susceptible to meropenem by phenotypic testing did not harbor a carbapenemase gene following WGS analysis
- CRKA with this antimicrobial susceptibility pattern could be excluded from further testing for detection of carbapenemase genes, alleviating some of the budgetary and workload burdens currently facing public health laboratories.

References

- CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 34th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2024. https://guides.library.cornell.edu/poster
- Hagey JV, Vlachos N, Kent AG, Diaz M, Halpin AL. (2023). CDCgov/phoenix: v2.0.0 (v2.0.0). Zenodo. https://doi.org/10.5281/zenodo.8147510