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Diagnosis of Antibiotic-Resistant K. Pneumoniae Sepsis by Serum Inflammatory Factors and Microbial Tests

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Abstract: This study aimed to investigate multidrug-resistant K. Pneumoniae sepsis through the combination of serum inflammatory factors and microbiological testing. Clinical data from 321 cases were analyzed: 50 patients suffered from sepsis caused by multidrug-resistant K. Pneumoniae (Group A), 221 patients with sepsis caused by other infections (Group B), and 50 healthy individuals undergoing physical examinations during the same period (Group C). Laboratory tests were conducted for all three groups, and the data were comprehensively analyzed. The results showed that the levels of inflammatory factors including procalcitonin (PCT), interleukin-6 (IL-6) and C-reactive protein (CRP) in group A were significantly higher than those in groups B and C ($P<0.001$). Furthermore, Group B patients had significantly higher inflammatory factor levelsthan Group C patients ($P<0.001$). Among the 452 strains of pathogens isolated from these sepsis patients, there were 302 strains of gram-negative bacteria, including 50 strains of multidrug-resistant K. Pneumoniae, accounting for 11.06% (50/452). There were 120 strains of gram-positive bacteria and 30 fungal strains. The resistance rate of K. Pneumoniae to cefazolin, cefotaxime, ceftazidime, cefepimea and aztreonam was over 44%. The resistance rate of K. Pneumoniae to imipenem, meropenem was over 40%. In conclusion, more attention should be paid to the clinical treatment of patients with multidrug-resistant K. Pneumoniae sepsis, and laboratory tests reflecting disease progresses such as the levels of serum inflammatory factors should be timely performed.

1. Introduction

Sepsis is a type of disease caused by infection that leads to a dysregulated response, further resulting in severe and life-threatening organ dysfunction. It can lead to complications such as acute respiratory distress syndrome, dissimulated intravascular coagulation, multiple organ dysfunction, multiple organ failure, and even death, making it a common critical illness in clinical practice. With the aging population, increasing incidence of tumors, and the rise of invasive medical procedures, the incidence of sepsis is continuously increasing globally at a rate of 1.5%-8.0% annually [1]. In recent years, the majority of the pathogens causing sepsis are gram-negative bacteria [2], with K. Pneumoniae sepsis ranking second among all gram-negative bacterial sepsis. If proper attention was not given, the disease progresses rapidly, leading to severe septicemia, typically characterized by low

blood pressure, acidosis, tachycardia, oliguria, multiple organ dysfunction, significantly impacting patients' daily life and quality of life. This disease is associated with high medical costs and mortality rates, causing significant physical and economic pressure on patients and their families. Numerous clinical studies have confirmed that monitoring serum inflammatory factor levels in sepsis patients can provide insights into the patient's condition, aiding in the comprehensive assessment of subsequent disease diagnosis, prognosis, and mitigating various risk factors for poor outcomes, ultimately improving the quality of life [3-5]. In this study, patients with sepsis were studied to explore the prognostic factors of patients with K. Pneumoniae sepsis, and provide the basis for timely evaluation of disease severity and treatment decisions.

2. Sample and Analysis Method

2.1 Subjects

This study collected clinical data of septic patients admitted to our hospital from January 2021 to December 2023. Hospital cases were retrieved through the medical record system. The patients met the criteria for K. Pneumoniae induced sepsis according to the study's inclusion criteria. There were 50 patients who suffered from sepsis caused by multidrug-resistant K. Pneumoniae (Group A), 221 patients with sepsis caused by other infections (Group B), and 50 healthy individuals undergoing physical examinations during the same period (Group C).

2.2 Inclusion criteria

(1) Patients admitted with a diagnosis of sepsis;
(2) All patients had blood culture of *K. Pneumoniae* or other microbes;
(3) No exposure to anti-inflammatory drugs and immunosuppressants.

2.3 Sample detection

(1) Detection of serum inflammatory factors

The levels of serum inflammatory factors of subjects in groups A,B and C were measured. On the morning after admission, 3ml of fasting venous blood samples were collected and serum was separated. Procalcitonin (PCT) and Interleukin-6 (IL-6) were tested using quantum dot immunofluorescence chromatography, C-reactive protein (CRP) was tested using immunoturbidimetry method.

(2)Microbiology

Automated identification: The identification board with the bacterial suspension is placed into the BD Phoenix automated microbiology system. The device initiates a series of pre-programmed biochemical reactions based on how the strain metabolizes various substrates, such as carbohydrate breakdown, amino acid metabolism, and enzyme activity assays.

Result output: Upon completion of the identification process, the system analyzes the results using software algorithms and automatically generates a report, which includes definitive identification of *K. Pneumoniae* and other relevant information.

Antimicrobial susceptibility testing: minimum inhibitory concentrations (MIC) are measured to determine the susceptibility (S - Sensitive, I - Intermediate, R - Resistant) of *K. Pneumoniae* against antibiotics according to authoritative guidelines by CLSI[6-7]. For this experiment, in vitro AST is performed for the following antibiotics using the automated method: ampicillin/sulbactam, piperacillin/tazobactam, Cefotaxime,cefazolin, cefepime, cefotaxime, ceftazidime, aztreonam, imipenem, meropenem, gentamicin, amikacin, ,tetracycline, ciprofloxacin, levofloxacin.

2.4 Statistical analysis

Data following a normal distribution are depicted by $\overline{x} \pm s$. Student's t-test, two-way ANOVA followed by Sidak's multiple comparison test were performed using IBM SPSS (V25.0). P<0.05 was statistically different.

3. Results

3.1 Distribution of pathogens

There were 452 strains of pathogens isolated from sepsis patients. 302 strains were gram-negative bacteria, including 50 strains of *K. Pneumoniae* accounting for 11.06% (50/452). There were 120 strains of gram-positive bacteria and 30 fungal strains. See Table 1.

Table 1: Analysis of pathogenic bacteria distribution in patients with sepsis

Pathogenic bacteria		Quantity (n=452)	Percent(%)
Gram-negative bacteria (n=302)	*K. Pneumoniae*	50	11.06
	E. coli	187	41.37
	Acinetobacter baui	4	0.88
	Pseudomonas Aeruginosa	6	1.33
	others	55	12.17
Gram-positive bacteria (n=120)	*Staphylococcus*	98	21.68
	Enterococcus	12	2.67
	other	10	2.21
Funguses		30	6.67
Total		452	100.00

3.2 Resistance of *K. Pneumoniae*

The resistance rates of *K. Pneumoniae* to cefazolin, cefotaxime, aztreonam, cefepime and ceftazidime were all above 44%. In contrast, resistance to the other four drugs including levofloxacin, imipenem, meropenem and trimethoprim-sulfamethoxazole was relatively low. See Table 2.

Table 2: Analysis of drug resistance of *K. Pneumoniae*

Antibacterial drug	**Quantity** (n=50)	**Drug resistance rate (%)**
Cefazolin	31	62
Aztreonam	26	52
Cefepime	24	48
Ceftazidime	24	48
Cefotaxime	22	44
Imipenem	23	46
Meropenem	20	40
Piperacillin/Tazobactam	15	30
Levofloxacin	11	22
Ampicillin/Sulbactam	29	58
Tetracycline	25	50
Gentamicin	16	32
Ciprofloxacin trimethoprim-sulfamethoxazole	16 10	32 20
Amikacin	5	10

3.3 Serum inflammatory factor levels among A, B and C groups

The levels of serum inflammatory factors (PCT, CRP, IL-6) in group A were significantly higher than those in group B and control group C (P<0.001). The levels of serum inflammatory factors (PCT, CRP, IL-6) in group B were also significantly higher than those in group C (P<0.001). See Figure 1.

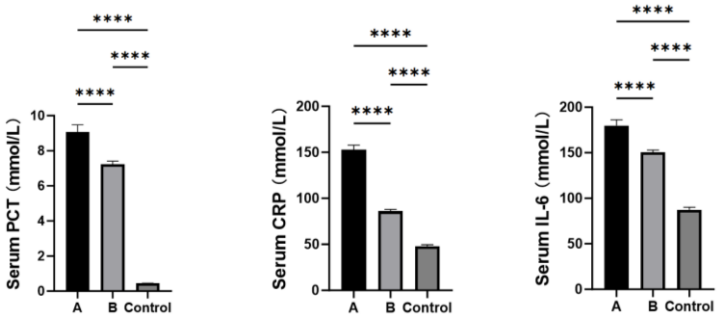

Figure 1: Levels of serum inflammatory factors among three groups. Four asterisks (****) indicate, that there are significant differences between groups (P<0.001).

4. Discussion

Sepsis can have adverse effects on various aspects of a patient's health and quality of life, leading to significant physical and mental stress for the patient and their family [8-9]. As an infectious disease, sepsis is a stress response of the body to infectious agents. When the body shows clear signs of inflammation, it can disrupt the stability of other organs and systems, including cardiovascular indicators, ultimately leading to conditions like septic shock, significantly reducing the patient's quality of life [10].

K. Pneumoniae is widely distributed in the human body. If clinical medication is used improperly, it can disrupt the body's microbial balance and trigger sepsis [11].*K Pneumoniae* is a well-known pathogen in clinical settings, and therefore, laboratory testing for drug resistance among these microbial populations can help detect disease progression timely, guide safe medication practices, and effectively reduce pathogen resistance.

Our study showed that the resistance rate of *K. Pneumoniae* to cefazolin, cefotaxime, cefepime, ceftazidime and aztreonam was over 44%. During laboratory testing, it is essential to focus on observing and analyzing key pathogens and resistance indicators of the disease, minimizing the use of antibiotics that show resistance, tailoring medication based on the patient's actual condition, and enhancing the effectiveness of disease diagnosis and treatment. Additionally, microscopic examination revealed the presence of a biofilm on resistant strains of *K. Pneumoniae*, which is a crucial factor contributing to their resistance, as the biofilm affects the regulation of bacterial resistance genes expression and extracellular polysaccharides, leading to resistance to various antibiotics [12].

Our study also showed the usefulness of three inflammatory factors in serum. Procalcitonin (PCT) belongs to a type of acute-phase reactant protein, with normally low levels in the blood. However, in the presence of sepsis, a significant increase in PCT levels can be observed.In this study, it was found that Group A patients had significantly higher PCT values compared to Groups B and C.Group B patients also exhibited significantly higher PCT values than the control group, indicating that as the severity of sepsis increaseDs, PCT levels rose accordingly. This suggests that PCT is useful for accessing the severity of sepsis with high diagnostic sensitivity and specificity. Dynamic monitoring of PCT facilitates early disease diagnosis, guides appropriate medication use, reduces unnecessary adverse drug reactions, and helps lower pathogen resistance rates.

C-reactive protein (CRP), another acute-phase reactant protein produced in the liver, is also significant in inflammatory responses [13]. Clinical studies have shown that CRP levels increase significantly in sepsis patients 12-18 hours after onset, gradually decreasing thereafter. The peak levels are maintained for 1-3 days. Comparing the CRP levels of three groups, higher CRP levels were observed in both Group A and Group B, indicating CRP can reflect the actual condition of sepsis patients to some extent. Moreover, the IL-6 levels in sepsis patients were also notably higher than in healthy individuals. These laboratory indicators can assist in subsequent diagnosis and treatment of diseases, enabling early prevention and diagnosis, providing targeted drug therapy, and ultimately improving patients' quality of life.

5. Conclusion

In conclusion, clinical attention should be paid to the diagnosis and treatment of patients with multidrug-resistant *K. Pneumoniae* sepsis, and antimicrobial susceptibility testing and serum inflammatory factors should be carried out to understand the drug resistance and actual condition, so as to provide guidance for safe and rational drug use, control the development of the disease, and improve the prognosis of patients.

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