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# Wastewater Metagenomic Surveillance Predicts Community Emergence of Carbapenem-Resistant *Enterobacteriaceae* Six Weeks Prior to Clinical Isolation

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## Abstract

Antimicrobial resistance (AMR) surveillance relies on clinical cultures, introducing detection delays. We implemented a longitudinal wastewater metagenomics pipeline across three tertiary hospitals and surrounding communities, sequencing 200 samples monthly over 18 months. Bioinformatic analysis of resistance genes (ARGs) using deep learning models (AMR-Guard) predicted the emergence of carbapenem-resistant *Enterobacteriaceae* (CRE) strains six weeks before first clinical isolation in 92% of outbreak events. Plasmid-associated *bla*KPC-3 and *bla*NDM-1 genes were detected in wastewater at concentrations as low as $10^3$ copies/mL, correlating with subsequent patient colonization. Genomic epidemiology confirmed clonal transmission between wastewater isolates and clinical strains. This environmental sentinel surveillance system enables preemptive infection control interventions and represents a paradigm shift from reactive to predictive AMR management.

**Keywords:** wastewater metagenomics, antimicrobial resistance, carbapenem-resistant Enterobacteriaceae, environmental surveillance, predictive epidemiology, plasmid-mediated resistance