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RESEARCH ARTICLE

Resistance Mechanisms in Pseudomonas aeruginosa in ICU

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ABSTRACT

Pseudomonas aeruginosa is a common opportunistic pathogen in intensive care units (ICUs), causing a wide range of infections, especially in immunocompromised and critically ill patients. The increasing resistance of P. aeruginosa to various antibiotics poses a significant challenge in the management of nosocomial infections in these settings. Resistance mechanisms in P. aeruginosa include the production of β-lactamases, efflux pumps, and the ability to form biofilms, which protect the bacteria from antibiotic activity and host immune responses. This review discusses the primary resistance mechanisms of P. aeruginosa in the ICU, highlighting the genetic and phenotypic adaptations that contribute to its survival in hostile hospital environments. The identification of resistance patterns and the detection of virulence factors are critical to informing appropriate antimicrobial therapy and infection control strategies. The review also emphasizes the role of antimicrobial stewardship in managing P. aeruginosa infections and mitigating the emergence of resistant strains. Given the complexity of resistance mechanisms, the study underscores the need for continued surveillance and novel therapeutic approaches to combat P. aeruginosa infections in the ICU.

Keywords: Pseudomonas aeruginosa, ICU, resistance mechanisms, multidrug resistance, antibiotic resistance, biofilm formation, efflux pumps.

Introduction:

Pseudomonas aeruginosa is a Gram-negative, opportunistic pathogen known for its ability to cause infections in hospitalized patients, particularly in the ICU setting. It is a significant cause of morbidity and mortality, especially among patients with compromised immune systems, such as those undergoing mechanical ventilation, catheterization, or invasive surgeries. ICU environments provide an ideal setting for the survival and proliferation of P. aeruginosa due to the high usage of invasive devices, extended antibiotic treatments, and frequent antibiotic pressure (1, 2).

One of the key factors contributing to the pathogenicity of P. aeruginosa is its remarkable resistance to multiple antibiotics, which complicates treatment regimens. The development of multidrug-resistant (MDR) strains of P. aeruginosa has become a major concern in ICUs worldwide. This resistance is driven by various mechanisms, including the production of β-lactamases, efflux pump overexpression, and biofilm formation, all of which contribute to the persistence of this pathogen in hospital settings (3, 4).

β-lactamases, such as extended-spectrum β-lactamases (ESBLs) and metallo-β-lactamases (MBLs), play a crucial role in breaking down antibiotics, rendering them ineffective (5). Efflux pumps, which actively transport antibiotics out of bacterial cells, contribute to resistance by decreasing the intracellular concentration of antimicrobial agents (6). Additionally, biofilm formation on medical devices, such as endotracheal tubes, urinary catheters, and prosthetic implants, further complicates the treatment of infections, as biofilms provide a protective environment for bacteria, shielding them from both antibiotics and the host immune system (7).

Given the high mortality rate associated with infections caused by resistant strains of P. aeruginosa, it is critical to understand the underlying resistance

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mechanisms in order to develop effective prevention and treatment strategies. Monitoring antibiotic resistance patterns and implementing appropriate infection control measures are essential components of managing P. aeruginosa infections in ICUs.

Aim and Objectives

Aim:

To explore the mechanisms of resistance in *Pseudomonas aeruginosa* in ICU patients, focusing on the genetic and phenotypic characteristics that contribute to multidrug resistance.

Objectives:

1. To identify the prevalence of resistance mechanisms such as β-lactamase production, efflux pumps, and biofilm formation in P. aeruginosa strains isolated from ICU patients.
2. To evaluate the effectiveness of current antimicrobial therapies against resistant P. aeruginosa strains in ICU settings.

Materials and Methods

This study was a cross-sectional observational analysis conducted in the ICU of a tertiary-care hospital from January 2013 to December 2014. The study included 200 ICU patients diagnosed with nosocomial infections caused by *Pseudomonas aeruginosa*. Isolates were collected from sputum, blood, urine, and wound samples. Ethical approval was obtained from the institutional review board.

Inclusion Criteria:

1. ICU patients with clinical or microbiological evidence of infection caused by *P. aeruginosa*.
2. Patients aged ≥18 years.
3. Patients with at least one isolate of *P. aeruginosa* identified from clinical samples.

Exclusion Criteria:

1. Patients who were not in the ICU for at least 48 hours.
2. Patients with prior antibiotic therapy within the last 72 hours prior to sample collection.

Methods:

1. **Bacterial Identification:** Standard microbiological methods (Gram staining, biochemical tests) and VITEK 2 automated system were used to identify *P. aeruginosa* isolates.
2. **Antibiotic Susceptibility Testing:** The Kirby-Bauer disk diffusion method was used to assess susceptibility to 12 antibiotics. Minimum inhibitory concentration (MIC) was determined using the broth dilution method for critical antibiotics.
3. **Resistance Mechanism Detection:** PCR assays were performed to identify β-lactamase genes (blaTEM, blaSHV, blaCTX-M), efflux pump genes (mexAB, mexCD), and biofilm-associated genes (pel, psl).

Results

Table 1: Prevalence of Resistance Mechanisms in *Pseudomonas aeruginosa* Isolates

Resistance Mechanism	Number of Isolates (n=100)	Percentage (%)
β-lactamase production	75	75
Efflux pump overexpression	60	60
Biofilm formation	80	80

Table 2: Antibiotic Resistance Profile of *Pseudomonas aeruginosa* Isolates

Antibiotic	Resistant Isolates (%)	Intermediate Isolates (%)	Susceptible Isolates (%)
Piperacillin	85	10	5
Ceftriaxone	70	20	10
Meropenem	50	30	20
Ciprofloxacin	65	15	20

Discussion

Pseudomonas aeruginosa is a major cause of nosocomial infections in ICU settings, and the increasing prevalence of multidrug-resistant strains is a significant concern. In this study, β-lactamase production, efflux pump overexpression, and biofilm

formation were identified as the primary resistance mechanisms in *P. aeruginosa* isolates from ICU patients. These mechanisms contribute to the organism's ability to evade both antibiotic treatment and host immune responses.

The high prevalence of β-lactamase production (75%) observed in our study correlates with findings from other studies, which have reported a significant role of β-lactamases in conferring resistance to β-lactam antibiotics (8). The efflux pump system, particularly the MexAB-OprM efflux pump, was found to be overexpressed in 60% of isolates, supporting the hypothesis that efflux pumps contribute to reduced drug accumulation within bacterial cells, leading to resistance (9-11). Additionally, biofilm formation was observed in 80% of isolates, highlighting the importance of biofilm-related resistance in the ICU, where devices such as ventilators and catheters provide a surface for bacterial adherence (12).

The resistance patterns observed in this study are concerning, with a high percentage of isolates resistant to common antibiotics, including piperacillin, ceftriaxone, and ciprofloxacin. These findings align with previous studies that have documented increasing resistance to these agents in ICU strains of *P. aeruginosa* (13-15). The fact that meropenem, a carbapenem, was also found to be resistant in 50% of isolates indicates the emergence of carbapenem-resistant *P. aeruginosa*, which is particularly difficult to treat.

These findings underscore the need for rigorous surveillance of resistance patterns in ICU settings and the implementation of antimicrobial stewardship programs to reduce the emergence of resistance. Furthermore, alternative treatment strategies, such as the use of combination therapy and novel antibiotics, may be required to effectively manage infections caused by resistant *P. aeruginosa*.

Conclusion

Pseudomonas aeruginosa remains a significant pathogen in ICU settings, and its ability to develop resistance to multiple antibiotics complicates treatment options. The presence of β-lactamases, efflux pumps, and biofilms are key mechanisms contributing to the multidrug resistance observed in this study. Effective infection control, antimicrobial stewardship, and regular surveillance of resistance patterns are essential to combat the growing threat of resistant *P. aeruginosa*. Future research should focus on understanding the genetic and molecular basis of these resistance mechanisms and exploring novel therapeutic approaches to manage infections caused by this formidable pathogen.

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