Original Article

A Study of Antimicrobial Resistance Rates in Clinical Burn Center Isolates of *Pseudomonas aeruginosa* in the South of Iran

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Abstract

Background: This research aimed to examine the frequency of resistance to antimicrobial agents and their variations in *Pseudomonas aeruginosa* clinical isolates, which are accountable for invasive infections in the southern part of Iran, from 2018 to 2022.

Methods: A retrospective study was conducted, involving the gathering of microbiological data from Taleghani Burn Hospital from 2018 to 2022. The primary variables under scrutiny were department, sample origin, the antiprogram system (e.g., disc diffusion and strip methods, and clinical laboratory standards), and the rate or percentage of resistant isolates investigated by antimicrobial susceptibility testing. The interpretation criteria employed for the study were those of the Clinical Laboratory Standards Institute (CLSI). And the percentage of resistant isolates was also taken into consideration.

Results: The disc diffusion and strip method is the most commonly used approach for antimicrobial susceptibility testing. According to the CLSI, resistance rates ranged from 3.64% (colistin) to 77.38% (amikacin). The rates of antimicrobial resistance remained relatively constant over time in 2018-2022. Approximately 67.62% of isolates were multidrug resistant, and the remaining 9.46% were extensively drug-resistant. Wound and urine isolates demonstrated higher resistance, except for amikacin and piperacillin, than those from blood culture and biopsy.

Conclusion: Antimicrobial resistance is widely prevalent in *P. aeruginosa*, a common bacterium in southern Iran. The findings revealed the highest resistance rates for commonly used antibiotics such as amikacin, piperacillin, ceftazidime, and meropenem. However, colistin and nitrofurantoin are more effective against this bacterium. The wound and urine isolates represented the highest resistance rates, indicating the need for prompt and appropriate treatment. Interestingly, the resistance rates for most antibiotics remained relatively stable during the study period, emphasizing the need to develop alternative treatments for *P. aeruginosa* infections.

Keywords: Antibiotic resistance, Burn, *Pseudomonas aeruginosa*, Infection, Microbiology

Introduction

Hospital-acquired infections are a primary concern for public health, with significant social and economic impacts worldwide (1,2). *Pseudomonas aeruginosa* is one of the many pathogens that can lead to infections. It is considered an opportunistic pathogen that poses a severe threat, especially in cases of invasive infections, as such infections tend to have high rates of morbidity and mortality (3).

What makes this microorganism a formidable foe is its innate ability to resist numerous antimicrobial treatments and develop resistance to broad-spectrum medications such as carbapenems and polymyxins (4-7).

In cases where non-multidrug-resistant (non-MDR) *P. aeruginosa* causes infections, there are various therapeutic options available. Some of the commonly used options are beta-lactams such as ceftazidime, cefepime, imipenem,

piperacillin/tazobactam, meropenem, and aztreonam, as well as fluoroquinolones and aminoglycosides. However, the treatment of infections caused by MDR *P. aeruginosa* can be quite challenging. In such situations, only a limited number of antimicrobials may be available, including colistin, which has potential toxicity issues. Newer antimicrobials such as ceftolozane/tazobactam and ceftazidime/avibactam, which have less clinical experience, may be used alternatively (8-10). To select the most effective antimicrobial treatment for a given infection caused by *P. aeruginosa*, it is essential to have a clear understanding of the local susceptibility and resistance rates. These rates can vary depending on different factors, such as the geographical region, local resistance patterns, and microbial factors such as the specific clone and resistance mechanisms involved. Unfortunately, the available data on antimicrobial resistance rates in *P. aeruginosa* isolates causing invasive infections in Iran are limited, making it challenging to develop effective treatment strategies for these infections (11-14).

Therefore, this research not only provides valuable insights but also has practical implications. First, it aims to determine the prevalence of antimicrobial resistance in *P. aeruginosa* isolates causing invasive infections in a burn center hospital in southern Iran, categorized by sample type. Second, it seeks to investigate how these antimicrobial resistance rates have changed from 2018 to 2022. These findings can directly impact patient outcomes by enabling the development of targeted and efficient treatment strategies, making this research highly relevant and applicable in the field of healthcare.

Methods

This study has provided a detailed retrospective analysis of the demographic and microbiological data collected from 2018 to 2022 in the Taleghani Hospital Burn Center in Iran. The data include various parameters such as age, gender, and underlying health conditions of the patients. The study has focused on the first isolates of each infection type per year, which includes bacteremia, wound infections, nosocomial urinary tract infections, and biopsies. Only the first 3 isolates were considered for patients with more than one isolate obtained per type of infection and year. The study variables were carefully selected, including the department, sample origin, the antiprogram system (e.g., disc diffusion and strip methods and clinical laboratory standards), and the rate or percentage of resistant isolates. The bacterial identification and susceptibility tests were conducted for specified antimicrobials at each site. The analyzed antimicrobials included piperacillin, ceftazidime, trimethoprim-sulfamethoxazole, imipenem, meropenem, nitrofurantoin, gentamicin, amikacin, ciprofloxacin, and colistin. The corresponding clinical category for each antimicrobial agent was determined based on the Clinical Laboratory Standards Institute (CLSI) 2020 (15). The parameters were statistically analyzed using SPSS for Windows statistical software (version 20; SPSS, Inc.,

Chicago, IL, USA). Categorical variables were evaluated using either the chi-square test or Fisher's exact test. A *P* value of less than 0.05 was considered statistically significant.

Results

Out of the 896 data points analyzed, the origin by type of unit or department was as follows:

About 20% were men, 5.1% were children, 66.3% were from the ICU, and 8.6% were women. The isolates were obtained from wounds (8.81%), urine (13.28%), blood culture (14.73%), biopsy (63.16%), and other samples (0.02%).

The results of disc diffusion and strip methods showed that the proportion of resistant isolates varied between 3.64% (colistin) and 77.38% (amikacin). Only the overall percentage of resistant isolates from 2018 to 2022 demonstrated statistically significant differences among all tested antimicrobials (Table 1).

Moreover, the resistance rates were consistent primarily from 2018 to 2022 (Table 1). However, there were a few exceptions. For example, ciprofloxacin and ceftazidime rates decreased from 70.3% in 2021 to 70% in 2022 ($P = 0.001$) and from 73.1% in 2020 to 72.5% in 2021 ($P = 0.03$), respectively. In addition, imipenem and colistin rates decreased from 67.6% in 2021 to 67.5% in 2022 ($P = 0.001$) and from 4.0% in 2020 to 3.6% in 2021 ($P = 0.006$), respectively.

No cases of pan-resistant isolates were identified based on the criteria by Magiorakos et al (16). However, 67.62% of the isolates were found to be MDR, while 9.46% were classified as extensively drug-resistant (XDR). Figure 1 depicts a modest rise in the percentage of MDR isolates from 50% in 2018 to 77.9% in 2022. On the other hand, there has been a decline in XDR isolates from 24.2% in 2018 to 1.8% in 2022. The microbial isolates extracted from urine and wound samples exhibited higher resistance to the tested antimicrobial agents, especially amikacin,

Table 1. Distribution of Resistance Rates per Year and Overall Resistance Rates Based on the Applied Breakpoint (CLSI)

Antimicrobial	Percentage Resistant (R) Isolates by					
	Year (%R)					Breakpoint
	2018	2019	2020	2021	2022	CLSI %R[a]
Nitrofurantoin	35.6	30	33.3	32.3	30.8	32.4
Colistin	3.3	3.5	4	3.6	3.8	3.64
Ceftazidime	72.2	71.4	73.1	72.5	74.1	72.66
Ciprofloxacin	67.7	71.6	70.2	70.3	70	69.69
Trimethoprim	61.7	60	61.4	61.5	60.7	61.06
Amikacin	76.2	78.3	76.9	76.9	78.6	77.38
Gentamicin	67.5	69.6	69.2	69.8	67.5	68.72
Imipenem	67.3	67.8	67.1	67.6	67.5	67.46
Meropenem	72.2	69.6	71.8	72.2	73.7	71.9
Piperacillin	72.4	73.5	72	72.6	73.4	72.78

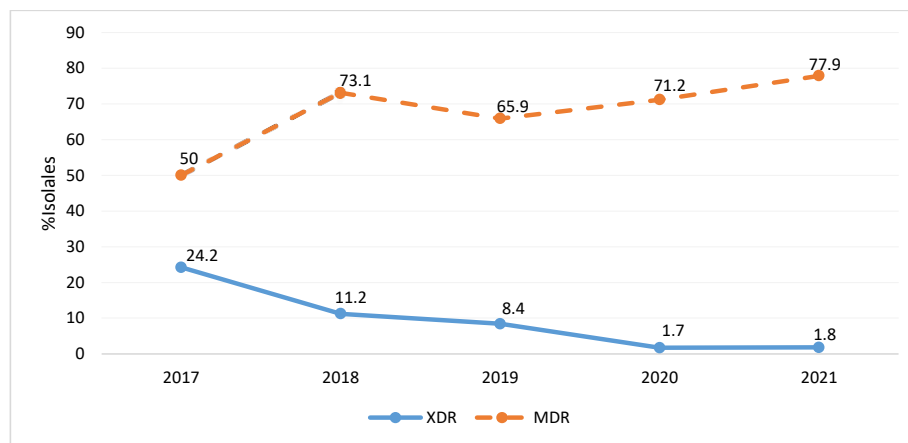*Note*. CLSI: Clinical laboratory standards institute; [a] Resistance isolates.

Figure 1. Annual Distribution of the Percentages of MDR and XDR *P. aeruginosa* Isolates. *Note*. *P. aeruginosa*: *Pseudomonas aeruginosa*; MDR: Multidrug-resistant; XDR: Extensively drug-resistant

ceftazidime, and imipenem (up to 40%). Meanwhile, the microorganisms obtained from blood and biopsy samples were less resistant to the same antimicrobial agents (as per Table 2).

Discussion

According to the results, *P. aeruginosa* was the hospitals' most commonly acquired pathogen. Its resistance to antimicrobial drugs has significantly increased in recent years, albeit with varying rates (14). Knowing the local rates of antimicrobial resistance and their trends over time is necessary for designing appropriate therapeutic strategies, particularly those that are empirical, as this justifies their requirement.

The findings of this research showed that the prevalence of antimicrobial resistance in *P. aeruginosa* at Taleghani Hospital in the southern region of Iran, Ahvaz, was relatively low compared to those reported in other studies (14,17,18), and resistance rates varied according to those of the CLSI.

The resistance rate was the highest with amikacin (77.38%), irrespective of the applied CLSI. Colistin was found to be the most active antibiotic, with a resistance rate of less than 10% (19).

These findings are in line with previous research outcomes, including those of a clinical burn care study in Iran that examined isolates collected between May 2012 and November 2014. In that study, the highest levels of resistance were detected with ciprofloxacin (93.3%), imipenem (60%), gentamicin (60%), and amikacin (66.6%). One of the most effective antimicrobials was trimethoprim (33.3%) (14). Similar or almost identical trends were observed in recent studies conducted in Iran. The results of a study performed in Tehran between September 2005 and October 2007 revealed that the highest resistance rates were associated with ciprofloxacin (72%), gentamicin (80%), and amikacin (73%) (20). These findings corroborate those of research conducted in Isfahan using 2016 samples. The research demonstrated that the highest resistance rates were related

Table 2. Distribution of Antimicrobial Resistance Rates by Sample Type

Antimicrobial	Percentage Resistant Isolates (%R) by Type of Sample			
	Biopsy[a] (63.16%)	Blood Culture[a] (14.73%)	Urine Culture[a] (13.28%)	Wound[a] (8.81%)
Nitrofurantoin	0	0	31.1	0
Colistin	1.9	3.0	5.0	6.3
Ceftazidime	36.7	40.2	38.7	43.0
Ciprofloxacin	21.7	25.0	29.4	36.7
Trimethoprim	12.0	6.8	11.8	12.7
Amikacin	47.5	53.0	43.7	48.1
Gentamicin	18.9	8.3	37.0	26.6
Imipenem	40.1	39.4	40.3	40.5
Meropenem	21.2	20.5	29.4	22.8
Piperacillin	35.1	40.2	26.9	26.6

Note. [a] Overall, 0.02% of other samples are not included.

to ciprofloxacin, imipenem, meropenem, amikacin, and ceftazidime, all of which were over 90%. Additionally, the resistance rates to piperacillin were 70.7%. The study identified colistin as the most effective antibiotic (21). In 2015, in a study conducted in Ardabil, researchers evaluated 94 strains of *P. aeruginosa* and reported that out of 83 isolates, the highest resistance rates were observed in imipenem (75.5%), gentamicin (86%), ciprofloxacin (87%), amikacin (85%), and piperacillin (82%). On the other hand, colistin was found to be the most effective antibiotic with a resistance rate of 0% (22).

Based on previous analysis (2018-2022), a thorough examination of antimicrobials revealed little to no significant developments or discernible patterns in the resistance rates. However, the resistance rate of piperacillin showed a noteworthy change; it was reduced by half (73.5–72%) in 2019 compared to 2020. These findings suggest that there should be significant changes in the hospitals in southern Iran regarding the distribution of resistant determinants or resistant clones. Observations of this trend date back to the early 2000s, as evidenced by the results of prior research performed in Iran (14,20).

No pan-resistant isolates were identified in our study.

However, the results indicated a relatively high prevalence rate of MDR isolates (67.62%) and a low prevalence rate of XDR isolates (9.46%). These combined resistance percentages are comparable to those found in some countries. For example, in India, the prevalence of pan-resistant isolates was 4%, while MDR and XDR isolates were found to have a prevalence of 50% and 2.3%, respectively (23).

The microbial isolates extracted from urine and wound samples represented comparatively higher resistance to the tested antimicrobials, particularly amikacin and piperacillin, than those isolated from other sources such as biopsy or blood. This outcome is consistent with that of previous research and may be linked to the escalated usage of antimicrobials for treating *P. aeruginosa*-induced wound and urine infections (18). This study's findings are subject to certain limitations, primarily due to the lack of verification by a reference laboratory of the reported data on *P. aeruginosa* susceptibility. Nonetheless, this study's comprehensive scope, encompassing numerous participating sites, types of samples, and years, confers a reasonably accurate understanding of *P. aeruginosa* susceptibility in the southern region of our country. In the absence of national standardized databases, such studies prove essential in obtaining such information. A further limitation of this work pertains to the absence of molecular epidemiology studies, such as the pulsed-field gel electrophoresis (PFGE) or multi-locus sequence typing (MLST), which would have enabled the determination of whether the observed prevalence of resistance is influenced by certain endemic situations, such as resistant clones or horizontal resistance determinants, in the participating sites (13,14,18). Certain factors, including the dosage of antimicrobials and the infection's focus, can affect isolates' susceptibility. This modification will result in a substantial reduction in resistance rates for several antimicrobials (24).

Conclusion

Antimicrobial resistance is widely prevalent in *P. aeruginosa*, a bacterium commonly present in southern Iran. The findings revealed the highest resistance rates for commonly used antibiotics such as amikacin, piperacillin, ceftazidime, and meropenem. However, colistin and nitrofurantoin were more effective against this bacterium. The wound and urine isolates demonstrated the highest resistance rates, indicating the need for prompt and appropriate treatment. Interestingly, the resistance rates for most antibiotics remained relatively stable during the study period, highlighting the need for developing alternative treatments for *P. aeruginosa*-related infections.

Authors' Contribution

Conceptualization: Elham Jafarzadeh.
Methodology: Masoud Kargar.
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Writing–review & editing: Masoud Kargar, Susan Amiri.

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