



ORIGINAL ARTICLE

Clinical characteristics and economic consequence of *Klebsiella pneumoniae* liver abscess in Taiwan



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Background: *Klebsiella pneumoniae* liver abscess (KPLA) has emerged as an endemic disease in Taiwan, and its prevalence has been increasing in east Asian countries in the past three decades. The utilization of healthcare resources associated with KPLA is assumed to be substantial, and may be of future concern. This study investigated the clinical characteristics and economic burden of KPLA in Taiwan in 2011 and 2012.

Methods: Adult patients with KPLA were identified retrospectively in a tertiary medical center in Taiwan from January 2011 to December 2012. The clinical characteristics, total and daily hospitalization expenditure, and the risk factors for the costs of KPLA were analyzed.

Results: Among patients with KPLA, the median cost was \$5290.80 in US dollars, and the mean cost was \$6337.50 ± \$4363.40. Length of hospital stay was the only independent risk factor for the high total hospitalization expenditure. The duration of antibiotic use was nearly the same as the length of hospital stay. The prolonged stay in the general ward (≥21 days) also contributed to the high total cost of hospitalization. The independent risk factors for the high average daily cost of hospitalization were a higher Charlson Comorbidity Index and the requirement of intensive care on admission.

Conclusion: The current study is the first to demonstrate the high economic burden resulting from KPLA in a medical center in Taiwan. Standardizing the treatment protocol for KPLA

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inpatients and introducing an outpatient parenteral antimicrobial therapy center to reduce the length of stay may reduce costs, whereas development of a vaccine may be necessary to tackle endemic KPLA in the future.

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Introduction

Pyogenic liver abscess is a common disease in Taiwan,¹ and the annual incidence of 11.99–17.59 per 100,000 population² is substantially higher than in Western countries, such as Denmark,³ Canada,⁴ and the United States⁵ with annual incidences of 1.0, 2.3, and 2.7–4.1 per 100,000 population, respectively. In the past three decades, *Klebsiella pneumoniae* has emerged as the main cause of pyogenic liver abscess in Taiwan and other East Asian countries, especially Korea and Singapore,^{2,6–15} whereas *Streptococcus* species and *Escherichia coli* are the predominant cause of pyogenic liver abscess in Western countries.^{4,5} The increasing prevalence of *K. pneumoniae* liver abscess (KPLA), and the associated distinctive invasive syndrome complicated by endophthalmitis, central nervous system infection, and septic metastatic lesions in other organs have contributed to the endemic features of the disease in Taiwan.^{1,2,6–9,11,12,16–21}

The clinical and microbiological characteristics of KPLA in Taiwan have been widely studied in the past three decades.^{2,6,7,9,11–14,18–26} The mortality rate of KPLA seemed to be decreasing in recent years in Taiwan because of increased physician awareness.^{2,22} However, concerns remain over the metastatic complications of KPLA,^{9,12,17–20,22} the long hospital stay,^{2,6,9,13,14} and the associated illness requiring critical care.²⁴ In addition, some patients experience major disability and poor long-term prognosis because of ocular or neurological complications arising from KPLA.¹⁷ As a result of the endemic features of KPLA in Taiwan, the associated utilization of healthcare resources is assumed to be substantial, but the economic burden of KPLA in Taiwan has never been determined.

In the current study, we aimed to investigate the clinical characteristics of KPLA and the associated economic consequence in a medical center in northern Taiwan in 2011 and 2012.

Methods

Study population

This retrospective cohort analysis was conducted at a 2900-bed tertiary medical center, Taipei Veterans General Hospital, from January 2011 to December 2012. In patients enrolled in this study, the diagnosis of KPLA was made by the presence of liver abscesses on abdominal ultrasonography or computed tomography, plus identification of the infectious organism isolated from liver pus or blood as *K. pneumoniae*. Patients younger than 20 years were excluded from the study. The study was approved by the

Institution Review Board of Taipei Veterans General Hospital.

Data collection

Patient medical records were reviewed by clinicians, and microbiological results of the liver abscess or blood were acquired from the Department of Microbiology in our hospital. Data on age, sex, underlying diseases, Charlson Comorbidity Index, clinical presentations, laboratory findings, Acute Physiology and Chronic Health Evaluation (APACHE) II scores within 48 hours after admission, origin and nature of the liver abscesses, radiological images, and patient management were collected. The unavailable parameters of APACHE II score were considered as within normal limits if there was no strong indication to measure within 48 hours after admission. The outcome measurements were: the requirement of intensive care on admission; the length of hospitalization; total expenditure related to KPLA, including emergency department costs; average daily hospital expenditure; and in-hospital mortality. A liver abscess of cryptogenic origin was defined as one in which no obvious extrahepatic source of infection could be identified and there was no underlying hepatobiliary disease.²¹ A liver abscess of biliary tract origin was defined when clinical features of cholecystitis/cholangitis or extrahepatic biliary ductal abnormalities on radiographic images were identified.²¹ Septic metastatic infection was defined as a distant site of infection with the same pathogen (*K. pneumoniae*) as in the pyogenic liver abscess. Definitive antibiotic therapy was defined as initial and continuous administration of antibiotics after susceptibility testing of cultures was available.²⁷ If the patient received various antibiotics after the culture results were available, the antibiotic with the longest duration of administration was considered as the definitive therapy. According to the policy of the Department of Infection Control in our hospital, amoxicillin-clavulanate, ampicillin-sulbactam, and first- or second- generation cephalosporins were defined as first-line antibiotics. Cephamycins, third- or fourth-generation cephalosporins, fluoroquinolones, tigecycline, piperacillin-tazobactam, colistin, and all carbapenems were defined as second-line antibiotics. The prolonged hospitalization was defined as hospital stays ≥ 21 days. The prolonged stay in the general ward was defined as being hospitalized in the general ward ≥ 21 days.

Cost data analysis

The total hospitalization expenditure of each episode of KPLA was assessed from the hospital's perspective as

described in a previous article.²⁸ The average daily cost was also analyzed. All costs, including accommodation, physician rounds, nursing care, pharmacy, medications, laboratory procedures and operations, other true costs per item or service, and food, of each inpatient since admittance to the emergency department until discharge from hospital were included, and were extracted from the hospital database. Fixed costs (e.g., costs of buildings, equipment, and salaried labor) were not included. The costs were converted to 2011 US dollars (1 Taiwan dollar = 0.03 US dollar) according to the Foreign Exchange Regime of the Central Bank of the Republic of China (Taiwan).

Statistical analysis

Analysis of categorical data was performed by Chi-square test or Fisher exact test. Numerical data were analyzed by the two-tailed Student *t* test or Mann-Whitney *U* test. Two-sided *p* < 0.05 were considered significant. To determine the factors associated with high average daily and total hospitalization expenditure for KPLA, a logistic regression analysis was performed.

Results

Clinical characteristics and economic consequence of KPLA

During the study period, a diagnosis was made in a total of 153 patients with microbiological evidence of pyogenic liver abscess. The most common identified organism was *K. pneumoniae* (70%), followed by *E. coli* (14.4%), and *Enterococcus* species (4.6%). Finally, 107 patients in whom KPLA was diagnosed were enrolled. Three patients were excluded from the subsequent analysis because of distinct characteristics and exceedingly high costs during the same hospitalization. Two of these patients received targeted therapy for malignancy after resolution of the liver abscesses. The other patient developed a liver abscess after transhepatic arterial chemoembolization for hepatocellular carcinoma. Table 1 demonstrated the clinical characteristics and economic consequence of the remaining 104 patients with KPLA during the study period. The mean length of hospital stay was 25.0 ± 15.2 days. The duration of antibiotic use (mean, 24.3 ± 14.2 days) was nearly the same as length of hospital stay. All patients received antibiotics throughout nearly the whole hospitalization course except for three patients staying in the hospital for an additional 3 days after discontinuation of antibiotics. The lowest estimated hospitalization cost was \$1644.50, the highest cost was \$27,431.80, and the median cost was \$5290.80.

Potential predictive factors for the high total cost of KPLA

To identify the independent risk factors for increased hospitalization expenditure, we stratified the patients into high cost and non-high cost groups using the median cost (\$5246.30) as the cutoff point. Three patients who died

Table 1 Clinical characteristics and economic consequence of 104 patients with *Klebsiella pneumoniae* liver abscess in Taiwan.

Characteristics	No. (%)
Male	72 (69.2)
Age, y	63.7 ± 15.9
Underlying disease	
Diabetes mellitus	51 (49.0)
Malignancy	13 (12.5)
Alcoholism	7 (6.7)
Chronic kidney disease ^a	5 (4.8)
Liver cirrhosis	4 (3.8)
Congestive heart failure	7 (6.7)
Chronic lung disease	5 (4.8)
Charlson Comorbidity Index	2.6 ± 2.0
Origin of liver abscess	
Cryptogenic	77 (74.0)
Biliary tract origin	27 (26.0)
Abscess location	
Right lobe	78 (75.0)
Left lobe	11 (10.6)
Both lobes	15 (14.4)
Abscess size, cm	
<5	46 (44.2)
≥5	58 (55.8)
Treatment	
Antibiotics + drainage	90 (86.5)
Antibiotics + operation	4 (3.8)
Antibiotics only	10 (9.6)
Metastatic infections	5 (4.8)
APACHE II score	14.0 ± 6.6
Length of hospital stay, d	25.0 ± 15.2
Duration of antibiotic use, d	24.3 ± 14.2
Requirement of intensive care on admission	23 (22.1)
Mortality rate	3 (2.9)
Total hospitalization cost (\$)	6337.5 ± 4363.4
Average daily hospitalization cost (\$)	280.9 ± 281.1

^a Baseline serum creatinine ≥2 mg/dL.

Data are presented as mean ± standard deviation or frequency with percentage (%).

APACHE = Acute Physiology and Chronic Health Evaluation.

were excluded from the analysis because of possible bias in the cost of hospitalization. One of these patients died within 24 hours after admission with very low cost of hospitalization, and two died from terminal cancer. Logistic regression analysis revealed that longer length of hospital stay [odds ratio (OR) 1.44; 95% confidence interval (CI), 1.24–1.67; *p* < 0.001] was the only independent risk factor for the high total cost of hospitalization (Table 2).

We further analyzed whether prolonged stay in the general ward (≥21 days) contributed to the high total cost of hospitalization. The variable “length of hospital stay” was replaced by prolonged stay in the general ward in the statistical analysis. Logistic regression analysis revealed that prolonged stay in the general ward was as well the independent predictor for the high total cost of hospitalization (OR 39.94; 95% CI 10.40–153.40, *p* < 0.001).

Table 2 Analysis of potential risk factors for the high cost of hospitalization from *Klebsiella pneumoniae* liver abscess in a tertiary care hospital in northern Taiwan.

Factor	Non-high cost of hospitalization	High cost of hospitalization	Univariate	Multivariate analysis	
	(n = 50) n (%)	(n = 51) n (%)	p	Odds ratio (95% CI)	p
Male	33 (66.0)	38 (74.5)	0.351	1.55 (0.33–7.25)	0.576
Age (y)	61.5 ± 15.2	65.8 ± 16.3	0.172	1.02 (0.98–1.07)	0.319
Charlson Comorbidity Index	2.4 ± 2.0	2.5 ± 1.6	0.887	—	—
Underlying disease					
Diabetes	24 (48.0)	24 (47.1)	0.925	—	—
Malignancy	7 (14.0)	4 (7.8)	0.327	—	—
Alcoholism	3 (6.0)	4 (7.8)	0.716	—	—
Chronic kidney disease ^a	2 (4.0)	3 (5.9)	0.665	—	—
Liver cirrhosis	2 (4.0)	2 (3.9)	0.984	—	—
Congestive heart failure	2 (4.0)	5 (9.8)	0.266	—	—
Chronic lung disease	3 (6.0)	2 (3.9)	0.633	—	—
Cryptogenic	38 (76.0)	38 (74.5)	0.862	—	—
Abscess in both lobes	6 (12.0)	8 (15.7)	0.593	—	—
Abscess size ≥5 cm	26 (52.0)	29 (56.9)	0.624	—	—
Treatment					
Antibiotics + drainage	42 (84.0)	47 (92.2)	0.539	—	—
Antibiotics + operation	0 (0.0)	4 (7.8)	—	—	—
Antibiotics only	6 (12.0)	2 (3.9)	0.152	—	—
Definitive treatment with 2 nd line antibiotics	34 (68.0)	38 (74.5)	0.470	—	—
Metastatic infections	0 (0.0)	4 (7.8)	—	—	—
APACHE II score ≥15	14 (28.0)	30 (58.8)	0.002	5.00 (0.74–33.67)	0.098
Requirement of intensive care on admission	5 (10.0)	17 (33.3)	0.007	2.79 (0.29–26.91)	0.374
Length of hospital stay, d	16.2 ± 5.2	34.1 ± 16.5	<0.001	1.44 (1.24–1.67)	<0.001
Prolonged stay in the general ward	8 (16.0)	41 (80.4)	<0.001	39.94 (10.40–153.40)	<0.001

^a Baseline serum creatinine ≥2 mg/dL.

Data are presented as mean ± standard deviation or frequency with percentage (%). APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval.

Potential predictive factors for prolonged hospitalization of KPLA

Table 3 showed the univariate analysis for the risk factors for prolonged hospitalization (≥21 days). A higher APACHE II score and the requirement of intensive care on admission seem to predispose for prolonged hospitalization, but they did not reach statistical significance in the logistic regression model. We further determined the risk factors for prolonged stay in the general ward and did not find the risk factors predisposing to prolonged stay in the general ward, as shown in Table 4.

Potential predictive factors for the high average daily cost of KPLA

For identifying the independent risk factors for increased hospitalization expenditure, the patients with KPLA were stratified into high and non-high average daily cost groups using the median average daily cost (\$249.40) as the cutoff point (Table 5). Logistic regression analysis revealed that a

higher Charlson Comorbidity Index (OR 1.49; 95% CI, 1.11–1.99; $p = 0.007$) and the requirement of intensive care on admission (OR 5.99; 95% CI, 1.65–21.71; $p = 0.006$) were the independent risk factors for the high average daily cost of hospitalization.

Discussion

K. pneumoniae is the predominant pathogen of pyogenic liver abscess in Taiwan, and is responsible for the endemic nature of this disease.² This study was the first to demonstrate the clinical characteristics and the economic consequences of KPLA in Taiwan in recent years. Our study showed that the only independent risk factor for the high total cost of hospitalization was the length of hospital stay. The independent risk factors for the high average daily cost of hospitalization were a higher Charlson Comorbidity Index and the requirement of intensive care on admission.

Kang and Hwang²⁹ have described the in-hospital costs of all cases of pyogenic liver abscess in 2007 in Taiwan using the National Health Insurance Research Database. Patients aged 65 years or older had a significantly higher mean cost

Table 3 Analysis of risk factors for prolonged hospitalization of patients with *Klebsiella pneumoniae* liver abscess in a tertiary care hospital in northern Taiwan.

Factor	Length of hospitalization <21 days (n = 45) n (%)	Length of hospitalization ≥21 days (n = 56) n (%)	p
Male	30 (66.7)	41 (73.2)	0.475
Age, y	62.1 ± 15.2	65.0 ± 16.4	0.371
Underlying disease			
Diabetes mellitus	21 (46.7)	27 (48.2)	0.877
Malignancy	7 (15.6)	4 (7.1)	0.187
Alcoholism	3 (6.7)	4 (7.1)	0.925
Chronic kidney disease ^a	3 (6.7)	2 (3.6)	0.483
Liver cirrhosis	2 (4.4)	2 (3.6)	0.823
Congestive heart failure	3 (6.7)	4 (7.1)	0.925
Chronic lung disease	3 (6.7)	2 (3.6)	0.483
Charlson Comorbidity Index	2.6 ± 2.0	2.3 ± 1.6	0.376
Origin of liver abscess			
Cryptogenic	33 (73.3)	43 (76.8)	0.690
Biliary tract origin	12 (26.7)	13 (23.2)	
Abscess location			
Right lobe	34 (75.6)	43 (76.8)	0.932
Left lobe	5 (11.1)	5 (8.9)	
Both lobes	6 (13.3)	8 (14.3)	
Abscess size, cm			
<5	23 (51.1)	23 (41.1)	0.315
≥5	22 (48.9)	33 (58.9)	
Treatment			
Antibiotics + drainage	38 (84.4)	49 (87.5)	0.659
Antibiotics + operation	0 (0)	4 (7.1)	
Antibiotics only	7 (15.6)	3 (5.4)	0.102
Definitive antibiotic use			
1st line antibiotics	16 (35.6)	13 (23.2)	0.176
2nd line antibiotics	29 (64.4)	43 (76.8)	
Metastatic infections	0 (0)	4 (7.1)	
APACHE II score	12.2 ± 6.3	15.3 ± 6.7	0.021
Requirement of intensive care on admission	6 (13.3)	16 (28.6)	0.071

^a Baseline serum creatinine ≥2 mg/dL.

Data are presented as mean ± standard deviation or frequency with percentage (%).

APACHE = Acute Physiology and Chronic Health Evaluation.

of hospitalization than those aged younger than 65 years (\$3082.10 ± \$3014.30 vs. \$2594.70 ± \$2457.90, $p < 0.001$). However, the mean cost of patients with KPLA in our hospital was \$6337.50 during 2011–2012, which was markedly higher than that determined from the 2007 nationwide population-based data. We also did not find that age 65 years or older was associated with higher costs. The low mortality resulting from improved diagnosis and management of KPLA in recent years has undoubtedly led to the increased healthcare expenditure for this disease. The high healthcare expenditure of KPLA indicates that the economic burden will be an important issue in the future. In contrast to the previous study by Kang and Hwang²⁹ of pyogenic liver abscess, which did not include emergency department expenditure, the cost estimated in our study better reflects the overall economic burden of KPLA. Another possible reason for the differences was the different study population. Our hospital serves as a primary

care hospital and a tertiary referral medical center, and hence patients might be slightly skewed to the severe side. In addition, the mean hospital stays were 17.8 ± 11.4 days in patients aged 65 years and older and 16.5 ± 10.1 in patients aged younger than 65 years in the nationwide population-based study. The long mean duration of hospitalization in our study (25.0 ± 15.2 days) likely contributes to the higher cost of the disease in our study. Last, the nationwide population-based study enrolled all liver abscess cases, not limiting to KPLA as the current study, and this may have contributed to the different results.

The only independent risk factor for the high total cost of hospitalization in the current study was the length of hospital stay. Previous research in Taiwan described variable durations of hospital stay for KPLA. Tsai et al² reported a mean KPLA hospitalization of 26.1 ± 16.4 days in a medical center in northern Taiwan during 1996–2004. In a medical center in central Taiwan, the mean hospital stay

Table 4 Analysis of risk factors for prolonged stay in the general ward of patients with *Klebsiella pneumoniae* liver abscess in a tertiary care hospital in northern Taiwan.

Factor	Length of hospitalization in the general ward <21 days (n = 52) n (%)	Length of hospitalization in the general ward ≥21 days (n = 49) n (%)	p
Male	36 (69.2)	35 (71.4)	0.809
Age, y	62.6 ± 16.0	64.9 ± 15.7	0.461
Underlying disease			
Diabetes mellitus	25 (48.1)	23 (46.9)	0.909
Malignancy	7 (13.5)	4 (8.2)	0.397
Alcoholism	4 (7.7)	3 (6.1)	0.757
Chronic kidney disease ^a	3 (5.8)	2 (4.1)	0.697
Liver cirrhosis	2 (3.8)	2 (4.1)	0.952
Congestive heart failure	3 (5.8)	4 (8.2)	0.637
Chronic lung disease	4 (7.7)	1 (2.0)	0.223
Charlson Comorbidity Index	2.5 ± 2.0	2.4 ± 1.6	0.670
Origin of liver abscess			
Cryptogenic	38 (73.1)	38 (77.6)	0.603
Biliary tract origin	14 (26.9)	11 (22.4)	
Abscess location			
Right lobe	38 (73.1)	39 (79.6)	0.738
Left lobe	6 (11.5)	4 (8.2)	
Both lobes	8 (15.4)	6 (12.2)	
Abscess size, cm			
<5	25 (48.1)	21 (42.9)	0.599
≥5	27 (51.9)	28 (57.1)	
Treatment			
Antibiotics + drainage	47 (90.4)	42 (85.7)	0.471
Antibiotics + operation	0 (0)	4 (8.2)	
Antibiotics only	5 (9.6)	3 (6.1)	0.519
Definitive antibiotic use			
1st line antibiotics	19 (36.5)	10 (20.4)	0.077
2nd line antibiotics	33 (63.5)	39 (79.6)	
Metastatic infections	1 (1.9)	3 (6.1)	0.305
APACHE II score	12.9 ± 6.3	15.0 ± 6.9	0.103
Requirement of intensive care on admission	10 (19.2)	12 (24.5)	0.523

^a Baseline serum creatinine ≥2 mg/dL.

Data are presented as mean ± standard deviation.

APACHE = Acute Physiology and Chronic Health Evaluation.

was 38.5 ± 21.6 days between January 1996 and April 2002 in the study by Yang et al,⁶ and the median hospitalization time was 19 days between July 2000 and June 2005 in the study by Chen et al¹⁴ Chan et al¹³ reported a mean length of stay of 17.4 ± 8.7 days in a medical center in southern Taiwan between January 2000 and June 2003, whereas Lee et al⁹ reported a mean length of stay of 23.3 ± 13.9 days in another medical center in southern Taiwan during 2001–2002. Antibiotic treatment for pyogenic liver abscess usually involves 2–3 weeks of parenteral administration followed by oral antibiotics to complete a total course of 4–6 weeks.^{30,31} How to reduce the duration of hospitalization is a challenge we face in the modern era of KPLA management.

In Singapore, *K. pneumoniae* is also the most common organism isolated from patients with pyogenic liver abscess.¹⁰ In Singapore, Chan et al¹⁰ conducted a prospective cohort study of all cases of KPLA treated from 2005 to 2011

at two outpatient parenteral antimicrobial therapy (OPAT) centers to assess the safety and efficacy of this treatment. The mean length of hospital stay was 15 ± 10 days, which was lower than in previous studies in Taiwan.^{6,9,13,14} They concluded that the management of KPLA via OPAT using a standardized protocol is a safe and effective alternative to inpatient intravenous antibiotics. In the current study, the duration of antibiotic use was nearly the same as hospitalization days. We cannot exploit the length of stay in the intensive care unit ward because of the high disease severity. The prolonged stay in the general ward was the independent risk factor for the high total cost. Therefore, adoption of OPAT to reduce the length of stay may be one of the ways to tackle the problem in Taiwan in the future.

The independent risk factors for a high average daily cost of hospitalization in the current study were a higher Charlson Comorbidity Index and the requirement of intensive care on admission. KPLA is a notable community-

Table 5 Analysis of potential risk factors for the high average daily cost of hospitalization from *Klebsiella pneumoniae* liver abscess in a tertiary care hospital in northern Taiwan.

Factor	Non-high average daily cost of hospitalization	High average daily cost of hospitalization	Univariate analysis	Multivariate analysis	
	<i>n</i> = 50 <i>n</i> (%)	<i>n</i> = 51 <i>n</i> (%)	<i>p</i>	Odds ratio (95% CI)	<i>p</i>
Male	36 (72.0)	35 (68.6)	0.711	1.05 (0.39–2.82)	0.917
Age, y	61.5 ± 16.5	65.8 ± 15.0	0.172	1.01 (0.98–1.04)	0.402
Charlson Comorbidity Index	1.9 ± 1.5	3.0 ± 1.9	0.004	1.49 (1.11–1.99)	0.007
Underlying disease					
Diabetes	23 (46.0)	25 (49.0)	0.761		
Malignancy	2 (4.0)	9 (17.6)	0.043		
Alcoholism	5 (10.0)	2 (3.9)	0.245		
Chronic kidney disease ^a	1 (2.0)	4 (7.8)	0.209		
Liver cirrhosis	3 (6.0)	1 (2.0)	0.322		
Congestive heart failure	2 (4.0)	5 (9.8)	0.266		
Chronic lung disease	2 (4.0)	3 (5.9)	0.665		
Cryptogenic	38 (76.0)	38 (74.5)	0.862		
Abscess in right hepatic lobes	36 (72.0)	41 (80.4)	0.324		
Abscess size ≥5 cm	26 (52.0)	29 (56.9)	0.624		
Treatment					
Antibiotics + drainage	42 (84.0)	47 (92.2)	0.214		
Antibiotics + operation	2 (4.0)	2 (3.9)	0.984		
Antibiotics only	6 (12.0)	2 (3.9)	0.152		
Definitive treatment with 2nd line antibiotics	33 (66.0)	39 (76.5)	0.247		
Metastatic infections	2 (4.0)	2 (3.9)	0.984		
APACHE II score ≥15	16 (32.0)	28 (54.9)	0.022	1.09 (0.41–2.96)	0.859
Length of hospital stay, d	25.7 ± 15.4	24.8 ± 15.1	0.781		
Requirement of intensive care on admission	5 (10.0)	17 (33.3)	0.007	5.99 (1.65–21.71)	0.006

^a Baseline serum creatinine ≥2 mg/dL.

Data are presented as mean ± standard deviation.

APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval.

acquired infection in Taiwan, and the high economic burden from KPLA due to the underlying comorbidities and disease severity is an unavoidable problem in Taiwan. Lin et al.³² conducted a population-based, cross-sectional study, using National Health Insurance administrative claims data in Taiwan to study the cost of community-acquired pneumonia during 2002–2004. The mean cost per patient with pneumonia was \$1957.00, which was markedly lower than the mean cost per patient of KPLA of \$6337.50 in our study. In view of this high economic burden and the increasing prevalence of KPLA in Taiwan, development of a vaccine for prophylaxis of KPLA, especially in a high-risk population, may be an important consideration for the future.

There are some limitations to our retrospective study. First, this was a hospital-based study. All data were collected from medical records, and the study population was restricted to patients from a tertiary medical center in northern Taiwan. Second, the cost data were only available in 2011 and 2012, and further longer follow-up is necessary to better determine the economic burden of KPLA. Despite these limitations, our study is believed to be the first to determine the hospitalization cost of KPLA in Taiwan.

In conclusion, the current study for the first time demonstrated the high economic burden of KPLA in our

hospital. The only independent risk factor for a high total cost of hospitalization was the length of hospital stay. The duration of antibiotic use was nearly the same as length of hospital stay. The prolonged stay in the general ward (≥21 days) also contributed to the high total cost of hospitalization. The economic burden of KPLA undoubtedly will be a challenge in the future in Taiwan. Therefore, standardizing the inpatient treatment protocol and introducing an outpatient parenteral antimicrobial therapy center for KPLA patients to reduce the length of stay are necessary in Taiwan. Development of a vaccine for high risk patients may also be necessary to tackle endemic KPLA in the future.

Conflicts of interest

The authors declare that they have no financial or nonfinancial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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