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ARTICLE

Clinical Characteristics and Risk Factors of Sepsis in Patients with Liver Abscess

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Abstract

Aims/Background Liver abscess (LA) is a serious medical condition that predisposes patients to sepsis. However, predicting sepsis in LA patients has rarely been explored. This study employed univariate and multivariate logistic regression analyses to identify independent risk factors for sepsis, which would provide guidance for clinical diagnosis and treatment.

Methods A total of 122 patients with LA treated in Peking University People's Hospital from 1 January 2016 to 31 October 2022 were recruited. Among the cases, 35 patients had sepsis (sepsis group) while the remaining 87 did not have sepsis (non-sepsis group). Clinical data were collected for all enrolled cases. Univariate analysis was performed to identify potential predictors, which were tested in multivariable logistic analysis to pinpoint the independent risk factors for sepsis in LA patients; these findings were utilized to develop a prediction model. Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficacy of the prediction model. Informed consent to participate was obtained from the patients or their relatives.

Results The incidence of shivering in the sepsis group was significantly higher than that in the non-sepsis group ($p < 0.05$). Through the univariate analysis, it was found that the reduction in platelet count and prothrombin time activity and the elevation of glycosylated hemoglobin (HbAlc) and procalcitonin (PCT) were more significant in the sepsis group than in the non-sepsis group ($p < 0.05$). Multivariate logistic regression analysis revealed that PCT and HbAlc were independent risk predictors of sepsis in LA patients within the derivation cohort ($p < 0.05$).

Conclusion Elevated levels of HbAlc and PCT were independent risk factors for sepsis associated with LA. Patients with LA exhibiting elevated PCT levels demonstrated a 21% increased susceptibility to sepsis, and those with elevated HbAlc levels showed a 38% heightened risk for sepsis.

Key words: liver abscess; clinical characteristics; sepsis; risk factors; prediction model

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Introduction

Liver abscess (LA) is a suppurative infection of liver parenchyma caused by various pathogens invading the liver and biliary system through bloodstream, or other cryptogenic factors (Almalki et al, 2019). Among them, bacterial LA is the most common, accounting for about 80% of the total incidence of LA, and is associated with a mortality rate of approximately 2%–12% (Bruns and Stallmach, 2022; Cecconi et al, 2018). According to relevant statistics, the incidence of bacterial LA at home and abroad is 2.3 to 17.6 per 100,000 people, but its incidence and mortality rates are increasing year by year (Chen et al, 2016).

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Despite advancements in our understanding of the underlying pathogens, diagnostic techniques, and therapeutic approaches, several severe LA-associated complications remain fatal, contributing to mortality rates ranging from 7.8% to 28.6% (Ejikeme et al, 2021). Sepsis, a grave complication of LA, can lead to multi-organ dysfunction, septic shock, and death (Feng et al, 2023; Gu et al, 2019). The prognosis for patients with LA who develop sepsis is generally unfavorable (Guo et al, 2017; Hotchkiss et al, 2016; Kim et al, 2019). Due to the inherent heterogeneity of this pathological condition, an accurate prediction of the prognosis for sepsis proves challenging (Ejikeme et al, 2021; Kokayi, 2021). Therefore, the identification of effective strategies for sepsis prevention and risk management becomes extremely crucial.

In this study, we retrospectively analyzed the clinical characteristics of 122 cases of LA, to establish a prediction model for doctors. The findings of this study and the resulting tool will serve as a valuable resource for clinicians, aiding in the prevention and management of sepsis in LA patients.

Methods

Patients

In this study, patients with LA treated in Peking University People's Hospital from 1 January 2016 to 31 October 2022 were recruited. The general data, clinical manifestations, history of underlying diseases, laboratory results (initial and worst values of blood routine test, biochemical test, coagulation test, C-reactive protein, procalcitonin [PCT] and glycosylated hemoglobin [HbAlc]), imaging findings, etiology and drug sensitivity test results, treatment and prognosis of the included cases were collected and analyzed.

The inclusion criteria (Almalki et al, 2019) of the present study are as follows: (1) fever, abdominal pain, shivering, nausea and vomiting, fatigue, anorexia, jaundice and other clinical manifestations; (2) LA diagnosis based on findings of abdominal B-ultrasound or computed tomography (CT), magnetic resonance imaging (MRI) and other imaging examinations; (3) positive results of microbial culture (blood culture, pus culture, tissue culture), or effective antibiotics treatment; and (4) confirmation of the lesion as LA after percutaneous liver puncture or surgical treatment. The exclusion criteria applied in the study include: (1) liver lesions caused by non-pathogenic microbial factors and other reasons; and (2) lack of clinical data.

A total of 122 cases were enrolled in this study and divided into sepsis group (n = 35) and non-sepsis group (n = 87), according to the Third International Consensus Definitions for sepsis and septic shock (Sepsis-3) updated in 2016 (Singer et al, 2016). The study was approved by the Medical Ethics Committee of the Peking University People's Hospital (Approval No. 2024PHB066-001). The ethics committee exempted patients from informed consent. This study was conducted in adherence with the guidelines outlined in the Declaration of Helsinki.

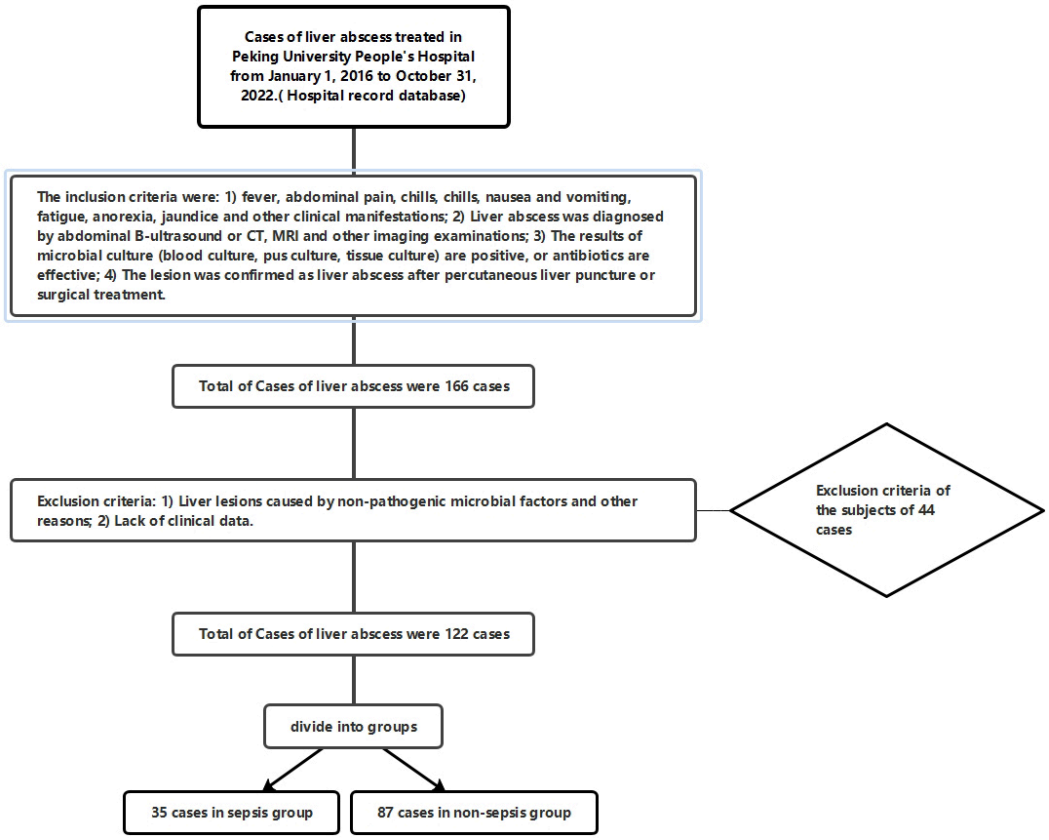

Fig. 1. Flowchart depicting the process of enrolling study participants.

Statistical Analysis

Data analysis was performed using the SPSS 19.0 statistical software (IBM SPSS Statistics, Chicago, IL, USA). Forest plot of logistics regression analysis was drawn using GraphPad Prism 9 (GraphPad Software Inc., San Diego, CA, USA). Normally distributed quantitative data are expressed as mean ± standard deviation, and comparison between the two groups was performed by *t*-test. Quantitative data with non-normal distribution are presented as median (P25, P75), and comparison between the two groups was performed by Mann–Whitney *U* test. χ^2 test or Fisher exact test was used to compare categorical data of the two groups. Univariate analysis was performed to identify potential predictors with a significance level of $p < 0.05$, which were then re-analyzed in multivariate logistic regression. Predictors identified with a statistical significance of $p < 0.05$ in the multivariable analysis were used to develop a prediction model. Receiver operating characteristics (ROC) curve was used to evaluate the diagnostic efficacy of the prediction model. $p < 0.05$ was considered statistically significant.

Results

A total of 122 LA cases were included in this study (Fig. 1), of which 61.5% were males and 38.5% were females, collectively with an average age of 59.7 ± 14.2 years. Most patients have underlying diseases, with the most common being diabetes, followed by biliary diseases. Three patients died during the study, bring-

Table 1. Baseline characteristics of the included study participants.

Variables	Number (%)
Gender	122 (100%)
Male	75 (61.5%)
Female	47 (38.5%)
Age (years)	59.7 ± 14.2
Past medical history	105 (86.1%)
Diabetic foot infection	51 (41.8%)
Diseases of the biliary system	34 (27.9%)
Viral hepatitis	5 (4.1%)
Liver cirrhosis	4 (3.3%)
Fatty liver disease	6 (4.9%)
Malignant tumor	20 (16.4%)
Previous history of hepatobiliary surgery	10 (8.2%)
Clinical symptoms	
Fever	119 (97.5%)
Abdominal pain	44 (36.1%)
Nausea and vomiting	20 (16.4%)
Shivering	60 (49.2%)
Jaundice	12 (9.8%)
Anorexia	18 (14.8%)
Weak	47 (38.5%)
Multiple parts of the abscess	12 (9.8%)
Pulmonary abscess	9 (7.4%)
Brain abscess	4 (3.3%)
Intraocular abscess	3 (2.5%)
Sepsis	35 (28.7%)
Septic shock	15 (12.3%)

ing the in-study mortality rate to 2.5%. Fever is the most common symptom among the patient, with patients' body temperature mainly ranging from moderate to high. Some patients experienced symptoms such as abdominal pain, shivering, nausea, and vomiting. In terms of related complications, 35 patients (28.7%) developed sepsis, including 15 patients (12.3%) with septic shock and 12 patients (9.8%) with multiple abscesses, including 9 patients (7.4%) with lung abscess, 4 patients (3.3%) with brain abscess, and 3 patients (2.5%) with intraocular abscess (Table 1).

The majority of patients showed elevated levels of white blood cells (WBC; 83.6%) and neutrophil granulocytes (NE; 91.8%), and some patients experienced a reduction of hemoglobin (HGB; 77.5%) and platelet (PLT; 36.7%). Biochemical analysis revealed prevalent observations such as decreased albumin (ALB; 85%), as well as increased alanine transaminase (ALT; 72.7%), aspartate transaminase (AST; 61.7%), gamma-glutamyl transferase (γ-GT; 89.8%), and alkaline phosphatase (ALP; 68.3%) levels. Additionally, elevated lactate dehydrogenase (LDH) levels were observed in some patients (48.3%), along with reduced prothrombin time activity (PTA; 65.2%). In terms of inflammatory indicators, an increase in C-

Table 2. Results of laboratory examinations.

Parameter	Count (%)	Median (p25, p75)
WBC (>9.5 × 10^9/L)	102 (83.6%)	13.22 (10.49, 18.45)
NE (>6.3 × 10^9/L)	112 (91.8%)	11.01 (8.73, 15.85)
HGB (<120 g/L × 10^9/L)	95 (77.5%)	104 (87.50, 119.50)
PLT (<125 × 10^9/L)	44 (36.7%)	152.50 (88, 216)
MPV (>13.5 fL)	11 (9.1%)	11.10 (9.93, 11.90)
ALB (<35 g/L)	104 (85%)	28.20 (25.13, 32.20)
ALT (>40 U/L)	89 (72.7%)	68.50 (40.25, 114.0)
AST (>40 U/L)	75 (61.7%)	56.00 (32.00, 121.0)
TBIL (>21.0 μmol/L)	54 (44.2%)	18.80 (12.60, 37.85)
γ-GT (>60 U/L)	110 (89.8%)	130 (86.75, 234.25)
ALP (>125 U/L)	83 (68.3%)	161.50 (116.25, 250.75)
LDH (>245 U/L)	59 (48.3%)	249.50 (185.25, 365.75)
PTA (<70%)	73 (65.2%)	65 (56.00, 74.75)
D-dimer (ng/mL)	101 (82.8%)	2800 (2010, 8522)
CR (μmol/L)	112 (91.8%)	73.00 (57.50, 120.50)
BUN (mmol/L)	112 (91.8%)	9.72 (4.68, 14.78)
CRP (>10 mg/L)	104 (85.2%)	152.25 (107.05, 200.00)
PCT (>0.5 ng/mL)	93 (76.5%)	2.61 (0.53, 19.27)
HbA1c (>6.0)	51 (41.8%)	7.25 (6.30, 9.90)

WBC, white blood cell; NE, neutrophile granulocyte; HGB, hemoglobin; MPV, mean platelet volume; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; γ-GT, gamma-glutamyl transferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; PTA, prothrombin time activity; CR, creatinine; BUN, blood urea nitrogen; CRP, C-reactive protein; PCT, procalcitonin; HbAlc, glycosylated hemoglobin.

reactive protein (CRP; >10 mg/L) was detected in 104 patients, which accounted for 85.2% of the cases, while a raised level of PCT (>0.5 ng/mL) was observed in 93 patients, which accounted for 76.5% of the cases. The details are shown in Table 2.

The imaging examination revealed that the median maximum diameter of LA was 6.45 cm. A range of 5 to 10 cm for the mean maximum diameter of LA is considered the most common. LA mainly occurs at the right lobe of the liver, and single LA is comparatively more common. In etiology examination, 77 cases (63.1%) were pathogen-positive, with *Klebsiella pneumoniae* being the most common, followed by *Escherichia coli*. The details are shown in Table 3.

All 122 cases were divided into the sepsis group and the non-sepsis group according to the Third International Consensus Definitions for sepsis and septic shock (Sepsis-3) updated in 2016 (Singer et al, 2016) and the data of the two groups were statistically analyzed. Regarding clinical symptoms, the incidence of shivering in the sepsis group was significantly higher than that in the non-sepsis group ($p < 0.05$). In terms of laboratory examination, the platelet count and prothrombin time

Table 3. Results of imaging and etiology examination.

Parameter	Number (%)/Median (p25, p75)
Maximum diameter of LA (cm)	6.45 (3.28, 8.65)
<5 cm	46 (37.2%)
5–10 cm	66 (54.5%)
>10 cm	10 (8.3%)
Location of the LA	
Right lobe of liver	86 (70.5%)
Left lobe of liver	29 (23.8%)
Bilateral lobe of liver	7 (5.7%)
Number of LA	
Single	69 (56.6%)
Multiple	53 (43.4%)
Pathogen-positive	77 (63.1%)
Klebsiella pneumoniae	55 (45.1%)
Escherichia coli	5 (4.1%)
Bacteroides fragilis	2 (1.6%)
Streptococcus constellates	2 (1.6%)
Enterobacter cloacae	2 (1.6%)
Enterococcus faecium	2 (1.6%)
Pseudomonas aeruginosa	2 (1.6%)
Acinetobacter baumannii	1 (0.8%)
Enterobacter sakazakii	1 (0.8%)
Staphylococcus epidermidis	1 (0.8%)
Enterococcus faecalis	1 (0.8%)
Candida albicans	2 (1.6%)
Hansay bartonella	1 (0.8%)

activity reduction as well as the elevation of HbAlc and PCT were more significant in the sepsis group than in the non-sepsis group ($p < 0.05$). All the factors found to display significant differences in Table 4 were included in the multiple logistic regression analysis, which revealed that PCT ($p = 0.017$, OR [95% CI] = 1.21 [1.12–1.26]) and HbAlc ($p = 0.011$, OR [95% CI] = 1.38 [1.20–1.57]) were independent risk predictors of sepsis in LA patients within the derivation cohort. Based on the data analysis, patients with LA exhibiting elevated PCT levels demonstrated a 21% increased susceptibility to sepsis, while those with elevated HbAlc levels showed a 38% heightened risk for sepsis. The details are shown in Tables 4,5, as well as Fig. 2.

Indicators related to early diagnosis of sepsis were statistically analyzed, and their sensitivity and specificity were analyzed with the help of ROC curves (Table 6). Indicators like PCT and HbAlc can predict the development of LA into sepsis, enabling the early diagnosis of sepsis caused by LA ($p < 0.05$). Based on the ROC curve analysis, the areas under the curve (AUC) were 0.781 (95% CI: 0.626–0.937) and 0.774 (95% CI: 0.627–0.921). The cut-off value for PCT was 1.7 ng/mL, with sensitivity and specificity 87.5% and 56.4%, respectively, whereas the

Table 4. Comparison between sepsis group and non-sepsis group.

Variables	Sepsis group (35 cases)	Non-sepsis group (87 cases)	Statistical values	*p*-value
Age (years)	61.23 ± 14.95	59.36 ± 13.80	$t = 0.686$	0.493
Length of hospital stay (days)	15.57 ± 7.89	16.43 ± 13.36	$t = -0.336$	0.738
Gender			$\chi^2 = 0.045$	0.832
Male	21	54		
Female	14	33		
Past medical history				
Diabetes	15	36	$\chi^2 = 0.022$	0.881
Biliary tract diseases	14	21	$\chi^2 = 3.070$	0.080
Malignant tumor	6	14	$\chi^2 = 0.020$	0.887
Clinical symptom				
Fever	35	85		1.000*
Abdominal pain	13	35	$\chi^2 = 0.100$	0.752
Shivering	25	35	$\chi^2 = 9.720$	0.002▲
Nausea and vomiting	8	12	$\chi^2 = 1.496$	0.221
Weak	12	35	$\chi^2 = 372$	0.542
Laboratory examination				
WBC (10^9/L)	12.91 (10.50, 13.75)	13.54 (10.40, 18.52)	Z = –0.292	0.100
NE (10^9/L)	10.70 (8.20, 15.17)	11.43 (8.72, 16.06)	Z = –0.173	0.110
HGB (g/L)	104.00 (69.75, 117.25)	104.0 (92.00, 118.00)	Z = –1.075	0.065
PLT (10^9/L)	117.50 (26.75, 201.00)	170.50 (98.25, 230.50)	Z = –2.175	0.013▲
MPV (fL)	11.55 (9.47, 12.18)	10.7 (9.90, 11.50)	Z = 1.144	
ALB (g/L)	28.10 (25.08, 32.28)	28.75 (25.20, 32.30)	Z = –0.230	0.073
ALB (<35 g/L)	32	77		0.755*
ALT (U/L)	68.00 (41.75, 114.00)	62.00 (39.00, 119.00)	Z = –0.412	0.123
AST (U/L)	63.00 (29.75, 152.75)	52.00 (32.00, 97.00)	Z = –0.877	0.210
TBIL (μmol/L)	28.15 (14.10, 55.85)	16.55 (11.90, 31.33)	Z = –2.327	0.054
γ-GT (U/L)	155.00 (105.5, 258.0)	127.00 (87.5, 236.0)	Z = –1.022	0.650

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Table 4. Continued.

Variables	Sepsis group (35 cases)	Non-sepsis group (87 cases)	Statistical values	*p*-value
ALP (U/L)	161.50 (119.50, 294.75)	158.00 (112.75, 237.25)	Z = –0.853	0.320
LDH	280.00 (201.50, 417.75)	235.00 (178.50, 318.25)	Z = –1.616	0.125
PTA (%)	60.00 (47.75, 68.00)	67.00 (58.00, 76.00)	Z = –2.554	0.043▲
D-dimer (ng/mL)	2800 (2010, 8522)	1156 (560, 3399)	Z = –2.871	0.113
CR (μmol/L)	73.00 (57.50, 120.50)	74.00 (55.00, 92.00)	Z = –0.864	0.213
BUN (mmol/L)	9.72 (4.68, 14.78)	5.71 (4.45, 9.27)	Z = –2.284	0.145
CRP (mg/L)	183.18 (125.73, 229.43)	142.47 (96.66, 190.00)	Z = –2.240	0.062
PCT (ng/mL)	4.33 (1.51, 26.49)	2.29 (0.50, 14.00)	Z = –1.613	0.023▲
HbAlc (%)	8.95 ± 2.72 (21/35)*	7.19 ± 1.71 (30/77)*	Z = –2.501	0.015▲
Culture positive for pathogenic bacteria	19	58	χ^2 = 1.643	0.200
Klebsiella pneumoniae	15	40	χ^2 = 0.796	0.754
Escherichia coli	2	3		0.624*
Liver abscess drainage	13	25	χ^2 = 0.823	0.364
Location of LA				0.781*
Right lobe of liver	25	61		
Left lobe of liver	9	20		
Bilateral lobe of liver	1	6		
Number of LA			χ^2 = 0.525	0.469
Single	18	51		
Multiple	17	36		

* *p*-value from the Fisher's exact test.

▲ Statistically significant difference.

WBC, white blood cell; NE, neutrophile granulocyte; HGB, hemoglobin; MPV, mean platelet volume; ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; γ-GT, gamma-glutamyl transferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; PTA, prothrombin time activity; CR, creatinine; BUN, blood urea nitrogen; CRP, C-reactive protein; PCT, procalcitonin; HbAlc, glycosylated hemoglobin.

Table 5. Multivariate logistic regression analysis for identifying predictors of sepsis caused by liver abscess.

Observation index	B	SE	Wald χ^2	*p*-value	OR	95% CI
PCT (ng/mL)	0.657	0.136	4.109	0.017	1.211	1.121–1.261
HbAlc (%)	0.318	0.206	3.218	0.011	1.380	1.201–1.572
PLT (10^9/L)	0.007	0.004	3.310	0.781	1.012	0.981–1.061
PTA (%)	0.033	0.030	1.197	0.562	1.061	0.912–1.121
Shivering	0.081	0.393	0.093	0.621	0.456	0.118–1.701

PLT, platelet; PTA, prothrombin time activity; PCT, procalcitonin; HbAlc, glycosylated hemoglobin.

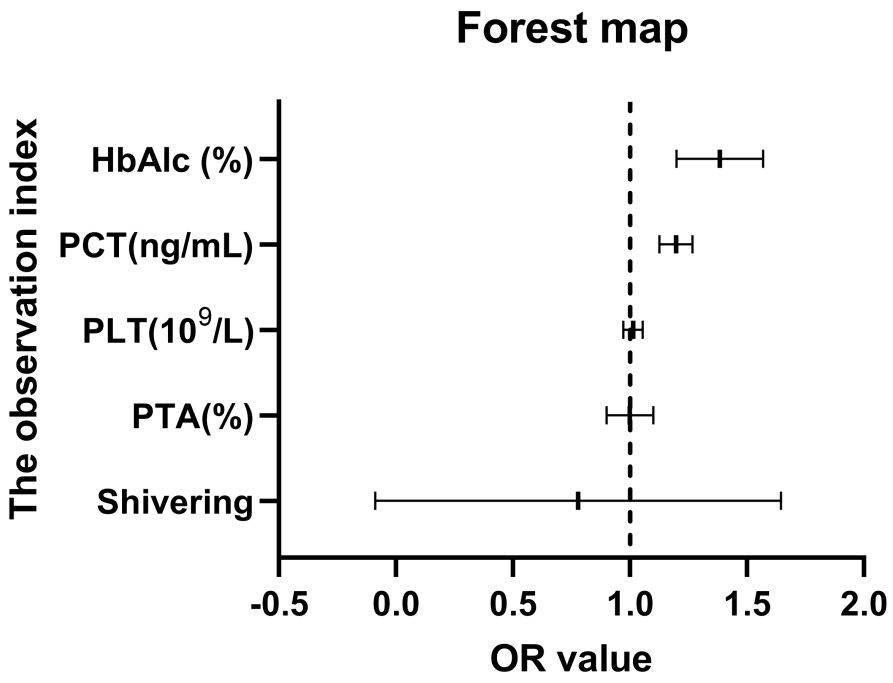

Fig. 2. Forest plot of logistics regression analysis. PLT, platelet; PTA, prothrombin time activity; PCT, procalcitonin; HbAlc, glycosylated hemoglobin.

cut-off value for HbAlc was 7.95%, with a 68.8% sensitivity and a 79.5% specificity (Table 6 and Fig. 3).

Discussion

Several studies revealed that the incidence of LA has been increasing year by year (Chen et al, 2016; Kumar et al, 2020). Epidemiological studies have shown that the proportion of LA in male (63.6%–64.0%) was higher than that in female (36.0%–36.4%), and about 76.8% of cases were aged ≥50 years (Kuo et al, 2013; Lee et al, 2020). In this study, male cases accounted for 61.5% and female cases 38.5%, whereas middle-aged and elderly people were the most common age group, with cases aged >40 years accounting for 90.4% of the total cases. Hepatic abscess has an occult onset and presents tremendous challenges for early diagnosis owing

Table 6. ROC curve analysis of sepsis predictors.

Observation index	AUC	Youden's index	*p*-value	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
PCT (ng/mL)	0.781	0.477	0.001	0.626–0.937	1.70	87.5	56.4
HbAlc (%)	0.774	0.507	0.002	0.627–0.921	7.95	68.8	79.5

AUC, areas under the curve; CI, confidence interval.

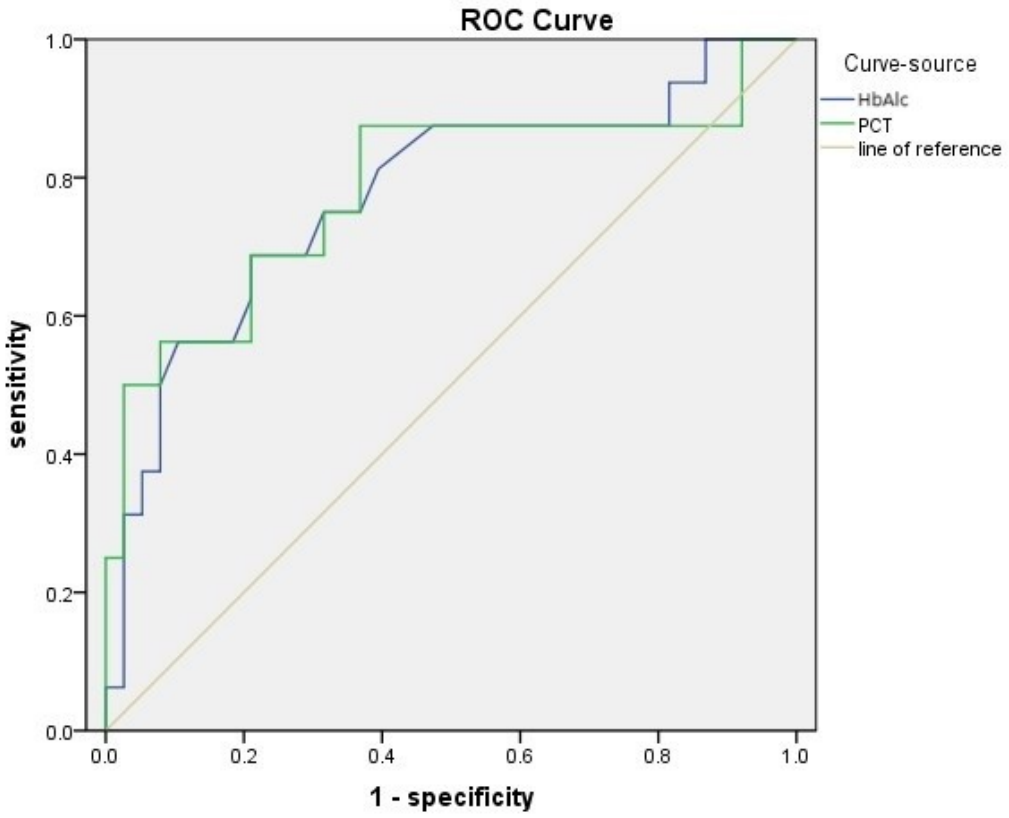

Fig. 3. ROC curves of HbAlc and procalcitonin.

to the lack of specificity in clinical manifestations (Li et al, 2021). Based on the present study, we found that fever, shivering, abdominal pain and fatigue are among the clinical manifestations of LA, with fever being one of the most common clinical symptoms. According to relevant studies, diabetes is an independent risk factor for LA (Li et al, 2018), and the risk of LA in diabetic patients is 3.6–11 times that of healthy people (Lee et al, 2020; Liu et al, 2021). The proportion of diabetes cases in this study was 41.8%, which falls within the range of 30% to 58% delineated in other studies (Miao et al, 2018; Mukthinuthalapati et al, 2020). In addition, biliary tract diseases accounted for 27.9% of LA cases in this study, which was the second most dominant cause of LA.

The most prominent result of the laboratory examination of LA cases in this study was the dramatically increased WBC count, which was predominantly contributed by the elevated neutrophil count. Decreased HGB levels and thrombocytopenia were displayed by severe cases in this study. Some cases presented liver

injury to varying degrees, but most of the liver injury cases were of mild to moderate severity, and liver failure was a rare occurrence. The levels of CRP and PCT in hepatic abscess were significantly higher.

Through imaging examination, we found that most LA cases (70.5%) occurred at the right lobe of the liver, a finding that is consistent with other literatures and substantiates that LA occurrence is mainly related to the anatomical structure of liver. The right lobe of liver is larger than the left lobe and supplied with a larger blood flow compared with its left counterpart. At the same time, the angle between the trunk of hepatic portal vein and the right anterior branch approximates to 180°. Therefore, the right anterior branch possesses the weakest resistance to the invading pathogenic microorganisms that enter the liver through portal vein, making the right lobe more vulnerable to liver abscess (Rodriguez-Villar et al, 2019; Shelat et al, 2016).

Single liver abscesses were predominant in this study, with the largest diameter of liver abscesses most commonly measuring at 5–10 cm. In this study, the most common etiology was biliary liver abscess (27.9%), followed by hematogenous liver abscess (26.2%), and the rest were cryptogenic liver abscess (45.9%). The data of this study were generally consistent with other literatures (Singer et al, 2016). Cryptogenic liver abscess refers to liver abscess caused by blood-borne infection that does not pass through biliary system but occurs independently in the absence of obvious infection source. This abscess variant occurs mostly in the young individuals with poorly controlled diabetes; of note, the range of clinical manifestations of this kind of abscess lack specificity. *Klebsiella pneumoniae* remains the most frequent pathogenic bacterium causing LA, although it is slightly more difficult to detect than other pathogenic causes (Wang et al, 2023). In this study, the positive rate of pathogenic bacteria culture was 63.1%, of which the positive rate of blood culture was 34.4%, and the positive rate of pus culture was 43.4%. Other study revealed low positive rate for pathogenic bacteria compared to other studies (Tseng, 2020; Wang et al, 2021), which is probably related to premature and excessive application of antibiotics (Yang et al, 2021). A relevant study showed that metagenomic next-generation sequencing (mNGS) could effectively improve the detection rate of pathogenic bacteria in the abscess tissue or drainage fluid samples with definite infection (Yoo et al, 2021). Relevant literatures show that the incidence of LA caused by *Klebsiella pneumoniae* infection is increasing on an annual basis worldwide, with the Asian areas becoming the major regions where *Klebsiella pneumoniae* emerges as the main pathogen causing LA (Zhang et al, 2019). Fifty-five cases of *Klebsiella pneumoniae* were detected in this study, accounting for 71.4% of all pathogens—an evidence that *Klebsiella pneumoniae* is the main pathogen of LA in our hospital. Presenting in five cases (4.1%), *Escherichia coli* stood as one of the most common pathogens causing LA.

Through comparative analysis, we found that the duration of hospital stay in the sepsis group was significantly longer than that in the non-sepsis group. The sepsis group was also more susceptible to shivering. In the context of laboratory examination, the degree of platelet decline was greater in the sepsis group than in the non-sepsis group. Separately, prothrombin activity decreased significantly in

the sepsis group. In this study, past medical history of diabetes was found to have no statistically significant impact on the risk of sepsis developing in patients with LA, but the level of HbAlc and PCT had a direct effect on the risk of sepsis in the LA cases. It has been suggested that diabetes is not an independent risk factor, but a significantly raised HbAlc in diabetic patients with poorly controlled blood glucose levels represents an independent risk factor for sepsis (Zhou et al, 2021).

The ROC curve analysis of the predictive factors for sepsis caused by LA unveiled that both PCT and HbAlc can predict the development of LA into sepsis ($p < 0.05$). Therefore, it is highly recommended to integrate the detection of PCT and HbAlc levels while carrying out the diagnosis of LA to evaluate the probability of sepsis progression.

Conclusion

In summary, LA is an infectious disease with atypical symptoms, such as fever, abdominal pain, nausea, vomiting, shivering and frailty, that are difficult to detect during the early stage. Among the causative agents of LA, Gram-negative bacteria are more common than Gram-positive bacteria, in terms of LA causation, with *Klebsiella pneumoniae* being the most prevalent pathogen. Univariate and multivariate logistic regression analyses were performed to develop a prediction model, which revealed that elevated levels of HbAlc and PCT were independent risk factors for sepsis associated with LA. Meanwhile, patients with LA exhibiting elevated PCT levels demonstrate a 21% increased susceptibility to sepsis, and those with elevated HbAlc levels show a 38% heightened risk of developing sepsis. For patients with LA demonstrating the PCT and HbAl levels exceeding 1.7 ng/mL and 7.95%, which are the cut-off values of these parameters, respectively, clinicians should be particularly vigilant of the potential development of sepsis and promptly initiate intervention and treatment.

Key Points

- LA is an infectious disease with atypical symptoms, that are difficult to detect during the early stage.
- Among the causative agents of LA, with *Klebsiella pneumoniae* being the most prevalent pathogen.
- Univariate and multivariate logistic regression analyses were performed to develop a prediction model, which revealed that elevated levels of HbAlc and PCT were independent risk factors for sepsis associated with LA.
- Patients with LA exhibiting elevated PCT levels demonstrate a 21% increased susceptibility to sepsis, and those with elevated HbAlc levels show a 38% heightened risk of developing sepsis.
- For patients with LA demonstrating the PCT and HbAlc levels exceeding 1.7 ng/mL and 7.95%, which are the cut-off values of these parameters.

Availability of Data and Materials

The data acquired/analyzed are available on the request of corresponding authors.

Author Contributions

KW, WG and WBG designed the study. KW, WG, JHZ and WBG collected the data. KW and YG performed the experiments. KW and WG analyzed the data. KW, WG, JHZ and WBG drafted the manuscript. All authors contributed to editorial changes of important content in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee of the Peking University People's Hospital (Approval No. 2024PHB066-001). The ethics committee exempted patients from informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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