# Antimicrobial Susceptibility Pattern of *Pseudomonas Aeruginosa* and Antibiotic Use in King Fahd Hospital of the University in Khobar, Saudi arabia

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Abstract :

Nosocomial infections caused by Pseudomonas aeruginosa in critically ill patients are often difficult to treat because of resistance to multiple antimicrobials. The purpose of this study was to evaluate antimicrobial resistance among P. aeruginosa isolates at King Fahad Hospital of the University from 1998-2004. We also evaluated the consumption of antipseudomonal agents over the same period. One thousand two hundred and eighty four nonduplicate isolates of P. aeruginosa were tested. Decreasing susceptibility to all antipseudomonal agents was observed with the greatest declines involving ciprofloxacin (96 -64%, $p$ <0.05), gentamicin (85-60%, $p$ <0.05)), ceftazidime (68-47%, $p$ <0.05), and cefepime (78-64%, $p$ <0.05). Despite the increasing use of pipracillin/tazobactam, susceptibility rate did not decrease significantly during the study period (83-77% $p$ >0.05). In addition, although ceftazidime and gentamicin use decreased, the proportion of P. aeruginosa that was susceptible to these agents continued to decrease for the first six years of the study and stabilized in 2004. Among the agents tested, meropenem, amikacin, imipenem and pipracillin-tazobactam, were the most active against P. aeruginosa, although susceptibility to any agent tested was still less than 90%. Ongoing surveillance studies are crucial in monitoring antimicrobial susceptibility patterns and the selection of empirical treatment regimen.

## Introduction :

Pseudomonas aeruginosa is one of the most common gram-negative pathogens associated with nosocomial infections (1). Infections caused by P. aeruginosa are frequently life threatening and often difficult to treat because of its intrinsic resistance to various antimicrobial agents and their ability to acquire adaptive resistance during a therapeutic course (2). The increasing prevalence of drug resistance among P. aeruginosa complicates decisions on treatment with antibiotics. In fact, resistance of P. aeruginosa to antimicrobials used for primary treatment has been shown to correlate with an adverse clinical outcome (3). Antibiotic use has proven to be one of the

most important factors in the development and maintenance of antimicrobial resistance (4).

The selection of appropriate antimicrobial therapy requires an active surveillance of emerging resistance trends and continuous education among health care providers.

The objectives of this study were to compare and correlate antimicrobial usage and resistance patterns and trends among P. aeruginosa at King Fahad hospital of the University from 1998 to 2004.

**Materials and methods :**

A retrospective study was conducted at King Fahad Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia, a 440-bed primary through tertiary care hospital. The microbiology laboratory database was used to identify all clinical cultures from patients that were positive for P. aeruginosa during a seven-year period from 1998 to 2004 without a duplication of strains. These isolates from different inpatients departments. All organisms were identified to the species level and testing for susceptibility was conducted using a custom microdilution MIC panel (Microscan WalkAway 96SI). In this study the susceptibilities to commonly recognized antipseudomonal agents were evaluated, including the aminoglycosides (gentamicin and amikacin), antipseudomonal cephalosporins (ceftazidime and cefepime), tazocin (piperacillin and tazobactam), carbapenems (imipenem and meropenem) and ciprofloxacin.

**Antibiotic use :**

In response to the increasing resistance patterns, the Hospital Antibiotic Committee adopted antibiotic utilization guidelines to reduce the use of third-generation cephalosporins as empirical therapy. Approval by the infectious disease consultant was required for the use of a third-generation cephalosporin. Pipracillin-tazobactam and cefepime were used as empirical therapy for nosocomial infections. Treatment with carbapenems (imipenem and meropenem) required the same approval except when needed for use in the intensive care units.

Records of acquisition of gentamicin, amikacin, ceftazidime, cefepime, pipracillin and tazobactam (Tazocin), ciprofloxacin, imipenem and meropenem were obtained from the pharmacy purchasing department.

**Statistical analysis :**

The results were analyzed using the SPSS-PC. X2 analysis was performed and $p<0.05$ was considered significant.

## Results

Susceptibilities of antipseudomonal agents for 1284 nonduplicate isolates of P. aeruginosa were evaluated during the 7-year period. Susceptibilities to different agents are shown in fig 1. Decreasing susceptibility to all antipseudomonal agents was observed with the greatest declines involving ciprofloxacin (96 -64%, $p$ <0.05), gentamicin (85-60%, $p$ <0.05), and ceftazidime (68-47%, $p$ <0.05). Although susceptibility data on cefepime were not available during the entire study period, there was a significant reduction in susceptibility rate (78-64%, $p$ <0.05). For most antimicrobial agents, a steady decrease in susceptibility occurred over the study period and has remained stable from 2003 to 2004. Among the agents tested, meropenem, amikacin, imipenem and pipracillin-tazobactam, were the most active against P. aeruginosa, although susceptibility to any of these agents was still less than 90%.

The change in antibiotic usage from 1998 to 2004 is shown in table1. Meropenem was introduced to the formulary in 1999 and cefepime in 2001. On the total consumption, the use of ceftazidime and gentamicin declined with a concomitant increase in the consumption of pipracillin/tazobactam, cefepime, and meropenem during the period of the study, whereas the use of amikacin and imipenem fluctuated. The use of ciprofloxacin was stable from1998 to 2002, with a 20% increase between 2003 and 2004.

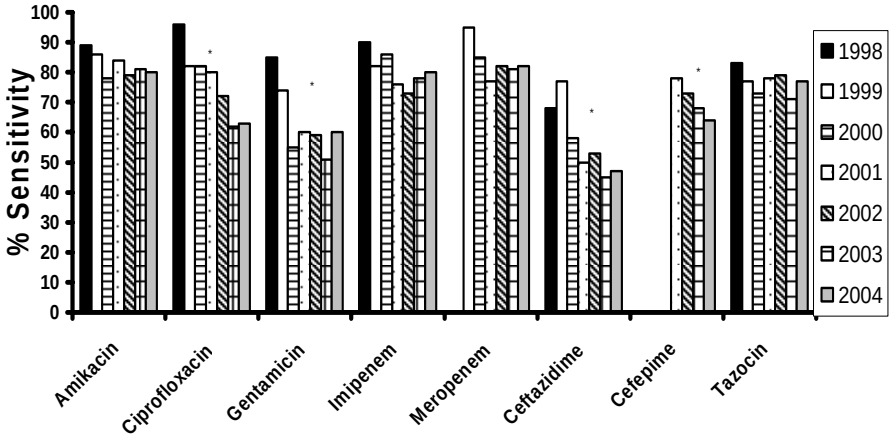


Figure1. Antimicrobial susceptibility rates for Pseudomonas aeruginosa, 1998-2004

Table (1)
Susceptibilities of Pseudomonas aeruginosa isolates and antibiotic usage

| Antibiotic | P. aeruginosa % susceptible | | Change (%) | Antibiotic Use | |
|---|---|---|---|---|---|
| | 1998 | 2004 | | 1998 | 2004 |
| Amikacin | 89 | 80 | -9 | 3000 g | 4500 g |
| Ciprofloxacin | 96 | 65 | -31(p<*0.05)* | 4000 g | 5000 g |
| Gentamicin | 85 | 60 | -25(p<*0.05)* | 18000 g | 10000 g |
| Imipenem | 90 | 80 | -10 | 2000 g | 2500 g |
| Meropenem | ND | 82 | | | 5000 g |
| Ceftazidime | 68 | 47 | -21 (p<*0.05)* | 18000 g | 3000 g |
| Cefepime | ND | 64 | | | 4000 g |
| Tazocin | 83 | 77 | -6 | 2000 g | 10000 g |

Meropenem was introduced to the formulary in 1999 (1000 g) and cefepime in 2001(1500gm)

**Discussion** :

Nosocomial infections caused by Pseudomonas aeruginosa are frequently life threatening and difficult to treat (1, 5). The organism's intrinsic susceptibility to a limited number of antimicrobial agents and the emergence of resistance during therapy, among initially susceptible strains, occurs with a relatively high frequency (6). Improvement of the clinical outcomes of patients with severe Pseudomonas aeruginosa infection depends on the rapid institution of adequate antimicrobial therapy (7). Unfortunately, instituting adequate empiric antimicrobial coverage is very difficult because of increasing resistance. Active surveillance of institutional susceptibility patterns can better assist clinicians in the selection of antimicrobials for the empiric therapy of nosocomial infections.

High rates of resistance to antimicrobial agents among clinical isolates of P. aeruginosa have been documented in the past decade in hospitals worldwide (8, 9). However there is considerable geographic variation in the rates of resistance to the various antimicrobial classes and to individual agents within each class (10).

The present study demonstrates increase in resistance among P. aeruginosa isolates to commonly prescribed antipseudomonal agents during the 7-year period from 1998 to 2004. Decreasing susceptibility to all antipseudomonal agents was observed with the greatest declines involving ciprofloxacin, ceftazidime, gentamicin, and cefepime. Other surveillance

studies have also shown decreasing susceptibility of P. aeruginosa isolates particularly to fluoroquinolones (11).

Ciprofloxacin, the most potent agent available in oral form for the treatment of P. aeruginosa infections, is in particular jeopardy. For instance in Europe, United States, and Latin America, rates of susceptibility to the drug are between 60-75 % (9).

Despite the increasing use of pipracillin/tazobactam, susceptibility rate did not decrease significantly during the study period. In addition, although ceftazidime and gentamicin use decreased, the proportion of P. aeruginosa that was susceptible to these agents continued to decrease in the first six years of the study and stabilized in 2004. In a report by Gentry et al a similar result indicated that, despite the substantial reduction in ceftazidime use, there was increased resistance among P. aeruginosa isolates (11). We noticed that several changes in antimicrobial use had no corresponding changes in susceptibilities. The possible explanation is that King Fahd hospital is a referral center. Our susceptibility profile therefore may be affected by patients admitted from different hospitals in the eastern province of the Kingdom. Another possibility is that the elimination of long-term resistance may require a longer period of time, as has been observed by other investigators (12).

Among the agents tested, meropenem, amikacin, imipenem and pipracillin-tazobactam, were the most active against P. aeruginosa, although susceptibility to any of these agents was still less than 90%. This trend has also been reported in the MYSTIC program (13), and from other hospitals in the kingdom of Saudi Arabia (14,15).

In conclusion, susceptibility of P. aeruginosa isolates was found to have declined substantially in the past seven years. The scarcity of adequate treatment options is very disturbing in an era of ever- increasing antibiotic resistance. Ongoing surveillance of susceptibility of P. aeruginosa and its resistance profile is necessary for the provision of adequate information to clinicians in selecting adequate antimicrobial therapy. In addition improved antibiotic stewardship and infection-control measures will be needed to prevent or slow the emergence and spread of resistant P. aeruginosa in the healthcare setting.

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# نمط حساسية المضادات الحيوية لبكتيريا الزائفة الزنجارية (البسيدوموناس أيروجينوزا) واستعمالها في مستشفى الجامعي بالخبر – المملكة العربية السعودية

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**الملخص :**

تعتبر العدوى المكتسبة بالمستشفيات والناتجة عن جرثومة السيدوموناس أيرجينوزا والتي تصيب المرضى الذين يعاونون من أمراض خطيرة من الصعب علاجها وذلك لمقاومتها لكثير من المضادات الحيوية.

**الهدف :** تهدف هذه الدراسة لتقييم مقاومة جرثومة السيدوموناس أيرجينوزا للمضادات الحيوية وكمية المضادات الحيوية المستعملة لعلاج هذه الجرثومة في نفس فترة الدراسة.

**الطريقة :** أجريت الدراسة بمستشفى الملك فهد الجامعي بالخبر في الفترة ما بين ١٩٩٨م و ٢٠٠٤م خلال هذه الفترة تم الفحص على ١٢٨٤ عينة لجرثومة السيدوموناس أيرجينوزا.

**النتائج :** أظهرت الدراسة تناقصاً في حساسية جرثومة السيدوموناس أيرجينوزا لكثير من المضادات الحيوية المستعملة وكانت ذات دلالة إحصائية. وقد أجريت التحليلات الإحصائية بإستخدام spss نسخة ١٥ .

**الخلاصة :** بينت هذه الدراسة أن حساسية السيدوموناس إيرجينوزا للمضادات الحيوية قد تناقصت خلال فترة الدراسة وبناءً على ذلك فإنه ينصح بتقييم مستمر لمقاومة هذه الجرثومة لمختلف المضادات الحيوية المستعملة لإمكانية مقاومتها.