Pseudomonas aeruginosa Infections among Patients and Healthcare Workers

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Abstract

Pseudomonas aeruginosa is rod-shaped, an aerobic, gram-negative, and opportunistic bacterium that doesn't make spores. It can cause various infections in immunocompetent and immunocompromised individuals, including surgical sites, urinary tract, pneumonia, burns, soft tissues, and otitis externa. Furthermore, it possesses variable virulence factors enabling it to resist treatment with the most available antibiotics. The purpose of this chapter was to show how common *Pseudomonas aeruginosa* isolates are among patients and healthcare professionals, as well as how they resist different types of antibiotics. This chapter demonstrates significant health problems related to *Pseudomonas aeruginosa* and derives more attention to this bacterium. Since only limited antibiotics are effective against it, therefore, all isolates must be investigated by antimicrobial susceptibility testing to identify the effective ones. From the used antibiotics, only Colistin showed a bactericidal effect by inducing a mechanism involving hydroxyl radicals that cause cell death. The application of this test limits antibiotic use and prevents the patients from developing resistance, in addition, it aids in the managements of treatment strategies.

Keywords: *Pseudomonas aeruginosa*, Patients, Multidrug-resistant bacteria, Healthcare workers

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Introduction

Pseudomonas aeruginosa is a widespread encapsulated, Gram-negative, monoflagellated non-spore forming rod, aerobic, and is a member of the Pseudomonadaceae family (Diggle & Whiteley, 2020). It possesses a pearlescent appearance with a grape-like odor, and the growth temperature ranges from 25-37°C, even though it can grow at 42°C, this feature aids in distinguishing it from other *Pseudomonas* species (Oberhofer, 1979). *P. aeruginosa* can be isolated from both humans and animals, in addition, it can be present in a variety of environments, such as water and soil. In humans, infections of the skin, soft tissues, otitis media, cystic fibrosis, ulcerative keratitis, surgical sites, and urinary tract, are among the nosocomial and hospital-acquired diseases caused by this bacterium (Del Barrio-Tofino et al., 2020).

It can withstand a broad variety of physical circumstances and endure in both public and medical facilities, furthermore, it has strong resistance to numerous antibiotics such as β-lactams, aminoglycosides, and quinolones making difficulties in the treatment of infected people (Pang et al., 2019). Furthermore, it often overcomes the host defenses by secreting several tissue-damaging toxins such as outer membrane proteins (*OprI*), exoenzyme S (*ExoS*), and exotoxin A (*ToxA*) (Khattab et al., 2015). In clinical environments, *P. aeruginosa* form considerably a strong biofilm that efficiently protects it from the host's defenses during chronic infections. This characteristic allows it to colonize the ventilator equipment in intensive care units (Rocca et al., 2020).

Resistance to antibiotics was noticed during the middle of the 20th century when antibiotics failed in treating several human diseases (Qureshi et al., 2023; Abbas et al., 2025). Due to the misuse and overuse of β-lactam antibiotics, resistant bacteria rapidly grown. The β-lactamases enzymes are the major causes for the development of resistant Gram-negative and Gram-positive bacteria, especially those belonging to the Pseudomonadaceae family. To reduce the hazard of pseudomonal resistance during treatment, it is necessary to use two antibiotics from different classes, such as cephalosporin or penicillin and an aminoglycoside (Pachori et al., 2019).

The Classification of *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a member of the "Pseudomonadaceae" family (Silby et al., 2011), which is classified into 5 classes based on the homology of rRNA/DNA and cultural features (Carroll et al., 2016).
Kingdom: Bacteria
Phylum: Proteobacteria
Class: Gamma Proteobacteria
Order: Pseudomonadales
Family: Pseudomonadaceae
Genus: *Pseudomonas*
Species: *aeruginosa*

Virulence Factors of this Bacterium

The majority of *P. aeruginosa* strains possess virulent factors on their surface enabling them to attach, colonize, and invade host tissues. The virulence factors stimulate the secretion of cytokines from the injured tissues that help in the invasion and secretion of toxins (Liao et al., 2022). This bacterium can invade numerous body organs and reduce the immune system, causing infections, which can't be completely cured. The main virulence factors contributing to the bacterial colonization are, the Lipopolysaccharide (LPS), the flagella and type IV Pili, (Saleh, 2021). In addition, there are other extracellular virulence factors such as exotoxins A, alkaline proteases, elastases, pyocyanin, biofilm formation, and quorum sensing (Vadakkan et al., 2024).

The main constituents of the outer membrane of Gram-negative bacteria are the lipopolysaccharide (LPS). The main component of LPS is Lipid A, a hydrophobic domain (called endotoxin), a distal polysaccharide (sometimes known as O-antigen), and a non-repeating core oligosaccharide. The main function of LPS is the stimulation of the host's immune responses, both innate and adaptive, that causes dysregulation of the inflammatory responses raising the rates of mortality and morbidity (Rocha et al., 2019). The type IV pili of *P. aeruginosa* are motorized pili which included three subtypes IVa, IVb, and Type IVb-tad, each of them is composed from frequent copies of the pilin (15 kDa protein). The pilin has a major influence on biofilm formation, the regulation of virulence factors, and the transfer of antibiotic resistance genes. Also, it is linked to the adhesion, the swarming motility and twitching of bacteria on various surfaces (Talà et al., 2019).

The flagella of *P. aeruginosa* are hair-like projections emerging from the bacterial surface and mostly are composed of flagellin protein subunits (Liao et al., 2022). Flagella encourage the biofilm formation in *P. aeruginosa,* as a mechanism for the motility of bacteria by the protein FliD of the flagellar cap and flagellin that simplifies chemotaxis and mobility. Due to their strong immunogenicity, they can activate the human immune system through Toll-like receptor 5 (TLR5) (Ozer et al., 2021). The *P. aeruginosa* exotoxin A (PEA) produced by type 2 secretion system (T2SS) and controlled by iron and glycose metabolisms, is a potent toxin. Exotoxin A(PEA) enhances apoptosis through blocking elongation factor 2 (EF-2) adenosine diphosphate (ADP) ribosylation, which enables the host cells to synthesize proteins (Michalska & Wolf, 2015).

Pseudomonas aeruginosa secrete many extracellular proteases that are responsible for host tissue invasion and destruction. Also, *P. aeruginosa* secrete Elastases A and B (lasA and lasB) to elastin lysis, which is a fundamental part of blood vessels and lung tissue and causes weakened lung function as well as pulmonary hemorrhage (Yang et al., 2015).

Alkaline protease (AprA), a virulence agent secreted by the type I secretion system, is controlled by the quorum sensing circuit (Pena et al., 2019). Degradation of complement components, Interferon-gamma (IFN-g), and Tumor necrosis factor alpha inhibitors (TNF-a) by AprA can weaken the body's natural defenses against infection (Liao et al., 2022). Its ability to make pyocyanin is the trait that most distinguishes it from other Pseudomonads and other Gram-negative, non-fermenting bacterial species. Pyocyanin is a chloroform-soluble, greenish-blue pigment that gives wound pus its distinctive blue color and can inhibit the proliferation of epidermal cells. Additionally, pyocyanin is toxic to hosts, which increases the severity of disease, damages tissue, and causes organ malfunction (Alatraktchi et al., 2020). Bacterial cells communicate with one another through a process called quorum sensing (QS), during QS, bacteria generate and secrete tiny chemicals known as autoinducers or quormones, they return to the cell once their concentration hits a particular level causing a coordinated reaction that helps the group survive. This response is initiated by two forms of 2 alkyl-4 quinolones (AQs) and autoinducers N-acyl-homoserine lactones (AHLs). QS regulates the synthesis of various virulence factors (that includes elastase, lipase, alkaline protease, pyocyanin, exotoxin A, and rhamnolipids) and promotes *P. aeruginosa* to build biofilms (Rezzoagli et al., 2020).

A matrix of exopolysaccharides (EPS) preserves populations of bacteria known as biofilms that have attached themselves to biotic or abiotic surfaces. EPS acted as efficient barriers that prevented cationic antibiotics, biocides, and antimicrobial agents from penetrating the tissue (Pinto et al., 2020). Infections caused with *P. aeruginosa* that produce biofilms are severely life-threatening and persistent in patients with cystic fibrosis. One important factor in the pathophysiology of *P. aeruginosa* is biofilm because biofilm isolates the bacterium and display intrinsic resistance to immune responses, medications, and harsh environmental conditions (Haidar et al., 2024).

Pathogenicity of *Pseudomonas aeruginosa*

Pathogenesis of infection has been linked to several secreted virulence factors used by *P. aeruginosa*. Lipopolysaccharide, phospholipase, alkaline protease, pili, flagella, and exotoxin A are all examples. Antibiotic lactamase inactivation and modification, the purine degradation set of the outer membrane, multidrug discharge pumps, efflux pumps, and low outer membrane permeability may all contribute to *P. aeruginosa* resistance to multiple antibiotics, making treatment challenging and limiting available options (Jarjees et al., 2021).

Although the skin is normally able to prevent harmful microbes from penetrating the body's tissues, burns and wounds may establish an environment that is more conducive to the growth and dissemination of bacteria, such as *Pseudomonas* species, which pose a risk to many patients. Patients with leukemia and those who are immunocompromised are particularly vulnerable to microorganisms because they can penetrate the bloodstream, leading to bacteremia and subsequently septicemia (Jalil et al., 2017). *P. aeruginosa* is one of the most prevalent nosocomial infections, producing high rates of morbidity and mortality in patients, that can lead to life-threatening illnesses and toxic infections in patients. They also have a role in both chronic and acute infections, especially in those who lack a functional immune system, and is the most prevalent Gram-negative bacteria that cause infection in burn patients, leading to sepsis and death (Reynolds & Kollef, 2021). *P. aeruginosa* is the major colonizer of burn wounds. It rapidly propagates within the wounded tissues, and frequently causes widespread infections, making it a common bacterium in medical facilities, especially in critical care units (Markou & Apidianakis, 2014).

The most common cause of hospital-acquired infections (HAIs) among patients is *P. aeruginosa,* which can cause a variety of diseases, including ventilator-associated pneumonia, dermatitis, gastrointestinal infections, urinary tract infections (UTIs), diabetic foot, bone, and joint infections, bacteremia, soft tissue infections, skin infections like folliculitis and external otitis, and many other infections, particularly in patients with extensive burns and those with weakened immune systems (Shortridge et al., 2019).

Additionally, *P. aeruginosa* corneal infections are most frequently caused by contact lens wearers; nevertheless, ocular surgery, ocular trauma, and prior ocular surface disease are also risk factors for keratitis in people who do not wear contact lenses (Enzor et al., 2021).

Pseudomonas aeruginosa Genome

Pseudomonas aeruginosa genomes are between 5 and 7 MB, making it one of the largest human pathogenic bacteria (Jurado-Martín et al., 2021). Cytosine and guanine (C+G) constitute up 66.6% of the genome, making it more complicated than other species. The genome is made up of chromosomal and extra-chromosomal elements known as plasmids. The genome of *P. aeruginosa* exhibits a mosaic structure because of several acquisitions throughout time from various donors. Also, there are various genomic islands and evidence of horizontal gene transfer, which comprise the existence of genes or gene fragments related to mobile elements such as plasmids, bacteriophages, and insertion sequences (Bachta et al., 2019).

Nearly 90% of *P. aeruginosa* genome is composed from 90% of the core genome, while the remaining 10% is made up of the accessory genome. The whole collection of genes (core and accessory) found in a phylogenetic group is named a pangenome (Whelan et al., 2021). Approximately all *P. aeruginosa* strains participate in a portion of the genome called the core genome; surrounded by "accessory" genomic components that are present in some species strains and absent in others (Ozer et al., 2014). Almost all genes involved in housekeeping functions, such as DNA replication, protein synthesis, and pathogenic factors, also, other genes that are not required for growth and survival, are concentrated in the core regions of the genome (Klockgether et al., 2011). The accessory genome is composed of non-conserved DNA segments of different lengths that are typically found in extrachromosomal elements. This region of the genome contains genes that encode resistance to diverse classes of antibiotics, therefore, it is considered as a critical region for the clinical consequences (Freschi et al., 2019).

The genome of *P. aeruginosa* are highly conserved in laboratory strains as well as in cultured strains isolated from clinical specimens and the environment. This wide genome imparts this bacterium a major array of physiological responses and metabolic pathways helping it to be adjusted to variable circumstances (Saleh, 2021).

In the core genome of *P. aeruginosa,* the β-lactamases and efflux pumps are determinants intrinsic antibiotic resistance. Whereas, the acquired antibiotic resistance is contained in the accessory genome (Sommer et al., 2020), making this genome to be extremely responsible for the prevalence of multidrug-resistant bacteria (Freschi et al., 2019). While the genomic islands of *P. aeruginosa* contain genes encoding virulence, adhesions, genetic mobility, toxins, biofilm formation, antibiotic resistance, and iron uptake, these functions help this bacterium to live well in various hosts causing their illness (Qin et al., 2022).

Antibiotics Resistance of *Pseudomonas aeruginosa*

Antibiotics are potent medications utilized to cure bacterial infections. The majority of microorganisms now exhibit antibiotic resistance due to the misuse of these medications (Livermore, 2018). *P. aeruginosa* is among the most adapted organisms in acquiring and developing resistance mechanisms to practically every kind of widely used antibiotic as well as to new antibiotics as soon as they are introduced (Qin et al., 2022). Since *P. aeruginosa* has the ability in acquiring extrinsic and intrinsic resistance to several routinely prescribed antimicrobial drugs, infections produced by this bacterium are notoriously tough to cure, ultimately creating *P. aeruginosa* strains resistant to multiple drugs (MDRPA) (Peymani et al., 2017). The ability of a bacterial species to naturally inhibit the effectiveness of a certain antibiotic across structural or functional characteristics is known as intrinsic antibiotic resistance (Arzanlou et al., 2017). The development of antibiotic-inactivating enzymes like beta-lactamases, efflux mechanisms that pump drugs out of the cell, and decreased outer membrane permeability have all demonstrated *P. aeruginosa's* high level of fundamental resistance to most antibiotics (Langendonk et al., 2021).

In contrast, bacteria may acquire antibiotic resistance by mutation or by horizontally transferring resistance genes. Mutations that permit the bacteria to insist on the presence of antimicrobial drugs cause changes such as, reducing antibiotic absorption, drug targets and overexpression of efflux pumps and antibiotic-inactivating enzymes (Munita & Arias, 2016). Apart from the important level of inherent antibiotic resistance in *P. aeruginosa*, acquired resistance is the main factor in the formation of multidrug-resistant strains, that increases the occurrence of persistent infections and enables this bacterium to challenge its elimination (Giovagnorio et al., 2023). For treating infections with *P. aeruginosa*, most of the used antibiotics must be able to enter cells and reach their intracellular targets. The molecular structure of antibiotics classified as β-lactams include monobactam, carbapenem, cephalosporin, and penicillin; have a β-lactam ring. The production and maintenance of the peptidoglycan are facilitated by enzymes known as penicillin-binding proteins (PBP), and these enzymes are blocked by β-lactam antibiotics, hence the recycling of peptidoglycan is altered leading to interference with the production of cell walls (Giovagnorio et al., 2023).

Enzymes known as β-lactamases cleave the amide bond of the β-lactam ring, rendering β-lactam antibiotics inactive (He et al., 2020). Antibiotics in the aminoglycoside family, such as Gentamicin, Amikacin, and Tobramycin, suppress the synthesis of proteins by interfering with and interacting with the ribosomal subunit (the 30S), resulting in a misreading of messenger RNA (mRNA). The alteration in aminoglycosides and the reduction in the cell permeability to antibiotics are the major causes of aminoglycoside resistance (Basavraj & Namdev, 2012). The quinolone class, of antibiotics, like Ciprofloxacin and Levofloxacin, hinder DNA replication through blocking the DNA gyrase enzymes and topoisomerase IV (Aldred et al., 2014). The most common reasons for ciprofloxacin resistance include upregulation of efflux pumps and mutations in the topoisomerase subunits ParC/ParE or the DNA gyrase subunits gyrA and gyrB (Rehman et al., 2019). By binding to the LPS on the outer membrane of Gram-negative bacteria, a class of polypeptide antibiotics called polymyxins promotes antibiotic uptake and increases the permeability of cell membranes. In clinical practice, two polymyxins are used: Polymyxin B and Polymyxin E, also known as Colistin, they kill bacteria by triggering a process that involves hydroxyl radicals that results in cell death (Pang et al., 2019).

Epidemiology of *Pseudomonas aeruginosa*

Because of its metabolic versatility, *P. aeruginosa* can thrive in a variety of settings making it possible to isolate it from numerous sources, such as soil, the human body, hospitals, and other water-rich areas (like swimming pools). In addition to non-domestic settings (like river water) and from the equipment used in medicine, including respirators, inhalers, anesthetic vaporizers, dialysis, ventilators and from sinks and toilets (Crone et al., 2020). This is because this bacterium can grow with relatively few nutrients and withstand a variety of environmental and physical circumstances (De Sousa et al., 2021). The most common kind of *Pseudomonas* that causes hospital-acquired illnesses is

Pseudomonas aeruginosa accounting for around 7.1–7.3% of all illnesses (Weiner et al., 2016). Also, it causes infection in intensive care unit (ICU) patients who have lower respiratory tract infections (LRTIs) throughout their hospitalization (ICU), and also responsible for higher percentage of healthcare-associated infections (Reynolds & Kollef, 2021). It also takes into account the second most prevalent infection linked to ventilator-associated pneumonia (Bhatt et al., 2018).

Research conducted in Duhok, Iraq, found that 40% of healthcare workers hands were infected (Mohammed Said et al., 2023). Because samples were taken at midday after healthcare workers had been in close contact with patients for a considerable amount of time, and because the wards were overcrowded with patients, the authors attributed this high rate in healthcare workers' hands to the sampling time. They also failed to wash their hands as frequently as they should have because of staff shortage. Hand cleanliness protects healthcare workers and stops pathogens from spreading to patients. In some studies, much lower rates were recorded from healthcare professionals' hands, with a 3.5% rate in Italy (Crivaro et al., 2009). In Egypt and Saudi Arabia, Mansour et al. (2013) reported rates of 10 and 6.7%, respectively among healthcare workers in two hospitals one in Egypt and the second in Saudi Arabia and attributed these rates to the healthcare workers' noncompliance with hand washing practices.

As regards patients, *P. aeruginosa* was shown to be prevalent in 55.5% of burn infections in Erbil and 44.4% of Duhok (Qader et al., 2020). In Sulaymaniyah province, Twenty-seven percent of isolates from burn patients were *P. aeruginosa* (Othman et al., 2014). Also, many studies performed in Iraq, have demonstrated that *P. aeruginosa* was present in burn infections at a high frequency, ranged between 32-66% in the provinces of Baghdad, Karbala, Hilla, and Kirkuk (Al-Saadi, 2009; Al-khafaji, 2016; Khorsheed & Zain Al Abdeen, 2017). Alternatively, 97.6% of *P. aeruginosa* isolates were found in another research done in Basra, Iraq (Alkhulaifi & Mohammed, 2023). It has been demonstrated that *P. aeruginosa* is the more frequent cause of middle ear infections in Tikrit City, accounting for up to 42% of all cases (Kamal et al., 2015). *P. aeruginosa* was also found to be isolated from 32.8% of burn patients in Najaf (Abdalhadi et al., 2021).

In Palestine, 50% of the population was affected (Al Laham et al., 2013). In Egypt, 90% (Shaaban et al., 2017). According to an Iranian investigation, 85% of infections with *P. aeruginosa* were found in Marand in East Azerbaijan (Jafari-Sales & Shadi-Dizaji, 2018), in Ethiopia 52.9% (Mekonnen et al., 2021).

A study carried out in Brazil showed that 71,4% of MDR *P. aeruginosa* isolates were found in burn patients (de Almeida et al., 2017). Another study conducted in India showed that *Pseudomonas* spp. were the more repeatedly isolated microorganisms, isolated from 43% of patients (Gupta et al., 2019). About 47 MDR *P. aeruginosa* strains in the USA were isolated from burn patients (Tchakal-Mesbahi et al., 2021). The isolation rate of *P. aeruginosa* may vary between nations due to drug usage, hospital management, hygiene strategies, geographic and climatic factors. The use of contaminated surgical instruments and both direct and indirect patient contact contribute to the spread of this pathogen. On the other hand, the pathogen can survive in treatments, eye drops, anesthetic masks, and liquid medications (Hatite Al-Daraghi & Abdulkadhim Al-Badrwi, 2020).

Prevention and Control

According to WHO guidelines, preventive measures must be applied in healthcare facilities to prevent the transmission of this bacterium and other nosocomial bacteria through the application of frequent hand hygiene, isolating the patients, taking precautions during contact with patients, environmental surveillance, and cleanliness. Controlling the use of antibiotics, they must be used in necessary cases only, and it is preferable during any infection to prescribe the antibiotics after performing a sensitivity test.

Conclusion

According to this review, *P. aeruginosa* was highly prevalent among patients and healthcare professionals in Duhok, Iraq. The significant prevalence of strains of *P. aeruginosa* that are resistant to different antimicrobial drugs in nosocomial organisms has made treating this bacterium extremely difficult. This is mostly because antimicrobial treatments are widely used, which considerably aids in the development of resistant bacterial strains by involving several mechanisms of resistance, such as synthesis of beta-lactamase enzymes that break down these medications. Therefore, for the purpose of preventing the spread of highly virulent and multidrug-resistant microorganisms in the community, it is advised to monitor antimicrobial resistance and promote rigorous adherence to infection control programs. Minimizing their spread, preventing outbreaks, and improving treatment are all necessary in these urgent conditions.

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