PSEUDOMONAS AERUGINOSA: EPIDEMIOLOGY OF BACTEREMIA AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN IN A TEACHING HOSPITAL IN KUALA LUMPUR

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ABSTRACT: A cross-sectional study of 109 patients with *Pseudomonas aeruginosa* bacteremia from the University of Malaya Medical Centre (UMMC) in the years 2000 and 2001 was conducted to describe epidemiological features, underlying diseases, possible source of infection, early mortality among patients as well as the antibiotic susceptibility pattern of patients' isolates. Further analysis of the 87 patient records that were available revealed that the mean age was 48.5 years (SD ± 25.1). Fifty-two per cent of cases were male and 48% female. Seventy-nine per cent of infections were nosocomially acquired, 33% of bacteremias were polymicrobial, 47% of patients had a continuous bladder drainage catheter (CBD) *in situ*, 33% had a central venous catheter (CVL) present at the time of bacteremia and 30% were ventilated. Sixty-eight per cent of patients had an underlying immunosuppressed state and 26% had undergone surgery involving general anesthesia in the week prior to isolating *P. aeruginosa*. Among the 23 patients with early mortality, 61% were on inappropriate antimicrobials.

Most of the patients' isolates were sensitive to imipenem (86%), ciprofloxacin (81%), ceftazidime (79%), gentamicin (78%) and cefoperazone (77%). Among the community acquired strains, however, there was 100% sensitivity to imipenem, ceftazidime, cefoperazone and ciprofloxacin. *(JUMMEC 2006; 9(1): 14-19)*

KEYWORDS: *Pseudomonas aeruginosa*, bacteremia, antimicrobial susceptibility

Introduction

Pseudomonas aeruginosa bacteremia has become an important cause of mortality and morbidity over the past few decades. Despite the advent of new antimicrobials and improved health standards, mortality ranges from 18-61% (1) which some studies have found is higher than mortality from other gram-negative bacteremias (2). This increased mortality may be reflective of more severe underlying illness or could be related to the greater inherent virulence of the organism (3), or the fact that the organism may develop resistance while the patient is on treatment (4).

P. aeruginosa, a gram-negative bacillus, is generally recognized as an opportunistic and nosocomial pathogen and rarely causes disease in healthy persons (2,3). It is recovered infrequently from the endogenous microbial flora of healthy individuals (2). It is a common pathogen, however, in patients hospitalized for more than a week and predisposing conditions to developing bacteremia include having an underlying immunosuppressed state, admission to intensive care units, respiratory therapy, surgical procedures, the presence of various catheters and antimicrobial therapy (2,3,5). Community-acquired cases have also increased and this may be related in part to the prevalence of HIV infection and reports that in HIV infected patients, *P. aeruginosa* bacteremia may be community-acquired (6).

There have not been any epidemiological studies on *P. aeruginosa* bacteremia in Malaysia. The objectives of this study were to describe the epidemiologic features, underlying diseases, possible source of infection, percentage of early mortality and the antimicrobial

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susceptibility pattern of isolates in patients with *P. aeruginosa* bacteremia at a tertiary level teaching hospital in Malaysia in the years 2000 and 2001.

Material and Methods

Patients

All 109 patients with *P. aeruginosa* bacteremia in the years 2000 and 2001 were identified from the computerized microbiology records of the Microbiology laboratory of the University of Malaya Medical Centre (UMMC), an 844-bed major teaching hospital in Kuala Lumpur, Malaysia. There were 45 cases in the year 2000 and 64 cases in the year 2001. However, only 87 patient records were available for further analysis.

Inclusion criteria for *P. aeruginosa* bacteremia was at least one positive blood culture from a patient with suspected bacteremia. Cases with polymicrobial bacteremia involving *P. aeruginosa* were also included in this study. The patients' demographic information as well as information regarding therapy with steroids, cytotoxic drugs, presence of hematological or other malignancies, other immunosuppressed states like burns and post-splenectomy, diabetes mellitus, central venous lines (CVL), continuous bladder drainage catheter (CBD) and mechanical ventilation was recorded. Patients who had undergone surgery in the week prior to the isolation of *P. aeruginosa* from the blood were also identified.

Microbiology

The microbiology data collected included the antimicrobial sensitivity pattern of all 109 bacteremic *P. aeruginosa* isolates as well as the types of organisms isolated in the polymicrobial cases. If the organism was isolated from another site of the body within a week prior to the positive blood culture, this was also recorded.

Blood cultures were processed by the Bactec 9240 system (Becton-Dickinson Microbiology System, USA). *P. aeruginosa* was identified by conventional bacteriological methods or by the API 20NE system (bioMérieux, France). Antibiotic susceptibility testing by disc diffusion was in accordance with the National Committee for Clinical Laboratory Standards (NCCLS) (7,8).

Definitions

Nosocomial infection was defined as a positive blood culture taken 48 hours after admission with no evidence of *Pseudomonas aeruginosa* infection at the time of admission. The bacteremia was considered to be community-acquired if *P. aeruginosa* was isolated within 48 hours of hospital admission and the patient had not been admitted in the previous two weeks (1). Patients were classified as immunosuppressed if they were on cytotoxics or steroids, had underlying malignancy, diabetes, HIV infection, systemic lupus erythematosus, burns, or had been splenectomized. Diabetes as an underlying factor was also analyzed separately.

Polymicrobial bacteremia was defined as the isolation of other organisms in addition to *P. aeruginosa* from the blood culture. If a specimen from any site of the body grew *P. aeruginosa* within a week prior to isolating the organism from the blood, it was considered a possible portal of entry; otherwise, the source of bacteremia was considered unknown. Early mortality was defined as death occurring within 72 hours of isolating the organism from a blood culture and antimicrobial therapy at the time of bacteremia in these cases was considered appropriate if the strain of *Pseudomonas aeruginosa* isolated was sensitive to any of the antimicrobials given to the patient and if the patient received adequate dosage of that antibiotic for at least 24 hours prior to death.

Results

Demography

Table 1 shows the characteristics of the study subjects. The mean age of the 87 patients was 48.5 years (SD ± 25.1; range: 13 days old to 92 years). Fifty-two per cent

Table 1. Characteristics of study subjects

Risk factors	No. of patients (%) (Total patients n=87)
Age (Year)	
0 – 12	11 (13%)
13 – 29	10 (11%)
30 – 49	17 (20%)
50 – 69	33 (38%)
> 70	16 (18%)
Sex	
Male	45 (52%)
Female	42 (48%)
Ward type	
Intensive care units	20 (23%)
Surgical	22 (25%)
Hematological	19 (22%)
Adult medical	15 (17%)
General paediatric	5 (6%)
Gynaecology	4 (5%)
Renal	2 (2%)

of patients were male and 48% were female. Twenty patients (23%) had been in an ICU at the time of bacteremia, 22 (25%) were from the surgical wards, 15 (17%) were from the adult medical ward, 5 (6%) were from the general paediatric wards, 19 (22%) from the haematology wards, 4 (5%) were from the gynaecology ward, and two patients (2%) were from the renal wards.

Underlying disease associated with P. aeruginosa *bacteremia*

Fifty-nine patients (68%) were classified as immunosuppressed at the time of bacteremia (Table 2). Twenty patients (23%) had underlying haematological malignancy, 22 (25%) had other non-haematological malignancies, 11 (13%) were on steroids, three (3%) had burns, three (3%) had systemic lupus erythematosus, two (2%) had been splenectomized and two (2%) had HIV infection. Twelve patients (14%) were diabetic.

Forty-one patients (47%) had a CBD *in situ*, 29 (33%) had a CVL present at the time of bacteremia and 26 patients (30%) were on ventilator. Twelve patients (14%) had undergone surgery involving general anesthesia in the week prior to isolating *P. aeruginosa* from the blood. Six patients (7%) had a tracheostomy and one patient had a ventriculo-peritoneal shunt.

Source of infection

Among the 87 bacteremic cases, sixty-nine (79%) were nosocomial in origin whilst 16 (18%) were community-acquired (Table 2). In two patients (2%), the information available was insufficient to determine a nosocomial or community origin. Among the patients with community-acquired bacteremia, nine (56%) had underlying carcinoma, haematological malignancy, or had undergone bone marrow transplant. The remaining seven patients had the following underlying conditions: polycystic kidneys and urinary tract infection with *P. aeruginosa,* HIV infection, diabetes with gangrene of the foot, liver cirrhosis, burns, upper gastrointestinal tract bleeding with polymicrobial bacteremia, and one was an infant with a prior history of being admitted to the special care nursery a month earlier.

The urinary tract was possibly the commonest identified site of entry (11%); this was followed by the respiratory tract (10%) and intravenous catheters (6%) (Table 2). Thirteen per cent of patients also had various wound swabs and drainage fluids growing *P. aeruginosa* in the week prior to isolation of the organism. However, it was not possible to determine accurately where the swabs and fluids had been taken from due to the retrospective nature of the study. In 62% of cases the site of entry was unknown.

Early mortality

Early mortality occurred in 26% (23/87 patients), and the *P. aeruginosa* bacteremia is likely to have been a contributing factor. Table 2 shows patient characteristics and underlying conditions in relation to early mortality.

Of the 23 patients with early mortality, 70% were male, 70% had monomicrobial bacteremia, 61% had nosocomial bacteremia, 61% were on inappropriate antibiotics, 61% had an underlying immunosuppressed state and 52% had a CBD catheter.

Microbiology

Twenty-nine cases (33%) were polymicrobial with various other organisms isolated in addition to *P. aeruginosa* (Table 3). Gram-negative bacilli and gram-positive cocci were isolated from 14 and 9 specimens respectively. Six specimens yielded both gram-negative bacilli and gram-positive cocci in addition to *P. aeruginosa*. The commonest organism isolated was *Staphylococcus aureus*, followed by *Enterococcus* spp. More than half (52%) of the polymicrobial bacteremia cases were from intensive care unit (ICU).

Antimicrobial sensitivity of isolates

All isolates had been tested for sensitivity against ceftazidime, cefoperazone, gentamicin, ciprofloxacin and imipenem. The majority of isolates (86%) were sensitive to imipenem, 81% were sensitive to ciprofloxacin; this was followed by ceftazidime (79%), gentamicin (78%) and cefoperazone (77%) (Table 4). Among the community-acquired strains, however, there was 100% sensitivity to imipenem, ceftazidime, cefoperazone and ciprofloxacin.

There were three strains resistant to piperacillin but sensitive to piperacillin/tazobactam, two strains were sensitive to imipenem but resistant to meropenem and another two were resistant to imipenem but sensitive to meropenem. Among the aminoglycosides, there were 11 isolates resistant to gentamicin but sensitive to amikacin, but none were sensitive to gentamicin and resistant to amikacin. There were four multi-resistant strains which were only sensitive to polymixin B. Two of these strains came from patients in the ICU, and one each from the adult surgical and medical wards.

Table 2. Patient characteristics and underlying conditions in relation to early mortality

Patient characteristic/ underlying condition	No. of patients (%) (Total patients n=87)	No. of patients dying within 72 hours (%) (Total patients n=23)	No. of patients dying in 72 hours/ total patients in the group (% total in the group)
Age (Year)			
0 – 12	11 (13%)	5 (22%)	5/11 (45%)
13 – 29	10 (11%)	2 (9%)	2/10 (20%)
30 – 49	17 (20%)	2 (9%)	2/17 (12%)
50 – 69	33 (38%)	10 (43%)	10/33 (30%)
> 70	16 (18%)	4 (17%)	4/16 (25%)
Sex			
Male	45 (52%)	16 (70%)	16/45 (36%)
Female	42 (48%)	7 (30%)	7/42 (17%)
Admission to an intensive care unit	20 (23%)	8 (35%)	8/20 (40%)
Immunosuppressed state	59 (68%)	14 (61%)	14/54 (24%)
All malignancies	42 (48%)	8 (35%)	8/42 (19%)
– Haematological malignancies	20 (23%)	7 (30%)	7/20 (35%)
– Other malignancies (bowel cancer, gynaecological, etc.)	22 (25%)	4 (17%)	4/22 (18%)
Diabetic patient	12 (14%)	2 (9%)	2/12 (17%)
Presence of CBD	41(47%)	12 (52%)	12/41(29%)
Presence of CVL	29 (33%)	6 (26%)	6/29 (21%)
On ventilator	26 (30%)	8 (35%)	7/26 (27%)
Recent surgery	12 (14%)	2 (9%)	2/12 (17%)
Source of bacteremia			
– Nosocomial	69 (79%)	16 (61%)	16/69 (23%)
– Community*	16 (22%)	7 (39%)	7/16 (45%)
Possible route of entry			
Respiratory tract	9 (10%)	2 (9%)	2/9 (22%)
Urinary tract	10 (11%)	2 (9%)	2/10 (20%)
Central venous catheters	5 (6%)	1 (4%)	1/5 (20%)
Others (swabs/drainage fluids)	11 (13%)	2 (9%)	2/11 (18%)
Type of bacteremia			
Monomicrobial	58 (67%)	16 (70%)	16/58 (28%)
Polymicrobial	29 (33%)	7 (30%)	7/29 (24%)
Treatment			
Appropriate	–	9 (39%)	–
Inappropriate	–	14 (61%)	–

* Of the community-acquired cases, nine had underlying malignancies or had undergone bone marrow transplant. The remaining seven had the following underlying conditions: polycystic kidneys with a urinary tract infection (*P. aeruginosa),* diabetes with gangrene of the foot, HIV infection, liver cirrhosis, burns, upper gastrointestinal tract (GIT) bleeding with polymicrobial bacteremia, and a history of having being admitted to the special care nursery a month earlier.

Table 3. Organisms isolated in polymicrobial cases involving *P. aeruginosa*

Microorganisms	No. of isolates
Gram-positive cocci	
Staphylococcus aureus (three isolates were methicillin resistant *S. aureus*)	6
Enterococcus spp.	5
Staphylococcus epidermidis	3
Gram-negative rods	
E. coli	4
Stenotrophomonas maltophilia	2
Enterobacter spp.	3
Klebsiella spp.	4
Acinetobacter spp.	4
Pseudomonas spp.	1
Yeast	1

Discussion

The majority of patients with *P. aeruginosa* bacteremia had an underlying immunosuppressed state or some device present that predisposed them to the development of infection, this being similar to findings in other published reports (1,3). The patients were mainly distributed among the intensive care units, surgical and haematological wards, whereas a predominance of patients from the general surgical and transplant services were found (6).

Although most of the cases (79%) were nosocomial infections, community-acquired cases were also seen (18%) and these findings were similar to a recent study (9). Research has shown that only 12% (1) of cases were community-acquired whereas a rate of 40% was reported (6). This was higher than their earlier study of 17% and the increase in community-acquired cases was partially attributed to the prevalence of HIV infection as in seven out of 11 episodes of *P. aeruginosa* bacteremia in these patients, the bacteremia was community-acquired (6). In our study, we had only one patient with underlying HIV infection among the community-acquired cases but most patients had some other underlying immunosuppressed state or predisposing factor.

Early mortality in our study was seen in 26.3% of patients. In a study of *Pseudomonas* septicemia in cancer patients 33% of patients died in the first 24 hours (10). In another study, 21 out of 23 patients had cancer, and the median period of survival from the positive blood culture was four days (11).

Polymicrobial bacteremia in this study was seen in 33% of the bacteremic cases, which was much higher than the 17% reported (12). Fifty-two per cent of these cultures were from ICU patients. However, contamination may have been responsible for some of the cases. Patients with polymicrobial bacteremia were clinically worse and had a higher mortality rate compared to patients with monomicrobial *P. aeruginosa* bacteremia (12). In our study, however, 70% of patients with early mortality had monomicrobial bacteremia with *P. aeruginosa*. The most common organism isolated along with *P. aeruginosa* was *Enterococcus* spp. (12), whereas in our study, *Staphylococcus aureus* was the commonest organism isolated, followed by *Enterococcus* spp.

It was not possible to determine with certainty the source of bacteremia in our patients, but 47% of the patients had a CBD catheter *in situ* and among those in whom a presumed source of infection was found, a urinary portal of entry was the commonest (11%), followed by the respiratory tract (10%). Studies have found that the respiratory tract was the commonest source for *P. aeruginosa* septicemia (6).

Table 4. Sensitivity of *P. aeruginosa* to antimicrobials

	Antibiotic									
	CAZ	CFP	GM	AN	CIP	IPM	MEM*	PIP	P/T*	SCF
Percentage sensitive	79	77	78	91	81	86	76	80	100	81
(No. tested)	(109)	(109)	(109)	(100)	(109)	(109)	(49)	(104)	(25)	(95)

Key:

S = sensitive

CAZ = ceftazidime, CFP = cefoperazone, GM = gentamicin, AN = amikacin, CIP = ciprofloxacin, IPM = imipenem, MEM = meropenem, PIP = piperacillin, P/T = piperacillin/tazobactam, SCF = cefoperazone/sulbactam

** Number of strains tested against these antimicrobials were few as they were not part of the routine testing panel in our laboratory at the time of this study. Isolates were only tested against these antimicrobials if multi-resistant or if specifically requested for by the clinicians.*

Conclusion

This study has highlighted the common epidemiological features of patients with *P. aeruginosa* bacteremia in our hospital, but being retrospective and not case controlled, firm statistical conclusions could not be made. As only 87 of the 109 patients' records were available for analysis, any bias in results cannot be excluded.

Most of our isolates were sensitive to imipenem, ciprofloxacin, ceftazidime, gentamicin and cefoperazone and for community-acquired isolates all were sensitive to imipenem, ceftazidime, cefoperazone, and ciprofloxacin. Therefore, if a *P. aeruginosa* septicemia was suspected or confirmed in a patient in our hospital, these antimicrobials would probably be effective as empirical therapy while awaiting results of sensitivity. Although not all isolates were tested against amikacin, among those tested, 91% were found to be sensitive. Four isolates were found to be resistant to all antibiotics except polymyxin B. Antibiotic selection for treatment of infections caused by *P. aeruginosa* is often problematic (4). In our study, 61% of patients with early mortality had been on inappropriate empirical antimicrobials. There have been conflicting reports about mortality in relation to whether patients had received appropriate or inappropriate antibiotics, with several studies failing to show a difference (1,13,14) and others showing a decrease in mortality when appropriate antibiotics were used (15,16,17,18).

Nonetheless, it does seem prudent to start empirical antimicrobials that are likely to be effective against *P. aeruginosa* if it is thought to be a likely pathogen, particularly, when dealing with immunosuppressed patients.

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