Increase in *bla*$_{NDM}$ among Carbapenemase-Producing, Carbapenem-Resistant Enterobacterales, United States, 2016–2023

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We report an increase of *bla*$_{NDM}$ among carbapenemase-producing, carbapenem-resistant Enterobacterales collected in the United States through the Emerging Infections Program's Multi-site Gram-negative Surveillance Initiative. Among 1,288 isolates identified, the percentage harboring *bla*$_{NDM}$ increased from 5.4% in 2016 to 39.8% in 2023.

Carbapenem-resistant Enterobacterales (CRE) are an urgent public health threat. In 2022, an estimated 13,387 CRE infections occurred among hospitalized patients in the United States (*1*). Different mechanisms may contribute to carbapenem resistance, but carbapenemase-producing CRE (CP-CRE) are of particular concern. Carbapenemase genes confer broad resistance to β-lactam antimicrobial drugs and are often located on mobile genetic elements, enabling them to spread between bacterial species. Metallo-β-lactamases (MBLs), including New Delhi metallo-β-lactamase (NDM)–producing CRE, are especially problematic because few antimicrobial drugs have activity against them (*2*). We report an increase in *bla*$_{NDM}$ among CP-CRE collected through the Centers for Disease Control and Prevention's Emerging Infections Program (EIP) Multi-site Gram-negative Surveillance Initiative.

The EIP Multi-site Gram-negative Surveillance Initiative conducts active, population- and laboratory-based surveillance of CRE (*3*–*5*). During 2016–2023, a total of 10 EIP sites participated in surveillance for carbapenem-resistant *Enterobacter cloacae* complex, *Escherichia coli*, and *Klebsiella* species (*K. pneumoniae*, *K. oxytoca*, and *K. aerogenes*) in isolates from a usually sterile site or from urine. Each site submitted a convenience sample of isolates to the Centers for Disease Control and Prevention for testing, including in-house reference broth microdilution incorporating an MBL screen, species identification, and real-time PCR for carbapenemase genes (*3*). We tested all isolates for *bla*$_{KPC}$, *bla*$_{NDM}$, and *bla*$_{OXA-48-like}$ genes; we also tested isolates with a positive MBL screen for *bla*$_{VIM}$ and *bla*$_{IMP}$ (*4*). We defined CP-CRE as isolates positive for a carbapenemase gene by real-time PCR and resistant to ertapenem, imipenem, or meropenem as determined by broth microdilution and Clinical and Laboratory Standards Institute breakpoints (Appendix Table, https://wwwnc.cdc.gov/EID/article/32/6/25-1404-App1.pdf) (*6*). Using the Pearson χ^2 test, we compared the percentages of *bla*$_{NDM}$

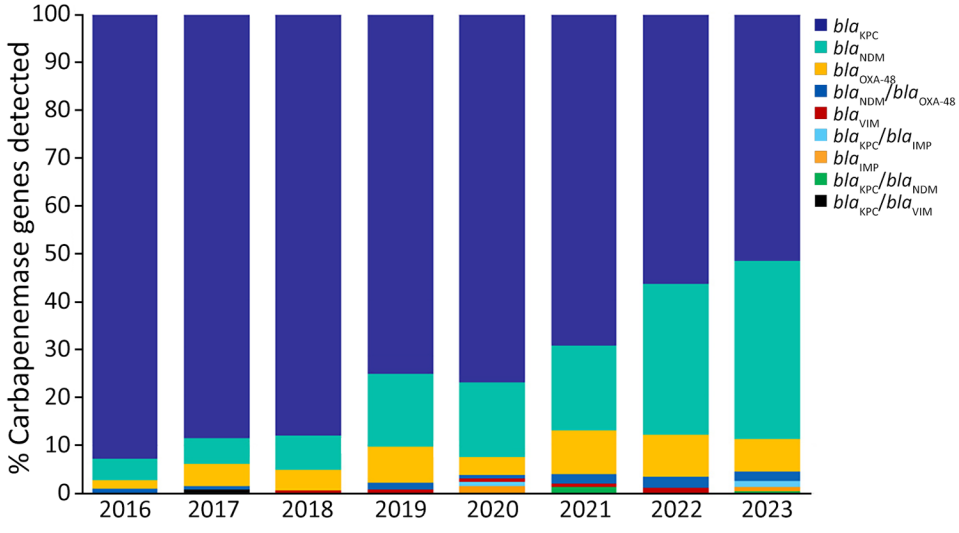

Figure. Percentage of carbapenemase genes detected by real-time PCR among 1,288 CP-CRE chosen for a study analyzing an increase in *bla*$_{NDM}$ among carbapenemase-producing, carbapenem-resistant Enterobacterales, United States, 2016–2023. IMP, imipenemase; KPC, *Klebsiella pneumoniae* carbapenemase; OXA-48, oxacillinase; NDM, New Delhi metallo-β-lactamase; VIM, Verona integron-encoded metallo-β-lactamase.

[1]HAIC MuGSI Working Group members are listed at the end of this article.

Table. Frequency of *bla*$_{NDM}$ by species from study investigating increase in *bla*$_{NDM}$ among CP-CRE, United States, 2016–2023*

Year	Total no. CP-CRE isolates	No. (%) isolates			
		All *bla*$_{NDM}$†	*Escherichia coli*	*Klebsiella* spp.	*Enterobacter cloacae* complex
2016	111	6 (5.4)	2 (1.8)	4 (3.6)	0
2017	149	9 (6.0)	5 (3.4)	4 (2.7)	0
2018	166	12 (7.2)	6 (3.6)	5 (3.0)	1 (0.6)
2019	145	24 (16.6)	13 (9.0)	9 (6.2)	2 (1.4)
2020	134	22 (16.4)	13 (9.7)	6 (4.5)	3 (2.2)
2021	153	32 (20.9)	17 (11.1)	10 (6.5)	5 (3.3)
2022	181	61 (33.7)	27 (14.9)	23 (12.7)	11 (6.1)
2023	249	99 (39.8)	57 (22.9)	29 (11.6)	13 (5.2)
Total	1288	265 (20.6)	140 (10.9)	90 (7.0)	35 (2.7)

*Data are updated for accuracy and may differ from online reports (accessed 2025 Aug 19) (*5*). CP-CRE, carbapenemase-producing, carbapenem-resistant Enterobacterales.
†Includes isolates carrying *bla*$_{NDM}$ (n = 245), dual mechanism *bla*$_{NDM}$+*bla*$_{OXA-48}$ (n = 17), and *bla*$_{NDM}$+*bla*$_{KPC}$ (n = 3).

among CP-CRE collected in 2016 and 2023. Annual reports with epidemiologic, clinical, and laboratory data are available online (*5*).

Among 1,288 CP-CRE identified, *bla*$_{KPC}$ was the most common carbapenemase gene detected among all confirmed CP-CRE during 2016–2023 (72.7%, 937 isolates), followed by *bla*$_{NDM}$ (20.6%, 265 isolates), *bla*$_{OXA-48-like}$ (7.5%, 96 isolates), *bla*$_{IMP}$ (0.6%, 8 isolates), and *bla*$_{VIM}$ (0.5%, 7 isolates) (Figure); 25 (1.9%) isolates harbored >1 carbapenemase gene (Appendix Table). The percentage of *bla*$_{NDM}$ isolates increased from 5.4% in 2016 (n = 6) to 39.8% in 2023 (n = 99) (p<0.00001). Conversely, *bla*$_{KPC}$ decreased from 92.8% in 2016 (n = 103) to 53.0% in 2023 (n = 132) (p<0.00001) (Figure). Again comparing 2016 and 2023, we observed an increase in *bla*$_{NDM}$ among *E. coli* (1.8% to 22.8%), *Klebsiella* spp. (3.6% to 11.6%), and *E. cloacae* complex (0.6% to 5.2%) (Table). NDM-producing Enterobacterales were more resistant to β-lactam combination agents than were *K. pneumoniae* carbapenemase–producing Enterobacterales (Appendix Table).

We report a notable shift in the type of carbapenemase genes among a convenience sample of 1,288 CP-CRE collected in the United States during 2016–2023. Although *bla*$_{KPC}$ remained the most common carbapenemase gene, we observed a decrease in the proportion of *bla*$_{KPC}$ coupled with an increase in *bla*$_{NDM.}$ This shift was most striking among *E. coli*, with *bla*$_{NDM}$ representing 73% of all carbapenemase-producing *E. coli* in 2023; in contrast, we observed *bla*$_{NDM}$ among only 14.3% of carbapenemase-producing *E. coli* in 2016.

The increase of *bla*$_{NDM}$ is alarming given that NDM-producing CRE are more resistant than other CRE isolates (*7*). Furthermore, newer β-lactam combination agents, including ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam, are ineffective against MBL enzymes, and treatment options are limited (*2*,*8*). Aztreonam/avibactam and cefiderocol have demonstrated in vitro efficacy, but resistance has also been reported (*7*).

Our study is limited because it is based on a convenience sample of isolates from population-based surveillance and might be affected by sampling bias. We collected isolates from 10 EIP sites and national trends may not be extrapolated based on these data. This study is not able to determine whether there are changes in the incidence of NDM-producing CRE, however, our findings align with recent reports of rising NDM-positive CRE in New York City and among the Antimicrobial Resistance Laboratory Network (*9*,*10*). Whole-genome sequencing analysis is needed to determine gene variants and whether increases are driven by specific sequence types.

In conclusion, we report a concerning increase in *bla*$_{NDM}$ among a convenience sample of CP-CRE collected across 10 EIP sites in the United States. Further investigation is needed to assess if this is a nationwide trend, to analyze epidemiologic data comparing characteristics of patients infected with *bla*$_{NDM}$-CRE and those with *bla*$_{KPC}$, and to examine whole-genome sequencing data to determine if the observed increase is related to clonal expansion. Our findings should alert clinicians to the increase in *bla*$_{NDM}$ and encourage mechanism testing in clinical laboratories.

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This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy (e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.). Similarly, the protocol was reviewed by all participating EIP sites and either was deemed nonresearch or received institutional review board approval with a waiver of informed consent. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of CDC or the Agency for Toxic Substances and Disease Registry.

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A description of the mortality rate among cranes was unclear in Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus and Mass Mortality in Eurasian Cranes, Germany, 2025 (A. Günther). The article has been corrected online (https://wwwnc.cdc.gov/eid/article/32/5/26-0170_article).