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ORIGINAL RESEARCH

Etiology, Risk Factors, and Antimicrobial Resistance in Recurrent Pyogenic Liver Abscesses: A Six-Year Analysis

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Aim: To perform a comparative analysis of the clinical data of patients with and without recurrent pyogenic liver abscess and explore the influencing factors, clinical characteristics, and pathogenic bacteria associated with the recurrence of liver abscesses.

Patients and Methods: A retrospective analysis was conducted on 436 recently diagnosed patients with pyogenic liver abscess admitted to the Affiliated Hospital of Chengde Medical College between June 2017 and June 2023. Patients with recurrence comprised the observation group, whereas those without recurrence comprised the control group.This analysis included the examination of clinical characteristics, pathogens, drug resistance patterns, and treatment modalities. Additionally, regression analysis was employed to investigate the factors influencing liver abscess recurrence.

Results: Of 436 patients initially diagnosed with pyogenic liver abscess, 58 experienced recurrence. The proportion of *Escherichia coli* infection was 23.3% in the observation group and 10.3% in the control group, indicating a statistically significant difference. Multivariate analysis identified diabetes mellitus and cerebral infarction as significant risk factors for recurrent pyogenic liver abscess.

Conclusion: In comparison with patients without recurrence, those who experienced recurrent pyogenic liver abscess following initial diagnosis exhibited a higher prevalence of *E. coli* as a pathogenic bacterium. In addition, a history of diabetes mellitus and cerebral infarction are high-risk factors for with pyogenic liver abscess recurrence for the first time.

Keywords: pyogenic liver abscess, relapse, *Klebsiella pneumoniae*, *Escherichia coli*, diabetes mellitus

Introduction

Pyogenic liver abscess (PLA) is an intrahepatic infection caused by pyogenic bacteria infiltrating the liver and accounts for approximately 80% of all liver abscess cases, Fungal liver abscesses are rare.[1,2] The incidence is notably higher in Asian countries, with approximately 12 to 18 cases per 100,000 individual persons annually and mortality rates varying from 2% to 31%.[3] Over the past 30 years, *Klebsiella pneumoniae* has replaced *Escherichia coli* as the predominant pathogen identified in PLA infections.[4] In recent times, owing to advancements in interventional radiology technology, percutaneous puncture drainage combined with antibiotics has emerged as the main treatment approach. This method is associated with reduced trauma and significant efficacy compared with antibiotic monotherapy and surgical interventions.[5,6] Limited research exists in the recurrence of PLA. This study investigated the clinical characteristics and pathogenic bacteria in patients with recurrent PLA and to analyze the risk factors contributing to recurrence.

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Methods

Sample Population

This retrospective study included 436 patients with newly diagnosed PLA admitted to the Affiliated Hospital of Chengde Medical College between June 2017 and June 2023.This study complies with the Declaration of Helsinki and was approved by the Institutional Ethics Committee of the Affiliated Hospital of Chengde Medical College.

Inclusion and Exclusion Criteria

Inclusion Criteria

① Diagnosis of liver abscess confirmed by ultrasound, computerized tomography(CT) or magnetic resonance imaging-(MRI);② Presence of symptoms such as fever, chills, and right upper abdominal pain; ③ Liver abscess diagnosis by puncture or surgical operation; ④ Identification of pathogenic bacteria in blood or pus cultures; ⑤ Improvement in patient's condition after antibiotic therapy.

Exclusion Criteria

① Incomplete patient information; ② Diagnosis of amebic liver abscess, tuberculosis, or other parasitic infections; ③ Non-initial onset of pyogenic liver abscess.

Research Methods

Demographic and clinical data, including gender, age, symptoms, laboratory results, bacterial culture results, treatment type, complications, and length of hospitalization were collected from the medical records of each patient. Treatment decisions, such as the use of percutaneous catheter drainage (PCD), were based on patient preferences and the effectiveness of antibiotic treatment for PLA. PCD catheter sizes typically ranging from 8 to 12 F were determined under ultrasound guidance. The number of drains can be increased depending on the number of liver abscesses, the size of the liver abscess, and the presence or absence of multilocular nature.Each patient received antibiotic treatment tailored to the doctor's expertise and bacterial culture. Intravenous antibiotics were administered for more than 2 weeks, followed by oral antibiotics for 2–4 weeks. Surgical treatment was provided when antibiotic therapy, percutaneous aspiration, or PCD was unsuccessful.

Pathogen Identification and Drug Susceptibility Test

Following percutaneous catheter aspiration (PCA) or PCD in PLA patients, 10 mL of pus was aseptically extracted using a sterile syringe and transferred into a culture bottle for examination. Patients with fever underwent blood culture. Pathogens were cultured using an ALERT3D120 automatic blood culture instrument [Biomeriere Diagnostic Products (Shanghai) Co., LTD., France] and inoculated onto blood agar and eosin-methylene blue plates. After 24 h of incubation, the pathogens were identified using automatic microbial identification and drug sensitivity analysis systems along with matching gram-positive and gram-negative bacterial identification cards [Meriier Diagnostic Products (Shanghai) Co., LTD.]. Drug susceptibility testing was performed using the disk diffusion method (Kirby-Bauer method) with drug susceptibility test papers and media from Oxoid Company, UK. A drug susceptibility test paper was placed on an agar plate inoculated with the test bacteria, resulting in the inhibition of bacterial growth within the inhibitory concentration zone surrounding the paper. After 24 h of incubation, the diameter of the inhibition zone was measured using a caliper to determine the sensitivity of the tested bacteria to the drugs under evaluation.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY). Data are presented as frequencies and percentages. Categorical variables were analyzed using the χ^2 test, whereas continuous variables were assessed using the *t*-test to determine significant differences between groups. Furthermore, logistic regression analysis was conducted to examine the association between liver abscess recurrence and other variables.

Results

Demographic and Clinical Characteristics

Comparison of the two groups of patients revealed no statistically significant differences in age, sex, size, and position of the liver abscess (Table 1).

Comorbidities in Patients with PLAs

More patients in the observation group had diabetes and cerebral infarction, and this disparity was statistically significant (Table 2).

Laboratory Examination

There were no statistically significant differences in infection markers (white blood cell count, C-reactive protein, procalcitonin) and liver function markers (albumin, ALT, total bilirubin) between the two groups (Table 3).

Culture Results of the Pathogen

Compared with the control group, the observation group exhibited a significantly higher prevalence of *E. coli. Klebsiella pneumoniae* was the predominant pathogen in both groups (Table 4).

Table 1 Demographics and Clinical Characteristics of 436 PLA Patients in the Two Groups

	Observation Group (n=58)	**Control Group (n=378)**	**P**
Age(mean SD)	60.58±11.02	58.99±14.06	0.333
Gender(n,%)			
Male	40 (69.0%)	239 (63.2%)	0.308
Female	18 (31.0%)	139 (36.8%)	
The size of PLA(mm)	68.39±23.62	67.22±27.01	0.759
The position of PLA(n,%)			
Left lobe	12 (20.7%)	90 (23.8%)	0.558
Right lobe	40 (69.0%)	245 (64.8%)	0.655
Both lobe	7 (12.1%)	43 (11.4%)	0.507
Multiloculated PLA(n,%)	24 (41.4%)	179 (47.4%)	0.569
Contains gas(n,%)	6 (10.3%)	39 (10.3%)	0.687
Individual PLA(n,%)	46 (79.3%)	313 (68.0%)	0.118
Symptoms (n,%)			
Fever	52 (90.0%)	346 (91.5%)	0.638
Abdominal pain	32 (55.2%)	188 (49.7%)	0.278
Vomit	15 (25.9%)	76 (20.1%)	0.240
Weakness	19 (32.8%)	119 (31.5%)	0.685

Abbreviation: PLA, Pyogenic liver abscess.

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Table 2 Comorbidities for PLAs

	Observation Group (n=58)	Control Group (n=378)	p
Diabetes	30 (51.7%)	140 (37.0%)	0.016
Hypertension	13 (22.4%)	89 (23.5%)	0.982
Malignant tumor	8 (13.8%)	51 (13.5%)	0.853
Abdominal operation	11 (19.0%)	77 (20.4%)	0.923
Cholecystolithiasis	9 (15.5%)	89 (23.5%)	0.224
Heart disease	5 (8.6%)	51 (13.5%)	0.800
Cerebral infarction	9 (15.5%)	27 (7.1%)	0.022

Table 3 Laboratory Examination of 436 PLA Patients in the Two Groups

	Observation Group (n=58)	Control Group (n=378)	p
ALT(U/L)	62.3±24.4	65.6±31.9	0.764
FIB(g/L)	5.72±1.16	5.94±3.85	0.388
ALB(g/L)	31.9±3.5	32.3±5.4	0.544
PLT($\times 10^9$/L)	211.9±131.6	218.1±147.1	0.649
PCT(ng/mL)	13.40±37.81	16.95±34.10	0.622
CRP(mg/L)	105.2±69.3	120.1±74.0	0.154
WBC($\times 10^9$/L)	9.9±5.3	10.8±5.3	0.898

Abbreviations: ALT, Alanine aminotransferase; FIB, Fibrinogen; ALB, albumin; PLT, Blood platelet; PCT, Procalcitonin; CRP, C-reactive protein; WBC, White blood cell count.

Table 4 Pathogen Species of 436 PLA Patients in the Two Groups

	Observation Group (n=58)	Control Group (n=378)	p
Pathogen culture positive	30 (52.6%)	203 (52.3%)	0.965
Klebsiella pneumoniae	21 (70.0%)	147 (72.4%)	0.783
E.coli	7 (23.3%)	21 (10.3%)	0.047
Enterococcus faecium	0	5 (2.5%)	
Aerobacter cloacae	2 (6.7%)	4 (2.0%)	0.146
Peptostreptococcus	1 (3.3%)	3 (1.5%)	0.489
Staphylococcus	0	4 (2.0%)	
Streptococcus formata	0	2 (1.0%)	
Streptococcus anginosus	0	3 (1.5%)	
Bacaeroides fragilis	0	2 (1.0%)	
Others	0	12 (6.0%)	

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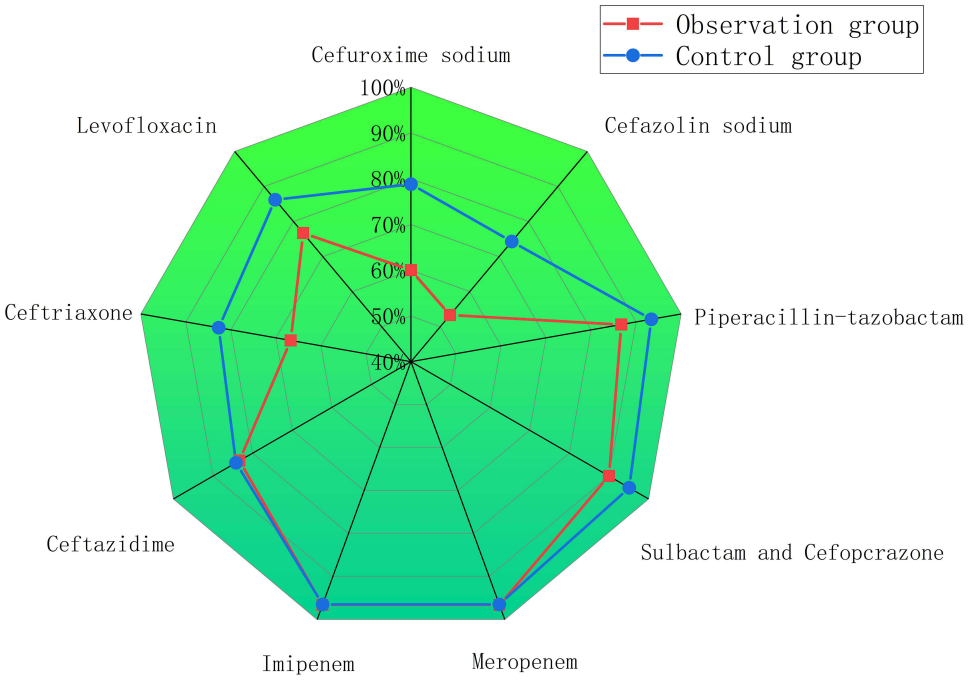

Figure 1 Comparison of antibiotic resistance in two groups of patients with PLA.

Drug Resistance of Pathogenic Bacteria

Only two patients exhibited comparable antibiotic susceptibility to imipenem and meropenem, with high sensitivity. In contrast, the observation group generally demonstrated lower susceptibility compared with the control group, exhibiting significant resistance (Figure 1).

Complications in Patients with PLAS During Hospitalization

The risks of ICU admission, septic shock, and septic shock syndrome during hospitalization were higher in the observation group than in the control group, although the difference was not statistically significant (Table 5).

High-Risk Factors for PLAS Recurrence

Multivariate analysis identified diabetes mellitus and a history of cerebral infarction as high-risk factors for recurrence in patients diagnosed with suppurative liver abscesses (Figure 2).

Table 5 Treatment and Complications in the Two Groups

	Observation Group 1 (n=58)	**Control Group (n=378)**	**p**
Pneumonia	21(36.2%)	139 (36.8%)	0.934
Admission to the ICU	10 (17.2%)	35 (9.3%)	0.063
Hospital stays(mean SD)	14.14±8.12	13.32±10.01	0.556
Septic shock	8 (13.8%)	29 (7.7%)	0.119
Invasion syndrome	5 (8.6%)	15 (3.9%)	0.115
PCD	36 (62.1%)	234 (61.9%)	0.981

Abbreviations: PCD, percutaneous catheter drainage; ICU, intensive care unit.

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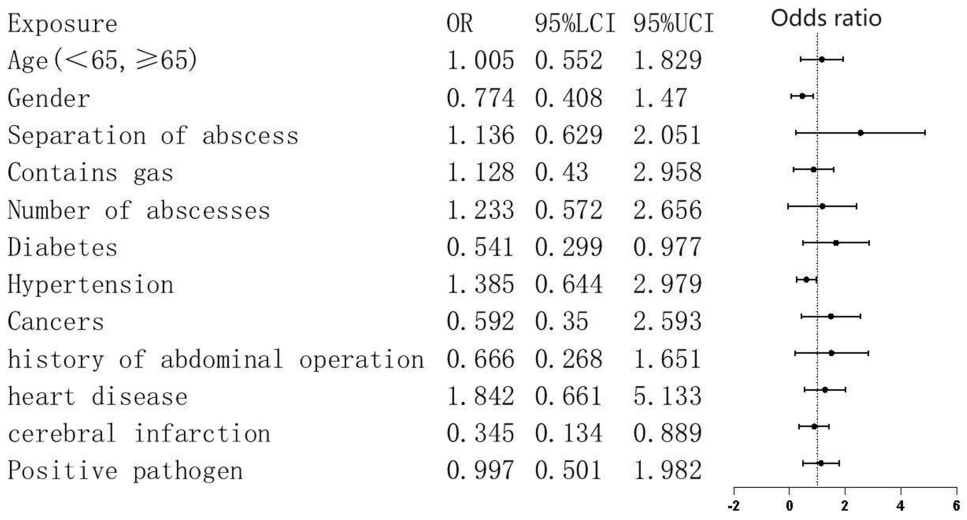

Figure 2 Risk factors for recurrence of PLA.

Discussion

In this study, the mean age at initial liver abscess onset was similar between the two patient groups. Around the age of 60 years, the liver abscesses were mainly located in the right lobe and were mostly singular, with male patients outnumbering females approximately two to one. Fever has emerged as the predominant symptom in patients diagnosed with bacterial liver abscesses, consistent with recent research.[7–10] A study conducted in the United States reported a recurrence rate of approximately 7% in patients with purulent liver abscesses.[11] In this investigation, the recurrence rate of patients with suppurative liver abscesses within one year was 13.3%, which is similar to the 13.7% reported by Czerwonko Matias et al,[12] and is lower than the 18.18% reported by Wang et al.[13] Some studies have reported that elderly patients with bacterial liver abscesses are at higher risk of recurrence.[14] However, this study did not identify age difference as a contributing factor to liver abscess recurrence, which could be attributable to regional variations or insufficient patient sample size.

The high incidence of suppurative liver abscesses includes conditions such as diabetes mellitus, obesity, liver transplantation, gallstones, coronary heart disease, cerebral infarction, history of proton pump inhibitor therapy, abdominal surgery, and malignant tumors.[15–18] Diabetes was the most prevalent comorbidity among patients diagnosed with bacterial liver abscesses in both groups. The proportion of patients with diabetes was 37% in the control group, which is consistent with previous studies.[1,19] In the observation group, 51.7% of patients had diabetes, a percentage significantly higher than that in the control group and other related studies. Multivariate analysis identified diabetes as an independent risk factor for liver abscess recurrence. Diabetic patients experiencing prolonged periods of hyperglycemia are prone to immune dysfunction, neuropathy, and impaired blood circulation, thereby facilitating bacterial growth and increasing susceptibility to infection.[20] Moreover, patients with diabetes are prone to vascular intima damage, which increases the risk of bacterial migration and the incidence of liver abscesses. Poor glycemic control hinders neutrophil activation and phagocytosis and promotes pathogen proliferation in tissues. Hence, strict control of blood glucose levels is imperative for treating patients with bacterial liver abscesses[21,22] to mitigate the risk of recurrence. Additionally, previous research has indicated that diabetes is also correlated with increased mortality among patients diagnosed with liver abscesses.[23]

Moreover, this study identified a history of cerebral infarction as an independent risk factor for bacterial liver abscess recurrence, which was not previously reported. Intestinal dysbiosis may occur in patients with cerebral infarction, as several studies have shown that such patients experience disruptions in their intestinal flora, which typically aids in reducing the occurrence of *K. pneumoniae*-induced liver abscesses.[24,25]

In this study, *K. pneumoniae* was the predominant pathogen in both groups of patients with liver abscesses, accounting for 70.0% and 72.4%, respectively, consistent with the results of previous studies.[7,8,26] It is also the most frequently identified pathogen in Asian patients with liver abscesses.[27] In this research, the prevalence of pathogens in the observation

group, specifically *Escherichia coli*, significantly exceeded that in the control group. Moreover, there was a higher incidence of multidrug-resistant bacteria, particularly against sensitive antibiotics, compared with the control group. However, cefoperazone sodium sulbactam sodium or piperacillin tazobactam sodium demonstrated relatively high sensitivity, although slightly lower than that of meropenem and imipenem. Therefore, early antibiotic administration is recommended for patients with liver abscesses. Cefoperazone sodium sulbactam sodium or piperacillin tazobactam sodium is recommended, in line with previous studies.[1] Pyogenic liver abscess is a severe infectious disease of the liver. When it is not known which antibiotic the bacteria are sensitive to, treatment should involve broad-spectrum antibiotics that are effective against both gram-negative and gram-positive bacteria, thereby avoiding the use of lower-grade antibiotics. Initial therapy should prioritize high-level antibiotics to prevent infection-induced sepsis and delay disease treatment.[28]

The observation group exhibited approximately a 100% higher incidence of septic shock, ICU admission rate, and invasion syndrome compared with the control group, although these differences did not achieve statistical significance, possibly Due to the insufficient sample size of this study, This difference may indicate a greater risk of recurrent infection in patients with liver abscesses who experience septic shock, require ICU care, or present with invasion syndrome. Hence, these outcomes should be considered in cases of potential relapse.

In terms of treatment, about 60% of the study patients underwent catheterization and drainage for liver abscesses, with the procedure's success rate exceeding 96%.[14] According to Losie Jennifer A, the use of puncture drainage treatment in patients with suppurative liver abscesses reduced the 30-day mortality.[29] Owing to its characteristic small trauma and simple operation, catheterization has become the most commonly used interventional treatment method.[30] In contrast, surgical drainage, which involves general anesthesia, trauma, and high cost, is less favored in clinical practice. Only one patient in the study underwent additional treatment for abdominal infection resulting from liver abscess rupture. Nevertheless, this approach was effective in the treatment of cases in which initial puncture and drainage were ineffective, with severe abdominal infection.

This was a retrospective study, and systematic documentation of patient medication post-discharge was not feasible. Medications used for managing certain chronic diseases can impact PLA recurrence; for instance, aspirin might lower the recurrence rate of bacterial liver abscesses.[31] Moreover, all patients in this study were from a province in northern China, suggesting that geographical factors may influence the epidemiology of bacterial liver abscesses.

Conclusion

In comparison with patients with suppurative liver abscess without recurrence, those experiencing recurrence exhibit a higher prevalence of pathogens. Furthermore, a medical history of diabetes mellitus and cerebral infarction are high-risk factors for liver abscess recurrence.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

Written informed consent for data use was obtained from all patients.This study was approved by the Ethics Committee of the Affiliated Hospital of Chengde Medical College.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

No potential conflict of interest was reported by the author(s).

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