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ORIGINAL ARTICLE

Epidemiology and clinical outcome of pyogenic liver abscess: an analysis from the National Health Insurance Research Database of Taiwan, 2000–2011

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Background: The epidemiology of pyogenic liver abscess continues to change and the issue of antimicrobial therapy is controversial. This study investigated the epidemiology and clinical outcomes of antimicrobial therapy.
Methods: The annual incidence rates, demographic data, underlying diseases, complications, length of stay, mortality rates, and antimicrobial therapy were analyzed using the data retrieved from the Longitudinal Health Insurance Database 2000, Taiwan, from 2000 to 2011.
Results: The annual incidence of pyogenic liver abscess for all age groups increased gradually in Taiwan from 10.83 per 100,000 person-years in 2000 to 15.45 per 100,000 person-years in 2011. Pyogenic liver abscess occurred more commonly in patients with male sex, of older age (>50 years), and lower family income. Among the 1522 adult patients with pyogenic liver abscess, 537 (35.3%) patients had diabetes mellitus, 165 (10.8%) patients had complications, 234 (15.4%) patients received mechanical ventilation, and 361 (23.7%) patients had a stay in intensive care; the mortality rate was 8.2% (125/1522). There were 426 (28%) patients treated with cefazolin and 158 (10.4%) patients treated with extended-spectrum cephalosporins. There were no statistically significant differences in the length of stay and mortality rates between these two groups (20.2 days vs. 23.1 days; and 7.5% vs. 10.1%, respectively).
Conclusion: The clinical outcomes of pyogenic liver abscess treated with cefazolin were

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comparable to those treated by extended-spectrum cephalosporins. Extended-spectrum cephalosporins should be used for severe complications, such as meningitis and endophthalmitis. Further surveillance of epidemiology and cohort analysis of antimicrobial therapy are important.

Introduction

Pyogenic liver abscess is usually a complication of biliary tract disease, and *Escherichia coli* is the most common pathogen of liver abscess in the world.[1–3] Liver abscess in Taiwan is caused mainly (~69–78%) by *Klebsiella pneumoniae*,[4,5] and has become an endemic disease during the past 3 decades since the first publication in Taiwan in 1986.[1,6–8] *K. pneumoniae* liver abscess is characterized by the high rates of metastatic infections (9.5–20.0%)[1,7,8] and mortality (6.0–11.3%),[8–10] and an association with diabetes mellitus (DM) (56.8–75.0%).[1,4,8]

A nationwide analysis of pyogenic liver abscess from the National Health Insurance Research Database (NHIRD) from 1996 through 2004 was published in 2008.[11] The annual incidence of pyogenic liver abscess increased from 11.15/100,000 population in 1996 to 17.59/100,000 population in 2004.[11] The population-based abscess-related death increased slightly from 1.38/100,000 in 1996 to 1.80/100,000 in 2004.[11] There were 33.3% (9904/29,703) of patients with pyogenic liver abscess had DM.

Patients with liver abscess treated with cefazolin had a greater chance of developing complications (22/59, 37.3%) than those receiving extended-spectrum cephalosporins (3/48, 6.3%) ($p < 0.001$) in a previous study.[12] Four (4.3%) patients from the group who were treated with cefazolin had metastatic infections in another study.[10] The limitations of these two studies were that they did not include a sufficient number of patients to be stratified by severity of infection and to evaluate the clinical efficacy. More large-scale studies are needed to determine whether extended-spectrum cephalosporins are superior to cefazolin.

The trends in the epidemiology of pyogenic liver abscess have changed gradually over the past 3 decades and antimicrobial therapy strategy remains in debate. This study was therefore conducted to evaluate the trend in epidemiology changes and to compare the clinical outcomes between two groups of patients treated with cefazolin or extended-spectrum cephalosporins by an analysis of the data retrieved from NHIRD, Taiwan, from 2000 to 2011.

Methods

Data sources: The National Health Insurance Research Database and Longitudinal Health Insurance Database 2000

The data used in this study were retrieved from the Longitudinal Health Insurance Database 2000 (LHID 2000) for the period of 2000–2011. LHID 2000 contains the reimbursement claims data of 1,000,000 beneficiaries, randomly sampled from the year 2000 Registry for Beneficiaries ($n = 23.75$ million) of the NHIRD. The NHIRD is managed and updated annually by the National Health Research Institute. The updated data in the NHIRD were provided by the Bureau of National Health Insurance, Department of Health, Taiwan.

Annual incidence and mortality

To avoid duplicate calculation due to transfer of patients between hospitals, only those newly-diagnosed patients who were hospitalized for pyogenic liver abscess for the first time were included for the calculation of incidence rate. The annual incidence rate of pyogenic liver abscess was defined as the number of newly-diagnosed patients with pyogenic liver abscess divided by the number of citizens in Taiwan in that year. The annual incidence rate included patients from all age groups. For the analysis of antimicrobial therapy, the adult patients with liver abscess were selected using the following two criteria: adult patients, ≥20 years old, admitted with a diagnosis of pyogenic liver abscess from January 1, 2000 to December 31, 2011; and a discharge diagnosis of ICD-9-CM 572.0 (abscess of the liver). Diagnoses of amebic liver abscess (ICD-9-CM 006.3) and injury to the liver (ICD-9-CM 864.00–ICD-9-CM 864.19) were excluded.

Hospital mortality was defined as death occurring in hospital or within 30 days after discharge.

Demographic variables

The following demographic characteristics of patients with liver abscess were analyzed. The ages were categorized into six groups: 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and ≥70 years. Urbanization of Taiwan was classified into four levels: 1 indicates the highest level of urbanization and 4 represents the lowest. Family income was ranked into four levels (in New Taiwan Dollars, NTD): 0, 1–15,840, 15,841–28,800, 28,801–45,800, and ≥45,801. Geographic areas of Taiwan were classified into northern, central, southern, and eastern. Occupations were divided into public and military, industry, business, low income, and others (including the retired).

Definition of comorbidities, complications, and antimicrobial therapy

The following comorbidities were analyzed: DM (ICD-9-CM 250), cirrhosis (ICD-9-CM 571.0–571.3, 571.5, and 571.6), cholelithiasis (ICD-9-CM 574), viral hepatitis including

hepatitis B (ICD-9-CM 070.2, 070.3, and V02.61) and hepatitis C (ICD-9-CM 070.41, 070.44, 070.51, 070.54, and V02.62), renal disease (ICD-9-CM 585 and 593.9), hepatocellular carcinoma (ICD-9-CM 155.0 and 155.2), other malignancies (ICD-9-CM 140—208.91) that exclude metastatic cancers (ICD-9-CM 196—199), and malignant neoplasms of ill-defined sites (ICD-9-CM 195).

The following infections related to liver abscess were defined as complications: endophthalmitis (ICD-9-CM 360.0), brain abscess (ICD-9-CM 324.0), intraspinal abscess (ICD-9-CM 324.1), bacterial meningitis (ICD-9-CM 320), lung abscess (ICD-9-CM 513), pneumonia (ICD-9-CM 480—486), acute respiratory distress syndrome (ICD-9-CM 518.5), osteomyelitis (ICD-9-CM 730), and abscess of the prostate (ICD-9-CM 601.0, 601.2, 601.8, and 601.9) during hospitalization.

The data relating to antimicrobial agents were retrieved from the LHID 2000 using the codes of the antibiotics from the National Health Insurance Administration Ministry of Health and Welfare website (http://www.nhi.gov.tw). Four groups of antimicrobial therapy were identified, i.e., cefazolin, extended-spectrum cephalosporins, cefazolin*extended-spectrum cephalosporins, and other antimicrobial agents. Cefazolin*extended-spectrum cephalosporins was used in the following two situations: cefazolin was used first as empiric therapy and then transited to extended-spectrum cephalosporins, or vice versa. The clinical outcomes between these four groups of patients were compared. The extended-spectrum cephalosporins included ceftriaxone, cefotaxime, ceftazidime, cefoperazone, and flomoxef. There were no available Acute Physiology, Age, Chronic Health Evaluation (APACHE) data in the NHIRD. The following three severe conditions of infection, i.e., complications, mechanic ventilation, and intensive care unit (ICU) stay, were therefore used instead to provide the risk stratification for severely ill hospitalized patients.

Statistical analysis

Student *t* test and analysis of variance were used for the analysis of continuous variables. Categorical data were compared by Chi-square test or Fisher's exact test. A $p < 0.05$ was considered to be statistically significant. All analyses were performed by SAS statistical software for Windows (version 9.3; SAS Institute, Inc., Cary, NC, USA).

Results

The annual incidence rates from 2000 to 2011 are shown in Table 1 and Fig. 1. The annual incidence of pyogenic liver abscess for all age groups increased gradually in Taiwan from 10.83 per 100,000 person-years in 2000 to 15.45 per 100,000 person-years in 2011. The average annual incidence of all age groups was 13.52 per 100,000 person-years during the period 2000—2011.

A total of 1522 adult patients with pyogenic liver abscess met the inclusion criteria and were enrolled in this study. The annual incidence of pyogenic liver abscess (for patients aged > 20 years) increased gradually from 14.82 per 100,000 person-years in 2000 to 16.03 per 100,000 person-years in 2011. The average annual incidence of patients >20 years was 14.59 per 100,000 person-years during the period of 2000—2011. There were only 10 patients with pyogenic liver abscess aged <20 years during the period being studied.

Table 1 The annual incidence and mortality of pyogenic liver abscess during the period 2000—2011 from the Longitudinal Health Insurance Database 2000, Taiwan

	All ages		Adults		
Year	*N*	Incidence[a]	*N*	Incidence[a]	Deaths
2000	107	10.83	105	14.82	13
2001	110	11.26	108	14.89	17
2002	136	14.07	135	18.14	12
2003	103	10.73	103	13.50	8
2004	136	14.26	135	17.33	12
2005	121	12.77	120	15.13	13
2006	148	15.73	146	18.12	7
2007	133	14.24	133	16.25	10
2008	123	13.27	122	14.67	9
2009	140	15.23	140	16.56	10
2010	135	14.80	135	15.72	5
2011	140	15.45	140	16.03	9
	1532[b]	13.52[c]	1522[b]	15.94[c]	125[d]

[a] Number per 100,000 person-years.
[b] Total number of patients with pyogenic liver abscess.
[c] Average annual incidence.
[d] Total number of deaths.

Table 2 shows the demographic characteristics of 1522 adult patients with newly-diagnosed liver abscesses. There were more men (63.6%) than woman (36.4%). The age at presentation ranged from 20.1 years to 96.1 years, with a mean age of 61.0 ± 15.1 years. It is worth noting that 76.8% of patients were ≧50 years old. The percentages of urbanization levels from 1 to 4 were 27.8%, 28.1%, 15.4%, and 28.6%, respectively. Patients with a family income of new NTD 15,841—28,800 accounted for the highest percentage (45.6%) of patients with pyogenic liver abscess. The percentages of patients with liver abscess in the northern (47.6%) and southern (30.9%) areas were greater than those in other geographic locations. Industry (43.2%) and business (26.0%) were the two most common occupations.

Table 3 shows the clinical characteristics of 1522 adult patients with liver abscess during the period 2000—2011. Among these individuals, the three most common underlying diseases were DM (35.3%), cholelithiasis (13.1%), and hepatocellular carcinoma (9.8%). Of the 1522 patients, 165 (10.8%) developed complications, 234 (15.4%) received mechanical ventilation, and 361 (23.7%) stayed in the ICU, with an average stay of 9.03 ± 12.5 days. The average length of stay in hospital (ALOS) was 20.9 ± 23.3 days. There were 596 (39.2%) patients with a length of stay (LOS) of ≤14 days, 646 (42.4%) patients with LOS of 15—28 days, and 280 (18.4%) patients with a LOS of ≥29 days. There were 426 (28.0%) patients treated with cefazolin and 158 (10.4%) were treated with extended-spectrum cephalosporins. The mortality rate was 8.2% (125/1522).

Among the 426 patients in the group treated with cefazolin, there were 25 (5.9%) patients with pneumonia, three (0.7%) patients with endophthalmitis, and one (0.2%) patient with meningitis. Among the 158 patients in the group

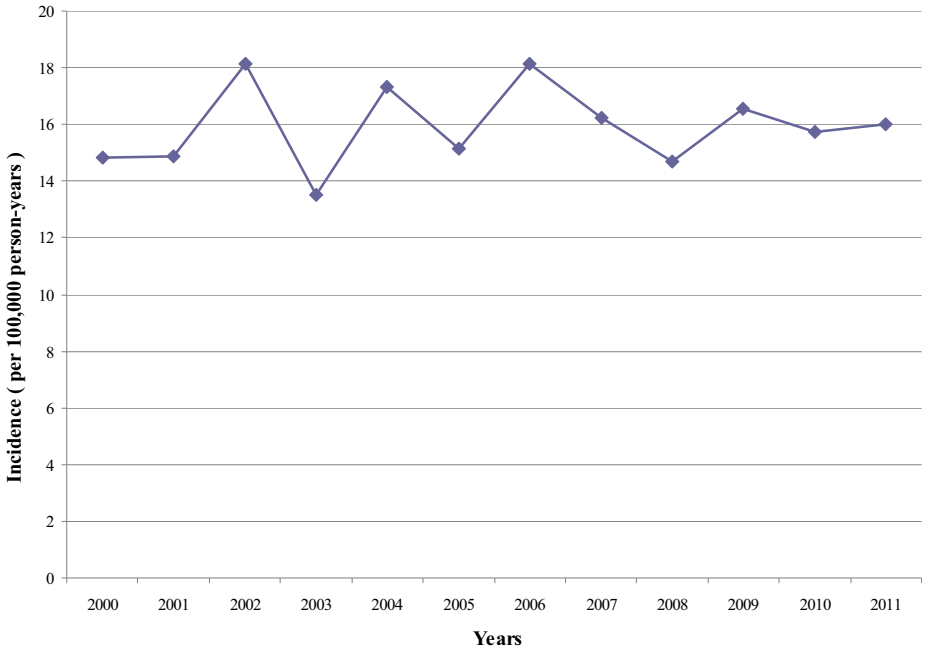

Figure 1. The incidence of pyogenic liver abscess per 100,000 population according to the Taiwan National Health Insurance Database during the period 2000—2011 (the Longitudinal Health Insurance Database 2000). The cases exclude individuals <20 years old.

treated with extended-spectrum cephalosporins, 27 (17.1%) had pneumonia, four (2.5%) had endophthalmitis and one (0.2%) had meningitis. Of the 79 patients treated with cefazolin*extended-spectrum cephalosporins, eight (10.1%) had pneumonia and five (6.3%) had endophthalmitis.

Table 4 compares the severity and clinical outcomes among the three groups of patients in the study. The complication rate of the 426 patients treated with cefazolin was lower than that of the 158 patients treated with extended-spectrum cephalosporins (8.0% vs. 20.9%, $p < 0.001$). There was no statistically significant difference in the use of mechanical ventilation between these two groups (14.6% vs. 20.9%, $p = 0.065$). The patients treated with cefazolin had a lower rate of ICU stay than those treated with extended-spectrum cephalosporins (18.3% vs. 37.3%, $p < 0.001$).

Although there was a statistically significant difference in the LOS among these three groups ($p = 0.004$), there was no significant difference in the LOS between the groups treated with cefazolin and extended-spectrum cephalosporins (20.2 $\pm$ 30.9 days vs. 23.1 $\pm$ 19.7 days). There was no significant difference in the mortality of these two groups of patients.

Table 5 lists the clinical outcomes of patients in the groups treated with cefazolin and extended-spectrum cephalosporins that had severe infections, including complications, mechanical ventilation, and ICU stay. Among the 67 patients with complications, 34 (50.7%) were treated with cefazolin and 33 (49.3%) were treated with extended-spectrum cephalosporin. There were no statistically significant differences in the ALOS (42.6 $\pm$ 100.0 days vs. 30.6 $\pm$ 29.8 days, $p = 0.508$) and mortality (20.6% vs. 18.2%, $p = 0.803$) between these two groups. Among the 95 patients who received mechanical ventilation, 62 (65.3%) were treated with cefazolin and 33 (34.7%) with extended-spectrum cephalosporin. These two groups had no statistically significant differences in the ALOS (32.2 $\pm$ 74.8 days vs. 30.9 $\pm$ 31.5 days, $p = 0.907$) or mortality (24.2% vs. 33.3%, $p = 0.341$). Of the 137 patients who had been admitted to ICU, 78 (56.9%) received cefazolin and 59 (43.1%) received extended-spectrum cephalosporin. There were no statistically significant differences in the ALOS (20.2 $\pm$ 14.1 days vs. 26.5 $\pm$ 25.4 days, $p = 0.091$) and mortality rate (24.4% vs. 20.3%, $p = 0.578$) of the two groups.

Discussion

In this study, the annual incidence of pyogenic liver abscess increased gradually in Taiwan from 10.83 per 100,000 person-years in 2000 to 15.45 per 100,000 person-years in 2011. The annual incidence rates of this disease are low in other countries, being 2.3 per 100,000 person-years in Canada from 1999 to 2003 according to population-based surveillance, for example.[13] In a nationwide study spanning a 26-year period in Denmark, the annual incidence rate of pyogenic liver abscess was 1.1 per 100,000 person-years from 1997 to 2002.[14]. The incidence of pyogenic liver abscess is much higher in Taiwan, which could be due to the spread of a pathogenic clone.[1] It has become an emerging infectious disease in Japan, Korea, and the United States.[15—19] How these international pathogenic clones are related remains to be clarified by molecular typing methods.

From the demographic data, there appear to be several variables that could increase the risk of developing pyogenic liver abscess. First, more males than females (63.6%

Table 2 Demographic data of 1522 patients with pyogenic liver abscess during the period 2000–2011 from the Longitudinal Health Insurance Database 2000, Taiwan

Sex, *n* (%)		
Female	554	(36.4)
Male	968	(63.6)
Age, y		
Mean (SD)	61.0	(15.1)
Range (median)	20.1–96.1	(61.5)
20–29	42	(2.8)
30–39	99	(6.5)
40–49	211	(13.9)
50–59	366	(24.0)
60–69	320	(21.0)
≥70	484	(31.8)
Urbanization[a]		
1	418	(27.8)
2	422	(28.1)
3	232	(15.4)
4	430	(28.6)
Family income (NTD[b])		
0	234	(15.5)
1–15,840	346	(22.7)
15,841–28,800	694	(45.6)
28,801–45,800	162	(10.6)
≥45,801	86	(5.7)
Area		
Northern	725	(47.6)
Central	288	(18.9)
Southern	471	(30.9)
Eastern	38	(2.5)
Occupation		
Public and military	97	(7.3)
Industry	577	(43.2)
Business	348	(26.0)
Low income	17	(1.3)
Others and retired	298	(22.3)

[a] Urbanization level: 1 indicates the highest level of urbanization and 4 the lowest.
[b] NTD = New Taiwan dollar.

vs. 36.4%) had such an abscess. Second, the incidence increased with age. Pyogenic liver abscess rarely occurred in children and adolescents; patients aged >50 years accounted for 76.8%. It is reasonable to assume that the elderly may have more comorbidities that predispose to pyogenic liver abscess. Third, pyogenic liver abscess occurred more commonly in patients with a lower monthly income. Patients with a monthly family income < NTD 28,800 accounted for 83.8% of patients with pyogenic liver abscess. Fourth, industry and business were the two most common occupations among patients with pyogenic liver abscess.

According to a number of studies, about 56.8–75.0% of patients with *K. pneumoniae* liver abscess had DM, and DM was considered a risk factor of this disease.[1,4,8] These are small-scale hospital-based studies, however, which could not reflect the exact percentage of DM. In the current study, the percentage of patients with DM was only 35.3%. This is similar to the finding of a recent study that retrieved data from the NHIRD, which showed that the percentage of DM in patients with pyogenic liver abscess was 33.3%.[11] In this study, 9.8% of patients with pyogenic liver abscess had hepatocellular carcinoma. In a population-based study using data from the NHIRD, the incidence of gastrointestinal cancer was 4.3-fold higher among patients with pyogenic liver abscess compared with controls (10.8/1000 person-years vs. 2.51/1000 person-years).[20] Similarly, another survey from the NHIRD reported that individuals with pyogenic liver abscess had a higher risk of liver cancer, biliary tract cancer, and colorectal cancer.[21] According to these large-scale population-based surveys, the evaluation of pyogenic liver abscess patients for hepatocellular cancer and colorectal cancer is an important new issue.

From population-based data from the NHIRD during the period 2000–2004,[11] of the 13,672 patients with pyogenic liver abscess, 155 (1.1%) had meningitis, 226 (1.7%) had endophthalmitis, 1141 (8.3%) had pneumonia, and 3252 (23.8%) had sepsis. Binary logistic regression analysis from the NHIRD from 1996 to 2004 found that underlying renal disease (odds ratio 2.45, 95% confidence interval 2.181–2.756; $p < 0.001$) and malignancy (odds ratio 2.136, 95% confidence interval 1.859–2.454; $p < 0.001$) increased the incidence and mortality rates of pyogenic liver abscess.[11]

Pyogenic liver abscess is a relatively common disease in Taiwan. It is well known that it should be treated by cephalosporin rather than carbapenem or fluoroquinolone; however, many patients cannot tolerate the adverse effects.[8,10,12] The clinical outcomes of treatment with

Table 3 Clinical characteristics of 1522 patients with pyogenic liver abscess during the period 2000–2011 from the Longitudinal Health Insurance Database 2000, Taiwan

Clinical characteristics	*n* (%)	
Underlying diseases		
Diabetes mellitus	537	(35.3)
Cirrhosis	99	(6.5)
Cholelithiasis	199	(13.1)
Viral hepatitis	93	(6.1)
Renal disease	26	(1.7)
Hepatocellular carcinoma	149	(9.8)
Other malignancies	83	(5.5)
Complications	165	(10.8)
Mechanical ventilation	234	(15.4)
Intensive care unit (ICU) stay	361	(23.7)
Length of ICU stay[a]	9.03 ± 12.5	
Length of stay[a]	20.9 ± 23.3	
Number of patients grouped by length of stay		
≤14 d	596	(39.2)
15–28 d	646	(42.4)
>28 d	280	(18.4)
Mortality	125	(8.2)
Antimicrobial therapy		
Cefazolin	426	(28.0)
Extended-spectrum cephalosporins	158	(10.4)
Cefazolin and extended-spectrum	79	(5.2)
Other	859	(56.4)

[a] Mean ± standard deviation, days.

Table 4 Comparison of severity and clinical outcomes among three treatment groups

Clinical characteristics	Cephalosporins						*p*
	Cefazolin ($n = 426$)		Extended-spectrum ($n = 158$)		Cefazolin*extended-spectrum cephalosporins ($n = 79$)		
	n	(%)	*n*	(%)	*n*	(%)	
Complications	34	(8.0)	33	(20.9)	15	(19.0)	<0.001[a]
Mechanical ventilation	62	(14.6)	33	(20.9)	20	(25.3)	0.027[a]
Intensive care unit (ICU) stay	78	(18.3)	59	(37.3)	30	(38.0)	<0.001[a]
Length of ICU stay[b]	6.13 ± 6.65		10.3 ± 15.0		10.1 ± 11.8		0.061[c]
Length of stay[b]	20.2 ± 30.9		23.1 ± 19.7		31.3 ± 21.9		0.004[c,d]
Number of patients grouped by length of stay							<0.001[a]
≤14 days	172	(40.4)	58	(36.7)	10	(12.7)	
15–28 days	185	(43.4)	65	(41.1)	39	(49.4)	
>28 days	69	(16.2)	35	(22.2)	30	(38.0)	
Mortality	32	(7.5)	16	(10.1)	10	(12.7)	0.259[a]

[a] *p* value was analyzed by *Chi*-square test.
[b] Mean ± SD, days.
[c] Analysis of variance.
[d] Difference between cefazolin group and cefazolin*extended-spectrum cephalosporin groups.

cefazolin were therefore compared with those of patients receiving extended-spectrum cephalosporins in this study. There were, however, 859 (56.4%) patients treated with other antimicrobial agents. There were several reasons for this finding, such as the preference for using carbapenem for sepsis, intolerance to adverse effects, superinfection with Enterobacteriaceae, resistance to cephalosporins, etc. We were unable to analyze these reasons by this retrospective study. The severe complications (such as infection of central nervous system, endophthalmitis, or superinfection by resistant microorganisms) should be treated by extended-spectrum cephalosporins, because of

Table 5 Comparison of clinical outcomes between two treatment groups in patients with severe pyogenic liver abscess (stratified by complications, mechanical ventilation, and intensive care unit stay)

Basal characteristic	Cephalosporin				*p*
	Cefazolin		Extended-spectrum		
	n	(%)	*n*	(%)	
Complications	34		33		
Length of stay, mean ± SD, d	42.6 ± 100.0		30.6 ± 29.8		0.508[a]
Number of patients grouped by LOS					0.802[b]
≤14 d	9	(26.5)	10	(30.3)	
15–28 d	11	(32.4)	12	(36.4)	
>28 d	14	(41.2)	11	(33.3)	
Mortality	7	(20.6)	6	(18.2)	0.803[b]
Mechanical ventilation	62		33		
Length of stay, mean ± SD, d	32.2 ± 74.8		30.9 ± 31.5		0.907[a]
Number of patients grouped by LOS					0.931[b]
≤14 d	19	(30.7)	11	(33.3)	
15–28 d	23	(37.1)	11	(33.3)	
>28 d	20	(32.3)	11	(33.3)	
Mortality	15	(24.2)	11	(33.3)	0.341[b]
ICU stay, number of patients	78		59		
Length of stay, mean ± SD, d	20.2 ± 14.1		26.5 ± 25.4		0.091[a]
Number of patients grouped by LOS					0.536[b]
≤14 d	30	(38.5)	18	(30.5)	
15–28 d	32	(41.0)	25	(42.4)	
>28 d	16	(20.5)	16	(27.1)	
Mortality	19	(24.4)	12	(20.3)	0.578[b]

[a] Student *t* test.
[b] Chi-square test.
ICU= intensive care unit; LOS= length of stay; SD= standard deviation.

better penetration into the central nervous system.[12,22–25] This is well known by physicians of internal medicine and the use of cefazolin for the aforementioned condition is rare.

There were no statistically significant differences in the length of stay and mortality rates between the groups treated with cefazolin and extended-spectrum cephalosporins (20.2 days vs. 23.1 days; 7.5% vs. 10.1%, respectively). It was possible that patients with mild infections were treated with cefazolin and patients with severe infections were treated with extended-spectrum cephalosporins. However, even for the patients with severe infections, complications, mechanical ventilation, and ICU stay there were no significant differences in the length of stay and mortality rates. We should be cautious when interpreting this finding because this retrospective study did not stratify the severity of complications. Prospective randomized, controlled clinical trials are needed to clarify the optimal antimicrobial strategy for pyogenic live abscess in individuals with severe complications.

The overall mortality rate (8.2%) in this study was comparable to those (6–11.3%) of previous hospital-based studies[8–10] and that (10.3%) of a population-based study.[11] The complication rate (10.8%) in this study was comparable to those (9.5–20%) of previous hospital-based studies.[1,7,8]

A previous report showed that patients receiving cefazolin treatment had a significantly higher likelihood of developing severe complications than those on extended-spectrum cephalosporin treatment (37% vs. 6.3%, $p < 0.001$).[12] By contrast, low rates of metastatic infections (4.3%), complications (septic shock 1.1%, acute respiratory failure 3.3%), and mortality (5.4%) for patients treated with cefazolin and aminoglycosides for > 3 days were shown in another study.[10] The majority (76.5%) of metastatic infections occurred within the first 3 days after presentation, so they could not be attributed to treatment. The authors therefore recommend that extended-spectrum cephalosporins be targeted to patients with high risk factors for the occurrence of metastatic infections. Further large-scale control studies are needed to clarify the clinical outcomes of different treatment strategies.

There were some limitations in this study. First, because the data were sourced retrospectively from the NHIRD, the detailed data of severity of underlying diseases for each patient were lacking. We were unable to stratify the risk factors by APACHE score or determine the causes of death, such as inadequate drainage, comorbidities, complications, superinfection, etc. Second, there was only the expenditure on each antimicrobial agent available rather than dosage regimens or date of therapy in the NHIRD. We were therefore unable to analyze the duration and sequence of therapy for each antimicrobial agent. Third, the data from treatment groups were not stratified by combination of aminoglycosides, therefore the *in vivo* synergistic effect was unknown. Fourth, there were no microbiological data available in the NHIRD, therefore we were unable to analyze the clinical outcome of treatment for a single pathogen.

In conclusion, the clinical outcomes of pyogenic liver abscess treated with cefazolin were comparable to those treated by extended-spectrum cephalosporins. However, extended-spectrum cephalosporins should be used for severe complications, such as infection of central nervous system and endophthalmitis. Further surveillance of incidence, investigation of risk factors, and cohort analysis of antimicrobial therapy are important issues for this disease.

Conflicts of interest

All authors declare no conflicts of interest.

Acknowledgments

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