



Assessment of Carbapenem Susceptibility and Multidrug-Resistance in *Pseudomonas aeruginosa* Burn Isolates in Tehran

Somayeh Moazami-Goudarzi¹, Fereshteh Eftekhari^{1*}

¹ Department of Microbiology, Faculty of Biological Sciences, Shahid Beheshti University, Tehran, IR Iran

* Corresponding author: Fereshteh Eftekhari, Department of Microbiology, Faculty of Biological Sciences, Shahid Beheshti University, G.C, Evin, Tehran, IR Iran. Tel.: +98-2129903208, Fax: +98-2122431664, E-mail: f-eftekhari@sbu.ac.ir

ABSTRACT

Background: *Pseudomonas aeruginosa* is an opportunistic pathogen which causes severe, acute and chronic nosocomial infections. These infections are difficult to eradicate since the organisms are usually multidrug-resistant. Carbapenems are considered as the most effective drugs against these isolates. However, recent emergence of carbapenem-resistant *P. aeruginosa* has become a major healthcare problem.

Objectives: The present study was conducted to determine the antibiotic susceptibility of *P. aeruginosa* burn isolates to 13 antibiotics including imipenem and meropenem.

Materials and Methods: One hundred and thirty three *P. aeruginosa* burn isolates were collected from Shahid Motahari Burn Hospital between July and December 2011. The majority of the isolates were from wounds (88.7%), followed by 5.26% from blood, 4.15% from subclavian catheters and 1.5% from urine. The antibiotic susceptibility profiles were studied by the agar disc diffusion.

Results: The results showed 99.2% resistance to carbenicillin, 98.4% to ticarcillin, 96.2% to ciprofloxacin, 95.4% to co-trimoxazole, 94.7% to imipenem and meropenem, 93.9% to piperacillin, 93.2% to azetronam, 92.4% to tobramycin, 91.7% to cefepime, 89.4% to amikacin and ceftazidime, and finally 87.2% to piperacillin-tazobactam. Overall, 100% of the isolates showed multidrug-resistance (resistance to ≥ 3 classes of antibiotics) including imipenem-resistant isolates.

Conclusions: The high rate of multidrug-resistance is alarming and it is crucial to screen for carbapenem resistance prior to antibiotic therapy.

Keywords: *Pseudomonas aeruginosa*; Antibiotic Susceptibility; Carbapenems

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► Implication for health policy/practice/research/medical education:

Suitable protocols are needed for appropriate use of antibiotics for treatment of multidrug resistant bacterial infections as well as avoiding the spread of resistance genes among bacteria.

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1. Background

Pseudomonas aeruginosa is the most common cause of 10% of all hospital-acquired infections (1). Infections occur particularly in immunocompromised hosts suffering from respiratory diseases, cancer and burns as well as cystic fibrosis with a significant rate of morbidity and mortality (2, 3). Burn injuries resulting in open and large wounds, including those with necrotic tissues, make these patients more susceptible to infection with *P. aeruginosa* (4, 5). Treatment of infections caused by *P. aeruginosa* is frequently complicated due to the limited susceptibility to antimicrobial agents and the emergence of antibiotic resistance during therapy. As a result, due to the severe adverse outcomes, the mortality rate among infected patients is likely to reach up to 40-50% (2, 5).

The Emergence of multidrug-resistant (MDR) strains in burn units, particularly in economically underdeveloped and developing countries, has become a major problem in the control of infections (6, 7). Multidrug-resistance, caused by a variety of resistance mechanisms, leaves few alternatives for treatment of some patients (4). Carbapenems are the selective drugs for treatment of MDR isolates (2, 6). However, the increasing frequency of carbapenem-resistant *P. aeruginosa* has recently become a worldwide serious concern. The prevalence of imipenem-resistant *P. aeruginosa* in Tehran has been reported to be within the range of 16% to 100% (8, 9). In fact, in the past two years, the rate of imipenem-resistant *P. aeruginosa* has increased from 69% to 97.5% in Shahid Motahari Burn Hospital (9, 10).

2. Objectives

Multidrug-resistant *P. aeruginosa* is the most prevalent bacterial isolate among the burn patients. The objective of the study was to determine the antibiotic susceptibility profiles of *P. aeruginosa* burn isolates in Shahid Motahari Burn Hospital in Tehran.

3. Materials and Methods

3.1. Bacterial Isolates

One hundred and thirty three *P. aeruginosa* burn isolates were collected from Shahid Motahari Burn Hospital between July and December 2011. The majority of bacterial isolates were recovered from wounds (88.72%), followed by blood (5.26%), cvp (subclavian catheters) lines (4.51%) and urine (1.5%). Two thirds of the specimens were from male patients and the rest were from females. All isolates were identified as *P. aeruginosa* by the standard microbiological tests such as Gram stain, oxidase test, growth on MacConkey agar (Liofilchem, Italy), oxidation-fermentation test, growth and fermentation on triple sugar iron agar (QBBL, UK), growth at 42°C, and pigment formation (11). The isolates were maintained at -20 °C in

brain-heart infusion broth (Oxoid, UK) containing 10% dimethyl sulfoxide (v/v).

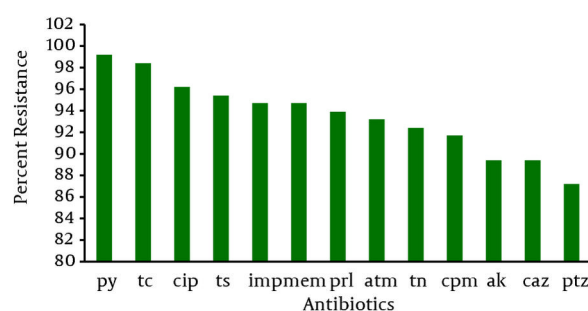
3.2. Antimicrobial Susceptibility

The Antimicrobial susceptibility profiles of the isolates were determined by the agar disc diffusion method according to the recommendations made by the Clinical and Laboratory Standards Institute (CLSI) (12). The following antimicrobial discs (MAST Diagnostics, Merseyside, UK) were used: imipenem (10 µg), meropenem (30 µg), aztreonam (30 µg), cefepime (30 µg), ceftazidime (30 µg), amikacin (30 µg), ciprofloxacin (5 µg), piperacillin (100 µg), piperacillin/tazobactam (110 µg), carbenicillin (100 µg), ticarcillin (75 µg), co-trimoxazole (25 µg) and tobramycin (10 µg). *P. aeruginosa* ATCC 27853 was used as the control in each run of antimicrobial susceptibility tests which were repeated at least 3 times and the average of inhibition zones was reported.

4. Results

The antibiotic susceptibility results showed 99.2% resistance to carbenicillin, 98.4% to ticarcillin, 96.2% to ciprofloxacin, 95.4% to co-trimoxazole, 94.7% to imipenem and meropenem, 93.9% to piperacillin, 93.2% to aztreonam, 92.4% to tobramycin, 91.7% to cefepime, 89.4% to amikacin and ceftazidime, and 87.2% to piperacillin-tazobactam (Figure 1). All isolates were MDR (resistant to at least 3 different classes of antibiotics).

Figure 1. Antibiotic Susceptibility of *P. aeruginosa* Burn Isolates.

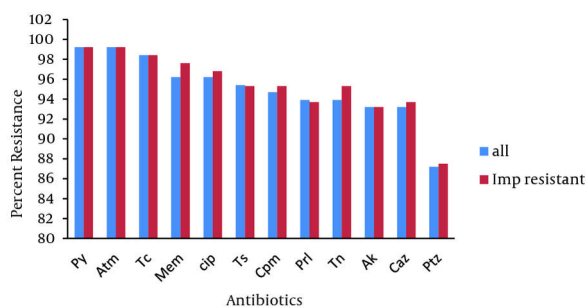


Py: carbenicillin, Tc: ticarcillin, Cip: ciprofloxacin, Ts: co-trimoxazole, Imp: imipenem, Mem: meropenem, Prl: piperacillin, Atm: aztreonam, Tn: tobramycin, Cpm: cefepime, Ak: amikacin, Caz: ceftazidime and Ptz: piperacillin/tazobactam.

Among the imipenem-resistant *P. aeruginosa*, there was 99.2% resistance to carbenicillin, 98.4% to ticarcillin, 96.8% to ciprofloxacin and aztreonam, 96% to meropenem, 95.3% to co-trimoxazole, 94.5% to tobramycin, 93.7% to cefepime and piperacillin, 91.4% to amikacin, 89.4% to ceftazidime and 87.5% to piperacillin-tazobactam (Figure 2). Since there was an overall high rate of imipenem resistance (94.7%), no statistical analysis could be performed to compare the susceptibility profiles of imipenem-resistant

strains with the susceptible isolates. However, resistance to ceftazidime, tobramycin, meropenem, cefepime and ciprofloxacin was slightly higher in imipenem-resistant strains (Figure 2), there was no relationship between antibiotic resistance and the source of the specimen.

Figure 2. Comparison of Antibiotic Susceptibility Between Imipenem Resistant and All of *P. aeruginosa* Isolates.



Py: carbenicillin, Atm: aztreonam, Tc: ticarcillin, Mem: meropenem, Cip: ciprofloxacin, Ts: co-trimoxazole, Cpm: cefepime, Prl: piperacillin, Tn: tobramycin, Ak: amikacin, Caz: ceftazidime and Ptz: piperacillin/tazobactam.

5. Discussion

Over the past 20 years, *P. aeruginosa* has been repeatedly recognized as the most prevalent organism which causes infection in burn centers in Tehran (5, 13, 14). Unfortunately, the organism appears to be resistant to almost all antimicrobial agents creating a great problem in clinical settings. In addition, the more recent emergence of carbapenem resistance in *P. aeruginosa* has limited the therapeutic options.

Multidrug-resistant *P. aeruginosa* is often the cause of outbreak of diseases in the burn units (5, 10). Different rates of MDR have been reported for *P. aeruginosa* burn isolates in various cities of Iran (5, 10, 13). The reports from Shahid Motahari Burn Hospital in Tehran have varied considerably from 2007 to 2011 in both MDR and carbapenem resistance. Salimi *et al.* found 16% imipenem resistance and 42% MDR in *P. aeruginosa* isolates collected in 2008 from the intensive care burn patients (14). Sadari *et al.* reported that 69% of *P. aeruginosa* burn isolates in 2008 were multidrug-resistant and MDR was more prevalent in the imipenem-resistant strains compared to the imipenem susceptible isolates (87% vs. 29%) (10). In 2007, Ranjbar *et al.* reported that all *P. aeruginosa* burn isolates from Shahid Motahari Burn Hospital were MDR of which, 97.5% were resistant to imipenem (9).

We found that 100% of *P. aeruginosa* isolates from Shahid Motahari Burn Hospital were MDR of which 94.7% were resistant to both imipenem and meropenem. The main reasons for various rates of drug resistance in such a short period of time from the same hospital

could be the use of different antibiotic regimes, presence of different persistent strains in hospitals and the quality of hygiene in different environments. Similarly, according to other studies in Iran, various degrees of imipenem resistance in *P. aeruginosa* have been reported. Beheshti and Zia reported 61.1% imipenem resistance in *P. aeruginosa* burn isolates from Imam Mousa Kazem Burn Center in Esfahan in 2011 (13). Haghi *et al.* reported 100% multidrug and imipenem resistance in *P. aeruginosa* burn isolates in Orumieh (13). Jamali and colleagues reported 61.8% imipenem resistance in the burn isolates of *P. aeruginosa* in 2009 (15). Studies in other countries have also shown different rates of imipenem resistance in *P. aeruginosa* burn isolates. Similar to these results, Shahid *et al.* found 100% MDR in *P. aeruginosa* burn isolates in India in 2003, (16). In 2004, Ozkurt *et al.* reported 69.92% imipenem resistance in *P. aeruginosa* burn isolates in Turkey (17). In a study conducted between 1996 and 1998 in Korea, 52% of *P. aeruginosa* were resistant to imipenem (18). In another study performed in Karachi, Pakistan in 2003, imipenem resistance in *P. aeruginosa* was 32.7% (19).

Antibiotic resistance in *P. aeruginosa* may be mediated via several distinct mechanisms including β -lactamase production, efflux pumps, modification of site-targeted drugs or outer membranes (4, 20). MDR is usually the result of a combination of different mechanisms in a single isolate or the action of a single potent resistance mechanism (20). The increase in antibiotic resistance is mostly due to extensive use of antibiotics such as ciprofloxacin, β -lactams and aminoglycosides in the burn centers as well as non-availability and high costs of other effective drugs.

We believe that it is important to conduct surveillance programs for appropriate empirical therapy and the practices of infection control. Meanwhile, it is necessary for health care practitioners and policy makers to address this problem by implementing suitable protocols for use of antibiotics not only to find strategies for treating such difficult infections, but also to avoid spreading of the resistance genes among bacteria.

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Authors' Contribution

None declared.

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