

Incidence and Antibiotic Susceptibility Pattern of *Pseudomonas aeruginosa* Isolated from Inpatients in Two Tertiary Hospitals

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Abstract

Pseudomonas aeruginosa (*P. aeruginosa*) has been reported as the most commonly isolated organisms in hospitals. The increasing resistance rate of *P. aeruginosa* to the common antimicrobial drugs has been reported worldwide. The present study aimed to investigate the incidence and antibiotic susceptibility pattern of *P. aeruginosa* from inpatients of two hospitals. Out of 1235 patient specimens, a total of 108 (8.7%) non-duplicated *P. aeruginosa* clinical isolates were identified, majority of them were from males (59.3%) and from patients above 60 years (31.5%). The most common incidence rate was from male ward (43.5%) followed by female ward (20.4%). Majority of *P. aeruginosa* strains were isolated from sputum specimen (38%) followed by urine specimen (14.8%). The results showed that 42.6% of the isolates were sensitive to all antibiotics while 36.1 % were found to be resistant to more than three antibiotics. The study showed that maximum antibiotic susceptibility rate of *P. aeruginosa* isolates was against amikacin (83.3%) followed by ciprofloxacin (75.9%). The maximum resistance rates among *P. aeruginosa* isolates were against Piperacillin/Tazobactam (38.5%), followed by cefepime (32.4%). It was concluded that among *P. aeruginosa* isolates, amikacin was the most susceptible antimicrobial drug while piperacillin-tazobactam and cefepime were most resistant ones. Interventions and strategies to stop high resistance rate and optimizing therapy are needed.

Keywords: *P. aeruginosa*; Amikacin; Piperacillin-tazobactam; Antibiotics; Resistance

Introduction

P. aeruginosa is an opportunistic pathogen capable of infecting virtually all tissues and becoming a major cause of morbidity and mortality. It can persist in both community and hospital settings due to its ability to survive on minimal nutritional requirements and to tolerate a variety of physical conditions [1]. The infections in hospitals mainly affect the patients in intensive care units and those having catheterization, burn, and/or chronic illnesses [2]. According to data from the US Centers for Disease Control and Prevention and the National Nosocomial Infection Surveillance System, *P. aeruginosa* is the second most common cause of nosocomial pneumonia (17%), the third most common cause of urinary tract infection (7%), the fourth most common cause of surgical site infection (8%), the seventh most frequently isolated pathogen from the bloodstream (2%) and the fifth most common isolate (9%) overall from all sites [3,4]. The choices for treatment for *P. aeruginosa* infections include; Aminoglycosides (amikacin, tobramycin, gentamicin), Carbapenems (imipenem, meropenem, doripenem), Cephalosporins, third-generation (cefoperazone, cefsulodin, ceftazidime), cephalosporins, fourth-generation (cefepime, ceftazidime, ceftazidime), Fluoroquinolones (ciprofloxacin, levofloxacin), Monobactam (aztreonam), Extended-spectrum penicillins (ticarcillin and/or ticarcillin-clavulanate, piperacillin and/or piperacillin-tazobactam, azlocillin), Polymyxin B/Colistin. However *P. aeruginosa* is intrinsically resistant to most of these drug classes and can rapidly develop resistance to other drugs during chemotherapy, making medical treatment difficult and

ineffective leading to a high mortality rate. Increases in the rate of antibiotic resistance to *P. aeruginosa* to the common antimicrobial drugs have been reported worldwide [1]. In Saudi Arabia, *P. aeruginosa* has been reported as the most commonly isolated organisms in hospitals [5]. The present study aimed to investigate the incidence and antibiotic susceptibility of *P. aeruginosa* in two Makkah hospitals.

Material and Methods

The present study was undertaken in two main tertiary care hospitals in Makkah, Hera General Hospital (HGH) (263 bed) and King Abdulaziz Hospital (KAH) (300 bed), during the period of 5 months, from September 2014-January 2015. A total of one thousand and two hundred and thirty five of patients (n=1235) from two hospitals, HGH (766) and KAH (469) in Makkah, Saudi Arabia were enrolled in the study. Among the patients, 725 were males and 510 patients were females. The patients were divided into eight age groups: less than 1 year old (n=233), 1-10 years old (n=85), 11-20 years old (n=35), 21-30 years old (n=122), 31-40 years old (n=130), 41-50 years old (n=200), 51-60 (n=163) years old, and more than 60 years old (n=267). The frequency of patients according to the wards as follows; male ward (n=295) female ward (n=233), Intensive care unit (n=135), surgery ward (n=125), obstetrics and Gynaecology (n=123), newborn intensive care unit (n=120), nursery (n=111) and pediatrics (n=93). The frequency of clinical specimens included in the study were: abscess (n=150), axillary (n=80), blood (n=56), Eye swab (n=35), high vaginal swabs (n=110), pleural fluid (n=118), pus swab (n=149), skin swab (n=65), sputum sample (n=195), tracheal aspirate (n=115), umbilical swab (n=66), urine samples (n=127), wound swab (n=119). All isolates

were obtained from inpatients of various body sites from each hospital. All specimen samples were taken from each patient. Demographic data (age, gender, site of infection and ward of hospitalization) of the patients were collected from the medical and laboratory records of each patient on a standardized collection form. Microbiological standard methods were used to isolate and identify the clinical isolates of *P. aeruginosa*. They include growth morphology, Gram stain, Conventional biochemical tests, oxidase positivity, the presence of characteristic pigments and API 20E (bioMérieux) strips. All collected strains were stored at -86°C in brain heart infusion containing 15% glycerol until used. Antimicrobial susceptibility was performed against all clinical isolates using disc diffusion susceptibility for various antibiotics. The isolates were tested against ceftazidime (30 µg), cefotaxime (30 µg), ciprofloxacin (10 µg), amikacin (30 µg), ceftazidime (30 µg), Piperacillin/Tazobactam (100/10 µg), Imipenem (10 µg) and colistin (10 µg). The disk diffusion susceptibility method was performed by applying a bacterial inoculum of approximately 1-2 × 10⁸ CFU/ml to the surface of Mueller-Hinton agar plate then antibiotic disks were placed on the inoculated agar surface. Plates were incubated for 18 hours at 35°C prior to determination of results. The diameter of each zone of inhibition was measured in mm. *P. aeruginosa* strains were classified as susceptible, intermediate, or resistant to each tested antibiotic based on the Clinical and Laboratory Standards Institute (CLSI) guidelines [6].

Results

Specimen	No (%)	Ward	No (%)	Age (year)	No (%)
Abscs	1 (0.9%)	Fw	22 (20.4%)	<1	14 (13.0%)
Axil	1 (0.9%)	Mw	47 (43.5%)	10-Jan	5 (4.6%)
Bld	1 (0.9%)	ICU	11 (10.2%)	20-Nov	3 (2.8%)
Eye	10 (9.3%)	Sw	8 (7.4%)	21-30	8 (7.4%)
HVS	4 (3.7%)	OBS	2 (1.9%)	31-40	14 (13.0%)
Plr	1 (0.9%)	NICU	11 (10.2%)	41-50	15 (13.9%)
Pus	1 (0.9%)	NSY	2 (1.9%)	51-60	15 (13.9%)
Skn	1 (0.9%)	Pedia	5 (4.6%)	>60	34 (31.5%)
Spm	41 (38%)				
Trach	15 (13.9%)				
Umb	3 (2.8%)				
Ur	16 (14.8%)				
Wd	13 (12.0%)				

Table 1: Distribution of *P. aeruginosa* clinical isolates according to the specimen type, clinical wards and e age group. Abscs: Abscess; Axil : Axillary; Bld : Blood; Eye: Eye swab; HVS: High Vaginal Swabs; Plr: Pleural Fluid; Pus: Pus Swab; Skn: Skin Swab; Spm: Sputum Sample; Trach: Tracheal Aspirate; Umb: Umbilical Swab; Ur: Urine Sample; Wd: Wound Swab; Fw: Female Ward; Mw: Male Ward; ICU: Intensive Care Unit; Sw: Surgery Ward; OBS : Obstetrics and Gynaecology; NICU: Newborn Intensive Care Unit; NSY: Nursery; Pedia: Pediatrics.

During a period of 5 months, a total of 108 (8.7%) of isolates were identified as *P. aeruginosa* in clinical specimens obtained from patients of various body sites. The majority of *P. aeruginosa* isolates were from HGH 65 (60.2%) while KAH was 43 (39.8%). The results revealed that males were more infected than females with *P. aeruginosa* with a percentage 64 (59.3%). Table 1 shows that the majority of patients with *P. aeruginosa* infection were above 60 years old representing 34 (31.5%) of total patients number, whereas a 15 (13.9 %) of infected patients with this strain were between 41-50 and 51-60 years old. Most of *P. aeruginosa* were isolated from male ward 47 (43.5%) followed by female ward 22 (20.4%). Regarding clinical specimens, majority of *P. aeruginosa* strains were isolated from sputum specimen (41 specimen) 38%, followed by urine specimen 16 (14.8%) and tracheal aspirates (15 samples) (13.9%). The antimicrobial susceptibilities of *P. aeruginosa* isolates during the study period are shown in Table 2. The study showed that the antibiotic susceptibility rates among *P. aeruginosa* isolates for amikacin, ciprofloxacin and cefotaxime were 83.3 %, 75.9% and 70.4%, respectively. The resistance rates among *P. aeruginosa* isolates for Piperacillin/Tazobactam, ceftazidime and ceftazidime were 38.5 %, 32.4% and 29.6% respectively. Forty six of the isolates (42.6%) was found to be sensitive to all antibiotics, while 39 (36.1%) of them were found to be resistant to more than three antibiotics. Only 4 of isolates (3.7%) were found to be resistant to one antibiotic, while 9 (8.3%) and 10 (9.3%) of isolates were found to be sensitive to 2 and 3 of antibiotics respectively.

Antibiotic	S No (%)	I No (%)	R No (%)
Ceftazidime	73 (67.6%)	4 (3.7%)	31 (28.7%)
Cefotaxime	76 (70.4%)	0 (0.0%)	32 (29.6%)
Ciprofloxacin	82 (75.9%)	0 (0.0%)	26 (24.1%)
Amikacin	90 (83.3%)	2 (1.9%)	16 (14.8%)
Cefepime	69 (63.9%)	4 (3.7%)	35 (32.4%)
Piperacillin/Tazobactam	65 (60.2%)	1 (0.9%)	42 (38.9%)
Imipenem	70 (64.8%)	11 (10.2%)	27 (25%)
Colistin	76 (70.4%)	26 (24.1%)	6 (5.5%)

Table 2: Antimicrobial susceptibility patterns of *P. aeruginosa*. S: Susceptible; I: Intermediate; R: Resistant.

Discussion

In the present study, a total of 108 (8.7%) of isolates were identified as *P. aeruginosa* in clinical specimens obtained from patients of various body sites in Makkah hospitals, most of which originated from HGH (60.2%), possibly due to the high number of patients referred to this hospital. Results revealed that males were more infected than females with *P. aeruginosa* with frequency (59.3%) which is similar to a previous studies in this locality [7,8]. The majority of patients were above 60 years old representing (31.5%), also similar to a previous study in this locality [7]. Very young and very old patients had overall higher rates of infection than did other age groups; however, the risk of infection in different age groups differed between sites [9]. Most of *P. aeruginosa* were isolated from male ward (43.5%) in contrast to studies that reported that most *P. aeruginosa* strains were isolated from ICUs, followed by male ward [10,11]. Regarding clinical specimens, majority of *P. aeruginosa* strains were isolated from sputum specimen (38%),

followed by urine specimen (14.8%) and tracheal aspirates (13.9%). Local and international studies showed a similar preference for infection sites [8,11,12]. In the present study, 42.6% of the isolates were sensitive to all antibiotics while 36.1% were found to be resistant to more than three antibiotics. Rates of antibiotic resistance in *P. aeruginosa* are increasing worldwide. Multidrug resistant *P. aeruginosa* was defined in the presence of resistance to at least three of the following antibiotic classes: penicillin, cephalosporin, carbapenem, aminoglycoside, cotrimoxazole, and fluoroquinolones [13]. So this finding could suggest the possibility MDR infections in Makkah.

In the present study, the resistance rates among *P. aeruginosa* isolates Piperacillin-tazobactam was very high (38.5%). Piperacillin-tazobactam resistance among *P. aeruginosa* strains is an emerging problem; because the chromosomal β -lactamases of *P. aeruginosa* are of low effectiveness against tazobactam and the rate of resistance to piperacillin-tazobactam is likely of a magnitude similar to that for the rate of resistance to piperacillin [14]. One study [15] reported (52.5%) piperacillin-tazobactam-resistant *P. aeruginosa* which may be affected by multiple antibiotics treatment [15]. Cefepime, a fourth-generation cephalosporin, is one of the few agents that remaining has reliable activity against *P. aeruginosa*. The increased prevalence of resistance to cefepime among *P. aeruginosa* has been reported [16]. Prior treatment with cefepime can lead to emergence of cefepime-resistant *P. aeruginosa* [16]. In addition, resistance may arise by the acquisition of plasmids encoding β -lactamases. The rate of strains with acquired resistance to ceftazidime has been estimated to range from 10% to 40% [17]. The data of the present study showed higher level of susceptibility to ceftazidime and cefotaxime than cefepime which may reflect the increased use of cefepime and the decreased use of ceftazidime in recent years in Makkah hospitals. In the present study, resistance rates against ciprofloxacin and imipenem were (24.1%) and (25%) respectively. *P. aeruginosa* rapidly acquires high-level resistance to these drugs which may have impacts on both clinical and economic outcomes. Worldwide, about 30% of strains presented high-level ciprofloxacin resistance [18] and about (13% to 20%) presented high-level imipenem resistance [19]. One study [20] showed a very low colistin resistance rate (5.5%) against *P. aeruginosa*. Although resistance to colistin is generally rare, it is higher in the Mediterranean and South-East Asia (Korea and Singapore) [20]. Colistin is not preferred due to its nephrotoxicity. It remains one of the last-resort antibiotics for multidrug-resistant *P. aeruginosa*. Amikacin is the aminoglycoside most frequently used for pseudomonas infections [21]. Although resistance to aminoglycosides with antipseudomonal activities is too common and is present in all areas of the world [21], many studies have reported the excellent activity of amikacin against *P. aeruginosa* [22]. So it could be concluded that amikacin was the most susceptible antimicrobial drug and could be used empirically to treat *Pseudomonas* infections. Piperacillin-tazobactam and cefepime were most resistant drugs possibly due to the excessive use during the treatment. There is a need for interventions to stop this continued increase of resistance and strategies to optimize therapy.

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