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Original Article

Impact of advanced age on inpatients with pyogenic liver abscess in Taiwan: A nationwide claim-based analysis

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Abstract

Background: Pyogenic liver abscess (PLA) is seen as an endemic disease in population of Taiwan. The impact of advanced age on inpatients with PLA remains unclear.
Methods: Data was collected and analyzed from claims of discharges by inpatients with PLA, using the National Health Insurance Research Database of 2007.
Results: A total of 2319 subjects and 2651 related discharges were enrolled, including 939 subjects/1077 discharges ≥65 years and 1380 subjects/1574 discharges <65 years. Subjects ≥65 years had significantly higher ratios of females to males, nephropathy, biliary tract diseases, liver cirrhosis and gastroenterological cancers than those <65 years. Hepatic/intra-hepatic duct cancers accounted for the most comorbid gastroenterological cancers. Discharged of subjects ≥65 years had longer hospital stays, more in-hospital death/critical discharge, and a higher ratio of acute low respiratory conditions (ALRC) and urological infections than those of subjects <65 years ($p < 0.05$). The inpatient costs for subjects ≥65 years were significantly higher than those for subjects age<65 years in blood products, hemodialysis and total hospitalization. Co-morbidities, such as nephropathy, biliary tract diseases, liver cirrhosis, gastroenterological cancers, ALRC and urological infections were predictive variables associated with age ≥65 years in patients with PLA, as were being female and in-hospital death/critical discharge. Nephropathy and gastroenterological cancers were predictive variables associated with poor prognosis (in-hospital death/critical discharge) in both PLA patients age < and ≥65 years ($p < 0.05$). Diabetes mellitus featured predominantly, but had no impact on distribution and prognosis.
Conclusion: Advanced age (≥65 years) had an impact on the aforementioned characteristics and predictive variables in inpatients with PLA. Physicians should pay attention and treat aged PLA patients with greater care, especially those cares with comorbid nephropathy or gastroenterological cancers.

Keywords: aged; ICD-9-CM code; odds ratio; predictive variables; pyogenic liver abscess

1. Introduction

With the improvement of public health, pyogenic liver abscess (PLA) has replaced amoebic infections as the major form of liver abscesses in developed countries. The characteristics of PLA and its epidemiological distributions differ geographically. For instance, the pathogenic distribution of PLA is subtly different between Asia and Europe.[1] The role of co-morbid diabetes mellitus in PLA has interesting controversies, as discovered by studies around the world.[2–4] Present evidence indicates a noticeable prevalence of PLA among the population in eastern Asia. In Taiwan, PLA has seen as an endemic disease.[5] Local urban and rural hospital-based studies have described some of its characteristics, such as a predominant

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ratio of diabetes mellitus, a high prevalence of *Klebsiella pneumoniae* infections, and some risk factors relating to mortality.[6–11]

The geriatric society and the accelerated aging of healthcare populations are inevitable worldwide. In Taiwan, the aging of society has been evident since 1993. The role of advanced age in PLA should be a significant issue. However, relevant information about the impact of advanced age on patients with PLA still remains limited due to studies being single hospital–based.[12–14] Using a nationwide database, the aim of our study was to analyze and understand the aforementioned issues.

2. Methods

2.1. Data source

Retrospective claim-based analyses were conducted. We collected claim data of discharges by inpatients with PLA from the National Health Insurance Research Database (NHIRD) for 2007. The NHIRD was maintained by the National Health Research Institute, Republic of China (Taiwan), which provided anonymous and encrypted claim data of National Health Insurance for local research institutes.[15] Under the authorization of NHIRD, we screened inpatients' claim data (DD2007.DAT) and collected discharges with major diagnosis of PLA by the International Classification of Diseases, the Ninth Revision Clinical Modification (ICD-9-CM), code 572.

2.2. Study design

Subjects' general data, co-morbidities, claims for charges and predictive variables were analyzed. We classified subjects and related discharges into 2 groups respectively by age $\geq$65 year. For results of hospitalization, we defined in-hospital death and critical discharge (discharge with pre-dying condition for home death) as poor prognosis. The in-hospital costs and details were calculated and converted to United States dollars (USD). The co-morbidities were screened by relevant ICD-9-CM codes. The chronic comorbidities included diabetes mellitus (250.x), nephropathy (580.x-589.x), biliary tract diseases (574.x-576.x), liver cirrhosis (571.5), and gastroenterological cancers (150.x-159.x), and were analyzed by counts of subjects. The acute comorbidities included acute low respiratory conditions (ALRC) (466.x, 480.x-487.x) and urological infections (590.x, 595.x, 597.x, 599.x, 601.x), and were analyzed by counts of discharges. We did not enroll viral/chronic hepatitis because of incomplete records of discharges and ICD coding.

2.3. Statistical analyses

Data in the text and tables are expressed as mean $\pm$ SD. SPSS software (SPSS version 17.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The independent *t*-test, x^2 test, trend x^2 test and multiple logistic regression analysis were used to assess statistical significance. The predictive variables associated with advanced age ($\geq$65 year) or poor prognosis were presented as odds ratio (OR) and 95% confidence interval (CI). A p value <0.05 was considered statistically significant (2-tailed test). Under the regulations of research ethics, this study was conducted with the approval of the National Health Research Institute, Republic of China (No. 99238).

3. Results

During 2007, 2319 patients with a major diagnosis of PLA contributed to a total of 2651 discharges, including 939 subjects/1077 discharges age $\geq$65 years and 1380 subjects/1574 discharges aged <65 years. The mean frequencies of admissions did not differ significantly between the two groups ($p = 0.658$ by independent *t*-test).

The subjects' demographic characteristics are shown in Table 1. Subjects $\geq$65 years included significantly more females, and had more chronic comorbidities of nephropathy, biliary tract diseases, liver cirrhosis, and gastroenterological cancers than those <65 years. Diabetes mellitus featured predominantly, but the distribution did not differ between the two groups. Among comorbid gastroenterological cancers, hepatic/intra-hepatic duct cancers (ICD-9-CM code 155; n = 106) were most numerous; colon cancers (code 153; n = 13) and gallbladder/extra-hepatic duct cancers (code 156; n = 11) ranked second and third, respectively.

Table 2 shows demographic characteristics of discharges made by patients with PLA. Subjects discharged at age $\geq$65 years had longer hospital stays, more in-hospital death/critical discharge, and a higher ratio of acute comorbidities such as ALRC and urological infections than did those discharged at <65 years. The majority of admissions were served by department of internal medicine, followed by surgery.

The in-hospital costs and details are shown in Table 3. Subjects discharged at age $\geq$65 years had significantly higher

Table 1
The demographic characteristics of subjects with pyogenic liver abscess as major diagnosis in 2007 ($n = 2319$).

Parameters	Subjects		p[a]
	Age $\geq$65 years ($n = 939$)	Age <65 years ($n = 1380$)	
Mean age (years)	74.8 ± 6.7	50.1 ± 10.4	
Mean frequency of admission (times)	1.2 ± 0.5	1.1 ± 0.3	0.658
Gender (male/female)	514/425	936/444	<0.001
Major chronic comorbidities			
Diabetes mellitus (yes/no)	355/584	553/827	0.279
Nephropathy (yes/no)	68/871	53/1327	<0.001
Biliary tract diseases (yes/no)	141/798	130/1250	<0.001
Liver cirrhosis (yes/no)	34/905	26/1354	0.011
Gastroenterological cancers (yes/no)	87/852	62/1318	<0.001

[a] Independent *t* test and x^2 test.

Table 2
The demographic characteristics of discharges made by subjects with pyogenic liver abscess as major diagnosis in 2007 ($n = 2651$).

Parameters	Discharges by subjects		p[a]
	Age ≥65 years ($n = 1077$)	Age <65 years ($n = 1574$)	
Mean hospital stay	17.8 ± 11.4	16.5 ± 10.1	0.003
Results (stable discharge/in-hospital death or critical discharge)	1040/37	1553/21	<0.001
Sections of admissions (%)			0.213
Family medicine	11 (1.0)	8 (0.5)	
Internal medicine	920 (85.4)	1330 (84.5)	
Surgery	131 (12.2)	215 (13.7)	
Pediatrics	0 (0)	11 (0.7)	
Neurology	8 (0.7)	6 (0.4)	
Other sections	7 (0.6)	4 (0.3)	
Major acute comorbidities			
Acute low respiratory conditions (yes/no)	73/1004	69/1505	0.008
Urological infections (yes/no)	78/999	76/1498	0.011

[a] Independent t test, x^2 test and trend x^2 test.

daily costs for blood products/hemodialysis and total cost of hospitalization than did those discharged at<65 years. The difference in the daily costs of laboratory exams, radiological exams and drug prescriptions differed insignificantly between the two groups.

Under multiple logistic regression analyses, female gender (OR = 1.737), in-hospital death/critical discharge (OR = 2.112), nephropathy (OR = 2.024), biliary tract diseases (OR = 1.663), liver cirrhosis (OR = 1.956), gastroenterological cancers (OR = 2.331), ALRC (OR = 1.612) and urological infections (OR = 1.485) were predictive variables associated with advanced age (≥65 years) in patients with PLA (all $p < 0.05$; Table 4). For prognosis of PLA, ALRC served as a predictive variable for poor prognosis in PLA patients <65 years (OR = 6.569). Nephropathy and gastroenterological cancers were both predictive variables associated with poor prognosis in all PLA patients (OR = 5.623 and 3.241, respectively, in age≥65 years; 7.038 and 4.689, respectively, in age <65 years; all $p < 0.05$;Table 5).

Table 3
The costs of discharges made by subjects with pyogenic liver abscess as major diagnosis in 2007 ($n = 2651$).

Cost items (USD[b])	Discharges by subjects		p[a]
	Age ≥65 years ($n = 1077$)	Age <65 years ($n = 1574$)	
Daily costs of laboratory exams	24.2 ± 26.1	23.6 ± 28.2	0.547
Daily costs of radiological exams	15.5 ± 24.0	15.5 ± 27.7	0.981
Daily costs of blood products	2.3 ± 10.6	1.0 ± 6.9	<0.001
Daily costs of hemodialysis	5.5 ± 24.2	3.7 ± 21.7	0.046
Daily costs of drug prescriptions	46.9 ± 37.6	47.8 ± 52.0	0.634
Daily costs of hospitalization	180.7 ± 133.9	169.1 ± 169.7	0.062
Total costs of hospitalization	3082.1 ± 3014.3	2594.7 ± 2457.9	<0.001

[a] Independent t test.
[b] USD = United States Dollars.

Table 4
The significantly predictive variables associated with advanced age (≥65 years) in patients with pyogenic liver abscess ($n = 2319$).

Variables	B value	Odds ratio	95%CI[b]	p[a]
Gastroenterological cancers	0.846	2.331	1.655-3.283	<0.001
In-hospital death/critical discharge	0.748	2.112	1.209-3.691	0.009
Nephropathy	0.705	2.024	1.391-2.947	<0.001
Liver cirrhosis	0.671	1.956	1.166-3.283	0.011
Female	0.552	1.737	1.460-2.066	<0.001
Biliary tract diseases	0.509	1.663	1.284-2.155	<0.001
Acute low respiratory conditions (ALRC)	0.477	1.612	1.139-2.279	0.007
Urological infections	0.396	1.485	1.064-2.075	0.020

[a] Multiple logistic regression analysis.
[b] CI = confidence interval.

4. Discussion

In this study, the gender distribution of patients with PLA reflected age-related factors. With advanced age, the ratio of females in the population increased gradually due to having a longer life expectancy than males. Furthermore, in-hospital death/critical discharge accounted for a significantly higher ratio of discharges of subjects ≥65 years than of those <65 years (3.4% versus 1.3%). This issue reflected the fact that PLA still had underlying hazards in elderly patients and needed aggressive treatment. Similar conclusions were also found in reports from Southern Korea.[12] Although departments of internal medicine and surgery provided >95% of admission services for such illness in this study, other departments had relevant knowledge in caring for patients with PLA.

The in-hospital costs of PLA also reflected some aspects of medical economics. The total costs of hospitalization were higher in the subjects discharged by subjects ≥65 years due to longer hospital stays than in those discharged subjects <65 years old. However, the daily costs of laboratory exams,

Table 5
The significantly predictive variables associated with poor prognosis (in-hospital death/critical discharge) in patients with pyogenic liver abscess stratified by age 65 years.

Groups/Variables	B value	Odds ratio	95%CI[b]	p[a]
Age ≥65 years ($n = 939$)				
Nephropathy	1.727	5.623	1.932-16.364	0.002
Gastroenterological cancers	1.176	3.241	1.283-8.188	0.013
Age <65 years ($n = 1380$)				
Nephropathy	1.951	7.038	1.392-35.594	0.018
Gastroenterological cancers	1.545	4.689	1.270-17.306	0.020
Acute low respiratory conditions	1.882	6.569	1.722-25.059	0.006

[a] Multiple logistic regression analysis.
[b] CI = confidence interval.

radiological exams and drug prescriptions were similar between the two groups. The longer hospital stay in geriatric patients with PLA may imply complicated health status in this group. Further prospective evaluations for standard treatments of PLA are indicated.

The higher daily costs of blood products and hemodialysis imply underlying hematological and renal problems in geriatric inpatients with PLA. Previous studies have reported aforementioned problems as factors of poor prognosis, such as anemia, coagulopathy and acute/chronic renal failure.[2,5,8,16,17] Healthcare workers should keep this in mind while caring for geriatric patients with PLA.

Among co-morbidities, the insignificant role of diabetes mellitus (DM) was similar with that in previous local hospital-based studies.[2,5,6] However, some studies from Southern Korea and Denmark reported opposite results.[3,4,18] We consider that PLA shows some unique characteristics in the population of Taiwan. Further epidemiological comparisons among other populations are indicated for PLA.

There have been several claim-based reports reflecting the negative role of renal insufficiency for prognosis of PLA.[5,16] Yang et al.[19] reported that PLA combining with end-stage renal disease had a high mortality rate. Okano et al.[20] reported that complicated PLA, such as co-morbid acute renal failure, needed aggressive percutaneous drainage for effective control. In this study, nephropathy contributed as a predictive variable associated with age $\geq$65 years in PLA patients. The results are similar to those of reports from Spain.[13] We conclude that underlying renal diseases should be considered when assessing geriatric patients with PLA. This co-morbidity also explains the aforementioned higher daily costs of hemodialysis.

Biliary tract diseases have been viewed as a well-known co-morbidity for PLA in previous studies.[6,7,21,22] Our result also proved this parameter and imposed its association with age $\geq$65 years in patients with PLA. What is also interesting is the role that the gastroenterological cancers have played in PLA. In the United States, a large claim-based analysis reported cancer as a mortality-related factor for PLA.[16] Another study from Hong Kong also reported a similar role of hepato-biliary cancers in PLA.[23] Several case reports and series reflected interesting roles of colon cancers and metastatic liver tumors, with an initial presentation of PLA.[24–27] There are case series also reporting the relationships between PLA and hepato-biliary malignancies, especially in those patients receiving invasive therapies such as transarterial embolization.[28–31] In this study, the role of gastroenterological cancers in PLA and the detailed classifications also showed similar characteristics. Underlying malignancies in PLA should be kept in mind and investigated further in highly-endemic areas.

Extra-hepatic complications, such as pulmonary or urological infections, should be seen as problems associated with age $\geq$65 years in patients with PLA, although the incidence in their discharges was low (6.8 and 7.2%, respectively). Liu et al. [32] reported that undiagnosed PLA (diagnosed after admissions) often manifested symptoms of respiratory or urinary tract infections in emergency rooms. Another series of early case also reflected similar infections in advanced age patients with PLA.[33] We concluded that PLA in advanced age patients had more complications or co-morbidities than did PLA in young adults due to impaired - condition commonly in the elderly. Care providers should be aware of the possibility of extra-hepatic infections in geriatric patients with PLA.

Liver cirrhosis was viewed as a risk factor of poor prognosis in PLA patients by two epidemiological studies from the United States and Denmark.[16,34] Our results revealed a predictive role of liver cirrhosis associated with geriatric PLA patients, although liver cirrhosis itself did not achieve statistic significance as a risk factor for poor prognosis. We suggest that PLA patients with comorbid liver cirrhosis should be treated carefully, especially those of advanced age.

Among predictive variables associated with advanced age in patients with PLA, gastroenterological cancers, in-hospital death/critical discharge and nephropathy all included high ORs $\geq$2. The results reflected the underlying hazards and health risks in caring for geriatric PLA patients. We suggest that caring for PLA patients should be carefully evaluated, along with other possible co-morbidities and prognosis, especially for those patients with advanced ages. It should be noted that both nephropathy and gastroenterological cancers were predictive variables associated with poor prognosis in PLA patients. Clinical physicians should pay more attentions when PLA patients had aforementioned comorbidities.

The design of this study and the present parameters have certain limitations. Screening with ICD-9-CM codes may not entirely exclude artificial registry bias when establishing the dataset. Incomplete records of discharges or ICD coding may limit the investigation of some issues, such as viral/chronic hepatitis. The timing relationships between PLA and some co-morbidities, such as extra-hepatic infections and cancers, were not clarified by the claim-based analyses. The details of invasive procedures, serum markers, infecting microorganisms, and pathological types of cancers, could not be clarified due to limitations of the dataset itself. We utilized single-year dataset due to limitations of authorization. Overall, this nationwide claim-based analysis could illustrate the gross characteristics and in-hospital costs for PLA inpatients, and reveal the differences in those with advanced ages. Further linkages of datasets could solve partial problems.

In conclusion, advanced age ($\geq$65 years) had impact on the aforementioned characteristics and predictive variables in patients with PLA, such as a high ratio of females, long hospital stays, poor prognosis, higher costs for blood products/hemodialysis, and complicated co-morbidities. Physicians and other medical staff should pay attention and treat carefully aged PLA patients, especially those with comorbid nephropathy or gastroenterological cancers.

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