

# Strengthening genomic surveillance of carbapenemases in soils: a call for global attention



Antimicrobial resistance is a global health problem that no longer has borders and requires continuous surveillance under the aegis of One Health. The *Lancet Microbe* editorial highlighted the public gap in the knowledge about antimicrobial resistance.<sup>1</sup> If antimicrobial resistance is largely unknown to the general public, there is likely to be a similar gap in knowledge when discussing the role of the environment in its emergence. On Feb 7, 2023, the UN Environment Programme—the global authority for the environment with programs focusing on climate, nature, pollution, and sustainable development—published a report underlining the importance of strengthening environmental action in the One Health response to antimicrobial resistance.<sup>2</sup>

The rapid and unbridled spread of carbapenemase-producing pathogens is a concerning example of this crisis. WHO has classified carbapenemase-producing bacteria as a serious priority pathogen since these organisms cause life-threatening infections for which few treatment options are available.<sup>3</sup> Conversely, there are increasing rates of carbapenemase-producing bacteria in the environment including agricultural sectors. In this respect, the soil plays a key role in the evolutionary dynamics of antimicrobial resistance development since several environmental bacterial species have evolved in their ability to resist antibiotics long before the golden age of antibiotics.<sup>4</sup>

We systematically evaluated the global scientific literature documenting the occurrence of carbapenemase-producing strains in agricultural and non-agricultural soils. We noticed that rapid and global dissemination of clinically important carbapenemase enzymes (ie, NDM, VIM, IMP, KPC, and OXA) in Enterobacterales and non-fermenting Gram-negative bacteria has occurred in the last decade. Carbapenemases have also been identified in uncultured bacteria and species of *Paenibacillus* and *Bacillus* (appendix pp 2–3). Some studies also documented the presence of GES, a class-A  $\beta$ -lactamase, but it was not assigned as a carbapenemase due to the absence of variant analysis (appendix p 4).

To date, only four studies have described the complete sequence of single and multireplicon

plasmids housing NDM, VIM, and IMP in *Escherichia coli*, *Enterobacter cloacae*, *Citrobacter freundii*, *Citrobacter sedlakii*, and *Pseudomonas aeruginosa* strains recovered from agricultural and non-agricultural soils in China and Brazil, both of which are agricultural superpowers (appendix pp 2–3). These findings provide evidence for the dissemination of carbapenemases in clinically important pathogens and the scarce data for gene transfer in soils.

Data regarding the epidemiology of carbapenemase-producing strains in soils are even scarcer. Enterohemorrhagic *E coli* ST11 and high-risk clones of *E coli* ST354 and *P aeruginosa* ST235 are the only clones reported that carry metallo- $\beta$ -lactamases in soils. Despite scarce data, it is possible to observe the interspecies and intraspecies transmission of carbapenemase-encoding genes. Worryingly, the presence of high-risk clones of WHO critical priority pathogens in soils calls for attention, being worthy of further investigation and One Biosecurity policies.<sup>5–7</sup> Hence, the high resolution provided by whole-genome sequencing is essential for monitoring antimicrobial resistance, and being the key factor for epidemiological and genomic surveillance to determine possible routes of carbapenemase transmission to the environmental sector.

Novel carbapenemases, including B1 and B3 metallo- $\beta$ -lactamases (eg, PEDO, CPS, ESP, MSI, SPG, and THIN-B), have also been identified in uncultured microorganisms in soils and even on the chromosome of resident soil microbiome (appendix p 5). Although metagenomics provides rich data on soil resistome, the successful capture and expression of novel carbapenemases in pathogens are presumed in the example of the well-studied CTX-M extended-spectrum  $\beta$ -lactamases of *Kluyvera* species.<sup>8</sup> Therefore, functional metagenomic analysis utilising methods on the basis of selective media that enable the growth of novel carbapenem-producing strains, should be encouraged.

Over the last decades, anthropogenic activities have affected soils in many ways, modifying the soil microbial diversity and contributing to the spread and persistence of clinically relevant antimicrobial resistance

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See Online for appendix

genes in the environment. This situation worsened after the COVID-19 pandemic crisis since carbapenems have been extensively administered. Indeed, the frequency of multidrug-resistant and carbapenemase-producing strains has increased and the coexistence of carbapenemases is emerging.<sup>9,10</sup> Consequently, these strains might already be sheltered in soils, which provide ideal conditions for long-term harbouring, amplification, and dissemination to multiple sources. Furthermore, the presence of medically relevant carbapenemase-harbouring strains in soils located surrounding urban areas can accelerate their transfer to humans.

The prevalence of carbapenemases in soils remains underestimated. The absence of large-scale investigations with appropriate methodologies addressing the prevalence, risk factors, and drivers of carbapenemase-producing bacterial strains in soils represents a bottleneck to reaching assertive conclusions in this field. Accordingly, different soil sampling geographically distributed from sites unaffected and affected by anthropogenic activities are desirable for this purpose. As a matter of urgency, the scientific community and ecological authorities should pay attention to this issue and tackle the carbapenem resistance problem in soils as a new public health and ecological concern.

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