



Letter to the Editor

One Health implications of NDM-producing bacteria expanding beyond hospital walls: Zoonanthroponotic trends requiring global action

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Dear Editor,

Carbapenem resistance is a global public health threat that has contributed to the current antibiotic crisis [1]. Clinical consequences of carbapenem resistance have been frightening, leading the World Health Organization (WHO) to classify carbapenem-resistant *Enterobacteriales* and *Acinetobacter baumannii* as critical-priority pathogens requiring urgent new antibiotic treatment options [1]. While the production of carbapenemases has been the most important mechanism underlying carbapenem resistance, the global prevalence of bacteria producing New Delhi metallo- β -lactamase (NDM) enzymes has exceeded pre-pandemic trends, expanding beyond hospital walls [2]. In fact, there have been increased reports of NDM-producing bacteria in companion animals, even though carbapenems have not been approved for veterinary use [3]. Noteworthy, close relationships between humans and companion animals have exponentially boomed over the last decades and were strengthened during the COVID-19 pandemic [4]. Therefore, it is possible that human-pet bonds could be a key point for the appearance of these WHO critical priority pathogens in companion animals by a reverse zoonotic event, also called zoonanthroponosis.

To better understand this epidemiological situation, we investigated the global distribution, genomic background, and One Health implications of NDM-producing bacteria in companion animals. In this regard, 17,086 publicly available NDM-positive bacterial genomes in the National Database of Antibiotic Resistant Organisms (<https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/>) were analyzed, of which 198 (1.1%) were obtained from strains isolated from cats and dogs. Most genomes were from *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter hormaechei* subsp. *xiangfangensis*, and *Acinetobacter* spp. strains identified from 2014 onwards in American, Asian, and European countries (Fig. 1). NDM-harboring genomes (70.7%) also carried extended-spectrum β -lactamases, such as CTX-M-type and SHV-12. Worryingly, the temporal analysis revealed an increase of 4.5-fold over the last five years, suggesting a linear trend of increasing NDM-producing bacteria in companion animals.

Unlike the prevalence of NDM-1 in human-derived strains, the NDM-

5 variant was dominant in the analyzed genomes. Besides, NDM-1, NDM-7, and NDM-9 variants were also identified, and most of them were encoded on pandemic plasmids, such as IncX3 and IncF-type. The NDM-positive genomes were chiefly from high-income countries (79.3%), reinforcing the need for more resources in genomic epidemiological surveillance of antimicrobial resistance (AMR) in low- and middle-income countries. Indeed, although the scientific literature demonstrates an increase in pet-derived bacteria carrying carbapenemases [3], most studies are PCR-based, limiting more assertive conclusions about their genomic traits (e.g., clonal relatedness) and possible transmission routes. In this regard, the current One Health priority research agenda for AMR encompasses the intersections and interdependencies between human health, animal health, and environmental health.

Remarkably, molecular typing revealed a great diversity of sequence types (STs), evidencing those closely related to humans and classified as healthcare-associated or international high-risk clones, including *E. coli* ST10, ST131, ST167, and ST410; *K. pneumoniae* ST11, ST258, and ST307; *E. hormaechei* ST114 and ST171; and *Acinetobacter baumannii* ST25 (Fig. 1). These high-risk clones have gained medical notoriety due to their successful spread and persistence in human healthcare settings worldwide, being frequently responsible for life-threatening infections and presenting genetic convergence of virulence and AMR genes [5]. The high prevalence of human-associated clones of NDM-producing bacteria in pets supports a zoonanthroponotic trend, spotlighting the versatility of these high-risk lineages to be adapted at the human-animal interface, whereas their persistence in companion animals could be extended by the selective pressure resulting from the massive use of β -lactam agents in veterinary medicine.

In summary, the rapid spread of human-associated clones of NDM-producing bacteria in companion animals constitutes a serious One Health problem and a clinical challenge for veterinary clinicians. Pet ownership is rising globally and it is estimated that more than half of the global population share their homes with one or more pets. Since cats and dogs are becoming family members and their social roles have changed, cross-transmission of high-risk clones between humans and

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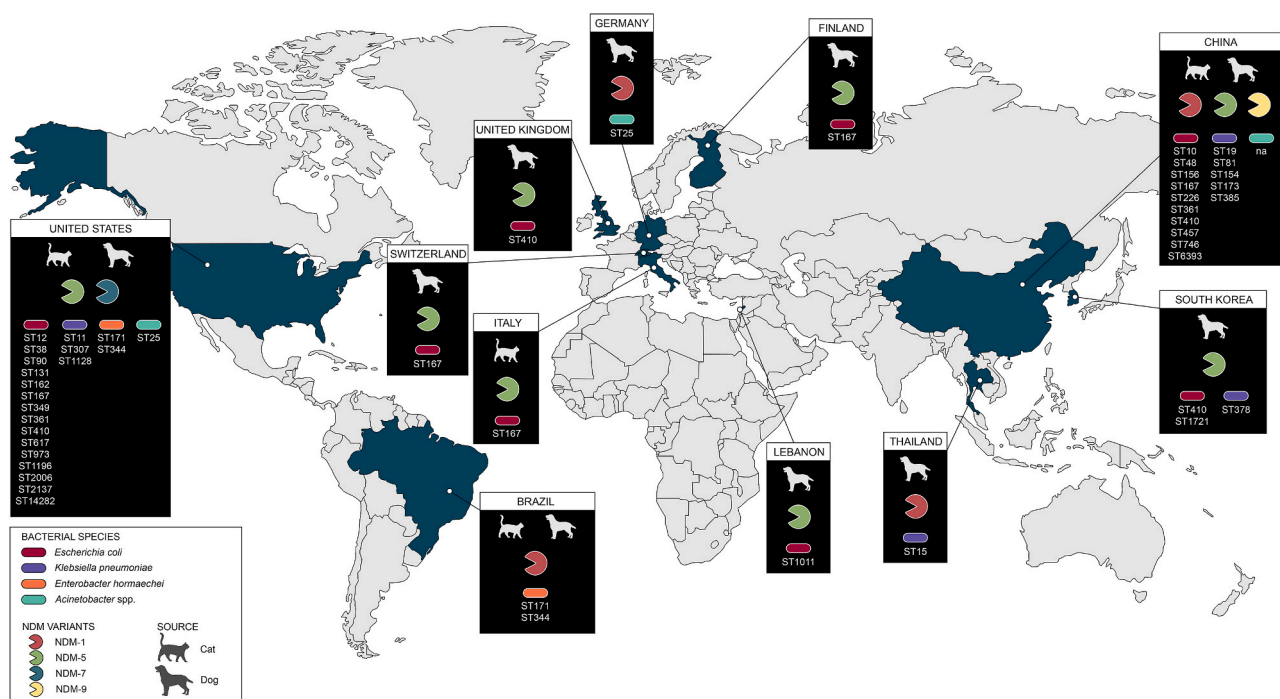


Fig. 1. Geographical distribution of NDM-harboring bacterial genomes of *Enterobacteriales* and *Acinetobacter* spp. isolated from cats and dogs.

their pets will continue to emerge. Considering that the carbapenem resistance problem has no longer hurdles and zoonoanthropotic transmission of NDM-positive bacteria to pets seems to be a global phenomenon that is silently occurring, global action for improving awareness, education, and training of physicians and veterinarians is required within the One Health agenda.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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