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Mini Review

Antibiotic Resistance Patterns in *Pseudomonas aeruginosa* Strains Isolated from Patients Hospitalized in Different Hospital Wards

Tanaz Zabihi ^{1*}, Maedeh Shahsanaei Goneirani ¹¹ Department of Microbiology, Taligene Pars Company, Isfahan Science and Technology Town, Isfahan, Iran**Corresponding Author:** Tanaz Zabihi, MSc in Microbiology, Department of Microbiology, Taligene Pars Company, Isfahan Science and Technology Town, Isfahan, Iran. Tel: +98-3142646414, E-mail: zabihitanaz@yahoo.com

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Abstract

The discovery of antibiotics followed by the extensive production of new antibiotics and their widespread use in the treatment of bacterial infectious diseases has led to bacterial resistance to antibacterial agents. Despite global efforts to improve the status of antimicrobial treatment, the phenomenon of resistance against gram-negative bacteria has increased in communities and hospitals. *Pseudomonas aeruginosa*, the most common human pathogen, is an oxidase-positive and glucose non-fermentative gram-negative bacillus considered an important opportunistic pathogen and the cause of mortality in patients with cystic fibrosis, neoplasms, and severe burns. Infection caused by *Pseudomonas aeruginosa* is one of the most important complications in hospitalized patients, and its incidence is increasing significantly in developed and developing countries. Based on the literature, it can be concluded that antibiotic resistance is higher in developing countries than developed ones, which is likely due to excessive antibiotic use in developing countries or the control of antibiotic use in developed ones.

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Introduction

The *Pseudomonas* genus is a complex of non-fermentative aerobic gram-negative bacteria commonly found in soil, water, and plants and often found in small numbers in the natural intestinal flora and skin of humans; it is considered the main pathogen in this group. *Pseudomonas* pathogens rarely cause disease and are categorized based on RNA/DNA similarity and conventional planting characteristics. *Pseudomonas aeruginosa* is widely distributed in nature and is often found in wet hospital environments. These bacteria can be colonized in healthy humans, acting as a saprophyte.¹ Several species of this genus cause diseases in animals and plants. Most *Pseudomonas* microorganisms do not infect humans, but some of them are potentially important pathogens for hosts with impaired immune systems. Usually human infections are severe and difficult to treat because of resistance to different conventional antibiotics and weak host conditions. *Pseudomonas aeruginosa* is the most common human pathogen in the *pseudomonas* genus. *Pseudomonas aeruginosa* is the third most common cause of

nosocomial infections after *Staphylococcus aureus* and *Escherichia coli* in some hospitals. These bacteria is a major pathogen and the leading cause of mortality in patients with cystic fibrosis, neoplasms, and severe burns.² In recent years, drug resistance has significantly increased in different pathogenic bacteria and has made the treatment of infections difficult. Therefore, there is a growing need for safe and effective drugs for use in treating drug-resistant infections.³ *Pseudomonas aeruginosa* is naturally resistant to several antibiotics and can be resistant to antibiotics such as penicillin, ceftazidime, ciprofloxacin, aminoglycosides, and carbapenems. The prevalence of antibiotic resistance is increasing; more than 10% of strains isolated across the world are resistant to multiple drugs.⁴

An Introduction to Drug Resistance

Resistance to antimicrobial agents and antibiotics among human pathogens has now entered the phase of multiple drug resistance (MDR). Despite the presence of numerous antibiotics and pharmaceutical factories and billions of dollars spent, the elimination of bacterial

diseases is still far from mind, mainly due to the presence of numerous bacteria that resist the antibiotic effects. It is worth noting that for antibiotics to function better, how these substances act in the body should be considered. First, antibiotics should identify their target. Next, they must reach their proper concentration after reaching the target, and then they must maintain that concentration for a sufficient period of time. Some treatment problems are caused by the antibiotic's inability to selectively reach the target, cross the blood brain barrier, or reach the bacteria present in an abscess. The concentration of the antibiotic is also important. In some cases, it has been observed that antibiotics are rapidly excreted from or metabolized in the body, and this reduces the serum concentration of antibiotic, resulting in the ineffective treatment of bacterial infections that require large amounts of drug and prolonged contact with antimicrobial agents for elimination. In some cases, however, the antibiotic concentration may increase rapidly in a particular organ or specific tissue, while infectious parts may remain out of its reach. The mechanism of antibiotic resistance can be genetic or non-genetic. Today, in addition to trying to produce semi-synthetic antibiotics from existing antibiotics to be effective against resistant strains, attempts have been made to extend the recommendations for the proper use of antibiotics as much as possible in order to prevent the emergence of resistant strains.⁵

Multidrug Resistance

Many bacteria are resistant to several classes of antibiotics (at least three different classes) and use various strategies to overcome the stress induced by an antibiotic's chemotherapeutic effect. These bacteria are called MDR, which are a major concern today in hospitals and other medical centers. MDR strains of *Pseudomonas aeruginosa* have been shown to exist in hospitals, isolated from the environment and hands of the personnel. Studies in Iran have shown that the multiple drug resistance of *Pseudomonas aeruginosa* strains has reached a worrying level in nosocomial infections.⁶ The main mechanism of resistance in these bacteria is the active transfer of drugs from the cell to the environment through pumps that send out a wide range of compounds harmful to bacteria, such as antibiotics. Additionally, the mutation of antibiotic target sites or the synthesis of enzymes changing the drug can induce MDR resistance in bacteria. In all of these cases, bacterial strains carrying resistive factors are selected through the use of antimicrobial molecules, because sensitive strains are eliminated, while resistant strains grow and survive.⁷

Treatment of Infections Caused by *Pseudomonas aeruginosa* Bacteria

One of the most important causes of nosocomial infections is the definite spread of drug resistance.⁸ Resistance to antimicrobial agents among numerous pathogens, especially pathogens affecting nosocomial

infections that impair the treatment of infections, has extended globally, leading to increased mortality rates in patients in different hospital wards.⁹ *Pseudomonas aeruginosa* is the most common human pathogen of the *pseudomonas* genus and the third most common cause of nosocomial infections after *Staphylococcus aureus* and *Escherichia coli*, which leads to mortality in patients suffering from cystic fibrosis, neoplasms, and severe burns.⁵ The term "nosocomial infection" refers to a serious disease unrelated to the underlying disease of the person seeking treatment in a hospital.⁶ Treatment for *pseudomonas* infection is difficult, and treatment with appropriate drugs is not always successful. *Pseudomonas aeruginosa* infections should not be treated with one drug, as resistant strains develop quickly. Penicillins effective against these bacteria include ticarcillin, mesocillin and piperacillin, usually prescribed with an aminoglycoside such as gentamicin, tobramycin or amikacin. Other drugs effective against *pseudomonas aeruginosa* include aztreonam, imipenem, new quinolones including ciprofloxacin, and new generation cephalosporins such as cefaprazone. Ceftazidime is also used in the initial treatment of *pseudomonas aeruginosa* infections.⁵

Discussion

Antibiotic resistance to gram-negative bacilli, especially *enterobacteriaceae*, *pseudomonas aeruginosa*, and *acinetobacter*, has become a growing problem around the world. Resistant bacteria can significantly impede the treatment maintenance.⁹ Several studies have addressed antibiotic resistance in different countries, most of which suggest using microbial and molecular techniques together as reliable and documented tools. Antibiotic resistance in aztreonam was 1% in France, 48.8% in Russia, 11.9% in the United States (USA), 23% in Spain, and 66.7% in Isfahan, Iran.^{7, 10-13} Antibiotic resistance to tobramycin has been reported as 25% in France, 5.4% in the USA, 10% in Spain, and 91.7% in Isfahan, Iran, which is alarmingly high; in other words, it is possible that in the near future, no other antibiotic will be effective against *pseudomonas* infections in Isfahan.^{7, 10, 12, 13} The antibiotic resistance to ticarcillin was 38% in France and 64% in Canada. According to the results of the present study, the resistance to this antibiotic was 83.3% in Isfahan, which is significantly higher than the above-mentioned regions and indicates the low effect of this antibiotic in Isfahan, possibly due to the wide use of this antibiotic in treatment regimens.^{13, 14} The antibiotic resistance to ceftazidime was reported as 9% in France, 12.3% in Brazil, 26% in Turkey, 4.6% in Japan, 35% in Russia, 12% in Canada, 11.1% in the USA, 15% in Spain, and 75% in Isfahan.^{7, 10, 11, 15, 16} Resistance to imipenem was 18.5% in France and 3.8% in Japan.^{12, 16}

Conclusion

According to the results of studies, it can be concluded that antibiotic resistance is higher in developing countries than developed countries, possibly due to the

excessive use of antibiotics in developing countries or the control of antibiotic use in developed countries.

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Authors' Contributions

TZ and MSG contributed equally to this research.

Conflict of Interest Disclosure

The authors declare that they have no conflicts of interest.

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