



NEW ERA MEDICAL JOURNAL



Narrative Review

Carbapenem Resistance Among Gram-Negative Bacteria: Emerging Trends, Clinical Implications, and Patient Outcomes

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ABSTRACT

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DOI: 10.62502/nemj/v2i3art1

Received: 21/02/2026

Accepted: 25/08/2026

Published: 12/09/2026

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Carbapenem resistance among Gram-negative bacteria has emerged as a major global public health concern, significantly complicating the management of healthcare-associated and community-acquired infections. This narrative review aims to summarize emerging epidemiological trends, underlying resistance mechanisms, clinical implications, patient outcomes, and recent therapeutic advances related to carbapenem-resistant Gram-negative bacteria. Relevant literature published between January 2000 and October 2026 was considered from databases including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The review focused on major resistant pathogens, including *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. Key resistance mechanisms included carbapenemase production, particularly KPC, NDM, and OXA-type enzymes, reduced outer-membrane permeability, and efflux pump activity. The reviewed evidence highlights the association between carbapenem resistance, limited treatment options, delayed effective antimicrobial therapy, prolonged hospitalization, increased healthcare costs, and elevated mortality risk. Newer antimicrobial agents and combination regimens offer additional treatment options; however, their effectiveness may be limited by emerging resistance, variable susceptibility patterns, and restricted availability. The findings emphasize the importance of rapid diagnostic testing, antimicrobial susceptibility-guided treatment, antimicrobial stewardship, infection prevention and control, and coordinated surveillance. Further high-quality multicentre studies are required to clarify regional resistance patterns, evaluate emerging therapeutic strategies, and improve patient outcomes.

Keywords: Carbapenem Resistance, Gram-Negative Bacteria, Carbapenemase, Antimicrobial Resistance, Clinical Outcomes, Antimicrobial Stewardship, Infection Control.

INTRODUCTION

Carbapenem resistance among Gram-negative bacteria has emerged as a major global public health concern because of its association with limited therapeutic options, increased healthcare costs, prolonged hospitalization, and adverse clinical outcomes. Carbapenems, including imipenem, meropenem, ertapenem, and doripenem, are broad-spectrum β -lactam antibiotics frequently used to treat severe infections caused by multidrug-resistant Gram-negative pathogens. However, the increasing prevalence of carbapenem-resistant Enterobacterales (CRE), *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* has compromised the effectiveness of these agents and complicated the management of serious hospital-acquired infections.^[1-4] The emergence and dissemination of carbapenem resistance are driven by several mechanisms, including the production of carbapenem-hydrolysing enzymes, reduced outer-membrane permeability, efflux pump overexpression, and alterations in penicillin-binding proteins. Clinically important carbapenemases include *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo- β -lactamase (NDM), Verona integron-

encoded metallo- β -lactamase (VIM), imipenemase (IMP), and oxacillinase-48-like enzymes (OXA-48-like).^[5–8] The genes encoding these enzymes are frequently associated with mobile genetic elements, facilitating horizontal transmission between bacterial species and contributing to the rapid spread of resistance within healthcare settings.^[9–11] The epidemiology of carbapenem resistance varies geographically according to antimicrobial prescribing practices, infection prevention measures, diagnostic capacity, and the distribution of resistant bacterial clones. International surveillance has documented substantial differences in resistance prevalence among countries and healthcare institutions, highlighting the importance of continuous microbiological surveillance and standardized antimicrobial susceptibility testing.^[12–15] In addition, inadequate antimicrobial stewardship, prolonged hospitalization, intensive care unit admission, previous exposure to broad-spectrum antibiotics, invasive medical devices, and severe underlying illness may increase the likelihood of acquiring carbapenem-resistant infections.^[16–19]

The clinical consequences of these infections extend beyond microbiological resistance. Patients with carbapenem-resistant bloodstream infections, pneumonia, urinary tract infections, and intra-abdominal infections may experience delayed initiation of effective antimicrobial therapy, treatment failure, septic complications, and increased mortality.^[20–23] Outcomes are influenced by infection severity, comorbidities, the infecting organism, resistance mechanism, and the availability of effective antimicrobial agents. Although newer β -lactam- β -lactamase inhibitor combinations and other targeted therapies have expanded treatment options for selected pathogens, therapeutic effectiveness depends on accurate pathogen identification, susceptibility results, and appropriate clinical application.^[24–27] Furthermore, the emergence of resistance to newer agents reinforces the need for integrated strategies combining rapid diagnostics, antimicrobial stewardship, infection prevention, and coordinated surveillance.^[28–30] This narrative review examines emerging trends in carbapenem resistance among clinically important Gram-negative bacteria, the molecular mechanisms and epidemiological factors underlying its dissemination, and its association with patient outcomes. It also discusses contemporary therapeutic approaches and future priorities for reducing the clinical and public health burden of carbapenem-resistant infections.

MATERIALS and Methods

Study Design: A narrative literature review was conducted to examine epidemiological trends, molecular

mechanisms, clinical implications, treatment strategies, and patient outcomes associated with carbapenem resistance among Gram-negative bacteria. The review covered literature published between January 2000 and October 2026.

Literature Search Strategy: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar were searched using relevant keywords, including “carbapenem resistance,” “Gram-negative bacteria,” “carbapenem-resistant Enterobacterales,” “KPC,” “NDM,” “OXA-48,” “clinical outcomes,” “mortality,” and “antimicrobial therapy.” Boolean operators (AND and OR) were used to combine search terms.

Eligibility Criteria and Data Extraction: English-language original research, observational studies, clinical trials, surveillance reports, and relevant reviews were considered if they addressed resistance epidemiology, mechanisms, risk factors, treatment, or patient outcomes. Duplicate and irrelevant publications were excluded. Data on study characteristics, bacterial species, resistance determinants, antimicrobial treatment, and clinical outcomes were extracted and assessed descriptively.

Data Synthesis: Findings were organized into five themes: epidemiological trends, molecular mechanisms, clinical risk factors, patient outcomes, and emerging treatments and prevention strategies. Given the narrative design and heterogeneity of the evidence, no pooled statistical analysis or meta-analysis was performed.

Study Selection and Ethical Considerations: The literature selection process is summarized in Figure 1 using a PRISMA-style flow diagram.

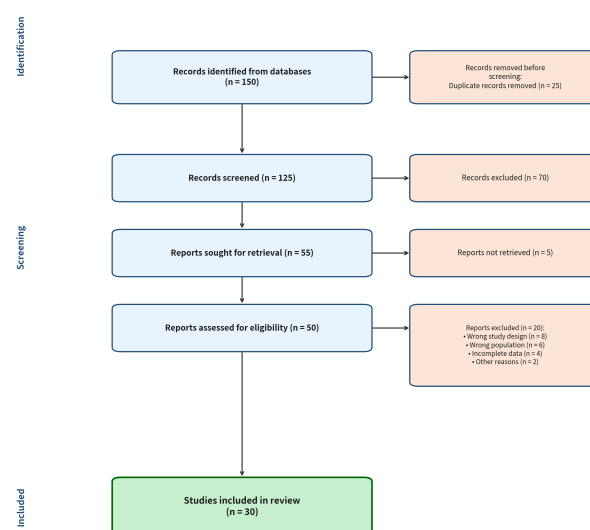


Figure 1. PRISMA-style flow diagram of literature identification, screening

As this was a review of published literature without direct participant recruitment or identifiable patient data, separate ethical approval was generally not required.

RESULT AND DISCUSSION

The literature examined in this narrative review demonstrates that carbapenem resistance among Gram-negative bacteria has evolved from a predominantly hospital-associated antimicrobial resistance problem into a major international public health challenge. The selected publications cover molecular resistance mechanisms, epidemiological dissemination, clinical risk factors, treatment strategies, and patient outcomes. Evidence from foundational studies published between 2007 and 2014 established the clinical significance of carbapenemase-producing Enterobacterales, while subsequent investigations increasingly focused on global dissemination, mobile genetic elements, treatment effectiveness, and newer antimicrobial agents. [1–17] Recent literature has expanded the evidence base through comparative clinical investigations, updated antimicrobial treatment guidance, and reviews of resistance epidemiology. Studies published in 2024–2026 also address regional resistance patterns and evolving therapeutic strategies. [18–30] However, because this is a narrative review, the findings are synthesized qualitatively rather than treated as a quantitatively exhaustive or statistically pooled dataset.

Epidemiological Trends and Dissemination of Carbapenem Resistance: The reviewed literature identifies carbapenem resistance as a heterogeneous phenomenon influenced by bacterial species, geographic location, healthcare exposure, antimicrobial selection pressure, and the distribution of resistance determinants. Early studies documented the international spread of carbapenemase-producing Enterobacterales and highlighted the emergence of KPC-producing *Klebsiella pneumoniae* as a significant cause of healthcare-associated infections. [1, 4–7] Subsequent epidemiological investigations emphasized that carbapenem resistance is not restricted to Enterobacterales. Carbapenem-resistant *A. baumannii* and *P. aeruginosa* also represent important clinical challenges, particularly in intensive care units and among patients with severe underlying illness. [11, 12, 14] These organisms differ in their intrinsic susceptibility profiles and resistance mechanisms, making species-specific surveillance and antimicrobial susceptibility testing essential. The evidence further indicates that resistance trends cannot be interpreted uniformly across regions. Differences in diagnostic capacity, antimicrobial prescribing, infection prevention practices, referral patterns, and surveillance coverage may influence reported resistance frequencies. Therefore, individual hospital studies and regional surveillance reports should be interpreted within their specific epidemiological contexts rather than assumed to represent global prevalence. [11, 12, 18, 24]

Molecular Mechanisms Underlying Carbapenem Resistance:

The reviewed studies identify carbapenemase production as a major mechanism responsible for resistance to carbapenem antibiotics. Important enzymes include KPC, NDM, VIM, IMP, and OXA-48-like β -lactamases. These enzymes differ in their biochemical properties and inhibitor susceptibility, influencing the selection of appropriate antimicrobial therapy. [2–5] KPC enzymes are class A serine carbapenemases, whereas NDM, VIM, and IMP belong to the metallo- β -lactamase group. OXA-48-like enzymes belong to class D β -lactamases. These distinctions are clinically relevant because available β -lactamase inhibitors do not have equivalent activity against all carbapenemases. [2–5, 24] Resistance may also result from the combined effects of reduced outer-membrane permeability, porin alterations, efflux pump activity, and other β -lactamases. The acquisition and dissemination of resistance genes through plasmids, transposons, and integrons contribute to the spread of resistance within and between bacterial populations. [13, 14]

Table 1. Major carbapenem-resistance mechanisms and their clinical significance

Mechanism or determinant	Principal characteristics	Clinical significance
KPC	Class A serine carbapenemase	Important in carbapenem-resistant Enterobacterales; may be susceptible to selected newer inhibitor combinations
NDM	Class B metallo- β -lactamase	Complicates treatment because conventional serine β -lactamase inhibitors do not directly inhibit NDM
VIM and IMP	Class B metallo- β -lactamases	Associated with resistance across several β -lactam agents
OXA-48-like	Class D carbapenemase	May be difficult to detect phenotypically and requires appropriate diagnostic interpretation

Porin loss and reduced permeability	Reduced antibiotic entry into bacterial cells	Can contribute to resistance, particularly in combination with β -lactamase production
Efflux pump overexpression	Increased removal of antibiotics from bacterial cells	May contribute to multidrug resistance in selected Gram-negative species
Mobile genetic elements	Transfer and dissemination of resistance determinants	Facilitate spread within bacterial populations and healthcare settings

Association Between Carbapenem Resistance and Patient Outcomes: The clinical-outcome literature consistently identifies carbapenem-resistant infections as a major therapeutic challenge. Studies of carbapenemase-producing *K. pneumoniae* bloodstream infections have investigated mortality predictors, treatment combinations, and the importance of timely administration of active antimicrobial therapy. [8–10] The adverse outcomes associated with these infections are influenced by multiple interacting factors, including the severity of infection, underlying comorbidities, source of infection, appropriateness of empirical treatment, and availability of effective definitive therapy. Consequently, observed mortality cannot be attributed exclusively to antimicrobial resistance without accounting for differences in baseline patient characteristics and illness severity. [8–10] Comparative treatment research has evaluated newer agents and alternative regimens for infections caused by resistant Enterobacterales. The ceftazidime-avibactam versus colistin comparison and the TANGO II trial contributed evidence supporting the evaluation of newer treatment options for selected carbapenem-resistant infections. [15, 16] Nevertheless, outcomes from these investigations should not automatically be generalized to all carbapenem-resistant Gram-negative organisms, particularly metallo- β -lactamase-producing strains or resistant *A. baumannii*.

Table 2. Clinical outcomes and their interpretation in carbapenem-resistant infections

Outcome domain	Findings from the literature	Interpretation
Mortality	Investigated extensively in bloodstream infections caused by	Influenced by infection severity, comorbidities,

	resistant Enterobacterales [8–10]	and treatment adequacy
Treatment failure	A major concern when empirical or definitive therapy lacks activity against the infecting isolate [10, 15, 16]	Requires interpretation alongside susceptibility results and clinical severity
Length of hospital stay	A relevant outcome in studies comparing resistant and susceptible infections	May be affected by baseline illness, complications, and discharge practices
Clinical cure	Evaluated in comparative studies of newer antimicrobial agents [15, 16]	Depends on pathogen, resistance mechanism, infection site, and treatment regimen
Microbiological eradication	Relevant to treatment evaluation and persistent infection	Must be distinguished from clinical improvement and long-term recurrence
Emergence of additional resistance	A concern during antimicrobial treatment of resistant pathogens	Supports susceptibility-guided therapy and ongoing microbiological monitoring

Therapeutic Advances and Antimicrobial Treatment Strategies: The reviewed clinical literature demonstrates a shift toward selecting antimicrobial treatment according to the organism, resistance mechanism, infection site, and susceptibility profile. Ceftazidime-avibactam and meropenem-vaborbactam have been investigated as treatment options for selected carbapenem-resistant Enterobacterales infections, particularly those involving KPC-producing organisms [15–17] Their suitability depends on the resistance determinants present and the results of antimicrobial susceptibility testing. The 2024 Infectious Diseases Society of America guidance provides a contemporary framework for treating antimicrobial-resistant Gram-negative infections, emphasizing pathogen-directed therapy and the importance of distinguishing between different resistance mechanisms. [24] Carbapenemase

identification can inform treatment selection, while conventional susceptibility testing remains essential for determining whether a particular agent is appropriate.

Table 3. Therapeutic approaches to carbapenem-resistant Gram-negative infections

Therapeutic approach	Potential role	Important consideration
Ceftazidime-avibactam	Selected KPC- and OXA-48-like-producing Enterobacterales infections	Not active against NDM and other metallo- β -lactamases by itself
Meropenem-vaborbactam	Selected KPC-producing Enterobacterales infections	Activity should be confirmed; not a universal option for all carbapenemases
Colistin-based regimens	Selected resistant infections when more suitable agents are unavailable	Toxicity and susceptibility limitations require careful consideration
Resistance-mechanism-guided treatment	Supports selection of an appropriate antimicrobial regimen	Requires reliable diagnostic testing and susceptibility interpretation
Antimicrobial stewardship	Reduces unnecessary antimicrobial exposure and supports appropriate prescribing	Must be integrated with local resistance surveillance and clinical protocols

Antimicrobial Stewardship, Surveillance, and Infection Prevention: The evidence supports combining antimicrobial stewardship with microbiological surveillance and infection prevention to limit the emergence and transmission of carbapenem resistance. Surveillance helps characterize local resistance patterns, identify emerging resistance determinants, and guide empirical treatment protocols. Infection prevention measures are particularly important in healthcare environments where vulnerable patients and invasive procedures increase opportunities for pathogen transmission. [11–14, 24] Antimicrobial stewardship complements these measures by promoting appropriate antibiotic selection, dosing, duration, and reassessment after microbiological results become available. Molecular diagnostics may improve the speed of resistance-mechanism identification, although their clinical value depends on appropriate interpretation and

integration into patient management. [13, 14, 24] Recent regional publications and surveillance-oriented studies may provide additional information on changes in resistance patterns and their economic and clinical consequences. However, differences in study design, diagnostic methods, and patient populations limit direct comparisons between countries and institutions.

The literature reviewed highlights five major findings:

1. Increasing epidemiological importance: Carbapenem resistance has become an important international concern involving Enterobacterales, *A. baumannii*, and *P. aeruginosa*.
2. Diverse resistance mechanisms: KPC, NDM, VIM, IMP, and OXA-48-like enzymes, together with permeability changes and other mechanisms, contribute to resistance.
3. Adverse clinical implications: Resistant infections are associated with substantial treatment challenges, and studies have examined their relationship with mortality and treatment failure.
4. Advances in treatment: Newer antimicrobial agents offer options for selected resistance mechanisms, but no single regimen is appropriate for every carbapenem-resistant organism.
5. Need for integrated control strategies: Surveillance, rapid diagnostics, antimicrobial stewardship, and infection prevention remain central to controlling the spread of resistance.

CONCLUSION

Carbapenem resistance among Gram-negative bacteria represents a major global clinical challenge, driven by diverse resistance mechanisms, widespread dissemination, and limited therapeutic options. Resistant infections are associated with substantial treatment difficulties and potentially adverse patient outcomes, particularly when effective antimicrobial therapy is delayed. Early resistance detection, susceptibility-guided treatment, antimicrobial stewardship, and robust infection prevention measures are essential to reduce the burden of these infections.

REFERENCES

1. Nordmann P, Naas T, Poirel L. Global spread of carbapenemase-producing Enterobacteriaceae. *Emerg Infect Dis*. 2011;17:1791–1798.
2. Queenan AM, Bush K. Carbapenemases: the versatile β -lactamases. *Clin Microbiol Rev*. 2007;20:440–458.
3. Bush K, Jacoby GA. Updated functional classification of β -lactamases. *Antimicrob Agents Chemother*. 2010;54:969–976.
4. Nordmann P, Dortet L, Poirel L. Carbapenem

- resistance in Enterobacteriaceae: here is the storm! Trends Mol Med. 2012;18:263–272.
5. Tzouvelekis LS, et al. Carbapenemases in *Klebsiella pneumoniae* and other Enterobacteriaceae. Clin Microbiol Rev. 2012;25:682–707.
 6. Schwaber MJ, Carmeli Y. Carbapenem-resistant Enterobacteriaceae: a potential threat. JAMA. 2008;300:2911–2913.
 7. Munoz-Price LS, et al. Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. Lancet Infect Dis. 2013;13:785–796.
 8. Falagas ME, et al. Deaths attributable to carbapenem-resistant Enterobacteriaceae infections. Emerg Infect Dis. 2014;20:1170–1175.
 9. Daikos GL, et al. Carbapenemase-producing *Klebsiella pneumoniae* bloodstream infections and antibiotic combination therapy. Antimicrob Agents Chemother. 2014;58:2322–2328.
 10. Tumbarello M, et al. Predictors of mortality in bloodstream infections caused by KPC-producing *Klebsiella pneumoniae*. Clin Infect Dis. 2012;55:943–950.
 11. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae. J Infect Dis. 2017;215(Suppl 1):S28–S36.
 12. van Duin D, Doi Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. Virulence. 2017;8:460–469.
 13. Partridge SR, et al. Mobile genetic elements associated with antimicrobial resistance. Clin Microbiol Rev. 2018;31:e00088-17.
 14. Bonomo RA, et al. Carbapenemase-producing organisms: a global scourge. Clin Infect Dis. 2018;66:1290–1297.
 15. van Duin D, et al. Colistin versus ceftazidime-avibactam for carbapenem-resistant Enterobacteriaceae infections. Clin Infect Dis. 2018;66:163–171.
 16. Wunderink RG, et al. Meropenem-vaborbactam versus best-available therapy: TANGO II trial. Infect Dis Ther. 2018;7:439–455.
 17. Ackley R, et al. Meropenem-vaborbactam versus ceftazidime-avibactam for carbapenem-resistant Enterobacteriaceae infections. Antimicrob Agents Chemother. 2020;64:e02313-19.
 18. Changing Epidemiology and Decreased Mortality Associated With Carbapenem-resistant Gram-negative Bacteria, 2000–2017. Clin Infect Dis. 2021.
 19. Comparison of clinical outcomes of patients infected with KPC- and NDM-producing Enterobacterales: a retrospective cohort study. Clin Microbiol Infect. 2021;27:1167.e1–1167.e8.
 20. Tamma PD, et al. IDSA guidance on the treatment of antimicrobial-resistant Gram-negative infections. Clin Infect Dis. 2024. doi:10.1093/cid/ciae403.
 21. Mortality factors and antibiotic options in carbapenem-resistant Enterobacterales bloodstream infections in a high-prevalence setting. 2024.
 22. Evaluation of ceftazidime-avibactam for carbapenemase-producing carbapenem-resistant Enterobacterales with OXA-48 and/or NDM genes.
 23. Li Q, et al. Carbapenem-resistant Gram-negative bacteria in ICUs: resistance genes, therapeutics, and prevention. Front Public Health. 2024;12:1376513. doi:10.3389/fpubh.2024.1376513.
 24. Carbapenem Resistance in India: A Systematic Review of Epidemiology, Diagnostic Strategies, and Therapeutic Approaches. BioMed Res Int. 2026. doi:10.1155/bmri/6806493.
 25. Epidemiology of carbapenem resistance and carbapenemase genes in Gram-negative clinical isolates from Egypt: a systematic review and meta-analysis. J Hosp Infect. 2026. doi:10.1016/j.jhin.2026.05.008.
 26. The changing epidemiology and long-term outcomes of patients with CRE infections. 2026.
 27. Distinct molecular epidemiology and outcomes of carbapenem-resistant Gram-negative infections in Lebanon. BMC Infect Dis. 2026.
 28. Clinical outcomes of carbapenem therapy in OXA-48-producing Enterobacterales infections: a French multicentre cohort, systematic review, and meta-analysis. 2026. doi:10.1080/22221751.2026.2671518.
 29. Mortality and cost of therapy of carbapenem-susceptible versus carbapenem-resistant Gram-negative infections among hospitalized patients in India: a multicentric surveillance (2022–2025). 2026.
 30. Karaba SM, et al. Comparative outcomes of ceftazidime-avibactam versus meropenem-vaborbactam for KPC-producing Enterobacterales infections. Antimicrob Agents Chemother. 2026. doi:10.1128/aac.01602-25.

How to cite: Kumar S. Carbapenem Resistance Among Gram-Negative Bacteria: Emerging Trends, Clinical Implications, and Patient Outcomes. New Era Medical Journal. 2026;2(3):1–6.