### ORIGINAL ARTICLE



# Clinical characteristics and management of 1572 patients with pyogenic liver abscess: A 12-year retrospective study

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#### Abstract

**Background & aims:** Pyogenic liver abscesses (PLA) are space-occupying lesions in the liver that produce high morbidity and mortality. The clinical characteristics and prognosis of abscesses is different depending on the bacterial culture results and require different strategies for management. The aim of this study was to investigate the clinical characteristics and prognostic factors of patients with PLA.

**Methods:** Clinical features, laboratory tests and etiology of PLA between 2006 to 2011 and 2012 to 2017 in a single hospital were retrospectively reviewed. The incidence and mortality of PLA caused by *Escherichia coli* and *Klebsiella pneumoniae* were compared and the risk factors for multiple organ dysfunction (MODS) and endoph-thalmitis were evaluated.

**Results:** Among the 1,572 PLA patients, the proportion with PLA increased from 333 (21.2%) in 2006-2011 to 1,239 (78.8%) in 2012-2017 without any investigation and treatment procedure differences. *K pneumoniae* was the main isolate in analysed pus cultures (85.6%). The mortality rate of patients with *K pneumoniae* infection was lower in the latter period (6.7% vs 0.7%, P = .035). Multivariate analyses revealed that age, fever, MODS and length of hospital stay were factors affecting poor prognosis (death + unhealed/uncured) in PLA patients after treatment and that cardiovascular disease, pleural effusion and pulmonary infection were risk factors for MODS, while diabetes mellitus was the only risk factor for endophthalmitis. Most patients (95.5%) with PLA recovered after abscess drainage/puncture and antibiotic therapy.

**Conclusions:** Pleural effusion, fever, MODS and length of hospital stays were factors useful in predicting PLA outcomes.

#### KEYWORDS

endophthalmitis, *K pneumoniae*, multiple organ dysfunction syndrome (MODS), pyogenic liver abscess, retrospective study

Abbreviations: CIs, confidence intervals; MODS, multiple organ dysfunction; PLA, pyogenic liver abscess; US, ultrasound.

Dalong Yin , Changyong Ji and Shugeng Zhang contributed equally to this manuscript.

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# 1 | INTRODUCTION

Pyogenic liver abscess (PLA) is an intrahepatic infection caused by purulent bacteria that invade the liver and are responsible for about 80% of all liver abscesses. The incidence is higher in Asian countries, with approximately 12 ~ 18 patients per 100,000 population per year<sup>1</sup> and an estimated mortality rate of 2 ~ 31%.<sup>2,3</sup> Over the last 30 years, *Klebsiella pneumoniae* has replaced *Escherichia coli* as the most common microorganism isolated from PLA infections.<sup>4</sup> In mainland China, > 80% of PLAs are caused by *K pneumoniae*.<sup>5</sup> As liver abscesses caused by *K pneumoniae* can produce invasive syndromes, including endophthalmitis, central nervous system infection, other extrahepatic infections and multiple organ dysfunction (MODS), increasing clinical attention has been paid to the study of the clinical characteristics, morbidity and mortality of PLA patients infected with *K pneumoniae*.<sup>6</sup>

PLA is characterized by a variety of nonspecific symptoms including upper right abdominal pain, fever, nausea and vomiting. The clinical manifestations of liver abscesses have also changed over the years because of the overuse of antibiotics, with an increased incidence of resistance to bacteria as well as a higher prevalence of patients with chronic or malignant diseases, likely because of ageing populations around the world.<sup>6</sup> Poor control of PLA infection can lead to sepsis, MODS and death,<sup>7</sup> thus posing major medical challenges for early detection of PLA and the selection of appropriate treatment.<sup>8</sup> To identify the risk and prognostic factors for PLA is therefore of great clinical significance. Previous studies have reported on changes in demographic and clinical characteristics of PLA.<sup>6,9</sup> However, predictors of mortality in PLA patients have not been unequivocally identified.

In the present study, the clinical, laboratory and etiology data from patients treated in a tertiary referral centre in northeast China with PLA between 2006 and 2017 were retrospectively collected to determine the changes in the proportion and clinical manifestations of PLA. The incidence and mortality rates of liver abscesses induced by *E coli* and *K pneumoniae* between a former 6-year study period (2006 - 2011) and a latter 6-year period (2012 - 2017) were also compared. The incidence and risk factors for patients with MODS and endophthalmitis were then compared to study prognostic factors on treatment outcomes for PLA patients.

# 2 | PATIENTS AND METHODS

# 2.1 | Design of study and patient population information

A retrospective study on consecutive patients with PLA, managed in our hospital between January 1, 2006 and December 1, 2017, was carried out. The research protocol was approved by our Institutional Ethics Committee (No. IRB-AF/SC-04/01.0). Patients were definitively diagnosed with PLA, excluding amoebic liver abscesses, based on clinical findings, abdominal ultrasound (US) or CT

#### Lay summary

In 1,572 Chinese patients with pyogenic liver abscess (PLA), 95.5% recovered after abscess drainage and antibiotic therapy. Age, fever, multiple organ dysfunction and length of hospital stay were factors affecting poor prognosis (death + unhealed/uncured) in PLA patients after treatment.

imaging/MRI  $\pm$  MRCP, serology and bacterial culture of pus from PLA. Patients were then treated with US or CT-guided percutaneous drainage of liver abscesses. At the same time, intravenous infusions of various combinations of antibiotics (cephalosporins, carbapenems or quinolones) were administered. The treatment courses were given until the body temperature of patients, C-rection protein levels and white blood cell counts had all returned to normal for at least 3 days.

### 2.2 | Clinical data and definitions of outcomes

The following data were extracted from the medical records: 1) demographic characteristics; (2) etiopathological factors; (3) coexisting conditions; (4) numbers and locations of abscesses; (5) laboratory examinations; (6) microbiological findings (7) diagnostic and therapeutic methods; and (8) treatment responses and mortality. For outcome indicators, 'cure' was defined as the absence of symptoms and signs, with laboratory tests and imaging results having returned to normal, and clinical evidence for total elimination of the bacterial infection. Improvement was defined as clinical evidence of improvement in a patient's condition, with elimination of bacterial infection but with only one of the symptoms, signs, laboratory tests and imaging results not having returned to normal. Unhealed/uncured was defined as no significant clinical improvement or worsening of the condition after treatment or, although the condition had improved, there were  $\geq 2$  abnormal items from symptoms and signs, laboratory tests or imaging results. The standards used to define PLA as having arterial, biliary, portal vein or other origins were: Arterial origin: caused by respiratory infection or otitis media; biliary origin: caused by cholecystitis, cholangitis and/or other billiary tract infections; portal vein origin: caused by gastrointestinal infection such as gastroenteritis or appendicitis; other origins: caused by trauma, tumour combined with infection or surrounding organ ulceration.

### 2.3 | Bacteria isolation and culture

All pus samples were processed in a central laboratory to identify the pathogens responsible for the liver abscesses. After direct inoculation on blood agar and China blue-plates for culturing, organism identification was confirmed using the VITEK 2 automated microbial identification system (bioMérieux).

### 2.4 | Statistical analysis

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All data were presented as the mean  $\pm$  SD. Statistical analyses were conducted using the GraphPad Prism (Ver. 6, GraphPad Software, La Jolla, US). A  $\chi 2$  or Fisher's exact test was employed to analyse categorical variables and a *t* test to analyse normally distributed continuous variables. Multivariate stepwise logistic regression analysis was used to identify potential factors in diagnosis. Univariate analysis was adopted to evaluate if the demographic, clinical, imaging, microbiological or laboratory factors correlated with mortality. Significant independent factors were then analysed in a multivariate stepwise logistic regression model to identify independent predictors of MODS. The odds ratios and 95% confidence intervals (CIs) were calculated. A *P*-value < .05 was considered to be a significant finding.

# 3 | RESULTS

### 3.1 | Characteristics of the study population

A total of 1,572 PLA patients (62.6% male) were enrolled with a mean age of  $58.5 \pm 13.5$  years. Arterial origin (70.6%) was the most common cause of a liver abscess, followed by biliary (16.0%) and portal venous causes (3.0%).

The number of abscesses was single in 77.5% of patients and 72.7% of the abscesses were located in the right hemiliver. In terms of comorbidities, 38.1% of the patients had a history of diabetes mellitus, 23.9% hypertension, 14.8% cardiovascular and 6.7% cerebrovascular in addition to 24.3% hepatobiliary and pancreatic as well as 2.0% kidney diseases and 0.5% of the patients had tumours, while 5.2% had hepatobiliary calculi. Fever occurred in 88.9%, abdominal pain in 51.3%, pulmonary infection in 20.6% and pleural effusion in 19.9% of patients. The pus culture results showed *K pneumoniae* to be the most common pathogen (85.6%), followed by *E coli* (4.5%). The duration of antibiotic treatment ranged from 5 ~ 28 days. Eventually, 24 (1.5%) patients developed endophthalmitis and 44 (2.8%) MODS (Table 1).

# 3.2 | Comparison of Proportions of PLA, MODS and Mortality Rates in the Two Study Periods

The proportions of PLA patients in the study periods from 2006 to 2011 and from 2012 to 2017 were 21.2% and 78.8% respectively. The incidences of MODS in patients with liver abscesses were 2.1% between 2006 and 2011 and 3.0% between 2012 and 2017 without significant difference, while the mortality rates for PLA patients caused by *K pneumoniae* were 6.7% vs 0.7% (P = .035),

respectively, indicating a significant mortality reduction in 2012 to 2017, but interestingly there were no deaths caused by *E coli* infections (Table 2).

# 3.3 | Comparison of the clinical characteristics of patients with PLA caused by K pneumoniae or E coli

The proportion of patients with diabetes mellitus and PLA induced by K pneumoniae (47.7%) was significantly higher than in patients with *E coli* infection (26.7%) (P = .024), whereas hepatobiliary and pancreatic diseases as well as hepatobiliary calculi occurred more frequently in E coli caused PLA patients (both P < .001). Patients with PLAs caused by *K* pneumoniae mainly came from an arterial origin (72.6%), while PLAs caused by *E coli* mainly came from either biliary (44.4%) or arterial (37.0%) origins. Fever was a clinical presentation in patients with PLA, whether the PLA was caused by K pneumoniae or E coli. However, the proportion of PLA patients with fever in PLAs caused by K pneumoniae was significantly higher than in those infected by *E coli* (91.7% vs 76.7%, P = .005). Considering the proportion of patients who were not drained percutaneously, the number of patients with E coli-infected PLAs was significantly higher than K pneumoniae-infected PLA patients (20.0% vs 6.1%, P = .004) (Table 3). There were no significant differences in other clinical features between these two groups of patients beside catheterization status with less untreated patients in the E coli PLA group.

When these clinical characteristics were then compared between the two study periods, with the exception of abdominal pain, the other clinical indicators exhibited no statistically significant differences (Table S2).

# 3.4 | Analysis of impact of different clinical indicators on prognosis

For the entire patient cohort, significant differences in prognosis existed between patients with the following four clinical features: pleural effusion, pulmonary infection, fever or gas in abscess when compared with those without these features. In addition, cerebrovascular disease appeared also to be a prognostic factor (P < .020). Surgical drainage significantly improved the recovery rate (P < .001), and an increase in hospital stay length was also correlated with recovery of patients (Table 4). Figure S1 shows a patient who was treated with CT-guided percutaneous drainage of a huge right liver abscess with gases before treatment. The patient recovered after treatment for 60 days using an indwelling catheter to drain the abscess and antibiotic therapy.

The proportion of PLA patients with MODS which resulted in deaths or unhealed/uncured conditions was as high as 63.6% (Table 4). Most laboratory test values for the PLA patients after hospital discharge were significantly better than their baseline values (Table S3).

### TABLE 1 Characteristics of patients with liver abscesses

Characteristics	N = 1,572	
Gender, n(%)		
Male	984 (62.6)	
Female	588 (37.4)	
Age (years), mean $\pm$ SD	58.5 ± 13.5	
Comorbidities, n (%)		
Diabetes mellitus	599 (38.1)	
Cardiovascular diseases	232 (14.8)	
Hypertension	375 (23.9)	
Kidney diseases	32 (2.0)	
Tumours	8 (0.5)	
Hepatobiliary and pancreatic diseases	382 (24.3)	
Hepatobiliary calculi	82 (5.2)	
Cerebrovascular disease	106 (6.7)	
Origin, n (%)		
Biliary	186 (16.0)	
Portal	35 (3.0)	
Arterial	823 (70.6)	
Others	121 (10.4)	
Clinical symptoms/signs, n (%)		
Pleural effusion	313 (19.9)	
Pulmonary infection	323 (20.6)	
Fever	1397 (88.9)	
Jaundice	81 (5.2)	
Abdominal pain	806 (51.3)	
No. of abscesses, n (%)		
Solitary	1176 (77.5)	
Multiple	342 (22.5)	
Location of abscess, n (%)		
Left hemiliver	236 (16.3)	
Right hemiliver	1,050 (72.7)	
Both hemilivers	158 (10.9)	
Gas in abscess, n (%)		
Yes	151 (9.6)	
No	1,420 (90.4)	
Pus culture, n (%)		
Escherichia coli	30 (1.9)	
Klebsiella pneumonia	576 (36.6)	
Combination infection	22 (1.4)	
Other bacteria <sup>ª</sup>	45 (2.9)	
Undetected <sup>b</sup>	315 (20.0)	
Not applicable	584 (37.2)	
No. of percutaneous punctures/ drainage, n (%)		

# TABLE 1 (Continued)

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Characteristics	N = 1,572
Once	641 (40.8)
Multiple	401 (25.5)
Surgical drainage, n (%)	
Yes	57 (3.6)
No	1,515 (96.4)
Catheterization status, n (%)	
No puncture	529 (33.7)
No catheterization	690 (43.9)
With catheterization	353 (22.5)
Length of hospital stay (days), n (%)	14.6 ± 9.6
Outcomes, n (%)	
Died in hospital	20 (1.3)
Uncured	50 (3.2)
Improved	761 (48.4)
Cured	741 (47.1)
Eyes, n (%)	
Normal	1,548 (98.5)
Endophthalmitis	24 (1.5)
MODS, n (%)	
Yes	44 (2.8)
No	1527 (97.2)

<sup>a</sup>The proportion of other bacteria detected by pus culture is shown in Table S1.

<sup>b</sup>indicates that samples were not send to a laboratory. MODS, multiple organ dysfunction.

# 3.5 | Analysis of Factors Affecting Poor Prognosis using a Multivariate Regression Model on PLA Patients after Treatment

After multivariate regression analysis, age, fever, MODS and length of hospital stay were shown to be factors that affected poor prognosis (death + unhealed/uncured) in PLA patients after treatment. Fever (OR: 0.284, P < .001) and length of hospital stay (OR: 0.878, P < .001) were protective factors for poor prognosis while age (OR: 1.026, P = .031) and MODS (OR: 109.627, P < .001) were risk factors for poor treatment outcomes (Table 5).

# 3.6 | Risk Factors for MODS on Multivariate Regression Analysis

After multivariate regression analysis, cardiovascular diseases, pleural effusion and lung infections were shown to be risk factors for MODS in PLA patients (Table 5). The results on univariate analysis are shown in Table S4.

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# 3.7 | Analysis of Risk Factors of Endophthalmitis in PLA Patients

Multiple regression analysis showed that the main risk factor for endophthalmitis in PLA patients was diabetes mellitus [no vs yes, OR: 0.434 95% CI (0.191-0.983), P = .045] (Table S5).

### 4 | DISCUSSION

This retrospective study on PLA patients was the first to evaluate the epidemiology of PLA in northeast China, to analyse the factors affecting poor prognosis of PLA after treatment and to determine the risk factors for MODS and endophthalmitis in affected patients.

The characteristics of PLA patients in northeast China supported the previously reported findings that PLA mainly occurred in middle-aged males with a single abscess in the right hemiliver.<sup>6,10,11</sup> The most common clinical presentation was fever (88.9%), followed by abdominal pain (51.3%), which were similar to the findings reported in previous studies.<sup>10,12-15</sup>

The present study revealed that the proportion of PLA patients in the latter 6 years of the study was nearly four times higher than that of the former 6 years, a finding most likely related to the fact that more patients underwent immunosuppressive therapy for cancer and/or organ transplantation. At the same time, the increased use of invasive techniques to treat hepatobiliary diseases and improvements in diagnostic accuracy of modern imaging techniques have also occurred.<sup>16,17</sup> Our investigations, however, revealed no significant difference in the overall mortality rates for PLA between the former and latter periods of the study, suggesting that early

	Years	Patients, n (%)		P-value
		Yes	No	
Proportion of PLA				NA
	2006 to 2011	333 (21.2)		
	2012 to 2017	1,239 (78.8)		
Incidence of MODS				.384
	2006 to 2011	7 (2.1)	326 (97.9)	
	2012 to 2017	37 (3.0)	1,201 (97.0)	
Overall PLA mortality				.163
	2006 to 2011	7 (2.1)	326 (97.9)	
	2012 to 2017	13 (1.0)	1,226 (99.0)	
K pneumoniae caused PLA mortality				.035
	2006 to 2011	2 (6.7)	28 (93.3)	
	2012 to 2017	4 (0.7)	542 (99.3)	
E coli caused PLA mortality				NA
	2006 to 2011	0 (0.0)	3 (100.0)	
	2012 to 2017	0 (0.0)	27 (100.0)	

Abbreviations: MODS, multiple organ dysfunction; NA, not applicable; PLA, pyogenic liver abscess.

diagnosis and treatment, with empirical use of antibiotics and image-guided drainage, are adequate to prevent death in patients with PLAs.

The symptoms of hepatic abscesses caused by E coli were milder in the present study than those caused by K pneumoniae, and there was less manifestation of extrahepatic invasion and more E coli caused hepatic abscesses also did not require percutaneous punctures/drainages, which reflected in lower mortality rates. PLA caused by K pneumoniae has been reported to be a worldwide problem associated with a significant mortality rate.<sup>18,19</sup> Up to the present time there have been a paucity of studies on the clinical characteristics and mortality rates of patients with PLA caused by K pneumonia, especially in China. This research found that K pneumoniae was the main organism that caused PLA, which is consistent with recent findings reported in other Asian countries.<sup>10,20</sup> All the studies found a gradual change in the bacterial spectrum of liver abscesses, with K pneumoniae in this study gradually becoming the dominant bacterium beeing 85.6% of all indentified strains, which is close to a previous recorded value for China of > 80%.<sup>5</sup> About 47.7% of patients with PLA caused by K pneumonia had diabetes mellitus, a figure similar to that of a 21-year retrospective study from southern China (49.7%). Poor glycaemia control impairs activation of neutrophils and phagocytosis, which promotes the growth of pathogens in tissues.<sup>21,22</sup> Thus, blood glucose levels should be strictly controlled during the management of patients with PLA caused by K pneumoniae. This study showed that the mortality rate of PLA caused by K pneumoniae in the latter six years of the study was significantly lower than in the former six years, implying better results after antibiotic therapy for PLA caused by K pneumoniae and might be attributed to approvals of novel antibiotics like ertapenem

> **TABLE 2** Comparison of PLA proportions, incidence rates of MODS and mortality rates between patient groups with liver abscesses in the two study periods

# **TABLE 3** Comparison of clinical characteristics data in PLA patients infected by *K* pneumoniae and *E* coli

		Escherichia coli (N = 30)	Klebsiella pneumonia (N = 576)	P-value
Comorbid conditions,	Diabetes mellitus	8 (26.7)	275 (47.7)	.024
n (%)	Cardiovascular diseases	7 (23.3)	82 (14.2)	.170
	Hypertension	7 (23.3)	156 (27.1)	.652
	Hepatobiliary and pancreatic diseases	19 (63.3)	110 (19.1)	<.001
	Hepatobiliary calculi	7 (23.3)	24 (4.2)	<.001
	Kidney diseases	1 (3.3)	10 (1.7)	.430
	Tumours	1 (3.3)	2 (0.4)	.140
	Cerebrovascular diseases	2 (6.7)	49 (8.5)	1.000
Origin, n (%)	Biliary	12 (44.4)	58 (15.1)	<.001
	Arterial	10 (37.0)	278 (72.6)	
	Portal venous	0 (0.0)	14 (3.7)	
	Others	5 (18.5)	33 (8.6)	
Clinical Symptoms/signs, n (%)	Pleural effusion	5 (16.7)	124 (21.5)	.526
	Pulmonary infection	6 (20.0 )	121 (21.0)	.895
	Fever	23 (76.7)	528 (91.7)	.005
	Jaundice	2 (6.7)	24 (4.2)	.373
	Abdominal pain	19 (63.3)	274 (47.6)	.092
No. of abscesses, n (%)	Solitary	23 (79.3)	448 (78.9)	.955
	Multiple	6 (20.7)	120 (21.1)	
Location of abscess, n (%)	Left hemiliver	7 (25.0)	78 (14.6)	.297
	Right hemiliver	19 (67.9)	399 (74.4)	
	Both hemilivers	2 (7.1)	59 (11.0)	
Gas in abscess, n (%)	Yes	1 (3.3)	53 (9.2)	.506
No. of percutaneous puncture/	None	6 (20.0)	35 (6.1)	.004
drainage, n (%)	Once	17 (56.7)	290 (50.4)	
	Multiple	7 (23.3)	250 (43.5)	
Surgical drainage, n (%)	Yes	1 (3.3)	2 (0.3)	.142
	No	29 (96.7)	574 (99.7)	.172
Catheterization status,	No puncture	6 (20.0)	35 (6.1)	.011
n (%)	No catheterization	15 (50.0)	366 (63.5)	.011
	With catheterization	9 (30.0)	175 (30.4)	
Outcomes, n (%)	Died in hospital	0 (0.0)	6 (1.0)	.544
Outcomes, II (76)	Uncured	1 (3.3)	7 (1.2)	.544
	Improved	15 (50.0)	266 (46.2)	
Ever $p(\ell)$	Cured	14 (46.7)	297 (51.6)	404
Eyes, n (%)	Normal	29 (96.7)	567 (98.4)	.401
	Endophthalmitis	1 (3.3)	9 (1.6)	
MODS, n (%)	Yes	1 (3.3)	11 (1.9)	.460
	No	29 (96.7)	564 (98.1)	

Abbreviations: MODS, multiple organ dysfunction; PLA, pyogenic liver abscess.

(in 2012) and imipenem (in 2013) by the Chinese National Medical Products Administration. On further analysis of the factors affecting poor prognosis (death + unhealed/uncured) for PLA patients, the length of hospital stay was a protective factor. This finding is most probably related to longer therapy with antibiotics. As a most common clinical symptom, fever is also a protective factor related to poor prognosis of PLA. In the early stages of onset of disease, patients with fever may easily be suspected by the doctor to have

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TABLE 4 Comparison of the prognosis information of death, unhealed/uncured, improvement and cured in patients with PLA

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		Death (N = 20)	Unhealed/ uncured (N = 50)	Improvement (N = 761)	Cured (N = 741)	P-value
Hospital stay (days), mean $\pm$ SD	)	$12.5 \pm 13.3$	$6.7 \pm 8.0$	$14.3 \pm 10.4$	15.6 ± 8.4	<.001
Comorbid conditions, n (%)	Diabetes mellitus (n = 599)	9 (45.0)	19 (38.0)	277 (36.4)	294 (39.7)	.453
	Cardiovascular disease (n = 232)	7 (35.0)	9 (18.0)	110 (14.5)	106 (14.3)	.133
	Hypertension ( $n = 375$ )	8 (40.0)	11 (22.0)	182 (23.9)	174 (23.5)	.427
	Hepatobiliary and pancreatic diseases (n = 382)	4 (20.0)	13 (26.0)	196 (25.8)	169 (22.8)	.330
	Hepatobiliary calculi (n = 82)	0 (0.0)	2 (4.0)	49 (6.4)	31 (4.2)	.360
	Kidney diseases (n = 32)	1 (5.0)	1 (2.0)	16 (2.1)	14 (1.9)	.520
	Tumours (n = 8)	0 (0.0)	2 (4.0)	1 (0.1)	5 (0.7)	.860
	Cerebrovascular diseases (n = 106)	1 (5.0)	3 (6.0)	39 (5.1)	63 (8.5)	.020
Origin, n (%)	Biliary (n $=$ 186)	1 (7.7)	4 (11.4)	94 (16.3)	87 (16.1)	.397
	Arterial (n $=$ 823)	9 (69.2)	24 (68.6)	400 (69.4)	390 (72.1)	
	Portal (n = 35)	0 (0.0)	0 (0.0)	20 (3.5)	15 (2.8)	
	Others (n = 121)	3 (23.1)	7 (20.0)	62 (10.8)	49 (9.1)	
Clinical Symptoms/signs,	Pleural effusion ( $n = 313$ )	8 (40.0)	16 (32.0)	160 (21.0)	129 (17.4)	<.001
n (%)	Pulmonary infection (n = 323)	10 (50.0)	14 (28.0)	168 (22.1)	131 (17.7)	<.001
	Fever (n = 1,397)	16 (80.0)	37 (74.0)	670 (88.0)	674 (91.0)	<.001
	Jaundice (n = 81)	3 (15.0)	2 (4.0)	44 (5.8)	32 (4.3)	.078
	Abdominal pain (n = 806)	9 (45.0)	28 (56.0)	395 (51.9)	374 (50.5)	.637
No. of abscess,	Solitary (n = 1,176)	15 (83.3)	35 (72.9)	554 (76.2)	572 (78.9)	.298
n (%)	Multiple (n = 342)	3 (16.7)	13 (27.1)	173 (23.8)	153 (21.1)	
Location of abscess, n (%)	Left hemiliver (n = $236$ )	2 (11.1)	7 (15.2)	120 (17.4)	107 (15.5)	.925
	Right hemiliver (n = $1,039$ )	13 (72.2)	34 (73.9)	498 (72.2)	505 (73.2)	
	Both hemilivers ( $n = 158$ )	3 (16.7)	5 (10.9)	72 (10.4)	78 (11.3)	
Gas in abscess, n (%)	Yes (n = 151)	5 (25.0)	11 (22.0)	69 (9.1)	66 (8.9)	.015
Pus culture, n (%)	Escherichia coli (n = 30)	0 (0.0)	1 (2.0)	15 (2.0)	14 (1.9)	.061
	Klebsiella pneumoniae (n = 576)	6 (30.0)	7 (14.0)	266 (35.0)	297 (40.1)	
	Combination infection (n = 22)	1 (5.0)	2 (4.0)	9 (1.2)	10 (1.3)	
No. of percutaneous	None (n = 529)	9 (45.0)	38 (76.0)	239 (31.4)	243 (32.8)	<.001
puncture/drainage, n (%)	Once (n = 641)	8 (40.0)	6 (12.0)	324 (42.6)	303 (40.9)	
	Multiple (n = 401)	3 (15.0)	6 (12.0)	198 (26.0)	194 (26.2)	
Surgical drainage, n (%)	Yes (n = 57)	0 (0.0)	0 (0.0)	1 (0.1)	56 (7.6)	<.001
Catheterization status, n (%)	No puncture (n = 529)	9 (45.0)	38 (76.0)	239 (31.4)	243 (32.8)	<.001
	Puncture without catheterization $(n = 690)$	8 (40.0)	9 (18.0)	345 (45.3)	328 (44.3)	
	Puncture with catheterization $(n = 353)$	3 (15.0)	3 (6.0)	177 (23.3)	170 (22.9)	
MODS, n (%)	Yes (n = 44)	14 (70.0)	14 (28.0)	12 (1.6)	4 (0.5)	<.001
	100 (11 = 44)	14 (70.0)	14 (20.0)	12 (1.0)	+ (0.5)	<.001

Abbreviations: MODS, multiple organ dysfunction; PLA, pyogenic liver abscess.

 TABLE 5
 Multivariate analysis of factors affecting poor

 prognosis and risk factors for MODS in PLA patients

	OR (95% CI)	P-value			
Factors affecting poor prognosis (death + unhealed/uncured)					
Age	1.026 (1.002-1.051)	.031			
Fever (Yes vs No)	0.284 (0.143-0.564)	<.001			
MODS (Yes vs No)	109.627 (44.026-272.979)	<.001			
Length of hospital stay (days)	0.878 (0.839-0.919)	<.001			
Risk factors for MODS					
cardiovascular diseases (Yes <i>vs</i> No)	2.132 (1.076-4.237)	.030			
Pleural effusion (Yes vs No)	2.688 (1.332-5.435)	.006			
Lung infections (Yes vs No)	4.367 (2.123-8.929)	<.001			

Abbreviations: MODS, multiple organ dysfunction; PLA, pyogenic liver abscess.

PLA prompting the initiation of treatment measures to avoid adverse outcomes.

In the present study, MODS was identified as a risk factor for poor prognosis of PLA with an OR value as high as 109.627, while coexisting -cardiovascular diseases, pleural effusion and pulmonary infection were risk factors related to development of MODS. The lung is typically the first organ to be involved in MODS, probably because of capillary leakage, alveolar congestion and surfactant inactivation.<sup>23</sup> The second organ commonly involved in MODS is the heart as increased levels of nitric oxide can cause myocardial dysfunction, which is closely related to MODS in sepsis.<sup>24</sup> Early control of the infected focus is very important in reducing inflammatory changes that lead to MODS.<sup>25</sup>

Finally, our study found the incidence of endophthalmitis in PLA patients to be 1.5%, which is within the range of 0.84%-6.9% reported worldwide.<sup>26-28</sup> Although rare, endophthalmitis is the most common and severe suppurative complication of a liver abscess.<sup>29</sup> As the present study showed diabetes mellitus to be a risk factor for endophthalmitis in patients with PLA and that 38.1% of PLA patients were associated with diabetes mellitus, routine and early ophthalmic examination of these patients can help in early diagnosis and treatment of this serious complication.

There are a number of limitations to our study. First, this was a single-centre retrospective study with its inherent defects. Second, the findings may not be applicable to other regions with different epidemiological or clinical practices. Third, the use of antibiotics was not documented in detail and there was no antibiotic susceptibility analysis. Fourth, the sizes of the liver abscesses were not analyszed.

# 5 | CONCLUSIONS

With increasing number of PLA patients in 2012-2017 compared to 2006-2011 treated in our centre, major improvements have been

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made in treatment outcomes. *K pneumoniae* was the main pathogen causing PLA. Pleural effusion, fever, MODS and length of hospital stay were important factors related to PLA treatment outcomes. For PLA patients with associated cardiovascular diseases, pleural effusion or lung infection, steps should be taken to early control the infected focus to prevent the development of MODS. Patients with PLA and diabetes mellitus should undergo an early eye examination to diagnose endophthalmitis.

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### CONFLICT OF INTEREST

None to declare.

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#### REFERENCES

- Chen Y-C, Lin C-H, Chang S-N, et al. Epidemiology and clinical outcome of pyogenic liver abscess: an analysis from the National Health Insurance Research Database of Taiwan, 2000–2011. J Microbiol Immunol Infect. 2016;49:646-653.
- Lo JZW, Leow JJJ, Ng PLF, et al. Predictors of therapy failure in a series of 741 adult pyogenic liver abscesses. J Hepatobiliary Pancreat Sci. 2015;22:156-165.
- Phaosawasdi K, Wilairatana P, Soonthornworasiri N, et al. Burden of Liver Abscess and Survival Risk Score in Thailand: A Population-Based Study. Am J Trop Med Hyg. 2016;95:683-688.
- Pope JV, Teich DL, Clardy P, et al. Klebsiella pneumoniae liver abscess: an emerging problem in North America. J Emerg Med. 2011;41:e103-e105.
- Qu T-T, Zhou J-C, Jiang Y, et al. Clinical and microbiological characteristics of Klebsiella pneumoniae liver abscess in East China. BMC Infect Dis. 2015;15:161.
- Siu LK, Yeh K-M, Lin J-C, et al. *Klebsiella pneumoniae* liver abscess: a new invasive syndrome. *Lancet Infect Dis.* 2012;12:881-887.
- He J, Ma L, Zhang J. Clinical analysis of bacterial liver abscess complicated with multiple organ dysfunction syndrome. J HEBEI Med Univ. 2011;32:1100-1101.
- Shi SH, Zhai ZL, Zheng SS. Pyogenic Liver Abscess of Biliary Origin: The Existing Problems and Their Strategies. *Semin Liver Dis.* 2018;38:270-283.
- Qian Y, Wong CC, Lai S, et al. A retrospective study of pyogenic liver abscess focusing on Klebsiella pneumoniae as a primary pathogen in China from 1994 to 2015. *Sci Rep.* 2016;6:38587.

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- Kong H, Yu F, Zhang W, et al. Clinical and microbiological characteristics of pyogenic liver abscess in a tertiary hospital in East China. *Medicine (Baltimore)*. 2017;96:e8050.
- 11. Li W, Chen H, Wu S, et al. A comparison of pyogenic liver abscess in patients with or without diabetes: a retrospective study of 246 cases. *BMC Gastroenterol*. 2018;18:144.
- 12. Ali AH, Smalligan RD, Ahmed M, et al. Pyogenic liver abscess and the emergence of Klebsiella as an etiology: a retrospective study. *Int J Gen Med.* 2013;7:37-42.
- Foo N-P, Chen K-T, Lin H-J, et al. Characteristics of pyogenic liver abscess patients with and without diabetes mellitus. Am J Gastroenterol. 2010;105:328-335.
- 14. Kaplan GG, Gregson DB, Laupland KB. Population-based study of the epidemiology of and the risk factors for pyogenic liver abscess. *Clin Gastroenterol Hepatol.* 2004;2:1032-1038.
- Huang X-P, Ding H, Yang X-Q, et al. Synergism and mechanism of Astragaloside IV combined with Ginsenoside Rg1 against autophagic injury of PC12 cells induced by oxygen glucose deprivation/ reoxygenation. *Biomed Pharmacother*. 2017;89:124-134.
- Huang C-J, Pitt HA, Lipsett PA, et al. Pyogenic hepatic abscess. Changing trends over 42 years. Ann Surg. 1996;223:600–607; discussion 607–609.
- 17. Meddings L, Myers RP, Hubbard J, et al. A population-based study of pyogenic liver abscesses in the United States: incidence, mortality, and temporal trends. *Am J Gastroenterol*. 2010;105:117-124.
- Shon AS, Bajwa RPS, Russo TA. Hypervirulent (Hypermucoviscous) Klebsiella Pneumoniae: A New and Dangerous Breed. *Virulence*. 2013;4:107-118.
- Siu LK, Fung C-P, Chang F-Y, et al. Molecular Typing and Virulence Analysis of Serotype K1 Klebsiella Pneumoniae Strains Isolated From Liver Abscess Patients and Stool Samples From Noninfectious Subjects in Hong Kong, Singapore, and Taiwan. J Clin Microbiol. 2011;49:3761-3765.
- Luo M, Yang X-X, Tan B, et al. Distribution of common pathogens in patients with pyogenic liver abscess in China: a meta-analysis. Eur J Clin Microbiol Infect Dis. 2016;35:1557-1565.
- Fung CP, Chang FY, Lee SC, et al. A global emerging disease of Klebsiella pneumoniae liver abscess: is serotype K1 an important factor for complicated endophthalmitis? *Gut.* 2002;50:420-424.

- Lin JC, Siu LK, Fung CP, et al. Impaired phagocytosis of capsular serotypes K1 or K2 Klebsiella pneumoniae in type 2 diabetes mellitus patients with poor glycemic control. J Clin Endocrinol Metab. 2006;91:3084-3087.
- 23. Ramírez M. Multiple Organ Dysfunction Syndrome. *Curr Probl Pediatr Adolesc Health Care*. 2013;43:273-277.
- Ferdinandy P, Danial H, Ambrus I, et al. Peroxynitrite is a major contributor to cytokine-induced myocardial contractile failure. *Circ Res.* 2000;87:241-247.
- Barie PS, Williams MD, McCollam JS, et al. Benefit/risk profile of drotrecogin alfa (activated) in surgical patients with severe sepsis. *Am J Surg.* 2004;188:212-220.
- Hu C-C, Ho J-D, Lou H-Y, et al. A One-Year Follow-up Study on the Incidence and Risk of Endophthalmitis after Pyogenic Liver Abscess. Ophthalmology. 2012;119:2358-2363.
- Sheu SJ, Kung YH, Wu TT, et al. Risk factors for endogenous endophthalmitis secondary to klebsiella pneumoniae liver abscess: 20year experience in Southern Taiwan. *Retina*. 2011;31:2026-2031.
- Van Keer J, Van Keer K, Van Calster J, et al. More Than Meets the Eye: *Klebsiella pneumoniae* Invasive Liver Abscess Syndrome Presenting with Endophthalmitis. *J Emerg Med.* 2017;52:e221-e223.
- Lee NK, Kim S, Lee JW, et al. CT differentiation of pyogenic liver abscesses caused by Klebsiella pneumoniae vs non-Klebsiella pneumoniae. Br J Radiol. 2011;84:518-525.

### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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