



Research Article

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Clinical Significance of Biochemical Indicators in Patients Infected with Drug-Resistant *Pseudomonas aeruginosa*

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Abstract

To evaluate the diagnostic and prognostic value of biochemical indicators Alanine Transaminase (ALT), Aspartate Transaminase (AST), Procalcitonin (PCT), Albumin (ALB), urea, and Creatinine (Cr) in patients infected with drug-resistant *Pseudomonas Aeruginosa* (PA). A retrospective analysis was conducted on clinical cases of drug-resistant PA from a tertiary hospital in Shanxi Province, China, between 2019 and 2023. Among 1950 PA-infected patients, 505 cases resistant to imipenem and/or meropenem were screened. The results showed that 89.91% of drug-resistant PA patients were aged ≥46 years. ALT, ALB, urea, and Cr exhibited significant differences across age or gender groups. Receiver Operating Characteristic (ROC) curve analysis revealed AUC values of 0.670 (ALT), 0.614 (AST), 0.388 (ALB), 0.629 (urea), 0.534 (Cr), 0.442 (PCT), and 0.759 (combined indicators). Notably, the combination of all six indicators did not improve the prognostic value compared to ALT alone. Elderly patients are more susceptible to imipenem and/or meropenem-resistant PA. ALT and ALB have diagnostic and prognostic value for drug-resistant PA infections, providing important guidance for clinical decision-making.

Keywords: Drug-resistant, *Pseudomonas aeruginosa*, Alanine transaminase, Albumin, Biochemical indicators, Diagnosis, Prognosis

Introduction

Pseudomonas aeruginosa (*P. aeruginosa*, PA) is a clinically important opportunistic pathogen, and controlling PA infections remains a major challenge in hospital infection management. It is an obligate aerobic Gram-negative bacillus with unique biological characteristics: an optimal growth temperature of 25-45°C, ability to proliferate at 42°C, and inability to survive at 4°C—traits that distinguish it from other opportunistic pathogens. Due to its strong survival in humid environments, PA often contaminates oxygen humidifiers, medical devices, and other hospital settings, making it a leading cause of hospital-acquired infections (especially ventilator-associated pneumonia [1]. Immunocompromised patients (e.g., those with severe pneumonia) face difficult treatment and poor prognosis after PA infection.

In recent years, PA resistance has increased steadily, with rising proportions of Multidrug-Resistant (MDR-PA) and Extensively Drug-Resistant (XDR-PA) strains [2-4]. This limits clinical treatment options significantly. PA resistance mechanisms are complex, including biosynthesis of Extended-Spectrum Beta Lactamases (ESBLs) and aminoglycoside-modifying enzymes, as well as integron-mediated regulation of Multidrug Resistance (MDR) gene activation [5]. Data from China's Antimicrobial Resistance Surveillance Program shows declining susceptibility of hospital-acquired PA to major antibiotics [6], and the US Centres for Disease Control and Prevention (CDC) classifies MDR-PA as a “serious threat” drug-resistant bacterium [7]. Thus, identifying accurate biomarkers for early diagnosis and disease assessment of drug-resistant PA infections is clinically critical.

Clinically, biochemical indicators are routinely used to assess health status, including liver function markers (ALT, AST, ALB) and renal function/ infection-related markers (Cr, urea, PCT) [8,9]. ALT is mainly distributed in hepatocytes, acting as a sensitive and specific marker for liver injury. AST is widely present in myocardial tissue with lower specificity than ALT. Resistant PA often overexpresses virulence factors (e.g., exotoxin A, elastase), which can directly damage hepatocytes or induce systemic inflammatory responses to disrupt hepatic microcirculation, leading to liver injury. Most anti-PA drugs are metabolized and excreted by the liver and kidneys; impaired liver or kidney function may alter drug concentrations, causing toxicity or subtherapeutic effects. Monitoring biochemical indicators can guide antibiotic dosage adjustment and assess infection severity/prognosis. ALB, the main plasma protein synthesized by hepatocytes, regulates colloid osmotic pressure, carrier transport, and nutrient maintenance. During acute infections, inflammatory mediators inhibit hepatic ALB synthesis, and increased vascular permeability causes ALB leakage into interstitial spaces, reducing serum levels making ALB a valuable marker for inflammatory responses in infected or critically ill patients. PCT, a marker of bacterial infections, rises rapidly within 2-4 hours of PA infection onset [10], earlier than traditional symptoms [11], and distinguishes Gram-negative bacterial infections (marked elevation) from viral/mycoplasmal infections (no significant or mild elevation) [11]. This helps differentiate PA infections from other pathogens, reducing diagnostic errors.

Despite their clinical utility, the role of biochemical indicators in PA infection diagnosis and assessment is not fully explored. Metabolic changes after PA infection are reflected in biochemical indicators, which may support early diagnosis, severity stratification, treatment efficacy evaluation, and prognosis prediction. This study collected clinical data of drug-resistant PA patients, analysed differences in biochemical indicators, and used Receiver Operating Characteristic Curves (ROC) to evaluate their diagnostic value providing a reference for early diagnosis of MDR-PA infections.

Materials and Methods

Study Subjects

Retrospective collection of PA-positive test cases from the Microbiology Laboratory of a tertiary hospital in Shanxi Province, China, between 2019 and 2023. Inclusion criteria: (1) Complete medical records; (2) Positive pathogen detection from specimens (sputum, bronchoalveolar lavage fluid, blood, etc.); (3) Sputum specimens meeting laboratory standards with repeated antimicrobial susceptibility testing confirming carbapenem (imipenem/meropenem) resistance. Exclusion criteria: (1) Multiple PA infection detections during hospitalization (only the first isolate was included); (2) Non-PA infections; (3) Incomplete patient information. Biochemical indicator data (ALT, AST, ALB, urea, Cr, PCT) during diagnosis were collected.

Study Group

Patients Were Divided into Four Age Groups: ≤18 years,

19-45 years, 46-65 years, and ≥66 years. Gender-based grouping included male and female patients.

Experimental Methods

Pathogen Culture and Identification: Specimens from suspected infection patients were collected and inoculated on blood agar plates, China blue agar plates, and chocolate blood agar plates, following the National Clinical Laboratory Operating Procedures [12]. The key steps: (1) Zone-inoculation of specimens onto appropriate media; Agar plates were incubated at 35°C, while others were incubated in 5% CO₂ for 24hours. (2) Characteristic grey-green/fluorescent PA colonies with a distinct odor were purified by subculture. (3) Purified colonies were suspended in 3mL of 0.45% (m/v) normal saline, standardized to 0.5-0.6 McFarland units, and analyzed using identification cards (results available in 4-8hours).

Antimicrobial Susceptibility Testing: The disc diffusion method was used, following CLSIM100-S32 guidelines. Antimicrobial discs included penicillins, β-lactamase inhibitor combinations, third-generation cephalosporins, novel cephalosporins, monobactams, carbapenems (imipenem, meropenem), aminoglycosides, and fluoroquinolones. The key steps: (1) Preparation of 0.5 McFarland turbidity bacterial suspension from 3-5 standard colonies. (2) Inoculation of Muller-Hinton agar plates using the three-wheel cross-streak method. (3) Placement of antimicrobial discs (center-to-center distance ≥24mm, distance from plate edge ≥15mm). (4) Incubation at 35°C for 16-18hours. (5) Measurement of inhibition zone diameter (to the nearest mm) against a black background with reflected light.

Clinical Data Collection: Patient data (name, gender, age, specimen source, antimicrobial susceptibility results, biochemical test results, prognosis) were extracted from the hospital's inpatient information system.

Statistical Analysis: Statistical analyses were performed using SPSS 25.0 software. Normal distributed data were expressed as mean ± standard deviation ($\bar{x} \pm s$) with one-way ANOVA for intergroup comparisons. Non-normally distributed data were expressed as median values (M, P25, P75) with non-parametric tests. Receiver Operating Characteristic (ROC) curves were plotted to calculate AUC value, optimal cut-off values, sensitivity and specificity [13]. Z-tests compared AUC values and logistic regression analyzed combined predictive factors [14]. Statistical was set at $p < 0.05$.

Results

General Characteristics

Table 1: Age distribution of patients with carbapenem-resistant *Pseudomonas aeruginosa*.

Age Group	Number of instances (n)	Composition Ratio (%)
≤18 years	7	1.39
19-45 years	44	8.71
46-65 years	204	40.4
≥66 years	250	49.5

In the present study, among 1950 PA-infected patients, 505 (25.90%) were resistant to imipenem and/or meropenem. Of these, 350 were male (69.31%) and 155 were female (30.69%); 45 patients (8.91%) died despite antibiotic treatment. The age distribution was dominated by 46-65 years (40.40%) and ≥ 66 years (49.50%), with a mean age of 63.89 ± 15.87 years (Table 1).

Specimen Sources

The top three specimen sources were sputum (71.88%), other secretions (6.14%), and bronchoalveolar lavage fluid (4.94%) (Figure 1).

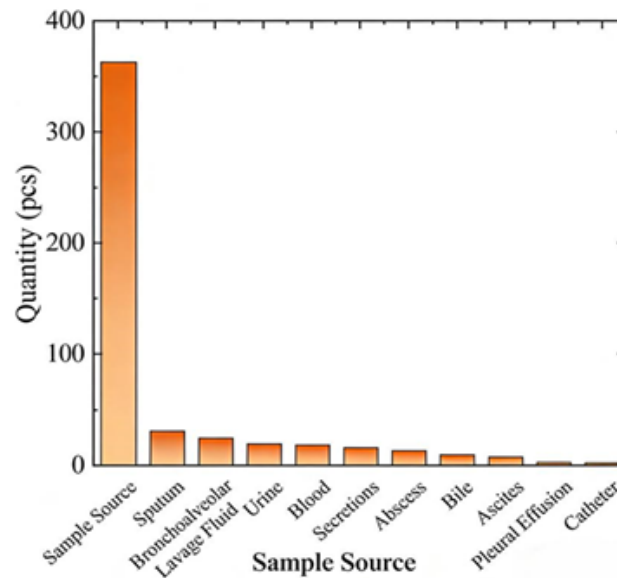


Figure 1: Sources of drug-resistant *P. aeruginosa* specimens.

Biochemical Indicator Results

Intergroup Differences by Age: Patients aged ≥ 66 years had

the highest levels of ALT, urea, and Cr, and the lowest ALB level with statistically significant differences across age groups ($p < 0.05$). AST and PCT showed no significant intergroup differences ($p > 0.05$) (Table 2).

Table 2: Comparison of biochemical indicators across age groups (median or mean \pm SD).

Indicator	≤ 18	19-45	46-65	≥ 66	p
ALT	3.23 (2.69, 4.07)	7.21 (6.24, 8.36)	18.10 (13.65, 23.36)	66.04 (45.27, 117.09)	<0.05
AST	27.50 (18.93, 49.13)	35.16 (24.37, 54.49)	29.73 (18.82, 59.18)	31.78 (20.04, 53.88)	0.587
ALB	38.05 \pm 5.37	34.67 \pm 5.16	32.4 \pm 5.83	30.74 \pm 5.67	<0.05
Urea	3.28 (3.20, 5.66)	5.97 (3.55, 9.23)	6.28 (3.95, 10.64)	7.48 (5.13, 12.33)	<0.05
Cr	38.02 (32.48, 44.70)	58.38 (43.25, 79.05)	51.90 (38.71, 64.67)	58.47 (42.53, 82.95)	<0.05
PCT	0.16 (0.08, 1.12)	0.27 (0.11, 0.64)	0.31 (0.12, 0.97)	0.35 (0.12, 1.51)	0.551

Table 3: Comparison of biochemical indicator between genders (median or mean \pm SD).

Indicator	Male	Woman	p
ALT	26.85 (14.54, 62.14)	28.3 (15.31, 57.13)	0.857
AST	33.13 (20.44, 59.01)	26.70 (17.90, 50.46)	<0.05
ALB	31.46 \pm 5.80	32.43 \pm 5.86	0.744
Urea	7.158 (4.82, 11.34)	6.14 (3.62, 9.94)	<0.05
Cr	57.34 (44.52, 77.25)	47.74 (33.74, 63.86)	<0.05
PCT	0.34 (0.12, 1.50)	0.31 (0.12, 0.84)	0.366

Intergroup Differences by Gender: Female patients had higher ALT and ALB levels than males, while males had higher AST, urea, Cr, and PCT levels. AST, urea, and Cr showed statistically significant gender differences ($p < 0.05$), while ALT, ALB, and PCT

did not ($p > 0.05$) (Table 3).

ROC Curve Analysis: The combined indicators had the highest AUC (0.759), followed by ALT (0.670), urea (0.629), AST (0.614), Cr

(0.534), PCT (0.442), and ALB (0.388). The combined test showed significantly higher AUC than AST, urea, and PCT ($p < 0.05$), but no

significant difference from ALT ($p = 0.164$). ALT had higher AUC than AST, urea, and PCT ($p < 0.05$) (Table 4, Figure 2).

Table 4: Diagnostic performance of biochemical indicators.

Project	AUC	Sensitivity	Specificity	Yorden Index	Optimum critical value	95% confidence interval
Joint trial	0.759	0.765	0.658	0.423	0.058	0.640, 0.877
ALT	0.67	0.765	0.561	0.326	30.135	0.519, 0.821
AST	0.614	0.647	0.578	0.225	36.405	0.488, 0.740
ALB	0.388	0.471	0.262	0.267	28.04	0.247, 0.529
Urea	0.629	0.647	0.591	0.238	8.11	0.494, 0.765
Cr	0.534	0.588	0.561	0.149	58.785	0.396, 0.672
PCT	0.442	0.588	0.215	0.197	0.11	0.299, 0.585

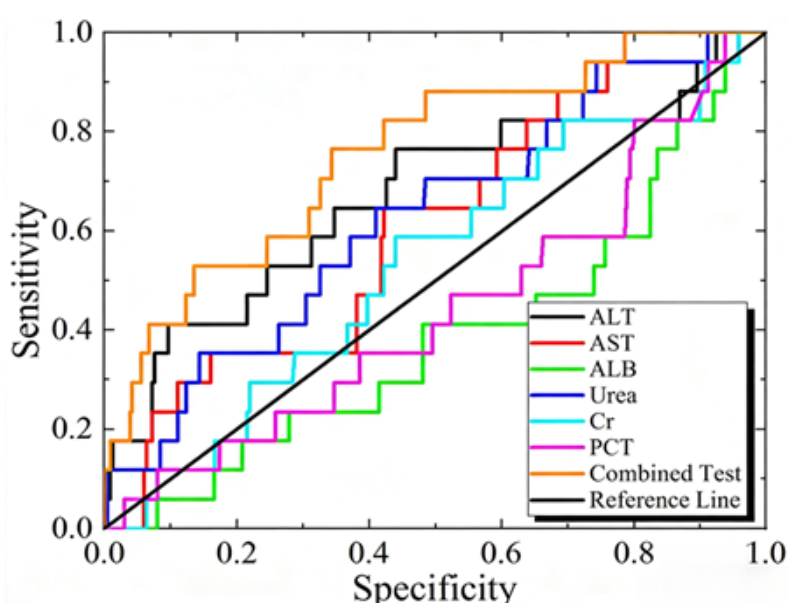


Figure 2: ROC curves for different biochemical indicators and combined tests.

Comparative analysis of AUC values using SPSS 25.0 revealed statistically significant differences between the combined test and AST, Urea, and PCT ($p < 0.05$), whereas no significant difference was observed when compared with ALT ($p > 0.05$). Individual

comparisons among biochemical indicators AST versus Urea, AST versus PCT, and PCT versus Urea also showed no statistical significance ($p > 0.05$), as detailed in (Table 5).

Table 5: Comparison of AUC values between indicators.

Comparison Pair	Z-value	P-value
Joint trial vs ALT	1.4	0.164
Joint trial vs AST	2.85	<0.05
Joint trial vs Urea	2.56	<0.05
Joint trial vs PCT	6.34	<0.05
ALT vs AST	1.13	<0.05
ALT vs Urea	1.04	<0.05
ALT vs PCT	5.04	<0.05
AST vs Urea	-0.59	0.554
AST vs PCT	4.19	0.154
PCT vs Urea	4.55	0.299

Discussion

Pseudomonas Aeruginosa (PA) is a leading cause of hospital-acquired Gram-negative bacterial infections, accounting for 13.80% of such cases [15]. Imipenem and meropenem, as core carbapenem antibiotics, exhibit high susceptibility rates against Gram-negative bacteria (80.10% and 76.45%, respectively) [15], making them frontline therapeutic options for PA infections. However, the global rise in Multidrug-Resistant *Pseudomonas Aeruginosa* (MDR-PA) has posed a severe threat to clinical treatment. MDR-PA enhances its pathogenicity through multiple mechanisms, including biofilm formation that shields bacteria from antibiotic penetration and overexpression of efflux pumps that actively expel antimicrobial agents [9]. Consequently, patients infected with MDR-PA often require higher antibiotic doses or combined regimens, which

may trigger excessive systemic inflammatory responses or induce hepatic and renal function impairment underscoring the urgency of identifying reliable biomarkers for early diagnosis and prognosis assessment.

This retrospective study analysed 1950 PA-infected patients over a five-year period (2019-2023), identifying 505 cases of imipenem and/or meropenem resistance (25.90% of total PA infections). Demographic analysis revealed that patients aged ≥ 66 years accounted for 49.51% of drug-resistant cases, with those aged 46-65 years comprising an additional 40.40%. This age distribution aligns closely with data from the Chinese Antimicrobial Resistance Surveillance Network (CHINET), highlighting that elderly populations are disproportionately vulnerable to carbapenem-resistant PA infections. The heightened susceptibility in older adults may be attributed to age-related decline in immune function, increased prevalence of underlying comorbidities (e.g., diabetes, chronic kidney disease), and a higher cumulative exposure to antibiotics all factors that facilitate the emergence and transmission of drug-resistant strains.

Specimen source analysis indicated that sputum was the most common sample type (71.88%), followed by other secretions (6.14%) and bronchoalveolar lavage fluid (4.94%). This finding is consistent with PA's tropism for the respiratory tract, as the bacterium thrives in humid environments and frequently colonizes medical devices such as ventilators and oxygen humidifiers leading to ventilator-associated pneumonia and other lower respiratory tract infections [1]. The predominance of respiratory specimens underscores the need for targeted monitoring of biochemical indicators in patients with respiratory symptoms suspected of PA infection, particularly in Intensive Care Units (ICUs) and other high-risk settings.

Statistical analysis of biochemical indicators revealed notable differences across age and gender groups. In age-stratified comparisons, ALT, ALB, Urea, and Cr showed statistically significant variations ($p < 0.05$). Patients aged ≥ 66 years exhibited the highest levels of ALT, Urea, and Cr, alongside the lowest ALB concentrations reflecting age-related declines in hepatic and renal function, as well as enhanced inflammatory responses during infection. These results are consistent with previous literature [16,17], which has linked advancing age to alterations in nutrient metabolism, protein synthesis, and organ function that influence biochemical marker levels. Gender-based comparisons showed that male patients had significantly higher AST, Urea, and Cr levels than females ($p < 0.05$), while females displayed marginally higher ALT and ALB concentrations (though not statistically significant). These gender differences may stem from physiological variations in hepatic enzyme activity, renal filtration rates, and hormonal influences on protein metabolism, which warrant further investigation in larger cohorts.

Notably, PCT an established marker of bacterial infection showed no significant differences across age or gender groups ($p > 0.05$) in this study, consistent with the findings of Min, et al., [15]. However, this contrasts with other reports suggesting PCT's

utility in diagnosing PA infections [16-19]. The discrepancy may be attributed to several factors: the limited sample size of our study, potential false-positive PCT elevations in patients with non-bacterial inflammatory conditions, or variations in the timing of PCT measurement relative to infection onset. Additionally, the heterogeneous nature of PA infections (e.g., differences in infection site, severity, and comorbidities) may have masked PCT's diagnostic utility, highlighting the need for standardized sampling protocols and larger-scale validation. ROC curve analysis was performed to evaluate the diagnostic value of individual biochemical indicators and their combination. The combined panel of ALT, AST, ALB, Urea, Cr, and PCT achieved the highest AUC (0.759), followed by ALT alone (0.670), Urea (0.629), AST (0.614), Cr (0.534), PCT (0.442), and ALB (0.388). Notably, the combined panel did not show a statistically significant difference in diagnostic efficacy compared to ALT alone ($p = 0.164$), while ALT outperformed AST, Urea, and PCT ($p < 0.05$). This indicates that ALT a classic marker of hepatic injury serves as a standalone reliable indicator for carbapenem-resistant PA infections. The elevated ALT levels in drug-resistant PA patients may be driven by direct hepatocellular damage from PA virulence factors (e.g., exotoxin A and elastase) or indirect injury via systemic inflammatory responses that disrupt hepatic microcirculation [8]. The clinical implication of this finding is substantial: ALT testing offers a simple, cost-effective tool for early screening of carbapenem-resistant PA infections, eliminating the need for complex multi-indicator panels and streamlining diagnostic workflows.

This study has several limitations that should be acknowledged. First, no control group (e.g., healthy individuals or patients with carbapenem-sensitive PA infections) was included, which limits the ability to determine the specificity of biochemical indicators for drug-resistant strains. Second, age-group analysis did not adjust for underlying comorbidities (e.g., diabetes, hypertension, chronic liver disease) that may independently affect biochemical marker levels and immune function. Third, cases of PA co-infection with other bacteria were not excluded, which may have confounded the results by introducing additional inflammatory stimuli. Fourth, the single-centre design and limited sample size may restrict the generalizability of the findings to other healthcare settings or populations.

Future research should address these limitations by expanding the sample size, incorporating a control group of carbapenem-sensitive PA infections and healthy individuals, and adjusting for confounding factors such as comorbidities and co-infections. Multi centre studies are needed to validate the diagnostic value of ALT across diverse patient populations and clinical settings. Additionally, longitudinal studies could explore the dynamic changes in biochemical indicators throughout the course of infection, which may provide insights into treatment response and prognosis. Further investigations into the mechanisms linking ALT elevation to PA drug resistance such as the role of bacterial virulence factors in hepatic injury could also enhance our understanding of the pathophysiological basis of this association.

In conclusion, elderly patients (≥ 46 years) are at a higher risk of carbapenem-resistant PA infections, likely due to age-related

immune decline and increased antibiotic exposure. ALT and ALB exhibit significant variations across age groups and hold diagnostic and prognostic value for drug-resistant PA infections. Notably, ALT alone demonstrates diagnostic efficacy comparable to a combined panel of six biochemical indicators, making it a practical and cost-effective tool for clinical practice. For patients with suspected or confirmed carbapenem-resistant PA infections, close monitoring of ALT levels is recommended to guide antibiotic dosage adjustment, assess liver function, and improve treatment outcomes. This study provides important insights into the clinical utility of biochemical indicators in managing drug-resistant PA infections, offering a foundation for optimized diagnostic and therapeutic strategies.

Author Contributions

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All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest Statement

The authors declare no conflicts of interest. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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