

elements on the same plasmid suggests that the CP-Hv pathotype could spread rapidly through horizontal transfer. This discovery demonstrates the critical role of genomic characterization of emerging resistance and virulence phenotypes by the AR Lab Network as part of US containment efforts.

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604. Gram-Negative Bacilli Carrying Multiple Carbapenemases: the United States, 2012–2018

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Background. Gram-negative bacilli carrying multiple carbapenemase genes (multi-CP-GNB) present an emerging public health threat; to date, most isolates reported in the literature have been from outside the United States. We reviewed multi-CP-GNB reported to CDC.

Methods. Reports of multi-CP-GNB isolates carrying genes encoding >1 targeted carbapenemases (i.e., KPC, NDM, OXA-48-type, VIM, or IMP) were received from healthcare facilities, health departments, and public health laboratories, and included isolates tested through the AR Laboratory Network (ARLN) beginning in 2017 as well as isolates sent to CDC for reference testing. Epidemiologic data were gathered by health departments during public health investigations.

Results. From October 2012 to November 2018, 111 multi-CP-GNB isolates from 71 patients in 20 states were identified. Two patients had three different multi-CP-GNB and one patient had two different multi-CP-GNB. The majority of cases (76%) were reported in 2017 or later, after ARLN testing began. Among patients with multi-CP-GNB, the most common organism-mechanisms combination was *Klebsiella pneumoniae* carrying NDM and OXA-48-type enzymes (table). Urine (44%) and rectal (20%) were the most frequent specimen sources for isolates. The median age of patients was 63 years (range 2–89 years); most had specimens collected at acute care hospitals (87%) or post-acute care facilities (9%). Of 50 patients with information available, 37 traveled internationally in the 12 months prior to culture collection. Among these, 88% were hospitalized for ≥1 night while outside the United States with 10 countries reported, of which India was most common (n = 18). All 5 patients with *Pseudomonas aeruginosa* co-carrying carbapenemases reported recent hospitalization outside the United States.

Conclusion. The multi-CP-GNB reported to CDC include diverse organisms and carbapenemase combinations and often harbored carbapenemases from different β-lactamase classes, which may severely limit treatment options. Healthcare exposures outside the United States were common; providers should ask about this exposure at healthcare admission and, when present, institute interventions to stop transmission in order to slow further US emergence.

Table: Unique Patients With Gram Negative Bacilli Producing Multiple Carbapenemases, by Organism and Mechanism, N=76**

Organism	IMP+NDM+ (n=2)	KPC+NDM+ (n=17)	KPC+OXA+ (n=1)	KPC+VIM+ (n=7)	NDM+OXA+ (n=47)	NDM+VIM+ (n=2)
Enterobacteriaceae (n=71)	0	17	1	6	47	0
<i>E. coli</i> (n=10)		2			8	
<i>Enterobacter</i> (n=10)		8		2		
<i>K. pneumoniae</i> * (n=48)		7	1	2	38	
<i>K. oxytoca</i> (n=1)				1		
<i>Citrobacter freundii</i> (n=1)				1		
<i>Providencia rettgeri</i> (n=1)					1	
<i>P. aeruginosa</i> (n=5)	2			1		2

*Includes organisms now classified as *Klebsiella aerogenes*

**71 patients had 76 isolates with unique organism-mechanism combinations

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605. Identification of a Novel CMY-Variant Enzyme in a Clinical *Escherichia coli* Strain with Treatment-Emergent Ceftazidime-Avibactam Resistance

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Background. Ceftazidime-avibactam (CZA) is a novel β-lactam / β-lactamase inhibitor with *in vitro* activity against multidrug-resistant Gram-negatives, including those harboring CMY-2 enzymes. Treatment-emergent resistance to CZA has been described in KPC-producing *Klebsiella pneumoniae* but has not been described in non-carbapenemase-producing, carbapenem-resistant *Enterobacteriaceae* (CRE).

Methods. A patient with an intra-abdominal infection due to a carbapenem-resistant *E. coli* (ertapenem MIC 16 μg/mL; meropenem MIC 2 μg/mL; CZA MIC 2 μg/mL; carbapenemase negative) was treated with CZA. On day 48 of therapy, a CZA resistant, carbapenem-sensitive *E. coli* was identified from abdominal drainage (CZA MIC ≥256 μg/mL; meropenem MIC 0.19 μg/mL). Illumina MiSeq whole-genome sequencing (WGS) was performed on both isolates to identify potential resistance mechanisms. The ResFinder database was used to identify known β-lactamase enzymes, and *in silico* modeling of β-lactamase structure was assessed.

Results. WGS revealed that both isolates were ST410 *E. coli*, with the sole difference in β-lactam resistance determinants between the two being a novel CMY β-lactamase harbored on an IncI-type conjugative plasmid in the second isolate. The novel CMY has 4 amino acid substitutions relative to CMY-2: A134E, Q140K, V231S, and N366Y. The V231S substitution is found in CMY-42 and has previously been associated with increased ceftazidime hydrolysis. The remaining three substitutions have not previously been identified. Previous studies have identified that substitutions at position 366 influence the rate of ceftazidime hydrolysis rate. Preliminary protein structure analysis suggests that positions 140 and 366 are in the active site. No other differences in β-lactam resistance determinants were identified between the first and second isolates.

Conclusion. To our knowledge, we have identified the first case of CMY-associated CZA resistance. Given the widespread and transferrable nature of CMY enzymes, this finding raises concern for additional cases of resistance with increasing usage of CZA. Further analysis is needed to identify the mechanism by which this enzyme confers CZA resistance.

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606. Identification and Characterization of HMB-2, a Novel Metallo-β-Lactamase in a *Pseudomonas aeruginosa* Isolate

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Background. Carbapenemases, a global health threat, are a diverse group of β-lactamases active against cephalosporins and carbapenems, which are often last resort treatments for multidrug-resistant gram-negative infections. The most common carbapenemases reported among *Pseudomonas aeruginosa* are metallo-β-lactamase (MBLs). We describe a novel MBL (designated HMB-2) identified in a *P. aeruginosa* isolate from a urine specimen collected in 2015 as part of CDC's Emerging Infections Program.

Methods. We performed antimicrobial susceptibility testing (AST) by broth microdilution, real-time PCR to screen for common carbapenemases (IMP, KPC, NDM, VIM, and OXA-48), and modified carbapenem inactivation method (mCIM) to test for carbapenemase production. The isolate underwent whole-genome sequencing (WGS) using Illumina MiSeq and PacBio RS II (Pacific Biosciences) platforms. Long read sequences were polished using Quiver and corrected by Pilon utilizing Illumina reads. We further characterized a putative novel MBL identified in WGS data by amplifying and cloning the gene into the pCR2.1-TOPO II vector (Invitrogen), which was then sub-cloned into a pET21 expression vector (Sigma-Aldrich). The resulting *hmb2+* pET21 plasmid was transformed into a susceptible *Escherichia coli* for AST, including the imipenem-EDTA method to confirm MBL activity.

Results. The isolate displayed resistance to carbapenems and demonstrated phenotypic carbapenemase activity (mCIM positive), but was negative for carbapenemase genes by PCR. WGS analyses identified a putative MBL gene located on the chromosome. The gene shared 98% DNA and protein sequence identity with an MBL reported in 2016 in a *P. aeruginosa* isolate from Germany (HMB-1) and thus was named *hmb-2*. The cloned *hmb-2* gene conferred resistance to carbapenems (meropenem and ertapenem) and third-generation cephalosporins (cefotaxime and ceftazidime) in transformed *E. coli*. The Minimum Inhibitory Concentration ratio for the imipenem-EDTA method was ≥4.

Conclusion. A putative, novel β-lactamase gene, *bla*_{HMB-2}, was identified and cloned. The imipenem-EDTA results indicated that HMB-2 is an MBL. This discovery