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Analysis of Clinical Characteristics and Risk Factors of *Pseudomonas aeruginosa* Bloodstream Infection in 55 Cases

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Abstract

Objective: *Pseudomonas aeruginosa* bloodstream infection presents a severe challenge to hospitalized patients. To investigate the clinical characteristics, risk factors and drug resistance of *Pseudomonas aeruginosa* bloodstream infection. **Methods:** Clinical data and laboratory results of patients with *Pseudomonas aeruginosa* bloodstream infection in the First Affiliated Hospital of Yangtze University from January 2019 to December 2022 were retrospectively analyzed. The factors associated with infection and death were analyzed by univariate analysis. **Results:** A total of 55 patients were enrolled in this study, The 28-day mortality rate was 14.5%. Univariate analysis showed that high procalcitonin, low albumin, ICU admission, central venous catheterization, indwelling catheter, and mechanical ventilation were associated with death. Multivariate Logistic regression analysis showed that hypoproteinemia and central venous catheters were independent risk factors for death in patients with *Pseudomonas aeruginosa* bloodstream infection. **Conclusions:** The drug resistance of *P. aeruginosa* bloodstream infection is not high, but the fatality rate is high. The combination of hypoalbuminemia after the onset of the disease and the use of central vein catheters can lead to increased mortality, suggesting that clinical identification of high-risk patients as early as possible, reducing the use of catheters, preventing the occurrence of *P. aeruginosa* bloodstream infection and improving the prognosis.

Keywords

Pseudomonas aeruginosa, Bloodstream Infections, Resistance, Risk Factors

1. Introduction

Pseudomonas aeruginosa is widely distributed in nature as a conditional pa-

thogen and can be normally colonized in the skin, respiratory tract, and gastrointestinal tract of humans and animals. *P. aeruginosa* is a Gram-negative non-fermenting bacillus that can cause serious hospital-acquired infections, especially in immunocompromised and neutropenic patients [1] [2]. In recent years, the clinical prognosis of patients with *P. aeruginosa* infection has improved with the widespread use of anti-pseudomonas antibiotics. Unfortunately, the emergence of drug-resistant *P. aeruginosa* due to natural and acquired drug resistance is of increasing concern [3] [4]. Hospital-acquired infections due to this bacterium are more common in lower respiratory tract infections, abdominal infections, and bloodstream infections, among which bloodstream infections are fatal, and their infection can prolong the patient's hospital stay, increase hospital costs, and trigger multi-organ failure in patients with a poor prognosis and mortality rates ranging from 18% to 61% [5]. Poor outcomes of the bloodstream infections caused by *P. aeruginosa* could be explained by its virulence and the underlying diseases or conditions of the patients. The previous studies revealed that the prognosis could be closely associated with the severity of underlying diseases and delayed usages of effective antibiotics [5] [6]. In this study, we retrospectively analyzed the clinical features, risk factors, and laboratory characteristics of *Pseudomonas aeruginosa* bloodstream infections to provide a basis for clinical diagnosis and treatment.

2. Materials and Methods

2.1. General Clinical Data

Patients with positive blood culture of *P. aeruginosa* bloodstream infection from January 2019 to December 2022 in various departments of the First Affiliated Hospital of Yangtze University were collected, and only the first isolated strain of *P. aeruginosa* was selected in the same patient with multiple isolations. Inclusion criteria: 1) Inpatients ≥ 18 years old with complete clinical information; 2) 1 or more positive blood cultures for *P. aeruginosa* and clinical evidence of the corresponding infection; 3) Multiple infections were taken for the first infection. *Pseudomonas aeruginosa* bloodstream infection was defined as more than one positive blood culture for *P. aeruginosa* and the presence of clinical signs and symptoms of its corresponding bloodstream infection, and the possibility of bloodstream infection and contamination by other pathogens was excluded.

Record all clinical information of the patients, including: 1) Patient's gender and age. 2) Underlying diseases, including hypertension, diabetes mellitus, solid tumors, cardiovascular diseases, hematologic diseases, anemia, hypoproteinemia, chronic kidney diseases, septic shock, and severe pneumonia. 3) Whether admitted to intensive care unit (ICU) with related invasive operations (including indwelling gastric tube, indwelling urinary catheter, central venous placement, mechanical ventilation, other site drainage tube), history of surgery, history of antimicrobial drug use. 4) 28-day survival of patients.

Exclusion criteria: 1) Outpatients. 2) Those with incomplete case information.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Yangtze University with approval number KY202377.

2.2. Bacterial Identification and Drug Sensitivity Test Methods

The strains were cultured and isolated according to the National Clinical Laboratory Practice (4th edition). Blood specimens from patients with suspected bloodstream infection were cultured using a BACTECTM FX automatic blood culture instrument (BD, USA). Positive specimens of strains were transferred to blood agar plates and chocolate agar plates. Antimicrobial susceptibility tests were performed using the Phoenix-100 (BD, USA), and it was interpreted according to the Clinical and Laboratory Standards Institute (CLSI) document M100-S32. The quality control strain was *Pseudomonas aeruginosa* ATCC 27853.

2.3. Statistical Methods

SPSS 23.0 statistical software and WHONET 5.6 were used. The measurement data conforming to normal distribution were expressed as mean ± standard deviation with t-test; variables not conforming to normal distribution were tested with Wilcoxon rank sum test; the count data were expressed as number of cases and percentages, and rates were compared with χ^2 test or Fisher's exact test. Logistic regression analysis was performed for risk factors, and differences were considered statistically significant at $P < 0.05$.

3. Results

3.1. Drug Susceptibility Testing

In vitro antimicrobial susceptibility tests showed 100% sensitivity to polymyxin B and amikacin; the resistance rate to imipenem and meropenem was low, only 3.6%; the resistance rates to quinolones antibacterial drugs was the highest, as shown in Table 1.

3.2. Clinical Characteristics

The average age of the 55 patients with *P. aeruginosa* bloodstream infection was (65.2 ± 12.7) years, 17 cases were under 60 years old and 38 cases were over 60 years old; 45 cases (81.8%) were male and 10 cases (18.2%) were female. The distribution of departments was mainly from urology 12 cases (21.8%), hematology 11 cases (20%), and ICU 10 cases (18.2%).

3.3. Underlying Diseases

Fifty-one patients (92.7%) were combined with at least 1 underlying disease, mainly including: hypertension in 26 cases (47.3%), diabetes mellitus in 12 cases (21.8%), and hematologic tumors in 11 cases (20.0%), as shown in Table 2.

Table 1. Susceptibility of 55 cases of *Pseudomonas aeruginosa* to antibacterial drugs.

Antibacterial drugs	*Pseudomonas aeruginosa* (n = 55)		
	Resistance (%)	Intermediary (%)	Susceptibility (%)
Ciprofloxacin	12.7	9.1	78.2
Amantadine	10.9	16.4	72.7
Piperacillin	7.3	9.1	83.6
Ceftazidime	5.5	5.5	89.1
Cefepime	5.5	14.5	80
Gentamicin	5.5	1.8	92.7
Levofloxacin	5.5	9.1	85.5
Piperacillin/tazobactam	3.6	3.6	92.7
Imipenem	3.6	10.9	85.5
Meropenem	3.6	0	96.4
Amikacin	0	0	100
Polymyxin B	0	0	100

Table 2. The risk factors for mortality of 55 cases of *Pseudomonas aeruginosa* bloodstream infection.

Variable	Death (n = 8)	Survival (n = 47)	*P* value
Age (years)	69.5 ± 10.7	64.5 ± 12.9	0.303
Male/case (%)	5 (62.5)	40 (85.1)	0.125
Underlying disease			
Diabetes mellitus	2	10	1.000
Hypertension	4	22	0.867
Chronic renal insufficiency	0	6	0.577
Hematologic tumor	2	9	1.000
Solid Tumors	2	5	0.580
Brain disease	2	7	0.844
History of gout	1	1	0.272
History of surgery	4	19	0.905
Laboratory tests			
C-reactive protein (mg/L)	171.9 ± 90.6	107.6 ± 95.9	0.086
Calcitoninogen (μg/L)	39.5 ± 34.9	14.9 ± 28.1	0.032
Peripheral blood leukocyte count ($\times 10^9$/L)	11.3 ± 9.9	10.9 ± 8.7	0.899
Hemoglobin (g/L)	94.8 ± 31.6	108.2 ± 32.3	0.280

Continued

Albumin (g/L)	30.2 ± 1.3	39.2 ± 4.3	0.000
Positive alarm time (h)	14.9 ± 9.7	21.6 ± 15.3	0.235
Number of cases of recurrent bacteremia	2	5	0.580
Admission to ICU	5	10	0.047
Indwelling catheter	7	19	0.029
Central venous catheter	8	23	0.007
Mechanical ventilation	4	2	0.001
Surgical procedures performed	7	24	0.125
Antimicrobial exposure	8	46	1.000

3.4. Receiving Invasive Treatment before Bloodstream Infection

94.5% of patients received at least 1 or more invasive operations within 14 d, mainly including: central venous placement in 31 cases (56.4%), urinary catheter in 26 cases (47.3%), performing surgical procedures in 31 cases (56.4%), and mechanical ventilation in 6 cases (10.9%), as shown in Table 2.

3.5. Clinical and Laboratory Characteristics of Bloodstream Infection

3.5.1. Clinical Manifestations

55 patients had fever in 55 cases (100%), septic shock in 14 cases (25.5%), multiple organ failure in 10 cases (18.2%) and gastrointestinal bleeding in 5 cases (9.1%), as shown in Table 2.

3.5.2. Laboratory Test Results

Peripheral blood leukocytes were 10.9 ± 8.8 (0.26 - 40.56) × 10^9/L, hemoglobin was 106.2 ± 32.2 (71 - 151) g/L, calcitoninogen was 18.4 ± 30.1 (0.12 - 100) μg/L, C-reactive protein was 116.9 ± 97.9 (1.97 - 425.8) mg/L, serum albumin 37.9 ± 5.1 (27.4 - 44.3) g/L, as shown in Table 2.

3.5.3. Plural Bacterial Bloodstream Infection

Among the 55 patients, 7 cases were combined with other pathogenic bacteria, including 4 cases of other Gram-negative bacilli (1 case each of *Enterobacter cloacae*, *Serratia marcescens*, *Klebsiella pneumoniae* and *Escherichia coli*) and 3 cases of positive cocci (1 case each of *Enterococcus faecalis*, *Enterococcus faecium* and *Staphylococcus aureus*), as shown in Table 2.

3.6. Treatment Regimen

All patients were treated with antimicrobial drugs at the time of infection symptoms, 24 cases (43.6%) used carbapenems, 18 cases (32.7%) used cephalosporins, 10 cases (18.2%) used quinolones, and 19 cases (34.5%) were combination regimens, including 12 cases of carbapenem-containing combination regimens, 5

cases of levofloxacin-containing combination regimens, and 2 cases were combined with polymyxin B.

3.7. Prognostic Regression

The 28-day mortality rate was 14.5% (8 patients' deaths). Univariate analysis between the death and survival groups showed that high calcitoninogen levels, hypoalbuminemia, ICU admission, central venous catheter, indwelling catheter, and mechanical ventilation were associated with poor patient prognosis, with a statistically significant difference between the two groups ($P < 0.05$). Further Multivariate Logistic regression analysis of factors with statistical differences in single factors showed that hypoalbuminemia and central venous catheter were independent risk factors for death from bloodstream infection in patients with *P. aeruginosa*, as shown in Table 3.

4. Discussions

Pseudomonas aeruginosa is a specialized aerobic conditionally pathogenic bacterium, which accounted for 7.96% in the 2021 CHINET data in China [6]. In a study reported by Wang Pan *et al.* [7], *P. aeruginosa* ranked 5th in bloodstream infections with a percentage of 6.72%. However, in a study by Chen *et al.* [8], *Pseudomonas aeruginosa* ranked 5th for bloodstream infections with a percentage of 3.6%. Bloodstream infections can prolong patients' hospital stay, increase clinical costs, and pose a challenge to clinical care.

In this study, the resistance of *Pseudomonas aeruginosa* to common antimicrobial drugs was low, with the highest resistance rate of 12.7% to levofloxacin and 0 to polymyxin B and amikacin, which was significantly lower than the resistance data of *Pseudomonas aeruginosa* [6] [7] [9]. However, polymyxin B is expensive, has toxicity to nerves and kidneys, and has some heterogeneous resistance [10], which often requires the combination of other antimicrobial drugs. Aminoglycosides have ototoxicity and nephrotoxicity and were often not used alone in pulmonary and bloodstream infections. *Pseudomonas aeruginosa* resistance mechanisms are complex and may be related to the production of various enzymes, decreased membrane permeability, expression of efflux pumps, altered target sites, and bacterial biofilm production [11]. Due to the widespread clinical use of carbapenems and some new β-lactamase inhibitor combinations such as ceftazidime-avibactam, resistances were largely increasing, clinics should also be alert to their resistance.

Table 3. Multivariate Logistic regression analysis of independent risk factors for prognosis of *Pseudomonas aeruginosa* bloodstream infection.

Risk factor	*P* value	OR (95% CI)
Hypoproteinemia	0.001	3.978 (1.768 - 8.953)
Central venous catheter	0.038	4.485 (1.083 - 18.577)

Pseudomonas aeruginosa bacteremia is a life-threatening infection in patients hospitalized with severe underlying conditions. *P. aeruginosa* bloodstream infections are generally clinically complex, with more than 90% of patients having serious underlying conditions, including diabetes, malignancy, and chronic renal failure [9]. Previous studies have shown that chronic renal failure, ICU admission, mechanical ventilation, and central venous catheter placement are risk factors for death from *P. aeruginosa* bloodstream infection [12]. Su *et al.* [13], reported that patients with MDR *P. aeruginosa* bloodstream infection had higher admission to the ICU, mechanical ventilation, poor prognosis, APACHE II score, and combined surgical procedures than the non-MDR *P. aeruginosa* bloodstream infection group. Patients who developed *P. aeruginosa* bloodstream infections in this study tended to have one or more underlying diseases that reduced the body's immunity, and approximately 100% of patients underwent various invasive procedures, all of which increased the risk of bloodstream infections. High calcitoninogen, low albumin, ICU admission, central venous line placement, indwelling catheter, and mechanical ventilation were associated with patient death. Multivariate Logistic regression analysis showed that hypoproteinemia and central venous line placement were independent risk factors for death in patients with *P. aeruginosa* bloodstream infection, similar to other studies in China [9] [14]. Because of the small number of cases of multi-drug resistant *P. aeruginosa* bloodstream infections in this study, no comparison of clinical characteristics and laboratory results between patients with resistant and sensitive *P. aeruginosa* bloodstream infections was performed.

The use of initial antimicrobial drugs may play a key role in the development of *P. aeruginosa* bloodstream infections, while overdose of β-lactams and fluoroquinolones is an independent risk factor for *P. aeruginosa* bloodstream infections [15]. According to the report [16], delayed application of sensitive antimicrobial drugs increased the 30-d morbidity and mortality rate in patients with *P. aeruginosa* bloodstream infections. The most used antimicrobial drugs are carbapenems, cephalosporins, and fluoroquinolones, which have been used with good efficacy. In this study 8 patients died with a mortality rate of 14.5%, which is lower than the mortality rates of 26.5% [17], 28.4% [18], 22.8% [19] reported in some domestic and foreign studies, probably because the number of cases of multi-drug resistant *P. aeruginosa* bloodstream infections in this study was low, and then reasonable treated with antimicrobial drugs, a good efficacy was achieved. In addition, a study [17] showed that combination antimicrobial therapy had no significant favorable effect on patient healing and that the mortality rate of patients treated with combination therapy was 35.6%, which was higher than that of monotherapy (19.8%, $P < 0.05$), but there was no statistical difference in mortality between combination therapy and monotherapy in this study because of the little cases of deaths.

In conclusion, *P. aeruginosa* bloodstream infections have a high morbidity and mortality rate, and hypoproteinemia and the use of central venous catheter were independent risk factors for death, and such patients should be actively

identified and prevented clinically, and targeted therapy should be administered as early as possible to reduce mortality.

This study has several limitations. 1) This was a single-centre study with a small number of cases, which may be biased; 2) The source of infection was not traced and the results may be affected. We will need to collect more cases from multiple centres at a later stage.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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