

Article

Antibiotic Resistance in *Pseudomonas Aeruginosa*: Resistance Mechanisms, Clinical Significance, and Current Challenges

Umrzoq Kuvondikov¹, Bazarov Khayrulla Kengashevich²

1. Department of Microbiology, Virology and Immunology, Faculty of Veterinary Diagnostics and Food Safety, Samarkand State University of Veterinary Medicine, Livestock and Biotechnology, Uzbekistan
2. Candidate of Veterinary Sciences, Associate Professor

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Abstract: *Pseudomonas aeruginosa* is an opportunistic Gram-negative bacterium associated with healthcare-associated infections and difficult-to-treat infections in vulnerable patients. Its clinical importance is driven by intrinsic resistance, the ability to acquire additional resistance determinants, multiple virulence factors, and biofilm formation. This review summarises major resistance mechanisms, including reduced outer-membrane permeability, efflux pumps, chromosomal AmpC beta-lactamase, acquired beta-lactamases, target mutations, and biofilm-associated tolerance. It also outlines the implications of carbapenem resistance, laboratory susceptibility testing, antimicrobial stewardship, and infection-prevention measures. Recent literature highlights the continuing global concern about multidrug-resistant *P. aeruginosa* and the need for local surveillance and susceptibility-guided therapy. This manuscript is a narrative review; it does not report a new clinical isolate collection or original experimental results. Therefore, no unverified local resistance percentages or patient-outcome estimates are presented.

Keywords: *Pseudomonas aeruginosa*; antimicrobial resistance; carbapenem resistance; biofilm; efflux pumps; beta-lactamases; antimicrobial susceptibility testing; infection prevention.

Introduction

Pseudomonas aeruginosa is a widely distributed environmental bacterium that can act as an opportunistic pathogen. In healthcare settings, it may cause pneumonia, bloodstream infections, urinary tract infections, surgical-site infections and wound infections, especially in patients with severe underlying disease, burns, invasive devices or prolonged hospital stays. The organism is particularly challenging because it can survive in moist environments, colonise medical equipment and persist in biofilms.

The Centers for Disease Control and Prevention identifies multidrug-resistant *P. aeruginosa* as a serious antimicrobial-resistance concern and notes that some strains are resistant to carbapenems, a class often used for severe infections. The World Health Organization's 2024 Bacterial Priority Pathogens List also underscores the public-health importance of resistant bacterial pathogens and the need to direct surveillance, prevention and research toward them [1], [2]. These international sources provide context, but their figures should not be interpreted as estimates for Uzbekistan or for a specific hospital.

The aim of this article is to summarise established mechanisms of antimicrobial resistance in *P. aeruginosa*, explain their clinical relevance, and outline evidence-based principles for diagnosis, treatment selection and infection prevention. The article is a narrative review based on published scientific literature and guidance documents. It does not claim to have conducted original sampling, laboratory experiments, molecular testing or statistical analysis. A formal systematic-review search strategy was not performed.

Materials and Methods

Intrinsic resistance and reduced permeability

The outer membrane of *P. aeruginosa* restricts the entry of several antimicrobial agents. Reduced expression or alteration of porin channels, particularly OprD, can decrease susceptibility to imipenem and contribute to carbapenem resistance. Resistance is often multifactorial: a porin change may occur alongside efflux-pump overexpression or beta-lactamase production.

Efflux pumps

Resistance-nodulation-division efflux systems, including MexAB-OprM and MexXY-OprM, can export different antimicrobial compounds from the bacterial cell. Their increased activity may contribute to reduced susceptibility to several drug classes. Efflux-pump activity should be interpreted as one component of the resistance phenotype rather than as proof of resistance to every substrate.

Beta-lactamases

P. aeruginosa naturally expresses the chromosomal AmpC beta-lactamase, whose expression may increase under particular conditions. Some isolates also acquire beta-lactamases such as extended-spectrum beta-lactamases or carbapenemases. Metallo-beta-lactamases, including VIM, IMP and NDM types, can hydrolyse many beta-lactams, including carbapenems. Detection of a resistance gene can support interpretation, but molecular findings should be considered together with validated phenotypic susceptibility results.

Mutations and acquired genetic elements

Chromosomal mutations affecting antimicrobial targets, porins and regulatory pathways can change susceptibility. Plasmids, integrons and other mobile genetic elements may carry resistance genes and facilitate their dissemination. The distribution of resistance determinants varies between regions, healthcare facilities and bacterial lineages; local surveillance is therefore essential.

Biofilm formation and persistence

Biofilms are structured microbial communities embedded in an extracellular matrix. They can develop on wounds, catheters, respiratory equipment and other surfaces. Biofilm-associated bacteria may show reduced antimicrobial susceptibility because of limited penetration, altered growth rates, physiological heterogeneity and persister subpopulations. This phenomenon is often described as tolerance and is not identical to heritable antimicrobial resistance measured by routine susceptibility tests [3], [4].

Results

Clinical significance and surveillance

P. aeruginosa can cause severe infections in intensive-care units and in patients with burns, respiratory support, urinary catheters or surgical wounds. Resistant infections may restrict treatment options and complicate clinical management. However, outcomes depend on multiple factors, including infection site, severity of illness, timeliness of effective therapy, comorbidities and local treatment resources; resistance alone should not be used to infer a specific mortality risk without appropriate data.

Surveillance data must be interpreted according to the population and setting from which they were collected. For example, CDC data for the United States reported that 8.2% of tested *P. aeruginosa* isolates in its 2024 dataset met the portal's multidrug-resistance definition, while 13.0% of tested isolates in a separate dataset were carbapenem-resistant [5], [6]. These are US surveillance figures with specific

denominators and definitions; they are not directly generalisable to Uzbekistan, other countries or individual institutions.

Laboratory diagnosis and antimicrobial susceptibility testing

Reliable diagnosis begins with appropriate specimen collection, culture and organism identification. Depending on the laboratory, identification may use conventional biochemical methods or validated automated and mass-spectrometry platforms. Antimicrobial susceptibility should be tested and interpreted using the current standards adopted by the laboratory, such as those issued by EUCAST or CLSI [7], [8]. The report should identify the guideline version used, because interpretive breakpoints and recommendations may change.[9]

When resistance patterns suggest a carbapenemase or another important mechanism, confirmatory phenotypic tests and/or molecular assays may be appropriate. Molecular tests can identify selected resistance determinants, but a negative panel does not exclude all mechanisms, and a detected gene does not replace susceptibility testing. For publication, authors should specify specimen sources, study dates, isolate inclusion criteria, sample size, laboratory methods, quality-control procedures and the denominator used for every percentage.[10][11][12]

Treatment principles and antimicrobial stewardship

Treatment should be selected by the responsible clinician according to the infection site and severity, susceptibility results, patient factors, drug availability and current local or international guidance. Newer antipseudomonal agents may be useful for selected resistant isolates, but activity is not universal and must not be assumed without susceptibility evidence. Combination therapy should not be presented as routinely superior for every infection; decisions require clinical assessment and relevant guidance.[13][14][15]

Antimicrobial stewardship supports appropriate drug choice, dose, route and duration, reassessment when microbiology results become available, and avoidance of unnecessary antimicrobial exposure. For severe infections, pharmacokinetic/pharmacodynamic principles and the minimum inhibitory concentration may inform dosing where appropriate. This article does not provide individual treatment advice or a substitute for local protocols.

Discussion

Infection prevention and future research

Prevention measures include hand hygiene, appropriate environmental cleaning and disinfection, correct sterilisation and maintenance of equipment, safe management of catheters and ventilators, and timely removal of devices that are no longer required. Healthcare facilities should monitor resistance trends and investigate possible transmission when clusters occur. In veterinary and environmental contexts, the One Health perspective is relevant because human, animal and environmental health are interconnected [3].

Research priorities include improved rapid diagnostics, surveillance of local resistance determinants, understanding of biofilm-associated persistence, and evaluation of new antimicrobials and non-antibiotic approaches such as bacteriophage-based strategies. Experimental approaches should be described as investigational unless supported by established clinical evidence.

Conclusion

Pseudomonas aeruginosa remains a clinically important opportunistic pathogen because its resistance can result from the combined effects of restricted permeability, efflux pumps, beta-lactamases, mutations, mobile genetic elements and biofilm-associated tolerance. Reliable management depends on high-quality microbiological diagnosis, susceptibility-guided therapy, responsible antimicrobial use and consistent infection-prevention practices. Local surveillance is necessary because resistance rates vary by place, population, sampling method and interpretive criteria. Further studies from clearly defined clinical or veterinary settings should report transparent methods and verifiable data before quantitative conclusions are drawn.

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