

Predictors of Septic Metastatic Infection and Mortality among Patients with *Klebsiella pneumoniae* Liver Abscess

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Background. Primary liver abscess caused by *Klebsiella pneumoniae* is an infection that is emerging worldwide and that is associated with severe morbidity and considerable mortality.

Methods. A retrospective analysis of 110 episodes of primary liver abscess caused by *K. pneumoniae* that required hospitalization during 2001–2002 was conducted to identify predictors of metastatic infection, mortality, and the efficacy of first-generation cephalosporins and percutaneous drainage. The potential role of *Klebsiella rmpA* and *magA* genes was also evaluated.

Results. The study included 59 men and 51 women, with a mean age of 61.8 years. Diabetes was noted in 67 patients (60.9%). Metastatic infection occurred in 17 patients (15.5%), with meningitis accounting for 11 patients (64.7%) and endophthalmitis accounting for 4 patients (23.5%). The overall mortality rate was 10.0% (11 patients). Most of the severe complications occurred within the first 3 days after hospital admission. Ninety-two patients (83.6%) received treatment with cefazolin for >3 days. Four patients (4.3%) of the group who received cefazolin had metastatic infection, 1 patient (1.1%) experienced septic shock, and 3 (3.3%) experienced acute respiratory failure. Five (5.4%) of those 92 patients died. Multivariable analysis revealed that *rmpA* (odds ratio [OR], 28.85), Acute Physiologic and Chronic Health Evaluation (APACHE) II score ≥ 20 (OR, 8.08), and septic shock (OR, 4.33) were statistically significant predictors of metastatic infection. Metastatic infection (OR, 6.73), severity of disease (APACHE II score ≥ 16 ; OR, 11.82), septic shock (OR, 8.30), acute respiratory failure (OR, 69.92), and gas formation revealed on imaging (OR, 13.26) predicted mortality. Pigtail drainage protected against both metastatic infection (OR, 0.25) and mortality (OR, 0.14).

Conclusion. Management of primary liver abscess caused by *K. pneumoniae* with use of first-generation cephalosporins and percutaneous drainage was associated with low rates of mortality, metastatic infection, and complications. These rates are comparable to those reported for third-generation cephalosporins.

Primary liver abscess caused by *Klebsiella pneumoniae* (KPLA) was first described in Taiwan in 1986 [1]. It currently accounts for ~78.5% of all liver abscesses in Taiwan [2, 3]. KPLA is being reported with increasing frequency in other countries in Southeast Asia, including Korea, Singapore, Japan, and Thailand [4–8], and

has become an emerging infectious disease in the United States and worldwide [9–14].

KPLA is often complicated by bacteremia, sepsis, and metastatic infection of the CNS, eye, and other sites [1, 15–17]. The rate of metastatic infection has a range of 3.5%–20% [5, 15, 16, 18]. The mortality rate has a range of 2.8%–10.8% [3, 18–22]. Diabetic persons are particularly susceptible [16, 18] and are predisposed to metastatic infection, including endophthalmitis [23, 24]. The most important *K. pneumoniae* virulence factors are heavy encapsulation of K1 and K2 strains; resistance to phagocytosis; the presence of *magA*, a capsule-associated virulence gene; and the presence of *rmpA*, a plasmid-mediated regulator of the extracellular polysaccharide synthesis [20, 25–30].

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The strains of *K. pneumoniae* that are associated with primary liver abscesses are susceptible to most antibiotics except aminopenicillins [31]. Optimal management includes the prompt administration of a cephalosporin and percutaneous drainage of the liver abscess with use of pigtail catheters [9, 18, 21]. There is currently considerable controversy about the treatment choice between use of a first- versus a third-generation cephalosporin [32]. The third-generation cephalosporins are purported to be more effective, because of their favorable penetration into the CNS and by reports from several uncontrolled retrospective studies [20, 32]. The standard antibiotic regimen used at our hospital for more than a decade is a combination of a first-generation cephalosporin (cefazolin) and an aminoglycoside (gentamicin) [18]. Third-generation cephalosporins are reserved for treatment of a subgroup of patients who develop meningitis or endophthalmitis.

The goals of the present retrospective analysis of 110 patients with KPLA were to identify the key host and microbial risk factors for sepsis, metastatic infection, and mortality and to determine whether the use of a first-generation cephalosporin at our hospital had efficacy comparable to that reported for third-generation cephalosporins. The data generated from this study will be used to design a prospective, comparative clinical trial of first- versus third-generation cephalosporins.

MATERIALS AND METHODS

Study population. The population consisted of all patients who were admitted to Kaohsiung Veterans General Hospital during a 2-year period (2001–2002) with a diagnosis of KPLA. Kaohsiung Veterans General Hospital is a 1200-bed, tertiary care teaching hospital located in southern Taiwan. A case was defined as the presence of ≥ 1 liver abscess, detected by sonography or CT, and culture-confirmed *K. pneumoniae* isolated from an abscess or blood. Age, sex, underlying diseases, clinical manifestations, laboratory findings, imaging, and management were determined by a retrospective analysis of the medical records. The major outcome measurements were severity of illness, occurrence and location of metastatic infection, and mortality.

Clinical and microbiological studies. The severity of illness was determined by the Acute Physiologic and Chronic Health Evaluation (APACHE) II score [33]. Septic shock was defined as sepsis associated with a systolic blood pressure decrease to <90 mm Hg and the need for intravenous hydration and vasopressors to maintain blood pressure. Acute respiratory failure was defined as the need for intubation with a mechanical ventilator. Location and severity of metastatic infection was determined by pertinent radiological and microbiological studies. Late complications were defined as metastatic infection, septic shock, acute respiratory failure requiring mechanical ventilation, and death occurring >72 h after presentation. The pres-

ence of *rmpA* and *magA* was determined by PCR of stored blood isolates of *K. pneumoniae* [34]. A modified string test was performed to detect the hypermucoviscosity phenotype [35].

Statistical analyses. Analyses were conducted using STATA, version 10.0 (STATA). Student's *t* test and the Wilcoxon rank-sum test were used for analysis of continuous variables. Categorical data were compared using Pearson's χ^2 test or Fisher's exact test. A *P* value $<.05$ was considered to be statistically significant. The cutoff for APACHE II score, to form a binary variable, was determined by using the receiver operator characteristic curve to predict mortality and metastatic infection. Logistic regression was used to analyze risk factors for metastatic infection and mortality. All variables with *P* values $<.10$ were included in the multivariate model. Diabetes mellitus (DM) was included in the multivariate model for metastatic infection, a priori. Forward selection with use of the likelihood-ratio test was used to select the final multivariate model for risk factors of metastatic infection and mortality.

RESULTS

Demographic characteristics. The demographic characteristics, underlying diseases, and clinical features of the 110 patients with KPLA are summarized in table 1. The population consisted predominantly of older, diabetic men. Other patients had hypertension (10 patients [9.1%]), coronary artery disease (10 [9.1%]), cerebrovascular diseases (6 [5.5%]), congestive heart failure (3 [2.7%]), chronic obstructive pulmonary disease (3 [2.7%]), and malignancy (8 [7.3%]). Most presented with fever, chills, and abdominal pain.

Laboratory and radiological studies. The laboratory, microbiological, and radiological findings and duration of hospitalization are summarized in table 1. At hospital admission, most patients had elevated or subnormal WBC, neutrophil, and platelet counts; increased band forms; increased levels of C-reactive protein and glucose; and abnormal results of liver function tests. Most of the liver abscesses were in the right lobe.

Univariate analysis revealed statistically significant differences between patients with and without metastasis for platelet counts ($P = .04$), alkaline phosphatase levels ($P = .03$), blood urea nitrogen levels ($P < .01$), and creatinine levels ($P = .01$). On multivariable analysis, there were no statistically significant differences for these variables.

Microbiological findings. *K. pneumoniae* was isolated from ≥ 1 site. Approximately two-thirds of the patients had bacteremia, and $>90\%$ had positive results from culture of liver aspirates (table 1). All but 2 isolates from 1 patient were susceptible to cefazolin (109 [99.1%] of 110 patients). All other isolates were susceptible to commonly used antibiotics, except ampicillin and piperacillin.

Forty-nine stored blood isolates were available for further

Table 1. Baseline characteristics, clinical manifestations, and microbiological findings of patients with primary liver abscess due to *Klebsiella pneumoniae* (n = 110).

Variable	Finding
Age, mean years \pm SD (range)	61.8 \pm 13.0 (33–86)
Characteristic	
Male sex	59 (53.6)
APACHE II score \geq 20	13 (11.8)
Diabetes mellitus	67 (60.9)
End-stage renal disease	5 (4.5)
Fever (body temperature \geq 38.3°C)	94 (85.5)
Chills	51 (46.4)
Abdominal pain and/or RUQ pain	50 (45.5)
RUQ tenderness on knocking	39 (35.5)
Altered mental status	16 (14.5)
Nausea and/or vomiting	14 (12.7)
General weakness	10 (9.1)
Laboratory finding	
WBC count \geq 10,000 cells/mm ³	74/109 (67.9)
Leukopenia (WBC count <4000 cells/mm ³)	8/109 (7.3)
Band percentage >5%	27/109 (24.8)
Neutrophil percentage >80%	75/105 (71.4)
Platelet count \leq 150,000 cells/mm ³	48/109 (44.0)
C-reactive protein level, ^a in mean mg/dL \pm SD (range)	27.5 \pm 17.5 (0.8–90.4)
SGPT level \geq 40 IU/mL	60/103 (58.3)
Alkaline phosphatase level >128 IU/mL	69/99 (69.7)
Serum creatinine level \geq 1.5 mg/dL	27/108 (25.0)
Glucose level \geq 200 mg/dL	57/109 (52.3)
Microbiological finding	
Bacteremia	66/108 (61.1)
Positive liver aspirate culture	88/95 (92.6)
<i>rmpA</i>	27/49 (55.1)
<i>magA</i>	21/49 (42.9)
Radiological imaging	
Abscess location	
Right lobe	64 (58.2)
Left lobe	33 (30.0)
Both lobes	13 (11.8)
Size of abscess, mean cm \pm SD (range)	5.3 \pm 2.9 (1.0–20.0)
Multiple abscesses	27 (24.6)
Gas formation in abscess	15 (13.6)
Immature abscess	38 (34.6)
Duration of clinical course, mean days \pm SD (range)	
Hospital stay	23.3 \pm 13.9 (1–111)
Time to defervescence	9.8 \pm 7.6 (0–49)

NOTE. Data are no. or proportion (%) of patients, unless otherwise indicated. APACHE, Acute Physiologic and Chronic Health Evaluation; RUQ, right upper quadrant; SGPT, serum alanine transaminase.

^a Data were available for 66 patients.

analysis. There were no statistically significant differences between the demographic characteristics, clinical manifestations, treatment management, and outcome of patients with these isolates, compared with that of the total study cohort. Twenty-seven (55.1%) and 21 (42.9%) of the blood isolates were found to carry *rmpA* and *magA*, respectively. Sixty-two percent of

isolates that had the *magA* gene also had the *rmpA* gene. Strains possessing *rmpA* were more prevalent among patients with metastatic infection than among those without (87.5% vs. 48.8%; $P = .06$). The hypermucoviscosity phenotype was detected in 26 strains (53.1%) and was not associated with the development of metastatic infection (19.2% vs 13.0%; $P = .71$) or death

(7.7% vs 8.7%; $P = 1.00$). The prevalence of *magA* in the hypermucoviscous strains was 42.3% (11 of 26 patients), and the prevalence of *rmpA* was 57.7% (15 patients).

Management. The initial antibiotic regimen consisted mostly of a combination of cefazolin and gentamicin (104 patients [94.5%]). Four patients (3.6%) who received a diagnosis of meningitis at hospital admission (including 1 with concomitant endophthalmitis) received a third-generation cephalosporin. Eighteen patients (16.4%) who were thought to have developed late metastatic infection were given treatment with third-generation cephalosporins. Seven of these patients were switched back to cefazolin after negative results of lumbar punctures. Pigtail drainage or aspiration of liver abscess was performed for 97 patients (88.2%). Early drainage was performed within the first 3 days after hospital admission for 76 patients (69.1%).

Complications. Complications included septic shock, acute respiratory failure requiring mechanical ventilation, and metastatic infections. Most of the severe complications occurred within the first 72 h after presentation. The rates of early and late complications are shown in table 2. Seventeen (15.5%) of the 110 patients had metastatic infections. Approximately one-third of these received a diagnosis of metastatic infection at the

time of presentation. Three-quarters were noted within 72 h after presentation. These 17 infections included meningitis (11 patients [64.7%]), endophthalmitis (4 [23.5%]), septic pulmonary emboli (5 [29.4%]), and other types (3 [17.6%]). Among the 4 patients with late metastatic infection, 2 had meningitis that became apparent on days 4 and 15 of hospitalization; 1 had endophthalmitis noted on day 6, and 1 had right-sided empyema noted on day 20.

Thirty-eight (34.5%) of the 110 patients developed severe complications (table 2). The overall mortality was 10% (11 patients), with an attributable mortality of 8.2% (9 of the 110 patients). Approximately one-half of the deaths (54.5% [6 patients]) occurred within the first 7 days. Nine (8.2%) were attributable to KPLA. Six patients died of septic shock (3 within 3 days and all within 8 days after hospital admission), 2 died of ischemic bowel disease, and 1 died of infection at the site of external ventricular drainage; 1 died of acute myocardial infection, and 1 died of ventricular arrhythmia. Ninety-two patients were given treatment with cefazolin for >3 days: of those, 4 patients (4.3%) had metastatic infection, 1 (1.1%) experienced septic shock, and 3 (3.3%) experienced acute respiratory failure. Five patients (5.4%) died.

Risk factors for metastatic infection. The characteristics of

Table 2. Overall rate of early and late complication of primary liver abscess due to *Klebsiella pneumoniae* (KPLA) ($n = 110$).

Complication or outcome	Overall	Presentation ^a	
		Early	Late ^b
Metastatic infection	17 (15.5)	13 (76.5)	4 (23.5)
CNS	11 (10.0)	9 (81.8)	2 (18.2)
Eye	4 (3.6)	3 (75.0)	1 (25.0)
CNS and eye	1 (0.9)	1 (100.0)	0 (0.0)
Lung	5 (4.5)	3 (60.0)	2 (40.0)
Other(s)	3 (2.7)	3 (100.0)	0 (0.0)
Severe complications			
Septic shock	28 (25.5)	27 (96.4)	1 (3.7)
ARF	15 (13.9)	12 (80.0)	3 (20.0)
ARDS	1 (0.9)	1 (100.0)	0 (0.0)
Septic shock or ARF	30 (27.3)
Septic shock, ARF, or metastatic infection	37 (33.6)
Septic shock, ARF, metastatic infection, or death	38 (34.5)
Mortality			
Overall	11 (10.0)	3 (27.3)	8 (72.7)
Attributable to KPLA ^c	9 (8.2)	3 (33.3)	6 (66.6)

NOTE. Data are no. (%) of patients. ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure requiring mechanical ventilation.

^a Early presentation, within 72 h after hospital admission; late presentation, >3 days after hospital admission.

^b The overall rates of late metastatic infection, septic shock, and mortality were 3.6%, 0.9%, and 7.3% (of 110 patients), respectively, and the rates were 4.3%, 1.1%, and 5.4%, respectively, of those (92 patients) who received cefazolin for >3 days.

^c Attributable death (i.e., due to KPLA) included septic shock (6 patients), ischemic bowel disease (2), and infection at the site of the external ventricular drain (1). Other deaths were due to acute myocardial infarction (1) and ventricular arrhythmia (1).

the 17 patients with metastatic infection are summarized in table 3. On univariate analysis, statistically significant risk factors for metastatic infection included higher APACHE II scores ($P < .01$); more-frequent development of severe complications ($P < .01$), including septic shock ($P = .001$), acute respiratory failure ($P < .01$), and acute respiratory distress syndrome ($P = .001$); and the presence of *ompA* ($P = .06$). On multivariate analysis, statistically significant risk factors were an APACHE II score ≥ 20 ($P < .01$) and septic shock ($P = .04$) (table 4). After controlling for age, sex, APACHE II score, DM, and pigtail drainage, *ompA* became a more statistically significant predictor of metastatic infection ($P = .03$). Pigtail drainage was protective ($P = .03$). The predictive values for metastatic infection are shown in table 5. An APACHE II score ≥ 20 , acute respiratory failure, and shock were the greatest positive predictive factors for metastatic infection at any site and for infection of the CNS or eye.

Mortality. On multivariate analysis, an APACHE II score ≥ 16 ($P < .01$), metastatic infection ($P = .02$), septic shock ($P = .05$), acute respiratory failure requiring ventilation ($P < .01$), and gas formation revealed on imaging ($P = .04$) were statistically significant predictors of death (table 6). Pigtail drainage protected against death ($P = .02$). Age, sex, DM, end-stage renal disease, an APACHE II score ≥ 20 , and septic shock were associated with gas formation revealed on imaging (data not shown). However, female sex ($P = .02$) and patient age of ≥ 70 years ($P = .04$) were the only factors that remained associated with gas formation revealed on imaging, after adjustment for age, sex, DM, end-stage renal disease, an APACHE II score ≥ 20 , and septic shock.

DM. Univariate analysis revealed that diabetic patients were more likely to have metastatic infection (19.4% vs. 9.3%; $P = .15$) and were more likely to die during hospitalization than were nondiabetic patients (13.4% vs. 4.7%; $P = .13$). Diabetic patients were statistically significantly older (mean age, 64.9 vs. 57.1 years; $P = .01$) and were more likely to have an APACHE II score ≥ 20 (17.9% vs. 2.3%; $P = .01$), septic shock (32.8% vs. 14.0%; $P = .03$), and gas formation revealed on imaging (22.4% and 4.7%; $P = .01$) than were nondiabetic patients. Multivariate logistic regression analysis, after controlling for age, sex, gas formation, APACHE II score, and septic shock, showed no statistically significant association between DM and metastatic infection (adjusted OR, 1.54; 95% CI, 0.33–7.08; $P = .58$) or death (adjusted OR, 1.39; 95% CI, 0.20–8.62; $P = .79$). There were also no statistically significant differences in severity of disease between diabetic patients and nondiabetic patients.

DISCUSSION

KPLA is associated with considerable mortality and severe complications, including metastatic infection affecting the CNS and

eye [1, 16, 18, 23]. Some authors advocate treatment with extended-spectrum cephalosporins instead of cefazolin, to optimize the outcome of KPLA, even though *K. pneumoniae* is susceptible to cefazolin [32]. In the current study, we found that 4.3% of patients who were given treatment with cefazolin and aminoglycosides for >3 days developed metastatic infection. The incidence of septic shock was 1.1%, the incidence of acute respiratory failure was 3.3%, and the incidence of mortality was 5.4%. These rates of metastatic infection, complications, and mortality are similar to those reported for patients given treatment with extended-spectrum cephalosporins [32]. In the current study, we found that metastatic infection can be predicted by severity of disease, as expressed by an APACHE II score ≥ 20 , septic shock, and the presence of the *ompA* virulence gene.

The majority of metastatic infections (76.5%) occurred within the first 72 h after presentation, during which time antibiotics treatment had not yet had time to become fully effective. Approximately one-third of patients included in the current study developed severe complications. This is comparable to the findings of a previous study [32]. In the current study, a higher percentage received a diagnosis of metastatic infection within the first 3 days after presentation (76.5% in the current study vs. 35.9% in a previous study [32]). One possibility is that these complications had already arisen at presentation. This implies that universal use of extended-spectrum cephalosporins will be ineffective in prevention of the occurrence of early complications. Prospective randomized, controlled clinical trials are needed to determine whether the use of extended-spectrum cephalosporins will effectively prevent metastatic infection among the remaining 23.5% of affected patients. An alternative strategy is to maintain high clinical vigilance for the development of these metastatic infections through early detection and management of high-risk patients.

The susceptibility of KPLA has not changed since it was first described >20 years ago [18, 31]. In the current study, the 1 strain (isolated from both blood and pus) that was resistant to cephalosporins was isolated from a patient who had been admitted to the hospital for treatment of urosepsis 1 month before sample testing. Both the in vitro susceptibility and clinical outcome in our study support the clinical practice of routinely using first-generation cephalosporins in combination with aminoglycosides as the initial antibiotic regimen for treatment of KPLA. First-generation cephalosporins have the advantage of lower cost and ready availability as first-line, unrestricted antibiotics.

This study also demonstrated that the occurrence of metastatic infection, clinical severity of disease (an APACHE II score ≥ 16 , septic shock, and acute respiratory failure), and gas formation revealed on imaging were statistically significant predictors of mortality among patients with KPLA. Patients with

Table 3. Characteristics of patients with metastatic infections associated with primary liver abscess due to *Klebsiella pneumoniae* ($n = 17$).

Patient	Age, years	Sex	Time until metastatic infection diagnosis, days	Infection(s) and/or infection site(s)	Underlying disease(s)	<i>mpA</i>	<i>magA</i>	Severe complication(s)	Initial antibiotic	Pigtail or aspiration	Cause of death	Outcome
1	62	M	0	Meningitis, endophthalmitis	DM	NA	NA	None	Cefpirome	Aspiration		Survived
2	42	M	0	Meningitis	AV block	+	+	None	Ceftriaxone	Aspiration		Survived
3	45	M	2	Meningitis, vertebral osteomyelitis, L2-L3, psoas muscle abscesses	COPD	NA	NA	None	Cefazolin	Pigtail		Survived
4	74	M	4	Meningitis, lung	DM	NA	NA	Septic shock	Cefazolin	Pigtail		Survived
5	75	F	0	Meningitis	DM, HTN, cholangiocarcinoma, aortic stenosis	+	–	Septic shock	Cefazolin	Pigtail		Survived
6	51	M	0	Meningitis	DM	–	+	Septic shock, ARF	Ceftizoxime	Pigtail		Survived
7	63	M	15	Meningitis	HTN, CAD	NA	NA	ARF	Cefazolin	Both	EVD infection	Died
8	66	F	1	Meningitis, SPE	DM, HTN with HCV, ESRD, CVA	NA	NA	Septic shock, ARF	Cefazolin	Pigtail	Septic shock	Died
9	72	M	2	Meningitis, SPE	DM, HTN, chronic renal insufficiency	NA	NA	Septic shock, ARF, ARDS	Penicillin	None	Septic shock	Died
10	66	M	1	Meningitis	DM	+	–	Septic shock, ARF	Cefazolin	Pigtail	Septic shock	Died
11	76	F	2	Meningitis	DM, HTN	NA	NA	Septic shock, ARF	Ceftizoxime	None	Septic shock	Died
12	44	F	1	Endophthalmitis, SPE, suspected meningitis	DM, HTN	NA	NA	None	Cefazolin	Pigtail		Survived
13	67	M	3	Endophthalmitis	IGT	+	+	None	Cefazolin	None		Survived
14	38	F	6	Endophthalmitis	DM, cervical cancer	+	–	Septic shock	Cefazolin	Pigtail		Survived
15	59	F	20	SPE, right-sided empyema	DM, cirrhosis, HCV-related, thyroid carcinoma	+	–	None	Cefazolin	Pigtail		Survived
16	74	M	0	Cellulitis of lower left leg	DM, HTN	+	+	None	Penicillin	Pigtail		Survived
17	72	M	0	Prostatic abscess	DM, CVA	NA	NA	Septic shock, ARF	Cefazolin	None	Septic shock	Died

NOTE. ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; AV, atrioventricular; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular disease; DM, diabetes mellitus; ESRD, end-stage renal disease; EVD, external ventricular drainage; HCV, hepatitis C virus; HCV, hypertensive vascular disease; HTN, hypertension; IGT, impaired glucose tolerance; L, lumbar spine; NA, not available; SPE, septic pulmonary emboli.

Table 4. Selected risk factors for metastatic infection among patients with primary liver abscess due to *Klebsiella pneumoniae* (n = 110).

Risk factor	Overall analysis		Adjusted analysis	
	Crude OR (95% CI)	P	Adjusted OR ^a (95% CI)	P
Age ≥64 years ^b	1.15 (0.41–3.24)	.79	0.76 (0.23–2.48)	.65
Male sex	1.72 (0.59–5.03)	.32	1.61 (0.48–5.40)	.44
APACHE II score ≥20 ^c	6.70 (1.90–23.58)	<.01	8.08 (1.87–35.00)	<.01
Diabetes mellitus	2.35 (0.71–7.75)	.16	1.75 (0.45–6.71)	.42
End-stage renal disease	1.39 (0.15–13.26)	.77	0.36 (0.03–5.11)	.45
Delay in presentation ^d	0.37 (0.10–1.39)	.14	0.33 (0.08–1.38)	.13
Septic shock	5.95 (1.99–17.78)	.001	4.33 (1.08–17.37)	.04
Acute respiratory failure	5.09 (1.52–17.06)	<.01	1.70 (0.33–8.73)	.52
<i>rmpA</i> (n = 49)	7.35 (0.83–65.21)	.07	28.85 (1.35–614.44)	.03
<i>magA</i> (n = 49)	1.47 (0.32–6.70)	.57	1.37 (0.24–7.96)	.72
Gas formation revealed on imaging	0.69 (0.14–3.35)	.65	0.46 (0.07–3.18)	.43
Pigtail drainage	0.30 (0.10–0.90)	.03	0.25 (0.07–0.87)	.03

^a Adjusted for age, sex, diabetes mellitus status, Acute Physiologic and Chronic Health Evaluation (APACHE) II score, and pigtail drainage.

^b Age cutoff was determined by the median age.

^c APACHE II score cutoff was determined by receiver operator characteristic curve for metastatic infection.

^d Delay was defined as duration of symptoms for ≥7 days before presentation.

metastatic infection had a high rate of severe complications (58.8%) and increased mortality (35.3%; $P < .01$). The higher rate of metastatic infections (15.5%), compared with those of other studies, and meningitis as the major type of metastatic infection (64.7%) may explain the greater overall mortality in the current series (10.0%) compared with that of others (6.5%) [32]. The major type of metastatic infection in the other studies was endophthalmitis [32, 36]. The mortality rate for *K. pneumoniae* meningitis had a range of 33.3%–48.5% reported in the literature [37, 38] and was 45.5% in our series.

Gas formation in the liver abscess, as revealed on imaging, has been reported to be associated with DM and increased mortality [39]. We also found that patients with gas formation were more likely to die (adjusted OR, 13.26; 95% CI, 1.20–146.41; $P = .04$); however, associations between DM and gas formation and death were not observed.

Percutaneous aspiration or pigtail drainage of the liver abscess in combination with antibiotics has become the main therapeutic modality for management of pyogenic liver abscesses [40, 41]. In our series, statistically significantly fewer patients with metastatic infection (58.8% vs. 82.8%; $P = .05$) or who died (45.5% vs. 82.8%; $P = .01$) had undergone pigtail drainage. This was because of the small size (<3 cm) or immaturity of many of the abscesses and the presence of multiple abscesses, which are not amenable to percutaneous pigtail drainage. Previous series reported high mortality rates associated with treatment with antibiotics alone and with multiple abscesses [40, 42]. In our series, percutaneous pigtail drainage protected against both metastatic infection (adjusted OR, 0.25; 95% CI, 0.07–0.87; $P = .03$) and mortality (adjusted OR, 0.14;

95% CI, 0.03–0.78; $P = .02$). The current study further supports the value of percutaneous pigtail drainage as the treatment of choice in the management of pyogenic liver abscess [41].

DM is a known risk factor for KPLA [9, 16, 18, 39]. The prevalence of DM in our series was 60.7%. There was a higher prevalence of DM among patients with metastatic infection (76.5% vs. 58.1%; $P = .15$) and among patients who died (81.8% vs. 58.6%; $P = .13$). There was a lower percentage of DM among those with positive results for *magA* (50.0% vs. 65.5%; $P = .28$). This supports the hypothesis that diabetic persons are more susceptible to invasion by non-K1/K2 isolates, which are considered to be less virulent than K1/K2 isolates [43].

The major strength of the current study is the large number

Table 5. Value of various clinical characteristics for prediction of metastatic infection.

Characteristic	Predictive value (%) of metastatic infection			
	Any site		CNS and/or eye	
	Negative	Positive	Negative	Positive
<i>rmpA</i>	95.5	25.9	95.5	18.5
Shock	91.5	35.7	93.9	32.1
Diabetes mellitus	90.7	19.4	90.7	14.9
APACHE II score ≥20	88.7	46.2	90.7	38.5
Acute respiratory failure	88.4	40.0	90.5	33.3
Gas revealed on imaging	84.9	11.8	88.4	11.8
Pigtail drainage	69.6	11.5	78.3	10.3
Pigtail drainage or aspiration	64.3	12.5	78.6	11.5

NOTE. APACHE, Acute Physiologic and Chronic Health Evaluation.

Table 6. Selected risk factors for mortality among patients with primary liver abscess due to *Klebsiella pneumoniae* (n = 110).

Risk factor	Overall analysis		Adjusted analysis	
	Crude OR (95% CI)	P	Adjusted OR ^a (95% CI)	P
Age ≥64 years ^b	2.95 (0.74–11.78)	.13	1.30 (0.22–7.73)	.78
Male sex	1.04 (0.30–3.64)	.95	0.60 (0.12–2.96)	.53
APACHE II score ≥16 ^c	11.58 (2.97–45.10)	<.001	11.82 (1.94–72.02)	<.01
Diabetes mellitus	3.18 (0.65–15.50)	.15	1.44 (0.21–9.65)	.71
End-stage renal disease	7.11 (1.05–48.27)	.05	6.37 (0.48–84.31)	.16
Delay in presentation ^d	0.72 (0.18–2.88)	.64	1.72 (0.26–11.37)	.58
Metastatic infection	9.60 (2.51–36.74)	.001	6.73 (1.39–32.63)	.02
Septic shock	10.53 (2.56–43.35)	.001	8.30 (1.02–67.37)	.05
Acute respiratory failure ^e	69.75 (12.24–397.55)	<.001	69.92 (4.74–834.39)	<.01
<i>rmpA</i> (n = 49)	0.80 (0.10–6.19)	.83	0.68 (0.06–8.25)	.76
<i>magA</i> (n = 49)	0.43 (0.04–4.49)	.51	0.79 (0.05–10.21)	.79
Gas formation on imaging	3.78 (0.97–14.73)	.06	13.26 (1.20–146.51)	.04
Pigtail drainage	0.16 (0.04–0.59)	<.01	0.14 (0.03–0.78)	.02

^a Adjusted for age, sex, Acute Physiologic and Chronic Health Evaluation (APACHE) II score, metastatic infection, and pigtail drainage.

^b Age cutoff was determined by the median age.

^c APACHE II score cutoff was determined by receiver operator characteristic curve for mortality.

^d Delay was defined as duration of symptoms for ≥7 days before presentation.

^e Requiring intubation and mechanical ventilation.

of patients who were given treatment in a single medical center over a relatively short time (2 years). The major limitations of the current study are that it was retrospective, that most patients received cefazolin and gentamicin, and that physicians were free to arbitrarily select third-generation cephalosporins for treatment. Prospective, randomized clinical trials are needed to determine whether third-generation cephalosporins are superior to cefazolin and gentamicin.

In conclusion, the current study demonstrates that the use of first-generation cephalosporins in combination with aminoglycosides and percutaneous pigtail drainage results in low rates of metastatic infection and complications. The majority of metastatic infections and complications were noted within the first 72 h after presentation. It is likely that those infections and complications had arisen by the time of presentation and were not preventable, regardless of the choice of antibiotics. We recommend that, until comparative trials are completed, extended-spectrum cephalosporins be targeted to patients with recognized risk factors that predict the occurrence of metastatic infection. First-generation cephalosporins appear to be effective in the absence of shock, acute respiratory failure, an APACHE II score ≥20, and the presence of the *rmpA* gene.

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