BMC Infectious Diseases

RESEARCH

Open Access

# Analysis of clinical and microbiological characteristics of invasive *Klebsiella pneumoniae* liver abscess syndrome

Li Gu[1], Yue Wang[2], Han Wang[3] and Dong Xu[1*]

## Abstract

**Background** Invasive *Klebsiella pneumoniae* liver abscess syndrome (IKPLAS) is emerging as a new disease worldwide, threatening human health. This study aimed to investigate the clinical and microbiological features of IKPLAS in order to detect this syndrome early and select antibiotics appropriately.

**Methods** Medical data from patients in Tongji Hospital, China, diagnosed with *Klebsiella pneumoniae* liver abscess (KPLA) between 2015 and 2023 was collected and analyzed retrospectively.

**Results** The study included 208 patients with KPLA, 41 with IKPLAS, and 167 with non-IKPLAS (NIKPLAS). Multivariate logistic regression analysis demonstrated that symptoms in other organ systems (including ocular, pulmonary, and neurological symptoms) ($p=0.001$) and a sequential organ failure assessment (SOFA) score ≥ 4 within 48 h of admission ($P=0.002$) were significant risk factors for IKPLAS. Patients with IKPLAS had a higher risk of developing multiple organ dysfunction (MODS), and a PCT ≥ 10 ng/mL was identified as an independent risk factor for MODS ($p=0.01$). IKPLAS was associated with significantly prolonged hospital stays and unfavorable outcomes (all $p<0.05$). There were no significant differences in microbiological characteristics between IKPLAS and NIKPLAS, including the antimicrobial susceptibility pattern and resistance profile of *Klebsiella pneumoniae* (KP) (all $p>0.05$). In this study, KP isolates were susceptible to most antibiotics, with low rates of drug resistance. Specifically, a total of five carbapenem-resistant strains (2.6%) and seven multidrug-resistant strains (3.6%) were detected, all of which were derived from the NIKPLAS group.

**Conclusions** Symptoms in other organ systems and the SOFA score ≥ 4 within 48 h of admission were significant predictors for IKPLAS. This study elucidated the antimicrobial susceptibility profile of liver abscess-associated KP strains, providing a reference for the early initiation of rational and effective antimicrobial therapy in patients with KPLA.

**Keywords** Invasive syndrome, *Klebsiella pneumoniae*, Pyogenic liver abscess, Sequential organ failure assessment, Drug resistance, Metastatic infection

*Correspondence:
Dong Xu
xdong@tjh.tjmu.edu.cn
[1]Department of Infectious Diseases, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China
[2]Department of Laboratory Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China
[3]Department of Gastroenterology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

## Introduction

*Klebsiella pneumoniae* (KP)-induced community-acquired liver abscess presenting with severe extrahepatic complications, particularly endophthalmitis, was first reported in Taiwan, China, in 1986 [1]. Over the past three decades, KP has emerged as the predominant cause of pyogenic liver abscess in Asia [2, 3].

Interestingly, *Klebsiella pneumoniae* liver abscess (KPLA) has a higher risk of septic metastatic infection than other bacterial liver abscesses [4], which is strongly correlated with hypervirulent KP infection [5]. Invasive *Klebsiella pneumoniae* liver abscess syndrome (IKPLAS) is defined as KPLA combined with one or more extrahepatic metastatic infections such as endophthalmitis, meningitis, lung abscess, septic pulmonary embolism, and pyogenic spondylitis [6–8]. IKPLAS often has an acute onset, rapid progression, and poor prognosis [9, 10]. The eye and central nervous system (CNS) are the most common sites for metastatic infection, which could progress to catastrophic and irreversible disability [11, 12].

The devastating nature of IKPLAS, coupled with the emergence of drug-resistant KP strains [13], urgently highlights the need for increased awareness of IKPLAS and the importance of rational antibiotic use. However, effective empirical antimicrobial therapy must be initiated as early as possible for better prognosis in patients with IKPLAS. Therefore, determining risk factors for IPKLAS and knowledge of antimicrobial susceptibility characteristics of KP isolates are essential for providing an early diagnosis and a reliable foundation for empirical therapy. Many studies on IKPLAS are limited to case reports, and only a few have investigated its various characteristics [14–17].

This study retrospectively analyzed the differences in clinical characteristics between IKPLAS and non-IKPLAS (NIKPLAS) to facilitate early detection of IKPLAS. It also clarified the antimicrobial susceptibility pattern of KP isolates, helping guide the rational use of antibiotics to some extent.

## Method

### Study population

This study retrospectively collected the medical records of patients with KPLA from Tongji Hospital between 2015 and 2023. The inclusion criteria were (1) monomicrobial *Klebsiella pneumoniae* isolated from pus and/or blood culture or detected by metagenomic next-generation sequencing (mNGS); (2) Imaging showing one or more liver abscess lesions. The exclusion criteria were (1) Amoebic liver abscess and liver abscess secondary to liver cysts and liver tumors; (2) The presence of organ failure before liver abscess formation. IKPLAS was defined as KPLA with contemporaneous metastatic infections at other body sites, whereas KPLA without extrahepatic metastatic infections was classified as NIKPLAS. IKPLAS was diagnosed based on a positive culture or mNGS result for monomicrobial *Klebsiella pneumoniae* in pus and/or blood, as well as imaging that indicated infectious lesions at other body sites during the same admission.

### Clinical data and definitions

The following data was extracted from the medical records: (1) patient demographics; (2) underlying conditions, including diabetes mellitus, biliary disease, history of intra-abdominal surgery including hepatobiliary surgery; (3) symptoms, including fever, chills and/or shivers, weakness, poor appetite, abdominal symptoms, and symptoms involving other organ systems (including ocular, pulmonary, and neurological symptoms); (4) laboratory tests at admission, including routine blood tests (white blood cell count, neutrophil percentage, platelet, and hemoglobin), inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) levels, and liver, kidney, and coagulation function tests; (5) radiological features of liver abscess including the location (unilobar [right or left] or bilobar), number (single or multiple), maximal diameter on CT images (where multiple abscess were detected, the largest was recorded), and gas in abscess; (6) sequential organ failure assessment (SOFA) score within 48 h of admission; (7) complications, including extrahepatic metastatic infections, sepsis, multiple organ dysfunction syndrome (MODS), and septic shock during the same admission; (8)hospitalization, treatment, and outcomes (treatment success and failure). Treatment success was defined as complete resolution of symptoms and signs, normalization or near-normalization of abnormal laboratory findings, radiological evidence (ultrasound or CT) of complete absorption or significant reduction (≥ 50%) in liver abscess size without new abscess formation or dissemination of infection, and eradication of bacterial infection confirmed by two consecutive negative blood or pus cultures. Treatment failure was defined as persistence or worsening of symptoms and signs during treatment, failure to normalize abnormal laboratory findings, radiological evidence of no significant improvement in liver abscess size or new abscess formation or dissemination of infection, and failure to eradicate bacterial infection.

### Microbiological data

Species identification was confirmed by Autof ms1000 automatic microbial mass spectrometry detection system (Autobio, China). Drug susceptibility testing was performed for all strains using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar (Zhongjin Technology Co., Ltd, Wuhan, China). The testing was conducted in accordance with the updated version of the Clinical and

Laboratory Standards Institute (CLSI) guideline for the year of implementation [18, 19]. The antibiotics tested included β-lactam antibiotics and β-lactamase inhibitor combinations (ampicillin, ampicillin/sulbactam, piperacillin/tazobactam, cefazolin, cefoxitin, cefuroxime, ceftazidime, cefotaxime, cefoperazone/sulbactam, cefepime, amoxicillin/clavulanic acid, and aztreonam), glycylcycline (tigecycline), quinolones (ciprofloxacin and levofloxacin), aminoglycosides (tobramycin, gentamicin, and amikacin (OXOID, UK), and other antibiotics (cotrimoxazole). The susceptibility testing was interpreted according to the CLSI guideline [20]. For tigecycline, the interpretive criteria for zone diameters were according to the breakpoints recommended by the Food and Drug Administration [21]. Carbapenem-resistant Enterobacterales (CRE) is defined as resistance to at least one carbapenem antibiotic, including imipenem, meropenem, doripenem, or ertapenem) [22]. Multidrug-resistant (MDR) strains are defined as isolates that exhibits intermediate (I) or resistant (R) phenotypes to at least one antimicrobial agent in three or more of the following antimicrobial categories: extended-spectrum cephalosporins (e.g., ceftriaxone, ceftazidime), fluoroquinolones (e.g., ciprofloxacin, levofloxacin), aminoglycosides (e.g., amikacin, gentamicin), carbapenems (e.g., imipenem, meropenem), and penicillins with β-lactamase inhibitors (e.g., piperacillin/tazobactam) [22].

### Metagenomic next-generation sequencing

Specimens (such as pus, blood, or tissue) were collected and then immediately transported to the hospital laboratory for mNGS detection. Sample processing, nucleic acid extraction, deoxyribonucleic acid (DNA) library preparation, high-throughput sequencing, bioinformatics analysis, and mNGS data interpretation were performed in accordance with the laboratory's standard operating procedures.

According to the manufacturer's instructions, DNA was extracted from all samples using Nucleic Acid Extraction Kit (vision medicals, Guangzhou, China). DNA libraries were constructed through DNA fragmentation, end-repair, adapter-ligation, PCR amplification, and magnetic bead purification. The quality of the libraries was assessed using Qubit (Thermo Fisher Scientific, MA, USA) and Agilent 2100 Bioanalyzer (Agilent Technologies, Palo Alto, USA). Library pools were then loaded onto an NextSeq CN500 sequencer (Illumina, San Diego, USA) for 75 cycles of single-end sequencing to generate approximately 20 million reads for each library.

Quality control for sequencing reads was conducted by removinglow-quality reads (Q < 30), short reads (< 36 bp), duplicate reads, and adapter sequences using Trimmomatic [23]. Human host DNA reads were filtered out by mapping to the human reference genome (hg38) using Burrows Wheeler Aligner software [24]. The remaining sequences were finally aligned to the microbial genome database (http://ftp.ncbi.nlm.nih.gov/genomes/) using Burrows Wheeler Aligner software.

Negative controls (NTC; sterile deionized water) and positive controls (synthesized fragments with known quantities) were established for each batch of experiments using the same wet lab procedures and bioinformatics analysis as the clinical samples. For detected microbes, including bacteria (excluding mycobacteria, *Nocardia* species, and *Legionella pneumophila*), fungi, virus, and parasites, a positive mNGS result was considered if at least 3 nonoverlapping reads were mapped to species level and were absent in the NTC or the detected reads were ≥ 10-fold than that in the NTC. For *Mycobacterium*, *Nocardia* species, and *Legionella pneumophila*, the result was considered positive if at least one species-specific read was detected, or the detected reads were ≥ 5-fold than that in the NTC.

### Statistical analysis

SPSS software (version 25.0; IBM Corporation, Armonk, NY, USA) was used for statistical analysis. The independent sample t-test or Mann-Whitney U test was performed for continuous variables, and the Chi-square test or Fisher's exact test was used for categorical variables. Quantitative data was expressed as mean ± standard deviation for normal distribution, median (interquartile range) for non-normal distribution, and percentage for count data. Multivariate logistic regression analysis was used to determine independent risk factors. A p-value < 0.05 was considered statistically significant.

## Results

### Clinical characteristics

This retrospective study included 208 patients with KPLA, predominantly male patients (83.7%), with a mean age of 52.25 ± 0.92 years. Forty-one (19.7%) patients were identified with IKPLAS, with 32 (78%) male patients and a mean age of 53.56 ± 1.48 years. The remaining 167 (80.3%) patients were deemed to have NIKPLAS, with 142 (85.0%) male patients and a mean age of 51.92 ± 1.09 years ($p > 0.05$) (Table 1). Twenty-seven patients with IKPLAS had one extrahepatic complication, and fourteen had two or more extrahepatic complications (Table S1). These extrahepatic complications included endophthalmitis ($n = 16$), lung abscess ($n = 19$), septic pulmonary embolism ($n = 1$), meningitis ($n = 4$), brain abscess ($n = 4$), kidney abscess ($n = 2$), spleen abscess ($n = 2$), psoas abscess ($n = 1$), subcutaneous soft-tissue abscess ($n = 3$), orbital cellulitis ($n = 3$), and spine infection ($n = 1$), suggesting that the lung and eye are most frequent sites for metastatic infections.

**Table 1** Comparison of clinical characteristics in patients with IKPLAS and NIKPLAS

| Variables | KPLA (*n* = 208) | IKPLAS (*n* = 41) | NIKPLAS (*n* = 167) | *P*-value |
|---|---|---|---|---|
| Age (years) | 52.25 ± 0.92 | 53.56 ± 1.48 | 51.92 ± 1.09 | 0.48 |
| Gender | | | | |
| Male | 174 (83.7%) | 32 (78.0%) | 142 (85.0%) | 0.28 |
| Female | 34 (16.3%) | 9 (22.0%) | 25 (15.0%) | |
| **Underlying conditions** | | | | |
| Diabetes mellitus | 105 (50.5%) | 28 (68.3%) | 77 (46.1%) | 0.01* |
| Biliary diseases | 41 (19.7%) | 5 (12.2%) | 36 (21.6%) | 0.18 |
| Abdominal surgical history | 10 (4.8%) | 0 (0%) | 10 (6.0%) | 0.11 |
| **Symptoms** | | | | |
| Fever | 196 (94.2%) | 41 (100%) | 155 (92.8%) | 0.08 |
| Chills/shivers | 91 (43.8%) | 22 (53.7%) | 69 (41.3%) | 0.15 |
| Weakness | 116 (55.8%) | 22 (53.7%) | 94 (53.6%) | 0.76 |
| Poor appetite | 109 (52.4%) | 23 (56.1%) | 86 (51.5%) | 0.60 |
| Abdominal symptoms | 104 (50.0%) | 15 (36.6%) | 89 (53.5%) | 0.06 |
| Symptoms in other organ systems [a] | 73 (35.1%) | 35 (85.4%) | 38 (22.8%) | < 0.001* |
| **Laboratory tests** | | | | |
| WBC (*10^9/L) | 13.24 ± 0.37 | 14.63 ± 0.92 | 12.90 ± 0.39 | 0.06 |
| NEUT% (%) | 83.00 (76.83, 89.28) | 86.50 (78.25, 91.60) | 81.90 (76.70, 88.10) | 0.06 |
| PLT (*10^9/L) | 204.50 (114.25, 204.50) | 199.00 (81.50, 311.00) | 206.00 (119.00, 291.00) | 0.52 |
| Hb (g/L) | 117.06 ± 1.48 | 113.37 ± 3.16 | 117.96 ± 1.67 | 0.22 |
| Alb (g/L) | 30.72 ± 0.38 | 28.68 ± 0.19 | 31.22 ± 0.41 | 0.01* |
| ALT (U/L) | 50.00 (27.00, 78.50) | 38.00 (23.50, 63.00) | 52.00 (28.00, 88.00) | 0.03* |
| AST (U/L) | 37.00 (23.25, 61.50) | 33.00 (24.00, 46.50) | 38.00 (23.00, 64.00) | 0.20 |
| ALP (U/L) | 157.00 (114.50, 231.00) | 157.00 (120.50, 218.80) | 157.00 (112.00, 232.00) | 0.98 |
| GGT (U/L) | 118.00 (72.00, 179.00) | 110.00 (64.00, 158.50) | 119.00 (74.00, 195.00) | 0.37 |
| TBiL (μmol/L) | 13.50 (8.58, 24.25) | 12.90 (8.90, 24.05) | 13.50 (8.30, 24.50) | 0.98 |
| Cr (μmol/L) | 71.00 (59.00, 90.75) | 73.00 (57.50, 90.00) | 71.00 (59.00, 90.00) | 0.99 |
| eGFR (mL/min/1.73 m^2) | 90.04 ± 1.94 | 85.84 ± 4.85 | 91.04 ± 2.10 | 0.29 |
| D-dimer (μg/mL) | 2.56 (1.46, 4.93) | 4.23 (1.79, 8.03) | 2.38 (1.40, 4.30) | 0.03* |
| FIB (g/L) | 6.96 ± 0.41 | 5.95 ± 0.30 | 7.21 ± 0.51 | 0.22 |
| CRP (mg/L) | 170.99 ± 6.72 | 152.58 ± 13.86 | 175.96 ± 7.64 | 0.16 |
| PCT ≥ 10 (ng/mL) | 64/162 (39.5%) | 18/31 (58.1%) | 46/131 (35.1%) | 0.02* |
| SOFA ≥ 4 [b] | 40 (19.2%) | 16 (39.0%) | 24 (14.4%) | < 0.001* |
| **Radiological features of abscess** | | | | |
| Location | | | | 0.36 |
| Right lobe | 170 (81.7%) | 32 (78.0%) | 138 (82.6%) | |
| Left lobe | 28 (13.5%) | 8 (19.5%) | 20 (12.0%) | |
| Both lobes | 10 (4.8%) | 1 (2.4%) | 9 (5.4%) | |
| Single | 172 (82.7%) | 35 (85.4%) | 137 (82.0%) | 0.64 |
| Maximal diameter | 6.60 (4.90, 8.45) | 6.10 (4.50, 7.80) | 6.75 (4.90, 8.73) | 0.19 |
| Gas in abscess | 24/205 (11.7%) | 3/39 (7.7%) | 21/166 (12.7%) | 0.56 |

Notes: The independent sample t-test and Mann-Whitney U test was performed for continuous variables, and the Chi-square test was used for categorical variables; *$P < 0.05$, statistically significant results; [a] Symptoms in other organ systems, including ocular, pulmonary, or neurological symptoms; [b] SOFA ≥ 4, assessed within 48 h of admission

Abbreviations: ALT, alanine aminotransferase; Alb, albumin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; CRP, C-reactive protein; Cr, creatinine; eGFR, estimated glomerular filtration rate; FIB, fibrinogen; GGT, glutamyl transpeptidase; Hb, hemoglobin; IKPLAS, invasive *Klebsiella pneumoniae* liver abscess syndrome; KPLA, *Klebsiella pneumoniae* liver abscess; NIKPLAS, non-invasive *Klebsiella pneumoniae* liver abscess syndrome; NEUT%, neutrophil percentage; PCT, procalcitonin; PLT, platelet; SOFA, sequential organ failure assessment; TBIL, total bilirubin; WBC, white blood cell

In terms of underlying conditions, approximately half of patients with KPLA had diabetes mellitus (DM), with 28 (68.7%) patients with IKPLAS and 77 (46.1%) patients with NIKPLAS ($p = 0.01$). Among patients with extrahepatic complications, DM was found in 62.5% of patients with endophthalmitis, 77.8% of patients with lung abscesses, and 37.5% of patients with CNS infections. Yet, only 51 (24.5%) patients with KPLA had biliary diseases or a history of intra-abdominal surgery, with no statistical difference between the IKPLAS and NIKPLAS groups (all $p > 0.05$).

The general symptoms did not differ between IKPLAS and NIKPLAS. Yet, patients with IKPLAS were more likely to have symptoms involving other organ systems (85.4% vs. 22.8%, $p<0.001$) (Table 1). In patients with IKPLAS, 16 patients presented ocular symptoms ($p<0.001$), with 100% (16/16) of them diagnosed with endophthalmitis; 11 patients presented neurological symptoms ($p=0.012$), with 54.5% (6/11) of them diagnosed with CNS infections; and 19 patients presented with pulmonary symptoms ($p<0.001$), with 89.5% (17/19) of them having lung abscess or septic pulmonary embolism (Table S2).

Patients with KPLA typically presented with elevated white blood cell counts, neutrophil percentages, and markedly increased CRP levels (all $p>0.05$) (Table 1). In comparison, more patients in the IKPLAS group had a PCT ≥ 10 ng/mL than in the NIKPLAS group (58.1% vs. 35.1%, $p=0.02$). Patients with IKPLAS had lower ALT (median 38 U/L) and albumin levels (median 28.68 g/L) than those with NIKPLAS (median 52 U/L and 31.22 g/L, respectively) ($p=0.03$ and $p=0.01$, respectively). Conversely, patients with IKPLAS had significantly higher D-dimer levels (median 4.23 vs. 2.38 μg/mL) and percentages of SOFA ≥ 4 (39.0% vs. 14.4%) than those with NIKPLAS ($p=0.03$ and $p<0.001$, respectively).

The maximal diameter of liver abscesses was 6.10 (4.50, 7.80) cm in the IKPLAS group and 6.75 (4.90, 8.73) cm in the NIKPLAS group. IKPLAS mostly manifested as single (35/41, 85.4%) abscesses in the right lobe (32/41, 78.0%), and infrequently gas-containing abscesses (3/39, 7.7%) (Table 1). However, the above imaging findings did not differ significantly between the two groups (all $p>0.05$).

Multivariable logistic regression analysis showed that symptoms in other organ systems (OR = 7.08, $p=0.001$) and SOFA ≥ 4 within 48 h of admission (OR = 5.14, $p=0.002$) were significantly associated with IKPLAS (Table 2).

**Table 2** Multivariable logistic regression analysis of risk factors for IKPLAS

| Variables | OR (95%CI) | *P*-value |
|---|---|---|
| Symptoms in other organ systems [a] | 7.08 (2.24, 22.37) | 0.001* |
| Diabetes mellitus | 0.88 (0.28, 2.73) | 0.82 |
| Alb (g/L) | 0.94 (0.84, 1.04) | 0.23 |
| ALT (U/L) | 0.99 (0.98, 1.004) | 0.15 |
| D-dimer (μg/mL) | 0.98 (0.87, 1.10) | 0.75 |
| PCT ≥ 10 (ng/mL) | 1.09 (0.32, 3.70) | 0.89 |
| SOFA ≥ 4 [b] | 5.14 (1.85, 14.25) | 0.002* |

Notes: *$P<0.05$, statistically significant results; [a] Symptoms in other organ systems, including ocular, pulmonary, or neurological symptoms; [b] SOFA ≥ 4, assessed within 48 h of admission

Abbreviation: Alb, albumin; ALT, alanine transaminase; CI, confidence interval; PCT, procalcitonin; OR, Odds ratios; SOFA, sequential organ failure assessment

### Microbiologic characterization of *Klebsiella pneumoniae*

Pus and/or blood cultures were collected in all the patients. In this study, 200 patients with KPLA had positive cultures results, while *Klebsiella pneumoniae* was detected by mNGS in 8 patients with negative culture results (Figure S1). Among the patients with positive culture results, only 192 patients with KPLA had complete drug sensitivity results, including 32 with IKPLAS and 160 with NIKPLAS.

There was no significant difference in the antimicrobial susceptibility pattern of the *Klebsiella pneumoniae* isolates from the IKPLAS and NIKPLAS groups (all $P>0.05$) (Table 3). In the IKPLAS group, a broad spectrum of antibiotics, including cephalosporins (except for cefazolin), quinolones, carbapenems, aminoglycosides, and β-lactamase inhibitor combination antibiotics, exhibited a susceptibility rate exceeding 90% for KP isolates. However, for KP isolates in the NIKPLAS group, the sensitivity rate of certain antibiotics, such as cefuroxime, cotrimoxazole, and ciprofloxacin, was below 90%. In patients with KPLA, the susceptibility rate of KP isolates to tigecycline is relatively low, at only 62%. For KP isolates in the NIKPLAS group, tigecycline exhibited a lower sensitivity rate than those in the IKPLAS group (60.0% vs. 71.9%).

In patients with KPLA, drug-resistant KP strains were detected, including CR strains (2.6%, 5/192) and MDR strains (3.6%, 7/192) (Table 3). All resistant strains were detected in the NIKPLAS group (all $p>0.05$).

### Complications and hospitalization conditions

Patients with IKPLAS appeared to have a higher risk of developing sepsis (46.3% vs. 36.5%, $p=0.25$), septic shock (19.5% vs. 9.0%, $p=0.10$), or MODS (17.1% vs. 6.0%, $p=0.02$) compared to those with NIKPLAS (Table 4). They were also more likely to be admitted to the Intensive Care Unit (ICU) (31.7% vs. 13.8%) and had longer ICU stays (median 14 days vs. 4 days) and hospital stays (median 22 days vs. 15 days) than those with NIKPLAS (all $p<0.05$).

Univariable logistic regression analysis showed that lower albumin levels, higher CRP levels, and PCT ≥ 10 ng/mL were associated with the development of MODS in patients with KPLA (Table S3). Multivariable logistic regression analysis revealed that PCT ≥ 10 ng/mL was the independent risk factor for MODS ($p=0.01$, OR = 18.40).

Before therapy, seventeen patients with IKPLAS developed disability due to metastatic infection. Among them, all 16 patients with endophthalmitis (16/16, 100.0%) experienced significant visual loss, and one patient with brain abscesses (1/4, 25.0%) developed right-sided hemiplegia. Of these patients with endophthalmitis, 87.5% (14/16) had monocular involvement, with the right eye being affected more frequently (9/14), while 12.5% (2/16)

**Table 3** Comparison of antibacterial susceptibility and resistance profiles between the IKPLAS and NIKPLAS groups

| Antibiotics | IKPLAS (*n* = 32) | | | NIKPLAS (*n* = 160) | | | *P*-value |
|---|---|---|---|---|---|---|---|
| | S | I | *R* | S | I | *R* | |
| Ampicillin | 0 (0.0%) | 0 (0.0%) | 32 (100.0%) | 0 (0.0%) | 0 (0.0%) | 160 (100.0%) | 1.000 |
| Ampicillin/sulbactam | 30 (93.8%) | 1 (3.1%) | 1 (3.1%) | 139 (86.9%) | 7 (4.4%) | 14 (8.7%) | 0.73 |
| Piperacillin/tazobactam | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 144 (90.0%) | 12 (7.5%) | 4 (2.5%) | 0.28 |
| Cefazolin | 28 (87.5%) | 3 (9.4%) | 1 (3.1%) | 136 (85.0%) | 14 (8.8%) | 10 (6.3%) | 0.92 |
| Cefoxitin | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 146 (91.3%) | 3 (1.9%) | 11 (6.9%) | 0.82 |
| Cefuroxime | 30 (93.7%) | 0 (0.0%) | 2 (6.3%) | 139 (86.9%) | 5 (3.1%) | 16 (10.0%) | 0.70 |
| Ceftazidime | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 151 (94.4%) | 1 (0.6%) | 8 (5.0%) | 1.000 |
| Cefotaxime | 30 (93.8%) | 1 (3.1%) | 1 (3.1%) | 148 (92.5%) | 3 (1.9%) | 9 (5.6%) | 0.70 |
| Cefoperazone/sulbactam | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 154 (96.2%) | 2 (1.3%) | 4 (2.5%) | 1.00 |
| Cefepime | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 151 (94.4%) | 0 (0.0%) | 9 (5.6%) | 0.89 |
| Amoxicillin/clavulanic acid | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 149 (93.1%) | 5 (3.1%) | 6 (3.8%) | 0.54 |
| Aztreonam | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 151 (94.4%) | 0 (0.0%) | 9 (5.6%) | 0.89 |
| Ciprofloxacin | 30 (93.8%) | 2 (6.2%) | 0 (0.0%) | 133 (83.1%) | 16 (10.0%) | 11 (6.9%) | 0.23 |
| Levofloxacin | 31 (96.9%) | 1 (3.1%) | 0 (0.0%) | 145 (90.6%) | 6 (3.8%) | 9 (5.6%) | 0.49 |
| Imipenem | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 156 (97.5%) | 1 (0.6%) | 3 (1.9%) | 1.00 |
| Meropenem | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 155 (96.9%) | 0 (0.0%) | 5 (3.1%) | 0.59 |
| Tobramycin | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 152 (95.0%) | 1 (0.6%) | 7 (4.4%) | 0.67 |
| Gentamycin | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 154 (96.2%) | 0 (0.0%) | 6 (3.8%) | 0.58 |
| Amikacin | 32 (100%) | 0 (0.0%) | 0 (0.0%) | 155 (96.9%) | 1 (0.6%) | 4 (2.5%) | 1.00 |
| Tigecycline | 23 (71.9%) | 9 (28.1%) | 0 (0.0%) | 96 (60.0%) | 55 (34.4%) | 9 (5.6%) | 0.26 |
| Cotrimoxazole | 31 (96.9%) | 0 (0.0%) | 1 (3.1%) | 143 (89.4%) | 3 (1.9%) | 14 (8.7%) | 0.70 |
| **Drug resistance** | **KPLA** (*n* = **192**) | | **IKPLAS** (*n* = **32**) | | **NIKPLAS** (*n* = **160**) | | **P-value** |
| MRD-KP | 7 (3.6%) | | 0 (0.0%) | | 7 (4.4%) | | 0.49 |
| CR-KP | 5 (2.6%) | | 0 (0.0%) | | 5 (3.1%) | | 0.59 |

Notes: The Chi-square test and Fisher's exact test were used for categorical variables; $^{*}P < 0.05$, statistically significant results

Abbreviations: CR, carbapenem-resistant; I, Intermediate; IKPLAS, invasive *Klebsiella pneumoniae* liver abscess syndrome; KP, *Klebsiella pneumoniae*; MDR, multidrug-resistant; NIKPLAS, non-invasive *Klebsiella pneumoniae* liver abscess syndrome; R, Resistant; S, Susceptible

**Table 4** Comparison of complications and hospitalizations in patients with IKPLAS and NIKPLAS

| Complications | KPLA (*n* = 208) | IKPLAS (*n* = 41) | NIKPLAS (*n* = 167) | *p*-value |
|---|---|---|---|---|
| Sepsis | 80 (38.5%) | 19 (46.3%) | 61 (36.5%) | 0.25 |
| Septic shock | 23 (11.1%) | 8 (19.5%) | 15 (9.0%) | 0.10 |
| MODS | 17 (8.2%) | 7 (17.1%) | 10 (6.0%) | 0.02* |
| **Hospitalization conditions** | | | | |
| ICU admissions | 36 (17.3%) | 13 (31.7%) | 23 (13.8%) | 0.01* |
| ICU length of stay (days) | 7 (3, 14) | 14 (7, 19) | 4 (3, 8) | 0.003* |
| Length of hospital stay [c] (days) | 16 (10, 24) | 22 (14, 31) | 15 (10, 22) | 0.002* |

Notes: Mann-Whitney U test was performed for continuous variables, and the Chi-square test was used for categorical variables; $^{*}P < 0.05$, statistically significant results; [c] Length of hospitalization, referring to the total days of first hospitalization for liver abscess, including ICU stays

Abbreviations: IKPLAS, invasive *Klebsiella pneumoniae* liver abscess syndrome; KPLA, *Klebsiella pneumoniae* liver abscess syndrome; ICU, intensive care unit; MODS, multiple organ dysfunction syndrome; NIKPLAS, non-invasive *Klebsiella pneumoniae* liver abscess syndrome

had bilateral involvement. In total, 18 eyes were affected by *Klebsiella pneumoniae* infection, with three eyes having no light perception and five eyes having only light perception (Table S4).

### Treatment and outcomes

The majority of patients with KPLA had percutaneous drainage (including percutaneous catheter drainage and percutaneous needle aspiration), with the NIKPLAS group having a comparatively higher rate ($p < 0.001$) (Table 5). Only one patient had surgical drainage for liver abscesses. There was no statistically significant association between treatment success and liver abscess drainage in the IKPLAS group ($P = 0.12$), as shown in Table S5. Similarly, no significant correlation was observed between treatment success and drainage in patients with liver abscesses ≥ 3 cm in diameter in the IKPLAS group ($p = 0.87$).

Regarding systemic antibiotics, β-lactamase inhibitor combination products and carbapenems were the main antibacterial agents for treating patients with KPLA. Compared with the NIKPLAS group, carbapenems and tigecycline were used more frequently in the IKPLAS group ($p = 0.01$ and $p = 0.04$, respectively). In contrast, ornidazole and cephalosporins/β-lactamase inhibitor combinations were used more often in the NIKPLAS group ($p = 0.03$ and $p = 0.002$, respectively). Eight patients with KPLA required ventilatory support, including seven with tracheal intubation and one with tracheostomy.

**Table 5** Treatment and outcome analysis of patients with IKPLAS and NIKPLAS

| Treatment | KPLA (*n* = 208) | IKPLAS (*n* = 41) | NIKPLAS (*n* = 167) | *p*-value |
|---|---|---|---|---|
| **Drainage** | | | | |
| Drainage by puncture | 192 (92.3%) | 31 (75.6%) | 161(96.4%) | < 0.001* |
| Percutaneous catheter drainage | 176 (84.6%) | 29 (70.7%) | 147 (88.0%) | |
| Percutaneous needle aspiration | 16 (7.7%) | 2 (4.9%) | 14 (8.4%) | |
| Drain by surgery | 1 (0.5%) | 0 (0.0%) | 1 (0.6%) | 1.00 |
| **Systemic antibiotics** | | | | |
| Cephalosporins | 22 (10.6%) | 3 (7.3%) | 19 (11.4%) | 0.45 |
| Fluoroquinolones | 68 (32.7%) | 13 (31.7%) | 55 (32.9%) | 0.88 |
| Carbapenems | 88 (42.3%) | 25 (61.0%) | 63 (37.7%) | 0.01* |
| Aminoglycosides | 3 (1.4%) | 1 (2.4%) | 2 (1.2%) | 0.49 |
| Tigecycline | 26 (12.5%) | 9(22.0%) | 17 (10.2%) | 0.04* |
| Ornidazole | 54 (26.0%) | 5 (12.2%) | 49 (29.3%) | 0.03* |
| Polymyxin | 4 (1.9%) | 2 (1.2%) | 2 (4.9%) | 0.18 |
| Cephalosporins/β-lactamase inhibitors | 107 (51.4%) | 12 (29.3%) | 95 (56.9%) | 0.002* |
| Piperacillin/tazobactam | 50 (24.0%) | 11 (26.8%) | 39 (23.4%) | 0.64 |
| **Invasive ventilator** | | | | |
| Tracheal intubation | 7 (3.4%) | 5 (12.2%) | 2 (1.2%) | 0.003* |
| Tracheostomy | 1 (0.5%) | 1 (2.4%) | 0 (0.0%) | 0.20 |
| **Outcomes** | | | | |
| Treatment success [d] | 185 (88.9%) | 20 (48.8%) | 165 (98.8%) | < 0.001* |
| Treatment abandonment [e] | 7 (3.4%) | 6 (14.6%) | 1(0.6%) | < 0.001* |
| Death | 1 (0.5%) | 0 (0.0%) | 1 (0.6%) | 1.00 |

Notes: The Chi-square test and Fisher's exact test were used for categorical variables; *$P < 0.05$, statistically significant results; [d] Treatment success, defined as complete resolution of symptoms and signs, normalization or near-normalization of abnormal laboratory findings, radiological evidence (ultrasound or CT) of complete absorption or significant reduction (≥ 50%) in liver abscess size without new abscess formation or dissemination of infection, and eradication of bacterial infection confirmed by two consecutive negative blood or pus cultures; [e] Treatment abandonment, referring to patients who chose to discontinue treatment and were discharged while in a catastrophic condition that did not improve despite aggressive treatment, with an unclear final outcome

Abbreviations: IKPLAS, invasive *Klebsiella pneumoniae* liver abscess syndrome; KPLA, *Klebsiella pneumoniae* liver abscess syndrome; NIKPLAS, non-invasive *Klebsiella pneumoniae* liver abscess syndrome

Tracheal intubation was more likely to occur in patients with IKPLAS (12.2% vs. 1.2%, $p = 0.003$), mainly in patients with metastatic infections involving the lungs and CNS.

Among eighteen eyes affected endophthalmitis, thirteen underwent vitrectomy, and one underwent enucleation. After vitrectomy, five eyes (5/13) had better visual prognosis (visual acuity > 0.01), and the visual acuity of two eyes remained unknown (Table S4).

In patients with IKPLAS, only 48.8% achieved treatment success, while 51.2% experienced treatment failure due to complications leading to irreversible disability or discontinuation of treatment (Table 5). In contrast, 98.8% of patients with NIKPLAS achieved treatment success ($p < 0.001$). Seven patients with KPLA abandoned treatment due to catastrophic and life-threatening conditions that did not improve despite aggressive treatment, and their outcomes remained unknown. This occurred more often in patients with IKPLAS (14.6% vs. 0.6%, $p < 0.001$). In the whole study, only one patient with NIKPLAS died, and no death was recorded in patients with IKPLAS (Table 5).

## Discussion

Despite its low prevalence, IKPLAS is a highly damaging and difficult-to-treat condition. Endophthalmitis and lung abscesses were the most common extrahepatic complications found in this study, followed by CNS infections. Patients with meningitis caused by *Klebsiella pneumoniae* are challenging to treat and have a high mortality rate [10]. In some patients, IKPLAS can lead to significant disability. In this study, almost all patients with endophthalmitis developed severe and irreversible visual loss, and one with brain abscess developed hemiplegia. For patients with IKPLAS, early detection and appropriate treatment are crucial, as they may improve unfavorable outcomes [25, 26].

IKPLAS should be considered when patients have symptoms involving other organ systems (such as ocular, pulmonary, and neurological symptoms) and SOFA scores ≥ 4 within 48 h of admission. If the patient with KPLA develops other symptoms, such as vision loss, cough with sputum, dyspnea, or consciousness disturbance, imaging of the corresponding organs or specialist examinations should be carried out promptly to clarify the presence of infections at distant sites. Early interdisciplinary consultation is essential if there is any suspicion of metastatic infection, which may contribute to early diagnosis and treatment [27].

The SOFA score is a crucial tool for estimating organ dysfunction and sepsis and allows for assessing the severity and prognosis of critically ill patients [28]. Feng et al. [17] showed that the SOFA score was a significant predictor of IKPLAS, which was confirmed in this study. This may be related to a higher risk of developing severe systemic infections and MODS in patients with IKPLAS. Consistently, this study revealed that IKPLAS may increase the risk for developing MODS, and a PCT level ≥ 10 ng/mL was identified as an independent risk factor for MODS. Furthermore, IKPLAS significantly increased the rate and length of ICU admissions, in

agreement with Qian et al. [29]. Although few patients with liver abscess required invasive mechanical ventilation, IKPLAS probably increased the patient's need for it. Lee et al. [9] also showed patients with metastatic infection had a higher risk of acute respiratory failure and acute respiratory distress syndrome.

Diabetic patients with KPLA are susceptible to metastatic infections [30]. However, in this study, DM was not demonstrated as an independent risk factor for IKPLAS. This finding may be attributable to the limited sample size of patients with IKPLAS. More importantly, DM with poor glycemic control may contribute to the development of the invasive syndrome [16, 31]. On the one hand, high glucose levels may selectively impair the phagocytosis and intracellular killing of K1/K2 KP serotypes by neutrophils [32]. On the other hand, hyperglycemia may enhance the expression of virulence-related genes in KP strains, thereby increasing their ability to resist phagocytosis and serum killing [33, 34]. As a result, strict monitoring and control of blood glucose levels may be necessary for diabetic patients with KPLA, which could help prevent the development of severe metastatic infections.

Some CT imaging features, such as thrombophlebitis, no rim enhancement, and gas-forming abscesses, were considered significant signs of extrahepatic metastatic infections [16, 31]. Moreover, smaller sizes of liver abscesses were significantly associated with IKPLAS [14, 15], probably because metastatic infections could occur in the early stages of KPLA [9]. However, this association was not confirmed in this study.

Our study showed that, although KP isolates from patients with liver abscesses were sensitive to most antibiotics, β-lactamase inhibitor combination products and carbapenems were frequently used to treat patients with KPLA in clinical practice. In order to delay the progression of drug-resistant strains, it's essential to strengthen the antimicrobial stewardship practice. The use of reserve antibiotics should be avoided to preserve the natural "wild-type" phenotype of KP strains for as long as possible [35, 36]. Furthermore, management of antimicrobial resistance in CR-KP strains is a major challenge for clinicians, as few effective antibiotics are available. For CR-KP infections, aminoglycosides (such as plazomicin), tetracyclines (such as eravacycline and tigecycline), and carbapenems in combination with novel β-lactamase inhibitors (such as meropenem-vaborbactam and imipenem-relebactam) may be considered [37]. However, the use of tigecycline may be limited in patients with KPLA. In this study, KP isolates exhibited relatively low susceptibility to tigecycline, with only 62% of isolates being susceptible.

In addition to antimicrobial therapy, vitrectomy is another important option for treating endophthalmitis. Early vitrectomy was associated with better final visual outcomes and significantly fewer eviscerations or enucleations [26]. However, there are controversial aspects to this finding [38]. The risk of retinal detachment makes vitrectomy a challenging procedure. Still, it is recommended that a vitrectomy should be considered if there is a poor response to antibiotic treatment within 48 h or if there is deterioration [39].

Our study has several limitations. First, the small sample size and the single-center, retrospective design of this study may limit the generalizability of the results. Additionally, some missing data points in this study may affect the accuracy of the findings. Therefore, multicenter, prospective, and larger-scale studies are required to further validate these results. Second, the number of research variables included in the study was relatively limited, which may have restricted the comprehensiveness of the analysis. This study did not examine the associations between IKPLAS and enhanced CT features, glycated hemoglobin, or fasting glucose.

## Conclusions

In summary, the presence of symptoms involving other organ systems, along with a SOFA score ≥ 4 within 48 h of admission, may facilitate the early detection of IKPLAS. Furthermore, this study elucidated the antimicrobial susceptibility profile of KP isolates from patients with liver abscesses, which may provide a reference for the rational and effective empirical antimicrobial treatment of patients with KPLA.

**Abbreviations**

| | |
|---|---|
| ALT | Alanine aminotransferase |
| Alb | Albumin |
| ALP | Alkaline phosphatase |
| AST | Aspartate aminotransferase |
| CRP | C-reactive protein |
| Cr | Creatinine |
| CI | Confidence interval |
| CNS | Central nervous system |
| CR | Carbapenem-resistant |
| CT | Computed tomography |
| DM | Diabetes mellitus |
| DNA | Deoxyribonucleic acid |
| eGFR | Estimated glomerular filtration rate |
| ESBL | Extended-spectrum β-lactamase |
| FIB | Fibrinogen |
| GGT | Glutamyl transpeptidase |
| Hb | Hemoglobin |
| IKPLAS | Invasive Klebsiella pneumoniae liver abscess syndrome |
| KP | Klebsiella pneumoniae |
| ICU | Intensive care unit |
| mNGS | Metagenomic next-generation sequencing |
| MODS | Multiple organ dysfunction syndrome |
| MDR | Multidrug-resistant |
| NEUT% | Neutrophil percentage |
| NIKPLAS | Non-invasive Klebsiella pneumoniae liver abscess syndrome |
| OR | Odds ratios |
| PCT | Procalcitonin |
| PLT | Platelet |
| SOFA | Sequential organ failure assessment |
| TBIL | Total bilirubin |

WBC White blood cell

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-10981-9.

Supplementary Material 1

**Acknowledgements**
Not applicable.

**Author contributions**
DX designed this study; GL, YW, and HW participated in data collection and analysis; LG drafted the manuscript; DX, YW, and HW critically revised the manuscript.

**Funding**
This study did not receive any funding.

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

## Declarations

**Ethics approval and consent to practice**
This study was carried out following the Declaration of Helsinki and approved by the Ethics Committee of Tongji Hospital, Huazhong University of Science and Technology (approval ID: TJ-IRB20231234), with informed consent waived due to the retrospective nature of this study.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

**Clinical trial**
Not applicable.

Received: 12 October 2024 / Accepted: 15 April 2025
Published online: 29 April 2025

**References**

1. Liu YC, Cheng DL, Lin CL. Klebsiella pneumoniae liver abscess associated with septic endophthalmitis. Arch Intern Med. 1986;146(10):1913–6.
2. Yin D, Ji C, Zhang S, Wang J, Lu Z, Song X, et al. Clinical characteristics and management of 1572 patients with pyogenic liver abscess: A 12-year retrospective study. Liver International: Official J Int Association Study Liver. 2021;41(4):810–8.
3. Chan KS, Chia CTW, Shelat VG, Demographics. Radiological findings, and clinical outcomes of Klebsiella pneumonia vs. Non-Klebsiella pneumoniae pyogenic liver abscess: A systematic review and Meta-Analysis with trial sequential analysis. Pathogens 2022; 11(9).
4. Lee JH, Jang YR, Ahn SJ, Choi SJ, Kim HS. A retrospective study of pyogenic liver abscess caused primarily by Klebsiella pneumoniae vs. non-Klebsiella pneumoniae: CT and clinical differentiation. Abdom Radiol (NY). 2020;45(9):2669–79.
5. Fang C-T, Lai S-Y, Yi W-C, Hsueh P-R, Liu K-L, Chang S-C. Klebsiella pneumoniae genotype K1: an emerging pathogen that causes septic ocular or central nervous system complications from pyogenic liver abscess. Clin Infect Dis. 2007;45(3):284–93.
6. Wang Y, Wang H, Liu Z, Chang Z. The Incidence of Septic Pulmonary Embolism in Patients with Klebsiella pneumoniae Liver Abscess: A Systematic Review and Meta-analysis. Gastroenterol Res Pract. 2022; 2022: 3777122.
7. Zhang CG, Wang Y, Duan M, Zhang XY, Chen XY. Klebsiella pneumoniae invasion syndrome: a case of liver abscess combined with lung abscess, endophthalmitis, and brain abscess. J Int Med Res. 2022;50(3):3000605221084881.
8. Hwang J-H, Lee SY, Lee J, Hwang J-H. Pyogenic spondylitis caused by Klebsiella pneumoniae: should the possibility of hypervirulent Klebsiella pneumoniae be considered? BMC Infect Dis. 2022;22(1):801.
9. Lee SS-J, Chen Y-S, Tsai H-C, Wann S-R, Lin H-H, Huang C-K, et al. Predictors of septic metastatic infection and mortality among patients with Klebsiella pneumoniae liver abscess. Clin Infect Dis. 2008;47(5):642–50.
10. Sun R, Zhang H, Xu Y, Zhu H, Yu X, Xu J. Klebsiella pneumoniae-related invasive liver abscess syndrome complicated by purulent meningitis: a review of the literature and description of three cases. BMC Infect Dis. 2021;21(1):15.
11. Chang Y, Chen J-H, Chen W-L, Chung J-Y. Klebsiella pneumoniae invasive syndrome with liver abscess and purulent meningitis presenting as acute hemiplegia: a case report. BMC Infect Dis. 2023;23(1):397.
12. Yang C-S, Tsai H-Y, Sung C-S, Lin K-H, Lee F-L, Hsu W-M. Endogenous Klebsiella endophthalmitis associated with pyogenic liver abscess. Ophthalmology. 2007;114(5):876–80.
13. Yang X, Sun Q, Li J, Jiang Y, Li Y, Lin J, et al. Molecular epidemiology of carbapenem-resistant hypervirulent Klebsiella pneumoniae in China. Emerg Microbes Infect. 2022;11(1):841–9.
14. Chang Z, Zheng J, Ma Y, Liu Z. Analysis of clinical and CT characteristics of patients with Klebsiella pneumoniae liver abscesses: an insight into risk factors of metastatic infection. Int J Infect Dis. 2015;33:50–4.
15. Shin SU, Park CM, Lee Y, Kim E-C, Kim SJ, Goo JM. Clinical and radiological features of invasive Klebsiella pneumoniae liver abscess syndrome. Acta Radiol. 2013;54(5):557–63.
16. Wang H, Guo Y, Yan B, Zhang Q, Pan T, Liu Z, et al. Development and validation of a prediction model based on clinical and CT features for invasiveness of K. pneumoniae liver abscess. Eur Radiol. 2022;32(9):6397–406.
17. Feng C, Di J, Jiang S, Li X, Hua F. Machine learning models for prediction of invasion Klebsiella pneumoniae liver abscess syndrome in diabetes mellitus: a singled centered retrospective study. BMC Infect Dis. 2023;23(1):284.
18. Clinical and Laboratory Standards Institute. M02 performance standards for antimicrobial disk susceptibility tests. 12th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2015.
19. Clinical and Laboratory Standards Institute. M02 performance standards for antimicrobial disk susceptibility tests. 13th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
20. Clinical and Laboratory Standards Institute. M100 performance standards for antimicrobial susceptibility testing. 32th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2022.
21. Food and Drug Administration. Antibacterial Susceptibility Test Interpretive Criteria. Available from: https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria. Accessed 15 March 2025.
22. Centers for Disease Control and Prevention. Antimicrobial resistance threats in the united States, 2021–2022. Atlanta, GA: U.S. Department of Health and Human Services; 2024.
23. Bolger AM, Lohse M, Usadel B. Trimmomatic: a flexible trimmer for illumina sequence data. Bioinformatics. 2014;30(15):2114–20.
24. Li H, Durbin R. Fast and accurate short read alignment with Burrows-Wheeler transform. Bioinformatics. 2009;25(14):1754–60.
25. Yonekawa Y, Chan RVP, Reddy AK, Pieroni CG, Lee TC, Lee S. Early intravitreal treatment of endogenous bacterial endophthalmitis. Clin Exp Ophthalmol. 2011;39(8):771–8.
26. Yonekawa Y, Chan RV, Reddy AK, Pieroni CG, Lee TC, Lee S. Early intravitreal treatment of endogenous bacterial endophthalmitis. Clin Exp Ophthalmol. 2011;39(8):771–8.
27. Serban D, Popa Cherecheanu A, Dascalu AM, Socea B, Vancea G, Stana D et al. Hypervirulent Klebsiella pneumoniae endogenous Endophthalmitis-A global emerging disease. Life (Basel) 2021; 11(7).
28. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001;286(14):1754–8.
29. Qian Y, Wong CC, Lai S, Chen H, He X, Sun L, 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.
30. Fung CP, Chang FY, Lee SC, Hu BS, Kuo BI, Liu CY, et al. A global emerging disease of Klebsiella pneumoniae liver abscess: is serotype K1 an important factor for complicated endophthalmitis? Gut. 2002;50(3):420–4.
31. Wang HH, Tsai SH, Yu CY, Hsu HH, Liu CH, Lin JC, et al. The association of haemoglobin $A_1C$ levels with the clinical and CT characteristics of Klebsiella

pneumoniae liver abscesses in patients with diabetes mellitus. Eur Radiol. 2014;24(5):980–9.
32. Lin J-C, Siu LK, Fung C-P, Tsou H-H, Wang J-J, Chen C-T, 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(8):3084–7.
33. Lee C-H, Chen IL, Chuah S-K, Tai W-C, Chang C-C, Chen F-J, et al. Impact of glycemic control on capsular polysaccharide biosynthesis and opsonophagocytosis of Klebsiella pneumoniae: implications for invasive syndrome in patients with diabetes mellitus. Virulence. 2016;7(7):770–8.
34. Tang L, Wang H, Cao K, Li Y, Li T, Huang Y, et al. Epidemiological features and impact of high glucose level on virulence gene expression and serum resistance of Klebsiella pneumoniae causing liver abscess in diabetic patients. Infect Drug Resist. 2023;16:1221–30.
35. Russo A, Fusco P, Morrone HL, Trecarichi EM, Torti C. New advances in management and treatment of multidrug-resistant Klebsiella pneumoniae. Expert Rev Anti Infect Ther. 2023;21(1):41–55.
36. Lei TY, Liao BB, Yang LR, Wang Y, Chen XB. Hypervirulent and carbapenem-resistant Klebsiella pneumoniae: A global public health threat. Microbiol Res. 2024;288:127839.
37. Theuretzbacher U. Global antimicrobial resistance in Gram-negative pathogens and clinical need. Curr Opin Microbiol. 2017;39:106–12.
38. Sheu S-J, Kung Y-H, Wu T-T, Chang F-P, Horng Y-H. Risk factors for endogenous endophthalmitis secondary to klebsiella pneumoniae liver abscess: 20-year experience in Southern Taiwan. Retina. 2011;31(10):2026–31.
39. Sadiq MA, Hassan M, Agarwal A, Sarwar S, Toufeeq S, Soliman MK, et al. Endogenous endophthalmitis: diagnosis, management, and prognosis. J Ophthalmic Inflamm Infect. 2015;5(1):32.

## Publisher's note