Antibiotic Sensitivity Pattern of Clinical Isolates of *Pseudomonas aeruginosa* at a Tertiary Care Hospital in Saudi Arabia

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ABSTRACT: Among gram-negative microorganisms *Pseudomonas aeruginosa* is the most common bacteria identified in different clinical specimens of hospitalized patients. A few studies have been conducted in Saudi Arabia regarding antibiotic susceptibility pattern. The purpose of this study was to evaluate the current levels of antibiotic susceptibility and to assess the resistance pattern of antibiotics among the clinical isolates of *P. aeruginosa* in the King Khalid Hospital, Alkharj, Kingdom of Saudi Arabia. This study was carried out during January, 2015 to May, 2015. A total of 180 different specimens such as sputum, urine, pus swabs, wound swabs etc. were collected from different patients admitted to the hospital. Thirty (30) clinical isolates of *P. aeruginosa* were isolated from different specimens of the patients suspected of having respiratory tract infection, urinary tract infection, wound infections, etc. The antibiotic susceptibility profiles of all the isolates were determined using Kirby-Bauer disk diffusion method. Piperacillin-tazobactam was found to be the most active antimicrobial agent with 96.7% susceptibility followed by cefepime (83.3%), ceftazidime (83.3%), and ciprofloxacin (76.7%). All isolates were resistant to ertapenem, cefuroxime, cefoxitin and nitrofurantoin. Anti-bacterial treatment strategies should focus on *P. aeruginosa*, for which the prevalence rates are increasing every year. The usage of piperacillin-tazobactam, cefepime, ceftazidime and ciprofloxacin must be reserved and only be given to the patients after susceptibility test to reduce the resistance of *P. aeruginosa* against these agents.

Keywords: Antibiotic, resistance pattern, *Pseudomonas aeruginosa*, sensitivity pattern

INTRODUCTION

Natural existence of *Pseudomonas* all over the world has been recognized early in the history of microbiology. The distribution of the members of the genus *Pseudomonas* is wide in nature, but the commonest human pathogen is *Pseudomonas aeruginosa* (*P. aeruginosa*). It is the most important human pathogen causing serious and life threatening infections in immunocompromised patients, especially those patients having respiratory disease, cancer receiving chemotherapy, and cystic fibrosis especially children and young adults. Besides, it is one of the leading causative organisms of nosocomial infections and is associated with a significant mortality rate. The main reason for high mortality rate is its notable resistance to the majority of the currently available antibiotics. Yet, comparative analyses of the emergence of resistance associated with different classes of antipseudomonal drugs are lacking.[1] It is of utmost importance to have the knowledge about the relative risks of resistance with different antibiotics in order to guide treating physicians in selecting appropriate therapeutic choices.[1] Continuous surveillance of *P. aeruginosa* resistance against different antimicrobial agents is a basic requirement to monitor the trends of susceptibility patterns and to appropriately guide the treating physicians in choosing empirical therapy, especially when new antibiotics may not be easily available in upcoming future.[2] To the best of our

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knowledge there are limited surveillance studies which report antibiotic resistance patterns among clinical isolates of *P. aeruginosa* in the Kingdom of Saudi Arabia.[3]

A significant increase in antibiotic resistance among gram negative bacteria isolated from admitted patients has been reported over the past few years, especially among critically ill patients.[4] It is well known that infections caused by multidrug resistant (MDR) gram negative bacteria, especially MDR *P. aeruginosa* have been associated with high morbidity, mortality and costs.[5] Patients suffering from nosocomial infections particularly those admitted in different intensive care units are usually infected with MDR strains of *P. aeruginosa.*[6]

The aim of the present study was to evaluate the current levels of antibiotic susceptibility and to assess the resistance pattern of anti-pseudomonal antibiotics among the clinical isolates of *P. aeruginosa* isolated from patients suffering from different infections, such as respiratory tract infection, wound infections and urinary tract infection admitted to the King Khalid Hospital, Al-Kharj, Kingdom of Saudi Arabia.

MATERIALS AND METHODS

This study was carried out in the Department of Microbiology, Prince Sattam bin Abdul-Aziz (PSAU), from January, 2015 to May, 2015. A total of 180 different specimens such as sputum, urine, pus swabs and wound swabs were collected from different patients admitted to King Khalid Hospital, Al-Kharj, Saudi Arabia. All these specimens were transported to the Microbiology Department of the College of Medical Sciences, PSAU, and processed immediately. The specimens were cultured on different media such as Blood agar, MacConkey agar, Cetrimide agar and cysteine-lactose-electrolyte-deficient agar. Colonies suspected of *Pseudomonas* were identified on the basis of colonial morphology, gram stain and biochemical tests and were re-confirmed as *P. aeruginosa* by using commercially available API 20 NE. A total of 30 isolates of *P. aeruginosa* were isolated from these specimens. Of these 17 specimens were collected from male and 13 from female patients. In addition, 50% (n=15) of our isolates were from neonates and children. The demography of the patients was given in Table 1.

Table 1. Demography of the patients included in the study.

Age (years)		Number of samples (%)
Males		17 (56.7)
Females		13 (43.3)
Age	0-10	15 (50)
	10-20	7 (23.3)
	20-30	0
	30-40	0
	>40	8 (26.7)

Antibiotic susceptibility testing. Antibiotic susceptibility testing was done by using Kirby-Bauer disk diffusion method.[7] The disk of gentamicin (10 μg), impenem (10 μg), amikacin (30 μg), piperacillin (100 μg), ciprofloxacin (5 μg), ceftazidime (30 μg), aztreonam (30 μg), meropenem (10 μg), cefepime (30 μg), ertapenem (10 μg), cefuroxime (30 μg), cefoxitin (30 μg), nitrofurantoin (300 μg) and levofloxacin (5 μg) were used for susceptibility testing. The results of disk diffusion method were interpreted in accordance to the Clinical and Laboratory Standards Institute (CLSI, 2015).[8]

RESULTS AND DISCUSSION

The antimicrobial susceptibility testing showed that *P. aeruginosa* strains were highly sensitive to most of the antibiotics tested, which are shown for sputum (Table 2), urine (Table 3), pus/wound swabs (Table 4) and in details in Table 5. The percentage of sensitivities was piperacillin-tazobactam (96.7%), ceftazidime (83.3%), cefepime (83.3%), ciprofloxacin (76.7%), meropenem (73.3%), levofloxacin (70%), imipenem (63.3%), gentamicin (56.7%), amikacin (43.3%), aztreonam (43.3%) and tobramycin (23.3%) and the percentage of resistance were 36.7 % to imipenem, 33.3% to aztreonam, 23.3% to levofloxacin, 16.7 % to meropenem and ceftazidime, 13.3% to ciprofloxacin and 10% to gentamicin and cefipime.

Table 2. Antibiotic sensitivity and resistance pattern of *P. aeruginosa* (n=12) from sputum of studied patients.

Number	Antimicrobial	Sensitive (%)	Resistance (%)
1	Amikacin	7 (58.3)	5 (41.7)
2	Gentamicin	6 (50)	6(50)
3	Tobramycin	1 (8.3)	11 (91.7)
4	Ertapenem	0 (0)	12 (100)
5	Imipenem	7 (58.3)	5 (41.7)
6	Meropenem	10 (83.3)	2 (16.7)
7	Cefuroxime	0 (0)	12 (100)
8	Cefoxitin	0 (0)	12 (100)
9	Ceftazidime	11 (91.7)	1 (8.3)
10	Cefepime	10 (83.3)	1 (8.3)
11	Aztreonam	6 (50)	5 (41.7)
12	Piperacillin-tazobactam	11 (91.7)	1 (8.3)
13	Nitrofurantoin	0 (0)	12 (100)
14	Ciprofloxacin	11 (91.7)	1 (8.3)
15	Levofloxacin	8 (66.7)	2 (16.7)

Table 3. Antibiotic sensitivity and resistance pattern of *P. aeruginosa* (n=10) from urine culture.

Number	Antimicrobial	Sensitive (%)	Resistance (%)
1	Amikacin	5 (50)	5 (50)
2	Gentamicin	6 (60)	4 (40)
3	Tobramycin	4 (40)	6 (60)
4	Ertapenem	0 (0)	10 (100)
5	Imipenem	6 (60)	4 (40)
6	Meropenem	6 (60)	1 (10)
7	Cefuroxime	0 (0)	10 (100)
8	Cefoxitin	0 (0)	10 (100)
9	Ceftazidime	8 (80)	2 (20)
10	Cefepime	9 (90)	0 (0)
11	Aztreonam	4 (40)	1 (10)
12	Piperacillin-tazobactam	10 (100)	0 (0)
13	Nitrofurantoin	0 (0)	10 (100)
14	Ciprofloxacin	8 (80)	1 (10)
15	Levofloxacin	8 (80)	2 (20)

Among gram-negative bacteria, *P. aeruginosa* is a leading causative organism of nosocomial infections. With the extensive use of antibiotics and increase in the number of immunocompromised hosts, *P. aeruginosa* has become one of the leading cause of gram-negative bacterial infections especially in immunocompromised patients who need prolonged stay in hospitals.[9] The increasing rate of *P. aeruginosa* strains in a wide spectrum of clinical settings determine them as emerging pathogens, especially in intensive care units (ICUs), and justifies the necessity for Antimicrobial Resistance Surveillance. Continuous monitoring of antibiotic resistance patterns in *P. aeruginosa* infection is very important in updating the current activity level of commonly used anti-pseudomonal antibiotics.[2]

A study from Saudi Arabia reported that 85% of the *P. aeruginosa* isolates are sensitive to ciprofloxacin.[3] However, our study showed about 76% of *P. aeruginosa* isolates are sensitive to ciprofloxacin which is lower than others.[3] This indicates that it is developing resistance gradually. Studies have shown that the large majority of Meropenem-resistant *P. aeruginosa* revealed resistance to imipenem, but almost half of the imipenem resistant strains were sensitive to meropenem. In addition, it was reported that the strains resistant to Meropenem were also resistant to ciprofloxacin and carbenicillin.[10] A number of recent studies have shown imipenem to be highly active antibiotic against *P. aeruginosa*,[11] while other

Table 4. Antibiotic sensitivity and resistance pattern of *P. aeruginosa* (n = 8) from pus / wound swabs.

Number	Antimicrobial	Sensitive (%)	Resistance (%)
1	Amikacin	1 (12.5)	7 (87.5)
2	Gentamicin	5 (62.5)	3 (37.5)
3	Tobramycin	2 (25)	6 (75)
4	Ertapenem	0 (0)	8 (100)
5	Imipenem	6 (75)	2 (25)
6	Meropenem	6 (75)	2 (25)
7	Cefuroxime	0 (0)	8 (100)
8	Cefoxitin	0 (0)	8 (100)
9	Ceftazidime	6 (75)	2 (25)
10	Cefepime	6 (75)	2 (25)
11	Aztreonam	3 (37.5)	4 (50)
12	Piperacillin-tazobactam	8 (100)	0 (0)
13	Nitrofurantoin	0 (0)	8 (100)
14	Ciprofloxacin	4 (50)	2 (25)
15	Levofloxacin	5 (62)	3 (37.5)

Table 5. Antibiotic sensitivity and resistance pattern of *P. aeruginosa* (n = 30) isolated from different specimens.

Number	Antimicrobial	Sensitive (%)	Resistance (%)
1	Amikacin	13 (43.3)	17 (56.7)
2	Gentamicin	17 (56.7)	13 (43.3)
3	Tobramycin	7 (23.3)	23 (76.7)
4	Ertapenem	0 (0)	30 (100)
5	Imipenem	19 (63.3)	11 (36.7)
6	Meropenem	22 (73.3)	5 (16.7)
7	Cefuroxime	0 (0)	30 (100)
8	Cefoxitin	0 (0)	30 (100)
9	Ceftazidime	25 (83.3)	5 (16.7)
10	Cefepime	25 (83.3)	3 (10)
11	Aztreonam	13 (43.3)	10 (33.3)
12	Piperacillin-tazobactam	29 (96.7)	1 (3.3)
13	Nitrofurantoin	0 (0)	30 (100)
14	Ciprofloxacin	23 (76.7)	4 (13.3)
15	Levofloxacin	21 (70)	7 (23.3)

has reported otherwise.[12] Our findings were almost similar to that reported by Patzer and Dzierzanowska, 2007.[12] The current study showed that *P. aeruginosa* was highly resistant to different aminoglycosides, including Amikacin (56.7%), Tobramycin (76.7%), and Gentamicin (43.3%). Our results were similar to that reported by Lila *et al*.[13] However, this result was in disagreement with one study, which asserts that Amikacin has the highest sensitivity against *P. aeruginosa*.[14] In our study resistance to 3 or more antibiotics (MDR) was about 20% which was much lower than that reported by others.[15] It is well known that inappropriate use of antibiotics gradually results in bacterial resistance.[16,17]

In our study, the rates of antimicrobial resistance of the isolates were 36.7 % to imipenem, 33.3% to aztreonam, 23.3% to levofloxacin, 16.7 % to meropenem and ceftazidime, 13.3% to ciprofloxacin, and 10% to cefipime. Antibiotic resistance patterns in different hospitals in Saudi Arabia and others nations as well have been reported within the past and antibiotics within the particular hospitals are recognized to the differential utilization. When compared our results with the previous studies from Saudi Arabia, [18] our study showed higher resistance rates to all antibiotics tested except piperacillin-tazobactam. Among the 30 clinical isolates of *P. aeruginosa* tested in our study, many strains were found to be multidrug-resistant (MDR). Patients with resistant MDR *P. aeruginosa* infection have a poor prognosis and it is consequently increasingly so that that close attention is paid to *P. aeruginosa* strains displaying high antibiotic resistance. Piperacillin-tazobactam was found to be the most active antibiotic with 96.7% susceptibility followed by cefepime (83.3%), ceftazidime (83.3%), ciprofloxacin (76.7%), and meropenem (73.3%), where about 30% of the isolates were MDR.

CONCLUSION

An increasing trend in the emergence of antibiotic resistance in *P. aeruginosa* has been observed in Saudi Arabia. Based on our findings, we conclude that antibacterial treatment strategies should focus on *P. aeruginosa* for which the prevalence rates are increasing gradually. The use of piperacillin-tazobactam, cefepime, ceftazidime and ciprofloxacin should be limited in use in terms of reservation in reducing the resistance of *P. aeruginosa* to these antibiotics. Antibiotic use and the corresponding resistance status of *P. aeruginosa* must also be considered to ascertain the rational utilization of antibiotics and the development of efficacious therapeutic strategies through implantation national of antibiotic policy.

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