ORIGINAL ARTICLE

Multi-Drug Resistant Pseudomonas Aeruginosa: A threat of nosocomial infections in tertiary care hospitals

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Abstract

Objective: To determine the resistance patterns of Pseudomonas aeruginosa to currently available anti-pseudomonal drugs and frequency of nosocomial infections caused by multi drug resistant Pseudomonas aeruginosa in hospitals.

Methods: Clinical isolates of Pseudomonas aeruginosa were collected from patients admitted in different hospitals of Karachi between July 2012 and June 2013. The isolates were identified by conventional and Analytical Profile Index 20NE kit methods while the antibiograms of these isolates were determined by Kirby- Bauer disc diffusion method.

Results: Of the 204 isolates, 79(39%) were obtained from intensive care units. Overall, 135(66%) isolates belonged to men, and 35(17.2%) belonged to 10-15 year age group. The overall antibiogram pattern showed high resistance to commonly used antibiotics like Ofloxacin 125(61.3%), Cefepime 117(57.3%), Ceftazidime 110(53.9%), Amikacin 108(53%). Of all the isolates, 129(63.2%) were considered multidrug resistant. The most effective antibiotics were Colistin, Polymyxin B and Meropenem.

Conclusion: Increasing multidrug resistance among nosocomial pathogens is an alarming situation in a hospital setting and requires prompt management of these cases.

Keywords: Pseudomonas aeruginosa, Multidrug resistance, antibiotic susceptibility. Antibiogram, MDRPA. (JPMA 65: 12; 2015)

Introduction

Pseudomonas (Ps.) aeruginosa has been recognised as a ubiquitious organism because of its extraordinary survival and adaptation abilities in a wide range of environments such as soil, water, sewage, hospitals etc. Among all gram-negative bacteria, Ps. aeruginosa has been considered a predominant opportunistic pathogen which usually infects persons having some underlying diseases and compromised immune status.[1,2] Therefore this organism has also been observed as one of the leading causes of nosocomial infections. In hospitalised patients, Ps. aeruginosa usually attacks patients with burns and wounds where they further complicate the primary condition and sometimes lead to bacteraemia.[3,4] Nosocomial pneumonia and urinary tract infections are the other prevalent types of infections associated with Ps. aeruginosa. In this connection, 40-60% mortality has been attributed to ventilator-associated pneumonia caused by Ps. aeruginosa.[4,5] It is also a major cause of morbidity and mortality in patients suffering from cystic fibrosis (CF) which is an autosomal recessive disorder. Moreover, this organism plays a significant role in the enhancement of complications in chronic obstructive pulmonary diseases.[6,7]

The capability of Ps. aeruginosa to generate resistance against commonly-used broad-spectrum antibiotics contributes greatly in its notorious fame.[1,8] This organism can combat against these drugs because of its ability to acquire multiple mechanisms of resistance such as low permeability of its membrane, efflux pumps, production of several antibiotic inactivating enzymes and biofilm formation.[4] Because of the unavailability of the successful therapeutic option, the treatment of severe infections with pseudomonas is now becoming more difficult. Only few anti-pseudomonal drugs such as some beta-lactams, aminoglycosides and fluoroquinolones can be considered good therapeutic options due to the emergence of resistance to most of the antibiotics giving rise to multiple drug resistant Ps. aeruginosa strains.[9]

The current study was planned to assess the resistance patterns of Ps. aeruginosa to currently available anti-pseudomonal drugs and to determine the frequency of nosocomial infections caused by this organism in Karachi hospitals. The outcomes of study, it was expected, would provide guideline for an effective treatment option and reference for an active measure of infection control.

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Materials and Methods

The epidemiological study comprised clinical isolates of four strains of Ps. aeruginosa that were collected from patients admitted in different hospitals of Karachi between July 2012 and June 2013. Demographic details including age, gender, location and clinical history of patients were recorded from hospitals' computerised databases. The isolates were collected from different wards of hospitals, including intensive care unit (ICU), Paediatric, General and Gynaecological wards as well as from different clinical specimens such as tracheal aspirate, bronchial washing, sputum, pus from wounds, urine and blood.

The isolates were identified by conventional methods using standard diagnostic criteria including microscopy, oxidase test, citrate utilisation test, triple sugar iron assay and motility test.[10] The identification of isolates that were not identified on the basis of conventional methods, was carried out by Analytical Profile Index (API) 20 NE kit (BioMerieux, France).

Antibiotic susceptibility test was done by using the disc diffusion Kirby Bauer method.[11] The antibiotics tested include Tazobactum/Piperacillin (10/100µg), Amikacin(30µg), Gentamicin (10µg), Ofloxacin(5µg), Levofloxacin (5µg), Ciprofloxacin (5µg), Ceftazidime (10µg), Cefepime(30µg), Meropenem(10µg), Imipenem (10µg), Polymyxin B (300 units) and Colistin(10µg). Ps. aeruginosa ATCC-27853 was used as reference strain.

Results

Of the 204 isolates, 79(39%) were obtained from ICU. followed by General Ward 58(28%) (Figure-1).

Among the antibiotics, Ofloxacin showed highest resistance with 125(61.3%) isolates being resistant to it. This was followed by Ciprofloxacin 122(60%), Cefepime 117(57.3%), Levofloxacin 115(56.4%), Ceftazidime 110(53.9%), Amikacin 108(53%), Gentamicin 104(51%) and Tazobactum/Piperacillin 81(37.9%). The most effective drug aginst Ps. aeruginosa with 100% susceptibility was Colistin followed by Polymyxin B 3(98.5%) and meropenem 175(85.8%) (Figure-2).

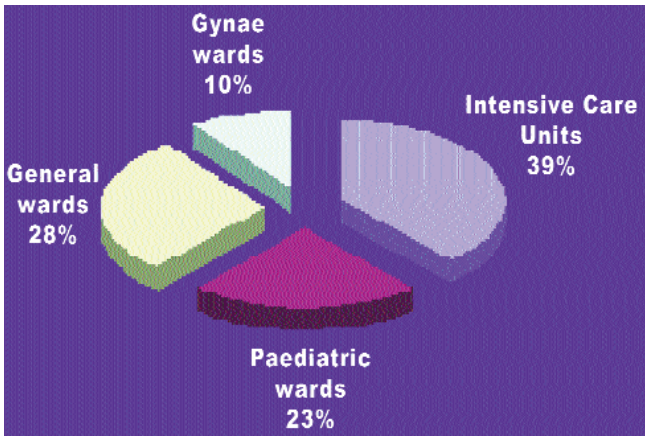


Figure-1: Prevalence of Pseudomonas aeruginosa in different hospital wards.

Besides, 129(63.2%) strains were multi drug resistant Ps. aeruginosa (MDRPA) as they were found to be resistant to 5 or more antibiotics. Among them 67(51.97%) were considered highly resistant as they showed resistance to all commonly-used anti-pseudomonal drugs, including Aminoglycosides, Cephalosporins and Quinolones.

The most common anatomical site of isolation of Ps. aeruginosa was respiratory tract 78(38.2%) followed by bronchial alveolar lavage 35(17.1%). Pus samples from wounds also revealed higher prevalence with 47(23%) isolates (Table-1).

Gender-wise distribution of Ps. aeruginosa strains revealed male propensity with 135(66.2%) cases. The incidence of MDRPA was also higher in male patients 93(72.1%) compared to females. The most susceptible age

Table-1: Distribution of MDRPA isolates in different clinical specimens.

S.No.	Clinical Specimen	Total No. Ps. aeruginosa strains isolated		Total No.of MDRPA strains isolated	
		No.	Percentage*A	No.	Percentage*B
1	Tracheal Aspirate	78	38.2	70	54.3
2	Bronchio alveolar lavage	35	17.2	18	13.9
3	Urine	26	12.8	14	10.8
4	Blood	18	8.8	1	0.8
5	Pus	47	23.0	26	20.2
	Total	204		129	

*A: %age calculated from total no. of Ps.aeruginosa isolates

*B:% age calculated from total no. of multidrug resistant Ps.aeruginosa isolates.

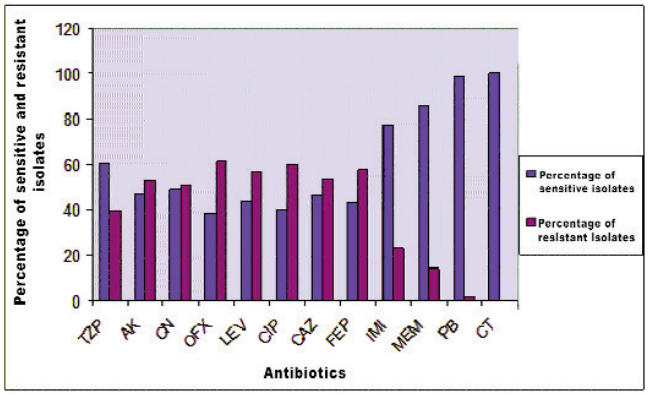
Ps: Pseudomonas

MDRPA: Multi drug resistant Pseudomonas aeruginosa.

Table-2: Distribution of MDRPA with respect to age and gender of patients.

Age Group	Male				Female				Total			
	No.of Ps.aeruginosa strains isolated		No. of MDRPA strains isolated		No.of Ps.aeruginosa strains isolated		No. of MDRPA strains isolated		Total No. of Ps. aeruginosa strains isolated		Total No. of MDRPA strains isolated	
	No.	%*A	No.	%*B	No.	%*A	No.	%*B	No.	%*A	No.	%*B
<10	18	13.3	9	19.4	11	15.9	6	16.7	29	14.2	15	11.6
10-19	21	15.5	18	9.7	14	20.4	6	16.7	35	17.2	24	18.6
20-29	11	8.1	6	6.4	6	8.7	2	5.5	17	8.3	8	6.2
30-39	9	6.7	7	7.5	9	13.0	3	8.3	18	8.8	10	7.7
40-49	20	14.8	7	18.3	9	13.0	6	16.7	29	14.3	23	17.8
50-59	23	17.1	18	19.3	9	13.0	4	11.1	32	15.7	22	17.0
60-69	21	15.6	14	15.1	7	10.2	8	22.2	28	13.7	22	17.0
>70	12	8.9	4	4.3	4	5.8	1	2.8	16	7.8	5	3.9
Total	135		93		69		36		204		129	

*A: %age calculated from total no. of Ps. aeruginosa isolates.
*B: % age calculated from total no. of multidrug resistant Ps.aeruginosa isolates.
Ps: Pseudomonas. MDRPA: Multi drug resistant Pseudomonas aeruginosa.



Key: TZP: Tazobactum, AK: Amikacin, CN : Gentacin, OFX : Ofloxacin, LEV : Levofloxacin, CIP: Ciprofloxin, CAZ: Ceftazidime, FEP: Cefepime, IMP: Imipenem, MEM: Meropenem, PB: Polymyxin B, CT: Colistin

Figure-2: Antibiotic resistance profile of Pseudomonas aeruginosa strains.

group was 10-19 years age group accounting for 35(17.2%) cases as well as for 24(18.6%) MDRPA isolates (Table-2).

Discussion

Ps. aeruginosa is a notorious gram-negative bacilli which is difficult to control with antibiotics or disinfectants. The factors which make this organism problematic are the inherent resistance of this specie to many classes of drugs, ability to acquire antibiotic resistance by mutation, and frequent involvement of this organism in serious infections.[12]

Being a ubiquitous organism in natural environments, Ps. aeruginosa is also a common opportunistic and nosocomial pathogen. In hospitalised patients, this organism colonises with higher rates, particularly when the patient is under administration of broad-spectrum antibiotics which also affects normal flora. Similarly, the disruption of natural barriers because of insertion of intravascular medical devices, endotracheal tubes and urinary catheters also predispose patients to acquire nosocomial infection by this pathogen.[13] In hospitalised patients having some underlying disease, pseudomonal pneumonia has been considered the most common nosocomial infection accounting for 30-33% of the total cases.[14] Ps. aeruginosa may also cause life-threatening conditions in hospitalised patients with compromised immune system.[3] The high morbidity and mortality because of pseudomonal infections may be reduced by early detection and prompt treatment of these infections.

The current study also highlighted the prevalence of infections by Ps. aeruginosa in different hospital settings and their resistance to most commonly-used antibiotics. The study focused on the collection of clinical specimens from patients who were admitted with some other disorder for a long period of time. The strains collected were identified and screened for their antibiotic susceptibility. Antibiotic resistance among bacterial isolates has been regarded as a growing clinical problem and a serious threat to public health. Similar threat was evident from antibiotic resistance profile of Ps. aeruginosa strains isolated from different patients in the present study. These clinical strains showed higher rates of resistance to most of the commonly-used antibiotics.

The most striking results were obtained from antibiotic

resistance profile of Quinolones family where the isolates showed marked resistance against Ofloxacin (61.3%), Ciprofloxacin (60%) and Levofloxacin (56.4%). This is in contrast with previous studies where clinical isolates were more susceptible to these antibiotics.[15,16] Aminogylycosides are considered frontline antibiotics against gram-negative bacterial infections, but in the present study higher resistance rates were recorded against Amikacin and Gentamicin which is inconsistent with earlier studies.[17,18] Cephalosporins are regarded as anti-pseudomonal drugs, particularly Ceftazidime which is a third generation cephalosporin and shows efficacy in such infections. But this drug also encountered higher resistance (53.9%) from Ps. aeruginosa isolates in this study. This finding simulates reports from Malaysia[19] whereas other studies reported much higher resistance against this antibiotic.[20]

Multidrug resistance is an emerging problem in clinical settings and has been reported from different parts of the world.[9,21,22] These strains may be a result of the emergence of multiple mechanisms of resistance after exposure to a number of different antipseudomonal drugs and cross-resistance between these drugs. In the present study, 63% of the total strains were considered multidrug resistant as they were found resistant to commonly-used pseudomonal drugs. Ps. aeruginosa acquires this multiple resistance to commonly-used antibiotics after their prolonged use in hospitalised patients.[23] These multidrug resistant strains were first reported from cystic fibrosis patients and were responsible for enhancing severity of the primary disease. The rising frequency of infections caused by MDRPA is a big problem for physicians all over the world. The resistant strains are associated with a three-fold higher rate of mortality, nine-fold higher rate of secondary bacteraemia, two-fold increase in length of hospital stay, and a considerable increase in healthcare costs.[24] As observed in the study, the multidrug resistant strains of Ps. aeruginosa were mainly obtained from ICUs which might be due to increasing invasive procedures that are required for diagnosis and chemotherapy and predispose patients to acquire nosocomial infections with such pathogens.

In the present study, the strains were mainly obtained from tracheal aspirate (38%) and pus samples (23%). This finding correlates to some extent with a previous study where higher prevalence was obtained from pus and urine samples.[25]

The age and gender-wise distribution of Ps. aeruginosa strains revealed high prevalence among male patients, whereas the most affected age group was 10-19 years. Similar rates of high prevalence among males were also indicated in literature and combination of factors such as male-dominant activities and relatively large body size of males might be behind more pseudomonal infections among males.[15]

Conclusion

The high rate of nosocomial infections and rising frequency of MDRPA in hospitals is an alarming situation. MDRPA has become a challenging nosocomial pathogen, forcing microbiologists to develop appropriate diagnostic tools, and physicians to optimise current antibiotic usage. The study may help in the strategic management of such multidrug resistant infections in terms of effective and prompt treatment. Surveillance efforts should consider resistant strains of Ps. aeruginosa as a high-priority area needing a solution.

Acknowledgement

We are grateful to Dean, Research Grant, Federal Urdu University of Arts, Science and Technology, Karachi, for financial assistance.

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