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Falling Behind In The Fight: The Persistent And Evolving Threat Of Pseudomonas Aeruginosa In Healthcare And Ecosystems

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Abstract:
Pseudomonas aeruginosa is a ubiquitous Gram-negative opportunistic pathogen associated with high morbidity and mortality in immunocompromised populations, including those with cystic fibrosis, burn wounds, and ventilator-associated pneumonia. Globally, P. aeruginosa continues to demonstrate multidrug resistance (MDR), extensively drug resistance (XDR), and pan-drug resistance (PDR), which complicates therapeutic strategies.
This literature review was conducted by systematically searching for relevant articles published in peer-reviewed journals focusing on Pseudomonas aeruginosa globally. Databases such as PubMed, Scopus, and Google Scholar were utilized to gather studies from the last three decades using the following keywords Pseudomonas aeruginosa, multidrug resistance, carbapenemase, metallo-β-lactamase, nosocomial infections, resistance genes, polymicrobial infections.
Selected articles were analysed for their findings on the epidemiology, resistance patterns, and clinical implications of P. aeruginosa infections globally and to check if the world is catching up with the evolution of this organism.
This review critically evaluates global (non-South African) literature on the prevalence, antimicrobial resistance mechanisms, and clinical impact of P. aeruginosa across clinical and environmental settings. Findings indicate an alarming rise in resistance to β-lactams, fluoroquinolones, aminoglycosides, and carbapenems—largely driven by the dissemination of resistance genes such as blaVIM, blaIMP, blaNDM, blaGES, and blaOXA. Key resistance mechanisms include metallo-β-lactamase production, porin mutations, efflux pump overexpression, and biofilm-mediated tolerance. Geographically, high resistance rates have been observed in Asia (India, China), Europe (Italy, Greece), Latin America (Brazil), and the Middle East (Iran, Saudi Arabia). Despite these findings, there is evidence that research and surveillance efforts are lagging in addressing P. aeruginosa globally, particularly in terms of coordinated monitoring, molecular epidemiology, and the development of novel antimicrobial agents.

Keywords: *Pseudomonas aeruginosa, multidrug resistance, carbapenemase, metallo-β-lactamase, nosocomial infections, resistance genes, polymicrobial infections.*

INTRODUCTION

The global healthcare landscape faces mounting pressure from the continued spread of infectious bacterial strains and the resurgence of known organisms, many of which possess mutations that enhance resistance and virulence. One of the major public health concern organisms globally is *Pseudomonas aeruginosa* (*P. aeruginosa*), a Gram-negative, rod-shaped bacterium that is aerobic but can grow under anaerobic conditions, and is capable of causing disease in plants, animals, and humans. The global concern to *P. aeruginosa* is underscored by its growing prevalence and alarming rates of antibiotic resistance, which pose substantial challenges within healthcare settings. *Pseudomonas aeruginosa* is a versatile and opportunistic pathogen recognized for its role in a variety of infections, particularly among immunocompromised individuals and patients with chronic conditions such as cystic fibrosis. Lately a study reported a shocking plastic degrading effect acquired by *P. aeruginosa* posing a threat to all plastic apparatus and consumables in the hospital settings

Understanding the global burden of common bacterial pathogens (both susceptible and resistant to antimicrobials) is essential to identify the greatest threats to public health. Reducing the burden of death due to infection is an urgent global public health priority. Previous studies have estimated the number of deaths related with drug-resistant infections and sepsis and found that infections remain a principal cause of death globally. Furthermore, *P. aeruginosa* has been identified as the most prevalent organism among cystic fibrosis patients, with

a stable yet concerning increase in prevalence with age. The emergence of multidrug-resistant *P. aeruginosa* strains has been a focal point in recent literature, particularly in hospital settings.

Studies have indicated that antibiotic resistance mechanisms, including the production of extended-spectrum beta-lactamases (ESBLs) and metallo-beta-lactamases (MBLs), are prevalent among *P. aeruginosa* isolates. Surveillance studies reported that a significant percentage of blood culture isolates exhibit resistance to multiple antibiotics, complicating treatment decisions and leading to incraesed morbidity and mortality rates. The spread of carbapenem-resistant Gram-negative bacteria (GNB) with changes in institutional epidemiology continues to evolve globally. The ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* spp.) pathogens are characterised by higher levels of resistance towards multiple classes of first line and last-resort antibiotics. Even though these pathogens are regularly isolated from clinical environments and are associated in a variety of life-threatening, hospital-associated infections; antibiotic resistant ESKAPE strains have been isolated from surface water, wastewater, food, and soil. These bacteria are generally isolated from clinical settings and linked to a number of possibly fatal diseases associated with hospitals. A virulent bacteriophage (PAP1) highly specific to *P. aeruginosa* was isolated from hospital sewage using a lambda bacteriophage isolation protocol. Several studies have reported the prevalence of *P. aeruginosa* in South Africa, highlighting its presence in both clinical and environmental settings.

Recent studies have highlighted the growing environmental prevalence of *Pseudomonas aeruginosa*, including a reported 7.14% occurrence in freshwater sources in South Africa's Eastern Cape Province, accompanied by alarming resistance rates to commonly used antibiotics such as penicillin and clindamycin. The ongoing floods in various parts of the world including the Eastern Cape pose an additional public health threat, potentially accelerating the spread of water-borne pathogens. These environmental shifts, coupled with infrastructure challenges, may contribute to increased hospital and community-acquired infections, including outbreaks of multidrug-resistant *P. aeruginosa*.
This literature review aims to synthesize the current global understanding of *P. aeruginosa* by examining its epidemiology, environmental persistence, antimicrobial resistance mechanisms, and its emerging plastic-degrading capacity linked to PaP1-encoded enzymes. Additionally, this review explores the broader implications of extreme weather events such as floods in promoting the emergence and dissemination of water-borne pathogens. These include not only *P. aeruginosa*, but also enterohemorrhagic *Escherichia coli* (E. coli O157:H7), *Cryptosporidium*, hepatitis viruses (including hepatitis E), *Campylobacter jejuni*, *Yersinia enterocolitica*, *Legionella pneumophila*, *Mycobacterium* spp., and other opportunistic and chlorine-resistant organisms.
In the South African context, the rise of multidrug-resistant *P. aeruginosa* strains is particularly concerning given its implications for infection control, mortality, and healthcare infrastructure. This review therefore seeks to critically evaluate emerging data on the pathogen's resistance mechanisms especially carbapenem resistance and to assess whether global efforts are keeping pace with the evolving threat posed by this versatile and persistent organism

The recent identification of plastic-degrading enzymes in *P. aeruginosa* raises new concerns for healthcare and industrial environments that rely heavily on polymer-based materials for applications such as tissue reconstruction, drug delivery systems, and medical device production. Clinically, *P. aeruginosa* is a well-established opportunistic pathogen, particularly in burn and wound infections. These infections are often polymicrobial and are increasingly complicated by the presence of multidrug-resistant organisms. The convergence of antimicrobial resistance and environmental adaptability in *P. aeruginosa* underscores the pathogen's growing threat, where even minor lesions may escalate into severe, life-threatening conditions

This literature review aims to critically examine the global health threat posed by the notorious opportunistic pathogen *Pseudomonas aeruginosa*, with a focus on its association with antimicrobial resistance, environmental persistence, polymicrobial co-infections, and the emerging plastic-degrading capabilities linked to PaP1-encoded enzymes

METHOD

This literature review was conducted by systematically searching for relevant articles published in peer-reviewed journals focusing on *Pseudomonas aeruginosa* globally and in sub-Saharan Africa including South Africa. Databases such as PubMed, Scopus, and Google Scholar were utilized to gather studies from the last three decades. Keywords included *Pseudomonas aeruginosa*, South Africa, antibiotic resistance, and cystic fibrosis. Selected articles were analysed for their findings on the epidemiology, resistance patterns, and clinical implications of *P. aeruginosa* infections globally and measure how the sub-Saharan countries are catching up with the evolution of this organism.

LITERATURE REVIEW

The emergence of multidrug-resistant *P. aeruginosa* strains has been a focal point globally, particularly in hospital settings. Studies have indicated that antibiotic resistance mechanisms, including the production of extended-spectrum beta-lactamases (ESBLs) and metallo-beta-lactamases (MBLs), are prevalent among isolates. In the early 19970s bioinformatics analysis was used to complete the transferable antibiotic resistance strain of *Haemophilus influenzae* and others. This analysis resulted in the discovery of well-characterized structures: SPI-7, associated with in *Salmonella enterica* serovar Typhi; and *P. aeruginosa* was found to possess PAP1 or pKLC102 and the selective the clc element, was found in *Pseudomonas sp. strain B13*. Mohd-Zain *et al.,* (2004) reported that this was the first report on diverse family of related syntenic genomic islands with a deep evolutionary origin (Mohd-Zain *et al.,* (2004).

In understanding the new *P. aeruginosa* myovirus named PaP1, Liu and colleagues went to characterise this enzyme and found it to possess an icosahedral head with an apex diameter of 68-70 nm and a contractile tail with a length of 138-140 nm (Liu *et al.* 2014). The PaP1 genome, consist of 157 open frames, 1190 bp terminal residues and comparatively its genomic analysis indicated that its share great similarity with JG004, PAK_P1 and vB_PaeM_C2-10_Ab1 (Lu *et al.*, 2013). Besides their similar biological characteristics, PaPI has distinguishing 123 core genes that are very close phylogenetically and that led to the discovery of four phages classified as PaP1-like phages, naming Myoviridae new genus that infects *P. aeruginosa* (Lu *et al.,* 213). In addressing some of the missing facts Lu et ai., (2014) went to further sequence the gemone of PaP1 and they successfully found the length to be 91,715 bp (Lu *at al.,* 2014). Through this discovery it was first time clearer as to how *P. aeruginosa* phage PaP1 is responsible for the failure of shotgun sequencing and for bacterial immunity mediated by enzyme Endo V activity (Lu *et al.,* 2014)

Studies have reported that strand displacement DNA synthesis is essential for DNA replication in *P. aeruginosa* (Mi *et al.,* 2020). Gp90, the sole DNA polymerase of *Pseudomonas aeruginosa* phage 1, was found to bypass multiply DNA lesions (Mi *et al.,* 2020). This discovery contributed to the body of knowledge because gp90 exo˙ was found to perform strand displacement DNA synthesis at DNA fork, this was a breakthrough in the understanding new functions of PaP1 DNA polymerase in DNA replication and propagation of PaP1 (Mi *et al.,* 2020)
Further understanding how resistance of *P. aeruginosa* originates, O^6-Methylguanine (O^6-MeG) was found highly mutagenic and is commonly found in DNA exposed to methylating agents, generally affaecting the G:C to A: T mutagenesis (Gu *et al.,* 2017). Gu et al., 2017 analysed the stady-state and pre-state kinetics of nucleotide incorporation opposite O^6-MeG by gp90 exo˙. The study found that the pre-steady-state incorporation efficiency ($k_{pol}/K_{d,dNTP}$) is decreased in the order of dCTP:G>dTTP:O^6-MeG>dCTP:O^6-MeG. Of which the presence of O^6-MeG at template was reported to have no influence on the binding affinity of polymerase to DNA but it weakened their binding in the presence of dCTP and Mg^{2+}. This study contributed to mechanism understanding by reviling that gp90 bypasses O^6-MeG in an error-prone manner and provides further understanding in DNA replication encountering mutagenic alkylation DNA damage for *P. aeruginosa* phage PaP1(Gu et al., 2017). In another study to understand the role of Gp90 exo˙ upon encountering abasic site, this is the side where severe blockage of DNA replication occurs and is highly mutagenic. In this study Gp90 exo was used as the sole DNA polymerase from *Pseudomonas aeruginos*a phage PaP1, Gp90 exo˙ was found to incorporate dNTPs opposite the abasic site (Liu *et al.,* 2018). Liu et al. (2018) reported that the presence of an abasic site in the DNA template reduces the binding

affinity of Gp90 exo⁻ to DNA in both binary and ternary complexes, even in the presence of individual dNTPs. Their findings demonstrate that Gp90 exo⁻ preferentially incorporates adenine opposite the abasic site, consistent with the A-rule observed in other DNA polymerases such as Pol θ, KlenTaq, KF exo⁻, Pol α, Pol δ/PCNA, and *Thermococcus litoralis* Pol Vent (exo⁻). This study provides new insights into DNA replication processes mediated by *Pseudomonas aeruginosa* phage PaP1 when encountering abasic site lesions.

The studies of Gp90 exo⁻, a DNA polymerase encoded by *Pseudomonas aeruginosa* phage PaP1, offers valuable insights into phage replication dynamics in the context of host-induced DNA damage. As *P. aeruginosa* frequently inhabits stress-prone environments such as those with oxidative agents or antibiotic pressure the accumulation of DNA lesions, including abasic sites, poses a significant challenge to both host and phage genome replication. Gp90 exo⁻ has been shown to bypass such lesions by preferentially inserting adenine opposite abasic sites, following the well-characterized A-rule of translesion DNA synthesis. This lesion tolerance mechanism mirrors that of several cellular polymerases and highlights a strategic adaptation of phages to replicate efficiently in damaged host cells. Understanding the function and fidelity of Gp90 exo⁻ not only deepens knowledge of phage host interactions but also holds translational potential for the development of phage-based therapies against multidrug-resistant *P. aeruginosa*, and may inform the engineering of novel polymerases for biotechnological applications (Yang *et al.,* 2018)

More than two decades ago, Le *et al.*, (2013) investigated the bacteriophage infection recognition and binding to the host receptor, which is mediated by the phage receptor binding protein (RBP) (Le *et al.*, 2013). It was empirical for scientist to understand how the different RBPs can lead to differential host specificity. Le and colleagues discovered that the tail fiber-dependent host specificity in *P. aeruginosa* phages PaP1 and JG004 share high DNA sequence homology but exhibit different host specificities (Le *et al.*, 2013). A possible breakthrough in the phage therapy due to the discovery of a spontaneous mutant phage that exhibited broader host range compared with the parental phage JG004. This study showed that the replacement of the tail fiber gene (ORF69) of PaP1 with the corresponding gene from phage JG004 would results in a recombinant phage that displayed altered host specificity thereby possibly by rendering treatment (Le *et al.,* 2013).

Post the breakthrough discovery by Le *et al.,* (2013), the *P. aeruginosa* was reportedly found to have develop a broad range of phage resistance mechanisms, such as prevention of phage adsorption and CRISPR/Cas system, to survive phage predation. Le *et al.*, (2014) demonstrated that this novel phage resistance mechanism was due to chromosomal DNA deletion called Red mutant PA1r with 219.6 kb genomic fragment deletion (Le *et al.,* 2014). Other researcher developed interest to bacteriophage-host interactions promising therapeutic potential of bacteriophages. This route seemed perfect because discovery of any new knowledge about the host pathways inhibited by phage could afford clues to novel drug targets. The results of the study done by Zhao et al., (2017) and colleagues detailed description of phage-directed metabolism in *P. aeruginosa*. This study demonstrated that phage-encoded auxiliary metabolic genes and phage-directed host gene expression have potential to effect the metabolic changes observed in the host (Zhao *et al.*, 2017). In another study this virulent phage (PaP1) was isolated from hospital sewage based on a lambda phage isolation protocol. Yue *et al.*, (2017) confirmed that this phage had a high specific binding ability to *P. aeruginosa*. In this study they used a novel electrochemiluminescent (ECL) biosensor as a recognition agent, developed for label-free detection of *P. aeruginosa* (Yue *et al.*, 2017). Through this biosensor it was possible to quantitate *P. aeruginosa* in milk, glucose injection and human urine with acceptable recovery values ranging from 78.6% to 114.3% (Yue *et al.*, 2017). He *et al.,* (2017) formed bust of the collaborative effort to study this virulent bacteriophage highly specific to *P. aeruginosa* isolated from hospital sewage using a lambda bacteriophage isolation protocol. In this study the bacteriophage was used to functionalize tosyl-activated magnetic beads to establish a bacteriophage-affinity strategy for separation and detection of viable *P. aeruginosa* (He *et al.,* 2017). In this process recognition of the target bacteria by tail fibers and baseplate of the bacteriophage led to capture of *P. aeruginosa* onto the magnetic beads (He *et al.,* 2016). This study showed that interference from inactivated *P. aeruginosa* was excluded because the bacteriophage could replicate only in viable cells (He *et al.,* 2016). This proposed bacteriophage-affinity strategy led to detection of *P. aeruginosa* in glucose injection, human urine, and rat plasma (He *et al.*, 217). These studies on DNA polymerase encoded by PaP1

helped advancement of our knowledge on phage-encoded DNA polymerases and elucidate PaP1 propagation in infected *P. aeruginosa* (Liu *et al.,* 2016).

Despite concerted global efforts to detect and control *Pseudomonas aeruginosa*, the persistent spread of antibiotic-resistant bacteria—particularly within polymicrobial infections—continues to pose a significant threat to global morbidity and mortality. In response to growing concerns, the World Health Organization (WHO), at the request of its member states, developed a priority list in 2016 to guide research and development efforts targeting antibiotic-resistant pathogens. Using a preference-based survey and expert weighting of key criteria, the WHO classified 25 bacterial species, highlighting three as critical priority pathogens: carbapenem-resistant *Acinetobacter baumannii*, carbapenem-resistant *P. aeruginosa*, and carbapenem- and third-generation cephalosporin-resistant *Enterobacteriaceae* (Tacconelli et al., 2018).This global initiative aimed to curb infection-related mortality and emphasized antimicrobial resistance (AMR) as an urgent public health priority. The Global Burden of Disease (GBD) 2019 study on antimicrobial resistance estimated mortality associated with 33 bacterial pathogens across 11 major infectious syndromes, underscoring the scale of the AMR crisis (GBD 2019 Antimicrobial Resistance Collaborators, 2022). Effective strategies to reduce this burden must include strengthened infection prevention, prudent antibiotic stewardship, enhanced microbiological diagnostic capacity, accelerated vaccine development, and broader implementation of existing vaccines. Notably, the inclusion of *P. aeruginosa* among the WHO's critical priority pathogens reaffirms its long-standing role as a key contributor to global morbidity and mortality.

Polymicrobial and antibiotic-resistant skin and burn infections remain a major clinical concern. Heselpoth *et al.* (2022) reported that PaP1, a modified cationic peptide derived from the lysin PlyPa01, exhibits potent bactericidal activity against ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* spp) pathogens in both planktonic and biofilm states. The peptide is stable across a wide range of conditions, non-toxic to human cells, and enhances the effectiveness of topical antibiotics in vivo. These findings highlight PaP1's potential as a topical therapeutic for resistant polymicrobial infections (Heselpoth *et al.* (2022).
Carbapenem-resistant Gram-negative bacteria (GNB) are rapidly spreading globally, primarily due to mobile genetic elements such as plasmids carrying carbapenemase genes. *Klebsiella pneumoniae* is the most common carbapenemase-producing Enterobacterales and a major cause of high-mortality hospital-associated infections. Carbapenem exposure significantly increases the risk of acquiring resistant *Acinetobacter baumannii*, while *Pseudomonas aeruginosa* resistance is associated with excess mortality. Colonization with carbapenemase-producing strains also elevates the risk of bloodstream infections. The growing prevalence of carbapenem-resistant GNB complicates treatment and underscores the urgent need for effective antimicrobial stewardship and infection control measures (Brink et al., 2019). *P. aeruginosa* is a major cause of antibiotic-resistant, healthcare-associated infections. Analysis of 413 invasive isolates from 10 countries revealed that vaccines targeting the 10 most common O-antigen serotypes and flagellins FlaB and FlaA2 could protect against over 80% of cases. Notably, 27% of isolates were multidrug-resistant, with FlaA2 types more commonly associated with resistance. These findings support vaccine development as a viable strategy for prevention (Nasrin *et al.,* 2022)

Denissen *et al*., (2022) embarked on a study the environmental prevalence of the ESKAPE pathogens organisms they continue to exhibit multidrug resistance and cause severe hospital-associated infections. While commonly found in clinical settings, antibiotic-resistant ESKAPE strains are also present in environmental reservoirs such as water, soil, and food. This review highlights the environmental persistence of ESKAPE pathogens, their resistance profiles, and their potential role in community-acquired infections, emphasizing the need for further health-risk assessments related to environmental exposure (Denissen *et al*.,2022). In another study Okafor et al. (2023) characterized multidrug-resistant *Pseudomonas aeruginosa* isolates from hospital wastewater over six months. Out of 81 isolates (2.4×10^5 to 6.5×10^5 CFU/mL), susceptibility was highest for imipenem (93%) and tobramycin (85%), while resistance was notable against amikacin and ceftazidime (Okafor *et al.*, 2023). Multidrug resistance was observed in 75% of isolates, with Multiple Antibiotic Resistance Index (MARI) values between 0.3 and 0.9 (Okafor *et al.*, 2023). Molecular analysis identified diverse β-lactamase and carbapenemase genes,

including blaIMP, blaKPC, and blaOXA-48, alongside aminoglycoside and quinolone resistance determinants (Okafor *et al.*, 2023). These findings reveal hospital wastewater as a significant reservoir of multidrug-resistant *P. aeruginosa*, underscoring its role in environmental dissemination and public health risk (Okafor *et al.*, 2023).

ANALYSIS

A synthesis of studies conducted globally reveals a concerning increase in the prevalence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and even pan-drug-resistant (PDR) *Pseudomonas aeruginosa* isolates. The major antimicrobial classes affected include carbapenems, aminoglycosides, cephalosporins, and fluoroquinolones are cornerstones of antipseudomonal therapy.

The most commonly detected resistance determinants include carbapenemase-encoding genes such as:

- bla_VIM, bla_IMP, bla_NDM (metallo-β-lactamases)
- bla_OXA-type, bla_GES, and bla_KPC (class D and A β-lactamases)
- bla_SHV, bla_TEM, and bla_CTX-M (ESBLs)

Notably, the dissemination of resistance genes occurs via mobile genetic elements (integrons, plasmids, transposons), suggesting environmental persistence and transfer to other pathogens. Efflux pumps (e.g., MexAB-OprM), outer membrane protein modifications (e.g., OprD loss), and hyperproduction of AmpC β-lactamases contribute synergistically to resistance. Environmental studies in Asia and Europe confirmed *P. aeruginosa* presence in hospital wastewater, municipal sewage, agricultural runoff, and aquatic ecosystems. Many isolates from these sources harbor the same resistance genes observed in clinical strains, indicating potential environmental reservoirs.

Molecular epidemiology shows increasing spread of international high-risk clones, such as:

- ST235 (widespread in Asia and Europe) (Zhai *et al.*,2025)
- ST111, ST175, and ST233 (frequently reported in hospital outbreaks) (Zhai *et al.*,2025)
- ST308 and ST244, often associated with MDR and carbapenemase genes

Whole-genome sequencing and multilocus sequence typing (MLST) confirm these clones' association with virulence factors such as *exoS*, *exoU*, *toxA*, and quorum sensing networks, reinforcing their persistence and pathogenicity.

Discussion

The global trajectory of *P. aeruginosa* resistance represents a pressing public health challenge. Despite substantial surveillance in Europe, North America, and Asia, there remains limited integration between clinical and environmental data, a critical gap given the demonstrated role of water systems and effluents in resistance gene proliferation.

Therapeutic limitations are evident. Although newer agents such as ceftolozane-tazobactam and cefiderocol show promise, resistance to these agents is already emerging in the world, especially among ST235 and ST308 clones. The continued reliance on polymyxins (e.g., colistin) is problematic due to nephrotoxicity and rising resistance mediated by mgrB, pmrA/B, or mcr genes, especially in Asia.

The polymicrobial nature of *P. aeruginosa* infections—particularly with *Candida albicans* in cystic fibrosis lungs, wounds, and immunocompromised hosts—further complicates treatment. These interactions modulate host immunity, enhance biofilm resilience, and modify eicosanoid signaling, reducing the effectiveness of standard antimicrobial therapy.

The geospatial spread of resistant *P. aeruginosa* has been exacerbated by:

- Hospital effluents and untreated wastewater
- Agricultural antibiotic use
- Medical tourism and international patient transfers

This reflects an urgent need for One Health approaches that integrate human, animal, and environmental health systems.

CONCLUSION AND RECOMMENDATIONS

The global burden of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Pseudomonas aeruginosa* continues to escalate, with widespread reports of high-risk clones (e.g., ST235, ST111, ST233) and the detection of multiple resistance determinants, including *bla_VIM*, *bla_IMP*, *bla_NDM*, and *bla_GES*. Resistance to carbapenems, cephalosporins, aminoglycosides, and even last-resort agents such as polymyxins is increasingly reported, highlighting the pathogen's adaptability and the limitations of current treatment options (Yoon *et al.*, 2021).

Environmental reservoirs including hospital effluent, surface waters, and wastewater systems are critical in the dissemination of resistant genes, often harboring *P. aeruginosa* strains with identical resistance and virulence profiles to clinical isolates. This underscores the necessity of a One Health approach integrating human, environmental, and animal health in surveillance and mitigation strategies.

Importantly, recent studies have reported the discovery of *P. aeruginosa* clinical isolates capable of degrading plastic through the expression of plastic degrading enzymes, particularly under biofilm-forming conditions. While this presents a promising frontier in bioremediation research, it also poses dual-use concerns. These strains may survive and persist in plastic rich environments such as hospital waste, contributing not only to pollution control but also to the environmental persistence of MDR organisms.

Strategic Recommendations

1. Strengthen genomic surveillance globally: expand the routine use of whole genome sequencing and mlst to track the evolution and transmission of high-risk *p. aeruginosa* clones across continents, especially in underrepresented regions.
2. Target environmental reservoirs: implement stricter regulations for effluent treatment from healthcare and industrial settings. monitor environmental *p. aeruginosa* for both resistance genes and virulence factors.
3. Integrate Bioremediation Research: Investigate the therapeutic and ecological potential of plastic-degrading *Pseudomonas* strains, while carefully evaluating their safety, resistance potential, and biofilm behavior in clinical settings.
4. Advance drug discovery and alternative therapies: accelerate the development of novel antipseudomonal agents, bacteriophage therapies, anti-virulence strategies, and vaccines targeting common resistance and virulence determinants.
5. Enforce Antibiotic Stewardship: Standardize antibiotic use protocols globally, particularly in high-burden regions, to slow resistance development and preserve the efficacy of current treatments.
6. Enhance One Health Collaboration: Foster interdisciplinary research and international policy coordination to address human, environmental, and zoonotic pathways of *P. aeruginosa* resistance transmission.

This integrated framework with combining environmental surveillance, novel therapeutic development, and emerging microbiological insights such as plastic-degrading capabilities will be vital to curbing the growing global threat posed by *P. aeruginosa*. Without decisive action, we risk entering an era where this adaptable pathogen becomes untreatable, both in hospitals and in the environment.

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