

# Clinical Characteristics of 606 Patients with Community-Acquired Pyogenic Liver Abscess: A Six-Year Research in Yantai

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**Objective:** This study was designed to analyze the clinical characteristics, etiological characteristics, drug resistance, and empirical use of antibiotics for community-acquired pyogenic liver abscess (PLA) to provide a basis for rational and effective empirical treatment of PLA in the local area.

**Methods:** The clinical data, etiological characteristics, drug resistance, and empirical anti-infective therapy schemes of 606 patients with PLA were collected and analyzed retrospectively.

**Results:** The included patients were mainly males, with a male-to-female ratio of 1.3:1. The average age of the patients was 60.3 ± 14.1 years. The underlying diseases were diabetes and biliary tract disease, accounting for 38.7% and 22.3%, respectively. The main clinical manifestations were fever (92.9%), abdominal pain (44.7%), and nausea (33.3%). Imaging findings: the proportion of patients with a single lesion was 74.7%, and 67% of the patients had involvement in the right lobe of the liver. The main pathogen was *Klebsiella pneumoniae* accounted for 74.9% in blood culture and 84.1% in pus culture, mainly extended-spectrum β-lactamase. In 272 strains negative for extended-spectrum β-lactamase (ESBLs), 100% were resistant to ampicillin and less than 50% were sensitive to nitrofurantoin. Only 36 ESBL-positive strains had higher than 80% sensitivity to carbapenems, β-lactamase inhibitor compound, and amikacin. Patients treated with different treatment methods showed significantly different average length of hospital stay (14 [9–21] vs 13 [8–18]). Empirical anti-infective therapy: Beta-lactamase complex, carbapenems, cephalosporins, and quinolones were used in 280 (37.6%), 180 (29.7%), 180 (29.7%), and 147 (24.3%) patients, respectively.

**Conclusion:** Patients with community-acquired PLA in this area are mainly males, and the underlying diseases are mainly diabetes and hepatobiliary system disease. The main clinical manifestation is fever, so patients with fever of unknown cause should pay attention to possible liver abscesses. Based on drug sensitivity tests, the empirical use of antibiotics is somewhat unreasonable.

**Keywords:** liver abscess, *Klebsiella pneumoniae*, epidemiological, community

## Introduction

Pyogenic liver abscess (PLA) is an infectious disease caused by pyogenic bacteria invading the liver through various channels, accounting for 13% of abdominal infectious diseases and 48% of visceral abscesses.<sup>1,2</sup> In recent years, the overall incidence rate of PLA has been increasing gradually, and the incidence rate is higher in Asian countries.<sup>3–5</sup> In the past 20 years, the infection rate of *Klebsiella pneumoniae* (*K. pneumoniae*) in the Asian population has gradually increased. At present, it has become the main pathogen causing PLA infection.<sup>6–8</sup> Patients with PLA may have nonspecific manifestations such as chills, fever, shivers, and pain in the liver area. When the infection is poorly controlled, PLAs, especially those caused by *K. pneumoniae*, can lead to sepsis, multiple organ dysfunction, and death; it has a mortality rate of 2%–31%.<sup>9</sup> However, due to the nonspecific manifestations of some patients, there are some misdiagnoses and missed diagnoses in clinics. To improve the diagnosis rate of PLA in the local area, effective empirical treatment must begin as soon as possible to improve the

prognosis of patients. The selection of antimicrobial drugs requires the combination with local PLA pathogenesis and clinical manifestations. In this retrospective study, we aimed to analyze the clinical characteristics, etiological characteristics, drug resistance, and empirical use of antibiotics for community-acquired pyogenic liver abscess (PLA), and therefore to provide a basis for rational and effective empirical treatment of PLA in the local area.

## Data and Methods

### Subjects

PLA met the diagnostic criteria proposed by Foo et al<sup>10</sup> in 2010. Exclusion criteria: (1) mixed infection, combined with fungal or parasitic infection; (2) the pathogenic culture results of the same patient were not the same; (3) the culture results were considered as contaminated bacteria. The study was approved by the ethics committee of the hospital.

### Research Methods

A total of 606 patients with PLA, diagnosed in Yantai Yuhuangding Hospital from 2015 to 2020, were analyzed retrospectively. The basic data, laboratory results, microbiological results, and treatment methods (eg, empirical anti-infective therapy scheme and drainage) were collected.

### Result Interpretation Criteria

The curative effect was evaluated after two weeks of hospitalization. (1) Effective: the symptoms were relieved, and the abscess shrunk after treatment. (2) Ineffective: the symptoms were not alleviated or worsened after treatment, the size of the pus cavity did not change, increases upon imaging examination (abdominal ultrasound, computed tomography [CT] or magnetic resonance imaging) were noted, or the death of the patient.

### Bacterial Isolation and Culture

#### Culture of Drainage Fluid and Blood

The patient's ultrasound-guided percutaneous drainage fluid was immediately sent to the bacterial room for culture. An inoculating nutrient broth was used to increase the amount of the bacteria. After 24 h, the bacteria were transferred to a blood plate and a MacConkey agar plate at the same time and cultured at 35°C for 24 h. A blood culture was carried out in strict accordance with the relevant methods in the BACTEC9050 blood culture user manual. After the positive alarm of the LED display screen of the instrument, smearing and seed transfers were performed at the same time. The method of seed transfer is the same as that of ordinary culture. For the pus culture, the pus was directly inoculated in a blood plate and a MacConkey agar plate and cultured at 35°C for 24 h.

#### Pathogen Identification and Drug Sensitivity Test

The separated bacteria were dissolved evenly in the identification culture medium. The turbidimeter was used to adjust the turbidity (0.5 Michaelis turbidity), and 25  $\mu$ L of the sample was taken from the dissolved identification culture medium into the drug sensitivity inoculation culture medium and placed in the corresponding well of the positive plate or negative plate. A full-automatic microbial analyzer, with its own bacterial identification/drug sensitivity system, was used for pathogen identification and drug sensitivity detection.

### Statistical Analysis

The original data of the patients were collected and sorted with Excel. The data were statistically analyzed using statistical software SPSS 22.0. Normally distributed and approximately normally distributed measurement data were expressed as the mean  $\pm$  standard deviation and compared between groups using *t*-tests. Non-normally distributed measurement data were expressed as the median and interquartile and compared between groups using non-parametric tests. The count data were expressed as numbers (proportion) and compared using two independent sample *Chi*-square tests or Fisher exact probability methods.  $P < 0.05$  was considered statistically significant.

## Results

### Basic Data of Patients with PLA

Of the 606 patients with PLA, 345 were males (56.7%), with a male-to-female ratio of 1.3:1. The age range of these patients was 18–97 years, with an average age of  $60.3 \pm 14.1$  years. The main underlying diseases were diabetes, cerebrovascular disease, and benign biliary disease, accounted for 38.7%, 27.9%, and 22.3% respectively (Table 1).

### Clinical and Laboratory Data of PLA

#### Clinical Manifestations

Fever (563 patients, 92.9%) was the most common clinical manifestation, followed by chills and chills (74.7%). Of all patients, 323 had a peak body temperature of  $>39^{\circ}\text{C}$ , accounting for 57.3% of the patients with fever. Abdominal pain was a clinical manifestation in 44.7% of patients, 33.3% had vomiting or nausea, 18.2% had fatigue and poor appetite, and 6.3% had jaundice. Some patients had other atypical clinical symptoms (Table 1).

#### Laboratory Tests

Elevated leukocytes were found in 408 patients (68.5%). There were 76.8% of the patients with elevated neutrophils; 289 (99.0%) of them had elevated C-reactive protein; and 202 (76.5%) had elevated procalcitonin. Other common abnormal laboratory indicators were as follows: 338 patients (56.8%) with anemia, 179 patients with albumin reduction (30.2%),

**Table 1** Clinical Features of Pyogenic Liver Abscess

Item		Number (Percentage)
Gender	Male	346(57.1%)
	Female	260(42.9%)
Average age (years old)	$60.3 \pm 14.1$	
Underlying disease	Hypertension	89(14.7%)
	Diabetes mellitus	234(38.6%)
	Coronary heart disease	36(5.9%)
	Cerebrovascular disease	169(27.9%)
	Malignant tumors	67(11.1%)
	Benign biliary disease or operation	135(22.3%)
Clinical manifestations	Fever	563(92.9%)
	Fear of cold, shiver	453(74.7%)
	Abdominal pain	271(44.7%)
	Nausea, vomiting	202(33.3%)
	Fatigue, poor appetite	110(18.2%)
	Jaundice	38(6.3%)
	Dyspnea	35(5.7%)
	Headache dizziness	25(4.1%)
	Unconsciousness	11(1.8%)
Peak body temperature ( $^{\circ}\text{C}$ )	$>39.0$	323(57.3%)
	$\leq 39.0$	240(42.7%)

423 patients (71.4%) with elevated  $\gamma$ -glutamyltransferase, 324 patients (54.7%) with elevated alkaline phosphatase, 301 patients (50.6%) with elevated alanine aminotransferase, 270 patients (45.4%) with elevated aspartate aminotransferase, 278 patients (47.2%) with elevated fasting blood glucose, and 462 (79.9%) patients with elevated lactate dehydrogenase.

### Ultrasonic or CT Results

Of these 606 patients, 451 patients (74.4%) had a single abscess. In 406 patients (67%), the abscess was in the right lobe.

## Analysis of Etiological Characteristics of PLA

Blood cultures were administered to 404 patients, and the positive rate was 26.1%. Among them, *K. pneumoniae* was dominant (79 patients, 74.5%), followed by *Escherichia coli* (*E. coli*; 13 patients, 12.3%). Pus cultures were performed on 409 patients, and the positive rate was 69.4% (284 patients). Among them, *K. pneumoniae* was dominant (233 patients, 82.1%), followed by *E. coli* (29 patients, 10.2%). The detection rate of positive cocci was very low in both the blood and pus cultures (Table 2).

### Drug Resistance of Pathogens

In the 272 strains negative for extended-spectrum  $\beta$ -lactamase (ESBLs), in addition to 100% resistance to ampicillin and less than 50% sensitivity to nitrofurantoin, their sensitivity to the commonly used cephalosporins III, cephalosporins and monocyclic  $\beta$ -Lactams, quinolones (ciprofloxacin, levofloxacin), aminoglycosides (tobramycin, gentamicin, amikacin), tetracyclines (tigecycline)  $\beta$ -lactamase inhibitor compound (Cefoperazone/sulbactam, amoxicillin/clavulanic acid, piperacillin/tazobactam), and carbapenems was higher than 90%, whereas the sensitivity rate to amikacin and meropenem was 100%. However, the susceptibility of *K. pneumoniae* to cotrimoxazole and levofloxacin was better than that of *E. coli*.

Thirty-three ESBL (+) strains had higher than 80% sensitivity to carbapenems (imipenem, meropenem, ertapenem, and biapenem), tetracyclines (tigecycline),  $\beta$ -lactamase inhibitor compound (cefoperazone/sulbactam, piperacillin/tazobactam), and amikacin. Only two strains were multidrug resistance and all of them were *E. coli* (Table 3).

**Table 2** Results of Blood Culture and Pus Culture

Item	Blood Culture (n=414)	Pus Culture (n=409)
Positive (n (%))	106 (25.6)	284(69.4)
KPN	79(19.1)	233(56.3)
ESBL (+)	1(0.2)	13(3.1)
ESBL (-)	78(18.8)	220(53.1)
<i>Escherichia coli</i>	13(3.1)	29(7.0)
ESBL (+)	4(1.0)	18(4.3)
ESBL (-)	9(2.2)	9(2.2)
<i>Enterococcus faecalis</i>	3(0.7)	3(0.7)
<i>Morganella morganii</i>	1(0.2)	2(0.5)
<i>Staphylococcus aureus</i>	0	3(0.7)
<i>Pseudomonas aeruginosa</i>	1(0.2)	1(0.2)
<i>Citrobacter freundii</i>	0	1(0.2)
Others	9(2.2)	12(2.9)
Negative	308(76.4)	125(30.6)

**Table 3** Analysis of Drug Resistance of Enterobacteriaceae Bacteria

	271 Cases with <i>K. pneumoniae</i>				35 Cases with <i>E. coli</i>			
	18 ESBL +Sensitivity N (%)	18 ESBL+Drug Resistance N (%)	253 ESBL- Sensitivity N (%)	253 ESBL- Drug Resistance N (%)	17 ESBL +Sensitivity N (%)	17 ESBL+Drug Resistance N (%)	18 ESBL- Sensitivity N (%)	18 ESBL-Drug Resistance N (%)
Amikacin	16 (88.9)	2 (11.1)	253 (100.0)	0 (0.0)	14 (82.4)	3 (17.6)	18 (100.0)	0 (0.0)
Imipenem	18(100.0)	0(0.0)	251 (99.2)	0 (%)	15 (88.2)	1 (5.9)	16 (88.9)	2 (11.1)
Tigecycline	18(100.0)	0(0.0)	240 (94.9)	10(3.9)	17 (100.0)	0 (0.0)	18 (100.0)	0 (0.0)
Ertapenem	18(100.0)	0(0.0)	250 (98.8)	0(0.0)	15 (88.2)	2 (11.8)	16 (88.9)	2 (11.1)
Cefoxitin	13(72.2)	5(27.8)	240 (94.9)	8(3.2)	10 (58.8)	5 (29.4)	13 (72.2)	1 (5.6)
Piperacillin/Tazobactam	17(94.4)	1(5.6)	250 (98.8)	2(0.8)	16 (94.1)	0 (0.0)	15 (88.2)	2 (11.1)
Cefoperazone-Sulbactam	16(88.9)	2(11.1)	251 (99.2)	2(0.8)	17 (100.0)	0 (0.0)	17 (94.4)	1 (5.6)
Cefepime	17(94.4)	1(5.6)	252 (99.6)	0(0.0)	12 (70.6)	5 (29.4)	16 (88.9)	2 (11.1)
Ceftriaxone	8(44.4)	10(55.6)	249 (98.4)	4(1.6)	3 (17.6)	14 (82.4)	15 (83.3)	2 (11.1)
Amoxicillin clavulanate	12(66.7)	6(33.3)	250 (98.8)	1(0.4)	8 (47.1)	4 (23.5)	8 (44.4)	4 (22.2)
Levofloxacin	14(77.8)	4(22.2)	250 (98.8)	3(11.9)	5 (29.4)	12 (70.6)	11 (61.1)	6 (33.3)
Trimethoprim/ Sulfamethoxazole	13(77.2)	5(22.8)	243 (96.0)	10(3.9)	2 (11.8)	15 (88.2)	9 (50.0)	9 (50.0)

## Empirical Anti-Infective Therapy

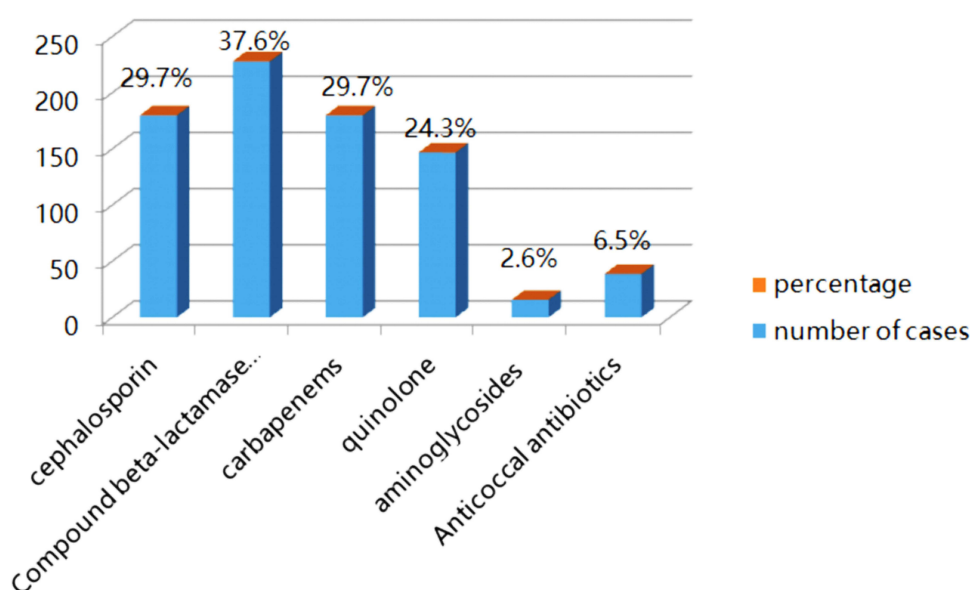
Of all patients, 228 were empirically treated with  $\beta$ -lactamase inhibitor compound for anti-infection treatment, and the proportion was the highest (37.6%). Of the total, 180 patients (29.7%) were empirically treated with cephalosporin, and 180 patients (29.7%) were empirically treated with carbapenems. In addition, 147 patients (24.3%) were empirically treated with quinolones, and 135 patients (22.3%) were treated with a single type of antibiotic. The remaining patients were treated with combined anti-infective therapy (cephalosporins combined with quinolones or aminoglycosides or nitroimidazoles, cefoperazone/sulbactam, or piperacillin/ sulbactam combined with nitroimidazoles). In 75 patients (12.3%), the anti-infection treatment was effective, and these patients underwent step-down treatment. A total of 105 patients (17.3%) received an upgraded treatment of carbapenem anti-infection. In 60 (9.9%) of these patients, the treatment was upgraded to antibiotics because of their serious condition, experience, or poor anti-infection treatment effect according to the drug sensitivity results (Figure 1).

## Efficacy Evaluation of Different Treatment Methods

Of all patients, 154 were treated with antibiotics alone and 452 were treated with antibiotics combined with puncture and drainage. Of the 154 patients treated with antibiotics alone, 143 patients (92.9%) achieved effective outcomes, and 11 patients (7.1%) achieved ineffective outcomes. In the combined treatment group, 423 patients (93.6%) achieved effective outcomes, and 29 patients (6.4%) achieved ineffective outcomes. A comparison revealed that there was no significant difference in the efficacy between the two treatment methods. However, the average length of the hospital stays of the patients who received combined treatment was significantly shorter than that of the patients who were treated with antibiotics alone (Table 4).

## Discussion

Pyogenic liver abscess is a serious infectious disease that threatens human health. It can develop into a life-threatening severe infection in patients with immunodeficiencies and older patients with underlying diseases. This study revealed that PLA usually occurs in males (the male-to-female ratio was 1.3:1). The average age was  $60.3 \pm 14.1$  years. These results are consistent with the results of previous studies. The main underlying diseases were diabetes and biliary tract disease, similar to those of previous studies. This is mainly because the liver has two sets of blood supply, namely the hepatic artery and the portal vein. The portal vein is connected to the gastrointestinal tract, and patients with underlying diseases of the biliary tract and intestinal tract will have an increased chance of an incidence of liver abscess.<sup>11–16</sup> In this study,



**Figure 1** Empirical use of antibiotics.

**Table 4** Comparison of Curative Effect Between the Two Groups with Different Treatment Methods

Item	Antibiotic Group (n=154)	Combined Group* (n=452)	P-value
Curative effect (n%)			
Effective	143 (92.9%)	423 (93.6)	0.527
Ineffective	11 (7.1%)	29 (6.4%)	
Length of hospital stay	14(9~21)	13(8~18)	0.029

**Note:** \*Combined group: antibiotics combined with puncture and drainage.

563 patients with PLA (92.9%) had a fever as the main clinical symptom and 323 patients (57.3%) had a high fever ( $>39.0^{\circ}\text{C}$ ). This is basically consistent with that reported in studies both locally and globally.<sup>17–19</sup> Therefore, in patients with a fever of an unknown cause, PLA should be carefully considered, especially for patients with a high fever. Other clinical symptoms of PLA can be jaundice, fatigue, poor appetite, and fading consciousness, suggesting that the clinical manifestation of PLA is not typical, so clinicians should be vigilant to avoid misdiagnoses and missed diagnoses that prolong the condition and affect the prognosis. This study revealed that patients with a single bacterial infection accounted for 93.0% of the patients. Among them, the detection rate of *K. pneumoniae* was 73.1%, slightly higher than that reported in the literature (64.0%).<sup>20</sup> The reason for this may be related to the patients' underlying disease.<sup>21</sup> The literature reported that diabetes mellitus was an independent risk factor for *K. pneumoniae* liver abscess.<sup>22</sup> In this study, the proportion of diabetes in the underlying diseases was the highest.<sup>23</sup> In our study, empirical anti-infection therapy was mainly compound  $\beta$ -lactamase inhibitor (36.0%), carbapenems (31.5%), and cephalosporins (31.3%). Singapore scholars studied patients with PLA with similar basic data treated with oral ciprofloxacin and injection of levofloxacin for 28 days. The results revealed that there was no difference in the treatment effects between the two groups.<sup>24</sup> Scholars in China's Taiwan region revealed that<sup>25</sup> there was no significant difference in the treatment effect of patients with PLA and even severe infection between quinolones and compound  $\beta$ -lactamase inhibitors. Quinolones can also shorten the time of administration of intravenous antibiotics and hospital stay. The reason may be that the main pathogen of PLA in China's Taiwan region and Singapore is *K. pneumoniae*.

The limitation of this study should also be acknowledged. In terms of the selection of empirical antibiotics, there was a lack of evaluation of the efficacy of different antibiotics in patients with the same basic data. In future research, pairing research will be conducted to provide the basis for a more reasonable and effective laboratory selection of antibiotics.

## Conclusion

The present study revealed that empirical treatment of patients with community-acquired liver abscess without risk factors of ESBL infection should also adopt compound  $\beta$ -lactamase inhibitors and even carbapenems. These findings may provide a basis for rational and effective empirical treatment of PLA in this region.

## Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Yuhuangding Hospital. Written informed consent was obtained from all participants.

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## Disclosure

The authors declare that they have no competing interests.

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