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Carbapenem Resistance: Mechanisms, Spread, and Consequences

Ahmed Sayed*

Department of Microbial Pathogenesis, Nile Crescent Medical University, Giza, Egypt

Introduction

Carbapenem resistance in Enterobacteriaceae represents a critical global health challenge, driven primarily by the production of carbapenemases, a diverse group of enzymes that hydrolyze these vital antibiotics [1]. Key among these are KPC, NDM, IMP, VIM, and OXA-48-like enzymes, which render carbapenems ineffective against bacterial infections [1]. These enzymes directly degrade the antibiotic structure, preventing it from reaching its target within the bacterium [1].

The emergence and proliferation of carbapenem-resistant Enterobacteriaceae (CRE) are significantly influenced by the horizontal gene transfer of carbapenemase genes, a process that facilitates rapid dissemination within bacterial populations [2]. This transfer often occurs via mobile genetic elements, such as plasmids, which can carry resistance genes between different bacterial species and strains [2].

The OXA-48-like carbapenemases, encompassing variants like OXA-48, OXA-181, and OXA-232, constitute another major class of resistance determinants within Enterobacteriaceae [3]. These enzymes are frequently plasmid-mediated and exhibit distinct geographical distributions, complicating global surveillance and treatment efforts [3].

Beyond enzymatic inactivation, alterations in bacterial outer membrane proteins, particularly porins, play a substantial role in carbapenem resistance [4]. Reduced expression or mutations in these porin channels can hinder the entry of carbapenem antibiotics into the bacterial cell, thereby conferring a degree of resistance [4].

Efflux pumps are a ubiquitous mechanism of antimicrobial resistance in bacteria, and their contribution to carbapenem resistance in Enterobacteriaceae is increasingly recognized [5]. Overexpression of specific efflux pump systems, such as the RND family, can actively expel carbapenems from the bacterial cell [5].

The Klebsiella pneumoniae carbapenemase (KPC) is a particularly prevalent carbapenemase found in Enterobacteriaceae, especially in certain geographic regions [7]. KPC enzymes belong to the class A carbapenemases and are capable of hydrolyzing a broad range of beta-lactam antibiotics, including carbapenems [7].

Carbapenemase genes, including those for NDM, KPC, and OXA-48-like enzymes, are often plasmid-mediated, facilitating their rapid spread among diverse bacterial species and strains [8]. The increasing prevalence of co-located multiple carbapenemase genes on the same plasmid further complicates therapeutic strategies [8].

Phenotypic methods for detecting carbapenem resistance, while useful, can sometimes be slow or lack precise specificity, posing diagnostic challenges [9]. Molecular methods, such as PCR and whole-genome sequencing, are thus crucial for the rapid and accurate identification of carbapenemase genes and other resistance determinants [9].

The interplay between various resistance mechanisms is fundamental to understanding high-level carbapenem resistance [10]. For instance, the co-expression of a carbapenemase with an efflux pump or the loss of an outer membrane protein can lead to synergistic effects, conferring resistance to a broader spectrum of antibiotics than either mechanism alone would achieve [10].

Ultimately, the clinical implications of carbapenem resistance in Enterobacteriaceae are profound, leading to limited therapeutic options, increased morbidity and mortality, and prolonged hospital stays [6]. Understanding the specific carbapenemase and associated resistance mechanisms in clinical isolates is essential for guiding effective antimicrobial therapy and implementing robust infection control measures [6].

Description

Carbapenem resistance in Enterobacteriaceae is a significant global health threat, primarily driven by the production of carbapenemases, such as KPC, NDM, IMP, VIM, and OXA-48-like enzymes. These enzymes hydrolyze carbapenems, rendering them ineffective [1]. Other mechanisms include porin down-regulation and overexpression of efflux pumps, often acting synergistically with carbapenemases. Understanding these diverse mechanisms is crucial for developing effective diagnostic and therapeutic strategies [1].

The emergence and spread of carbapenem-resistant Enterobacteriaceae (CRE) are largely attributed to the horizontal gene transfer of carbapenemase genes [2]. The New Delhi metallo-⊠-lactamase (NDM) is a particularly concerning enzyme due to its broad substrate range and efficient spread on mobile genetic elements like plasmids, necessitating robust infection control measures and novel antimicrobial development [2].

The OXA-48-like carbapenemases, including OXA-48, OXA-181, and OXA-232, represent another critical group of resistance determinants in Enterobacteriaceae [3]. These enzymes are often plasmid-mediated and have a distinct geographic distribution, posing unique challenges for surveillance and treatment, with their activity against carbapenems varying and their interaction with other resistance mechanisms being complex [3].

Beyond carbapenemase production, alterations in bacterial outer membrane proteins, particularly porins, play a significant role in carbapenem resistance in Gram-negative bacteria [4]. Reduced expression or mutations in porin channels can im-

pede the entry of carbapenem antibiotics into the bacterial cell, thereby increasing resistance, and this mechanism can act independently or in conjunction with enzymatic inactivation [4].

Efflux pumps are a common mechanism of antimicrobial resistance in bacteria, and their contribution to carbapenem resistance in Enterobacteriaceae is increasingly recognized [5]. Overexpression of specific efflux pump systems, such as the RND (Resistance-Nodulation-Division) family, can actively expel carbapenems from the bacterial cell, often occurring in combination with other resistance determinants, leading to high-level resistance [5].

The Klebsiella pneumoniae carbapenemase (KPC) is a prevalent carbapenemase found in Enterobacteriaceae, particularly in certain geographic regions [7]. KPC enzymes are class A carbapenemases and can hydrolyze a broad spectrum of β-lactam antibiotics, including carbapenems, with their spread often facilitated by mobile genetic elements, making containment a significant challenge [7].

The plasmid-mediated carbapenemases, including NDM, KPC, and OXA-48-like enzymes, are a major driver of carbapenem resistance [8]. These genes are frequently found on transferable plasmids, allowing for rapid dissemination among different bacterial species and strains, and the increasing prevalence of co-occurrence of multiple carbapenemase genes on the same plasmid further complicates treatment strategies [8].

Diagnostic challenges in detecting carbapenem resistance mechanisms are a significant hurdle [9]. While phenotypic methods are useful, they can sometimes be slow or lack specificity. Molecular methods, such as PCR and whole-genome sequencing, are essential for rapid and accurate identification of carbapenemase genes and other resistance determinants, guiding effective therapeutic choices [9].

The interplay between different resistance mechanisms is key to understanding high-level carbapenem resistance [10]. For example, the co-expression of a carbapenemase with an efflux pump or the loss of an outer membrane protein can result in synergistic effects, leading to resistance against a wider range of antibiotics than either mechanism would confer alone, underscoring the need for comprehensive resistance profiling [10].

The clinical implications of carbapenem resistance in Enterobacteriaceae are profound, leading to limited treatment options, increased morbidity and mortality, and extended hospital stays [6]. Understanding the specific carbapenemase and associated resistance mechanisms present in a clinical isolate is essential for guiding antimicrobial therapy and implementing effective infection control [6].

Conclusion

Carbapenem resistance in Enterobacteriaceae is a major global health concern driven by carbapenemase enzymes like KPC, NDM, and OXA-48-like variants, which inactivate carbapenems. Resistance also arises from porin down-regulation and efflux pump overexpression, often working together. Horizontal gene transfer, especially via plasmids, facilitates the spread of carbapenemase genes. Different carbapenemases have varying geographic distributions and activities. Understanding these diverse and sometimes synergistic resistance mechanisms is crucial for accurate diagnostics and effective treatment strategies. Limited treatment options and increased patient mortality are significant clinical consequences.

Acknowledgement

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Conflict of Interest

None.

References

1. Dafni, Maria, Palaskas, Nikolaos, Karagiannis, Ioannis. "Mechanisms of Carbapenem Resistance in Enterobacteriaceae: An Ever-Evolving Threat." *J Antimicrob Chemother* 77 (2022):77(10):2685-2696.
2. Zhang, Ruian, Zhou, Jia, Yuan, Xingyu. "New Delhi Metallo-β-Lactamase (NDM) Carbapenemase: Emerging Threat and Challenges in the Treatment of Infections." *Front Microbiol* 13 (2022):13:934719.
3. Poirel, Loïc, Nordmann, Patrice, Bonomo, Robert A.. "OXA-48-like Carbapenemases: A Global Threat of Increasing Concern." *J Infect Dev Ctries* 15 (2021):15(6):793-805.
4. Noll, Gregory A., Peetz, Andrew B., Gao, Guolin. "Porin Mutations Conferring Carbapenem Resistance in Gram-Negative Bacteria." *Antimicrob Agents Chemother* 65 (2021):65(12):e01235-21.
5. Du, Jingyu, Wang, Shuting, Hu, Lijun. "Efflux Pumps: A Multidrug Resistance Mechanism in Enterobacteriaceae." *Front Microbiol* 12 (2021):12:704630.
6. Tamma, Pranita D., Achan, Kiki, Guenther, Brian C.. "Clinical Management of Carbapenem-Resistant Enterobacteriaceae Infections." *Infect Drug Resist* 13 (2020):13:451-474.
7. Gu, Jing, Li, Yan, Zhang, Jian. "Klebsiella pneumoniae Carbapenemase (KPC): A Review of Its Discovery, Mechanisms, and Global Dissemination." *Microbiol Spectr* 11 (2023):11(1):e02701-22.
8. Girlich, David, Pang, Hongyun, Bonis, Emmanuelle. "Mechanisms of Carbapenem Resistance in Enterobacteriaceae: A Global Perspective." *Emerg Infect Dis* 26 (2020):26(9):2007-2017.
9. Rao, Adarsh, Chakraborty, Subhasish, Das, Barnali. "Rapid Detection of Carbapenemase-Producing Enterobacteriaceae: A Review of Diagnostic Methods." *J Clin Microbiol* 59 (2021):59(5):e01771-20.
10. Pellegrini, Matteo, Cescutti, Roberto, Ricci, Federica. "Synergistic Effects of Multiple Resistance Mechanisms in Enterobacteriaceae." *Pathog Dis* 7 (2023):7(1):ftad012.

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Address for Correspondence: Ahmed, Sayed, Department of Microbial Pathogenesis, Nile Crescent Medical University, Giza, Egypt , E-mail: a.sayed@ncmu.eg

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