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ORIGINAL ARTICLE

Bacteremic pneumonia caused by extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*: Appropriateness of empirical treatment matters

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Background: Clinical information about bacteremic pneumonia caused by extended-spectrum beta-lactamase (ESBL)-producing organism is limited.
Methods: A retrospective study was conducted at two medical centers in Taiwan. From May 2002 to August 2010, clinical information and outcome of adults with bacteremic pneumonia caused by ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* were analyzed. The primary outcome is the 30-day mortality.
Results: A total of 111 patients with bacteremic pneumonia caused by *E. coli* (37 patients, 33.3%) and *K. pneumoniae* (74, 66.7%) were identified. Their mean age was 69.2 years and 51.4% were male patients. Fifty-seven (51.3%) episodes were classified as hospital-acquired infections, 19 (17.1%) as health-care-associated infections, and four (3.6%) as community-

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acquired infections. Fifty-one (45.9%) patients received appropriate empiric antimicrobial therapy. The 30-day mortality rate was 40.5% (45 patients). In the multivariate analysis, several independent risk factors, including rapidly fatal underlying disease [odds ratio (OR), 5.75; 95% confidence interval (CI), 1.54–21.48; $p = 0.009$], severe sepsis (OR, 4.84; 95% CI, 1.55–15.14; $p = 0.007$), critical illness (OR, 4.28; 95% CI, 1.35–13.57; $p = 0.013$), and receipt of appropriate empirical therapy (OR, 0.19; 95% CI, 0.07–0.55; $p = 0.002$), were associated with 30-day mortality. The survival analysis consistently found that individuals with appropriate empiric therapy had a higher survival rate (log-rank test, $p < 0.001$).
Conclusion: ESBL-producing bacteremic pneumonia, especially health-care-associated infections, often occurred in adults with comorbidities. Appropriate empirical therapy was associated with a favorable outcome.

Introduction

Extended-spectrum beta-lactamases (ESBLs) are a heterogeneous group of enzymes responsible for the resistance of Gram-negative bacteria to beta-lactam antibiotics.[1] The first ESBL-producing organism was reported in Germany in 1983.[2] Pathogens harboring this characteristic phenotype spread worldwide and had a serious impact on clinical management of infectious diseases.[3] Besides, infections caused by ESBL producers are associated with a worse outcome than their non-ESBL-producing counterparts.[4]

Escherichia coli and *Klebsiella pneumoniae* are common ESBL-producing Enterobacteriaceae found worldwide,[5] and cause various infectious diseases in both hospital and community settings.[4,5] According to a previous multicenter study, *E. coli* and *K. pneumoniae* can be the pathogens of bacteremic nosocomial pneumonia (*E. coli*, 8.3% and *K. pneumoniae*, 13.1%).[6] In Taiwan, the annual prevalence rate of ESBL-producing phenotype among clinical *E. coli* and *K. pneumoniae* isolates was 11.5% and 12.1%, respectively, from 2002 to 2010.[7]

Because positive blood cultures are uncommon in patients with pneumonia, the pathogens responsible are usually isolated from respiratory samples.[8,9] Many studies tried to investigate the potential impact of bacteremic pneumonia due to a worse outcome.[6,10–12] However, clinical studies of bacteremic pneumonia caused by ESBL producers are limited. This study is intended to identify clinical features and risk factors for mortality in patients with bacteremic pneumonia caused by ESBL-producing *E. coli* and *K. pneumoniae*.

Materials and methods

Patients

A retrospective study among adults (age $\geq$ 18 years) was conducted in two medical centers in Taiwan, namely, the National Taiwan University Hospital in Northern Taiwan and the National Cheng Kung University Hospital in Southern Taiwan. The list of patients with *E. coli* and *K. pneumoniae* bacteremia between May 2002 and August 2010 was retrieved from the database of clinical microbiology laboratories in the two study hospitals. Information on individuals with ESBL-producing *E. coli* and *K. pneumoniae* bacteremic pneumonia between May 2002 and August 2007 was included in a previous study.[13] A diagnosis of pneumonia was made when there were symptoms of lower respiratory tract infections (e.g., cough, purulent expectoration, chest pain) and pulmonary infiltrates on the chest radiograph not attributable to other causes, coinciding with the isolation of the same isolate in sputum, bronchoalveolar lavage fluid, or appropriate respiratory specimens[14,15] as the ESBL producer isolated from blood samples. For those with more than one episode of bacteremia caused by the same isolate, only the first episode was included for analysis.

Antimicrobial susceptibility and ESBL phenotype detection

Blood samples collected in the blood culture bottles were incubated in the blood culture system of BACTEC 9240 (Beck Dickinson, Franklin Lakes, NJ, USA). Sputum samples were plated onto the blood agar. *E. coli* and *K. pneumoniae* were identified by the colony morphology and biochemical characteristics and confirmed by the VITEK identification system (bioMérieux Inc., Durham, NC, USA).

Antimicrobial susceptibility was determined by the disk diffusion method, using the method and interpretative criteria recommended by the Clinical and Laboratory Standards Institute (CLSI).[16] The production of ESBL was screened and confirmed in accordance with the standards of CLSI.[16]

Collection of clinical information

Medical records of eligible cases were reviewed. Clinical information, including demographic data, comorbidities, disease severity, complication of bacteremia, laboratory and microbiology data, antimicrobial treatment, and clinical outcome, was collected using a standardized case form.

Definitions

All study patients with pneumonia were classified into four groups, namely, community-acquired, health-care-associated, hospital-acquired, and ventilator-associated pneumonia, as defined by the Infectious Diseases Society of America and the American Thoracic Society.[15,17] In brief, hospital-acquired pneumonia comprises adults with pneumonia that were clinically evident after more than 48 hours of hospitalization. Ventilator-associated pneumonia is defined as pneumonia occurring more than 48 hours after the initiation of endotracheal intubation and mechanical ventilation. Health-care-associated pneumonia includes any patient who has been hospitalized in an acute care hospital for 2 or more days within the preceding 90 days, resided in a nursing home or long-term care facility, received recent intravenous antibiotic therapy, chemotherapy, or wound care within the preceding 30 days, or attended a hospital or hemodialysis clinic. Community-acquired pneumonia comprised those unable to fulfill the definitions of health-care-associated or hospital-acquired pneumonia. ESBL-producing isolates resistant to both fluoroquinolones (ciprofloxacin, levofloxacin, or both) and aminoglycosides (amikacin or gentamicin, or both) were defined as being multidrug resistant (MDR). According to the McCabe score, the severity of underlying medical illness was stratified as being fatal, ultimately fatal, or nonfatal.[18] The severity of bacteremia was evaluated by the Pittsburgh bacteremia score, and patients with four points or more were regarded as having a critical illness.[19] Patients with dysfunction of two or more organs were categorized as having severe sepsis.[20]

Antimicrobial therapy administered within 5 days after bacteremia onset was regarded as empirical therapy, and that administered afterward as definitive therapy. Antimicrobial agents were considered to be appropriate if the causative pathogen was *in vitro* susceptible to the antimicrobial agents. The primary outcome in the study was 30-day mortality.

Statistical analysis

The results were analyzed by the SPSS software (IBM Corp., Armonk, NY, USA) for MAC, version 21.0. Continuous variables were expressed as mean values ± standard deviations, and compared by the Mann–Whitney *U* test or Student *t* test. Categorical variables were expressed as percentages of the total number of patients analyzed, and compared by the Fisher exact test or χ^2 test, as appropriate. Variables with $p \leq 0.05$ by the univariate analysis were included in the multiple conditional logistic regression analysis. A p value < 0.05 was considered statistically significant and all tests were two tailed. Survival curves were prepared by the Kaplan–Meier method and analyzed by the log-rank test.

Results

During the study period, a total of 473 patients with bacteremia caused by ESBL-producing *E. coli* ($n = 228$) and *K. pneumoniae* ($n = 245$) were identified. Bacteremic pneumonia was noted in 30.2% (74/245) of *K. pneumoniae* bacteremia and in 16.2% (37/228) of *E. coli* bacteremia ($p < 0.001$). Overall, 111 (23.5%) patients fulfilling the eligible criteria were analyzed. The clinical characteristics of these patients are presented in Table 1. The mean age of the patients was 69.2 years and 48.4% were male patients. Chronic kidney disease (50, 45%) was the most common underlying disease, followed by diabetes mellitus (43, 38.7%) and malignancy (37, 33.3%). With respect to clinical settings in which pneumonia developed, four (3.6%) patients had community-acquired, 19 (17.1%) health-care-associated, 57 (51.3%) hospital-acquired, and 31 (27.9%) ventilator-associated pneumonia. *E. coli* more often caused community-acquired (10.8% vs. 0%, $p = 0.01$) or health-care-associated (27.0% vs. 12.2%, $p = 0.06$) bacteremic pneumonia than *K. pneumoniae*. Most ESBL-producing *E. coli* or *K. pneumoniae* isolates (88, 79.3%) were resistant to at least a fluoroquinolone, and nearly a half of the isolates (58, 53.3%) were MDR. However, the clinical characteristics of patients with bacteremic pneumonia caused by *K. pneumoniae* or *E. coli* were similar in terms of age, gender, underlying diseases, and severity of disease when bacteremia developed (Table 1). Of note, there were no significant differences in the mortality rate of patients with bacteremic pneumonia caused by ESBL-producing *K. pneumoniae* or *E. coli* (Table 1). Therefore, the patients with *E. coli* and *K. pneumoniae* bacteremia were grouped together for further analysis.

In the univariate analysis, the presence of rapidly fatal underlying disease ($p < 0.001$), severe sepsis ($p < 0.001$), receipt of inappropriate empirical therapy ($p < 0.001$), inappropriate definitive therapy ($p < 0.001$), and solid tumor ($p = 0.016$) were associated with the 30-day mortality (Table 2). MDR was not significantly related to the mortality (46.7% vs. 53.3 %, $p = 0.34$). By the multivariate logistic regression analysis, the presence of rapidly fatal underlying disease [odds ratio (OR), 5.75; 95% confidence interval (CI), 1.54–21.48; $p = 0.009$], severe sepsis (OR, 4.84; 95% CI, 1.55–15.14; $p = 0.007$), and critical illness (OR, 4.28; 95% CI, 1.35–13.57; $p = 0.013$), were independently associated with the 30-day mortality (Table 2). By contrast, the receipt of appropriate empirical therapy (OR, 0.19; 95% CI, 0.07–0.55; $p = 0.002$) was independently associated with a better outcome.

To clarify the impact of empirical therapy, survival analysis was performed, which revealed that the 30-day mortality rate was lower in patients receiving appropriate empirical therapy (Fig. 1A) and in those with severe sepsis (Fig. 1B). Fifty-one (45.9%) patients had received appropriate empirical antimicrobial therapy. Of these patients, 49 (96.1%) received monotherapy, including a carbapenem ($n = 39$ patients; ertapenem, imipenem, or meropenem), a fluoroquinolone ($n = 4$; ciprofloxacin or levofloxacin), a β-lactam/β-lactamase inhibitor ($n = 4$), and cephamycin ($n = 2$). The 30-day mortality rate of empirical carbapenem monotherapy was 25.6% (10/39) and that of fluoroquinolone monotherapy was 25% (1/4). Even if empirical therapy is defined as the agents used within 3 days of bacteremia onset, the 30-day mortality rate of those receiving appropriate empirical therapy was significantly lower than that of those receiving inappropriate empirical therapy (23.9%, 11/46 vs. 52.3%, 34/65; $p = 0.003$). As for

Table 1 Clinical characteristics of 111 patients with bacteremic pneumonia caused by extended-spectrum beta-lactamase-producing *Escherichia coli* or *Klebsiella pneumoniae*

Characteristics	All ($n = 111$)	*E. coli* ($n = 37$)	*K. pneumoniae* ($n = 74$)	p
Age (mean ± standard deviation), y	69.2 ± 15.0	67.8 ± 16.2	69.9 ± 14.4	0.49
Sex, male	57 (51.4)	21 (56.8)	36 (48.6)	0.55
Underlying disease				
Chronic kidney disease	50 (45.0)	12 (32.4)	38 (51.4)	0.07
End-stage renal disease with hemodialysis	33 (29.7)	9 (24.3)	24 (32.4)	0.51
Diabetes mellitus	43 (38.7)	14 (37.8)	29 (39.2)	1.00
Malignancy	37 (33.3)	16 (43.2)	21 (28.4)	0.14
Immunosuppressant therapy	29 (26.1)	14 (27.5)	15 (25.0)	0.83
Liver cirrhosis	12 (10.8)	6 (16.2)	6 (8.1)	0.21
None	16 (19.4)	7 (13.7)	9 (15.0)	1.00
Type of pneumonia				
Community-acquired	4 (3.6)	4 (10.8)	0 (0.0)	0.011
Health-care-associated	19 (17.1)	10 (27.0)	9 (12.2)	0.06
Hospital-acquired	57 (51.3)	14 (37.8)	43 (58.1)	0.07
Ventilator-associated	31 (27.9)	9 (24.3)	22 (29.7)	0.66
Critical illness (Pittsburgh bacteremia score ≥ 4)	47 (42.3)	17 (45.9)	30 (40.5)	0.68
Severe sepsis	58 (52.3)	23 (62.2)	35 (47.3)	0.16
Appropriate empirical antimicrobial therapy	51 (45.9)	12 (32.4)	39 (52.7)	0.047
Appropriate definitive antimicrobial therapy	90 (81.1)	29 (78.4)	61 (82.4)	0.62
Sepsis-related mortality	41 (36.9)	15 (40.5)	26 (35.1)	0.68
30-d mortality	15 (40.5)	16 (43.2)	29 (39.2)	0.69
Crude mortality	62 (55.9)	21 (56.8)	41 (55.4)	1.00

Data are presented as *n* (%), unless otherwise specified.

Table 2 Logistic regression analysis for risk factors of 30-d mortality among patients with bacteremic pneumonia caused by extended-spectrum beta-lactamase producing *Escherichia coli* or *Klebsiella pneumoniae*

Variables	Number of cases (%)		Univariate analysis			Multivariate analysis		
	Fatal ($n = 45$)	Surviving ($n = 66$)	Odds ratio	95% confidence interval	p	Odds ratio	95% confidence interval	p
Age (mean ± standard deviation), y	71.4 ± 13.1	67.1 ± 16.1			0.21			0.15
Sex, male	21 (46.7)	36 (54.5)	0.73	0.34–1.56	0.45			
Comorbidities								
Chronic kidney disease	20 (44.4)	30 (45.5)	0.96	0.45–2.06	1.00			
Diabetes mellitus	20 (44.4)	23 (36.7)	1.50	0.69–3.25	0.33			
Solid tumor	18 (40.0)	12 (18.2)	3.00	1.26–7.12	0.016	2.09	0.53–8.29	0.30
Immunosuppressant therapy	11 (24.4)	18 (27.3)	0.86	0.37–2.06	0.83			
Liver cirrhosis	8 (17.8)	4 (6.1)	3.35	0.94–11.90	0.07			
Chronic lung disease	1 (2.2)	4 (4.1)	0.35	0.04–3.26	0.65			
None	4 (8.9)	12 (18.2)	0.44	0.13–1.46	0.27			
Rapidly fatal underlying disease	18 (40.0)	6 (9.1)	6.67	2.38–18.67	<0.001	5.75	1.54–21.48	0.009
Type of pneumonia								
Community-acquired	1 (2.2)	3 (4.5)	0.48	0.05–4.74	0.65			
Health-care-associated	9 (20.0)	12 (18.2)	1.13	0.43–2.94	0.81			
Hospital-acquired	20 (44.4)	37 (56.1)	0.63	0.29–1.35	0.25			
Ventilator-associated	16 (35.6)	15 (22.7)	1.88	0.81–4.34	0.20			
Critical illness (Pittsburgh bacteremia score ≥ 4)	30 (66.7)	17 (25.8)	5.76	2.51–13.22	<0.001	4.28	1.35–13.57	0.013
Severe sepsis	37 (82.2)	21 (31.8)	9.91	3.94–24.95	<0.001	4.84	1.55–15.14	0.007
Appropriate empirical antimicrobial therapy	11 (24.4)	40 (60.6)	0.21	0.09–0.49	<0.001	0.19	0.07–0.55	0.002
Time to appropriate therapy (mean ± standard deviation), d	6.9 ± 6.0	2.8 ± 2.4			<0.001			

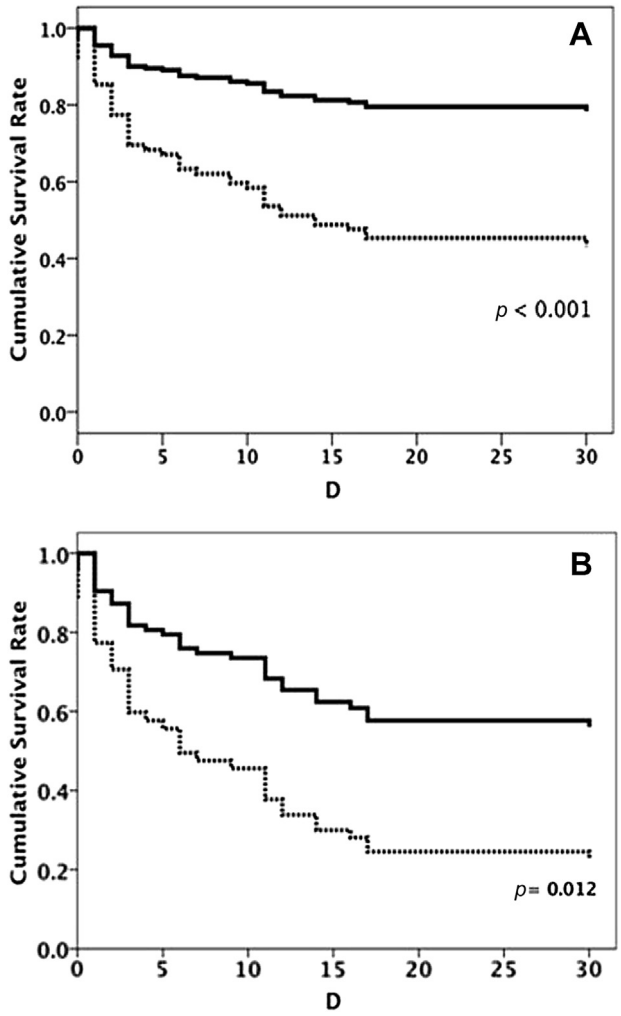

Figure 1. Survival curves of patients with ESBL-producing bacteremic pneumonia with and without appropriate empirical therapy (A), and of severe sepsis patients with and without appropriate empirical therapy (B). The unbroken line represents appropriate empirical therapy, and the broken line represents inappropriate empirical therapy.

definitive therapy, appropriate therapy has a survival beneficial effect at 30 days, when compared with inappropriate definitive therapy (28.9%, 26/90 vs. 90.5%, 19/21; $p < 0.001$). None of those receiving empirical β-lactam/β-lactamase inhibitor or cephamycin therapy died. In a subgroup analysis, the patients with rapidly fatal underlying disease (11.8% vs. 30%, $p = 0.022$), solid tumor (17.6% vs. 35.0%, $p = 0.054$), and *E. coli* infections (67.6 % vs. 47.3 %, $p = 0.047$) were more likely to receive empirical inappropriate therapy (Table 3).

Discussion

This study demonstrated that 96.4% of ESBL-producing bacteremic pneumonia was regarded as hospital- or health-care-associated infections, and approximately one half of the study population received an inappropriate empirical antimicrobial therapy, which is associated with a higher 30-day mortality rate (40.5%). The clinical characteristics of ESBL-producing *E. coli* and *K. pneumoniae* bacteremic pneumonia were described to emphasize the importance of appropriateness of empirical antibiotics.

Many studies have described the worldwide increase in ESBL-producing *E. coli* and *K. pneumoniae* isolates during the past decade.[7,21,22] In addition, a previous study also reported that bacteremia caused by ESBL producer was associated with a longer hospital stay and delayed treatment.[23] Diversity of clinical diseases caused by ESBL producers, such as bacteremia, urinary tract infection, and intra-abdominal infection, had been reported and analyzed.[4,24,25] Studies suggest that bacteremia associated with hospital-acquired pneumonia may lead to a fatality rate up to 50%,[6,10,26] and is independently associated with higher mortality, which was possibly related to the high level of antibiotic resistance.[6] *Pseudomonas aeruginosa* is the leading pathogen of hospital-acquired pneumonia, and the 30-day mortality rate of *P. aeruginosa* bacteremic pneumonia may be up to 51%.[27] However, adequate empirical therapy can decrease mortality in these patients.[27] In our study, the mortality rate of bacteremic pneumonia due to ESBL-producing Enterobacteriaceae was 40%, and 50% of the patients received inappropriate antibiotic therapy initially.

Previous studies of bloodstream infections caused by ESBL-producing Enterobacteriaceae have reported conflicting results regarding the impact of the appropriateness of empirical therapy on mortality.[28–30] Diverse study designs, categorizations of clinical settings, and origins of bacteremia made the data incomparable between these studies. Primary bacteremia and respiratory infections-related bacteremia had the highest mortality, whereas bacteremia that originated from a urinary tract infection had the lowest mortality.[31] In the aforementioned studies, inappropriate empirical antibiotic therapy was an independent risk factor for mortality in nonurinary tract infections. Accordingly, our study found that inappropriate empirical or definitive therapy was significantly related to the 30-day mortality (by the Kaplan–Meier analysis, $p < 0.001$). Twenty-five (22.5%) patients died within 5 days after bacteremia onset, and 80% of them received inappropriate empirical therapy. This highlights the importance of initiating early appropriate therapy.

Furthermore, we analyzed the role of fluoroquinolones in treating pneumonia caused by ESBL producers. Empirical fluoroquinolone monotherapy is not inferior to carbapenem in terms of the crude 30-day mortality rate. However, high resistance to fluoroquinolones (79.3%) was found in our cohort, and therefore, choosing it as empirical therapy for covering possible ESBL-producer pneumonia may not be suitable. However, in areas with low resistance to fluoroquinolones, it can be a suitable choice for empirical therapy to treat bacteremic pneumonia caused by ESBL producers.

When we compared the patients who received appropriate therapy with that of those who received inappropriate therapy, it was found that patients with underlying solid tumor more often received inappropriate empirical therapy. In our earlier analysis, empirical carbapenem therapy was prescribed more often to patients with hematological malignancy (53.8% vs. 32.2%).[24] Because

Table 3 Characteristics of patients receiving appropriate and inappropriate empirical antibiotic therapy

Variables	Empirical therapy		*p*
	Appropriate ($n = 51$)	Inappropriate ($n = 60$)	
Age (mean ± standard deviation), y	66.9 ± 15.2	71.1 ± 14.6	0.15
Sex, male	29 (56.9)	28 (46.7)	0.34
Comorbidities			
Chronic kidney disease	27 (52.9)	23 (38.3)	0.13
Diabetes mellitus	18 (35.3)	25 (41.7)	0.56
Immunosuppressant therapy	14 (27.5)	15 (25.0)	0.83
Solid tumor	9 (17.6)	21 (35.0)	0.054
Liver cirrhosis	5 (9.8)	7 (11.7)	1.00
Rapidly fatal underlying disease	6 (11.8)	18 (60.0)	0.022
Causative pathogen			
Escherichia coli	12 (23.5)	25 (41.7)	0.047
Klebsiella pneumoniae	39 (76.5)	35 (58.3)	
Severity of disease			
Severe sepsis	23 (45.1)	35 (58.3)	0.19
Organ dysfunction at onset of bacteremia			
Respiratory dysfunction	31 (60.8)	28 (46.7)	0.18
Shock	23 (45.1)	38 (63.3)	0.059
Hepatic dysfunction	12 (23.5)	19 (31.7)	0.40
Renal dysfunction	8 (15.7)	11 (18.3)	0.80
Neurological dysfunction	8 (15.7)	18 (30.0)	0.12
Hematological dysfunction	7 (13.7)	16 (26.7)	0.11
Mortality rate			
Sepsis-related	9 (17.6)	32 (53.3)	<0.001
30-d	11 (21.6)	34 (56.7)	<0.001
Crude	24 (47.1)	38 (63.3)	0.13

Data are presented as *n* (%) unless otherwise specified.

neutropenia is frequently encountered in patients with a solid tumor, physicians tended to administer broad-spectrum antibiotics early during the treatment period in this group of patients, whereas they administer more appropriate empirical therapy in patients with hematological malignancy (57% vs. 30%). Another possibility is that those with a solid tumor were older and more likely to have advanced tumors, and thus empirical antimicrobial therapy would be conservative. Likewise, the underlying rapidly fatal diseases were mainly referred to malignancy and led to a similar scenario as in the aforementioned clinical setting. With regard to the causative pathogens, those with *E. coli* bacteremia more often received inappropriate empirical therapy. It is likely that *E. coli* was dominant in community-acquired and health-care-associated pneumonia, for which physicians rarely considered ESBL producers as causative pathogens and less likely prescribed carbapenem therapy as empirical therapy.

In ESBL-producer infections, carbapenems have been widely considered as the drugs of choice. With these aforementioned findings and the increasing prevalence of ESBL-producer infections, carbapenem therapy should be considered for critically ill patients with multiple risk factors for the treatment of infections caused by MDR organisms. However, such an escalation strategy may be detrimental to the antimicrobial resistance crisis and cause a greater extent of carbapenem resistance in Gram-negative bacteria.[32,33] Thus, it is important to find clinical clues for early identification of infectious diseases caused by ESBL-producing Enterobacteriaceae. Susceptible population included those with previous colonization or infections due to ESBL producers, serious illness with prolonged hospital stay or invasive medical device, prior therapy with fluoroquinolones or oxyimino-β-lactam agents (such as cefuroxime, cefotaxime, ceftriaxone, ceftazidime, or aztreonam).[3,34] When confronting these patients with pneumonia, clinicians should consider ESBL producers as one of the potential pathogens.

Recent studies focused on increasing ESBL-producer infections, especially urinary tract infections, in the community setting.[4,25,35,36] Only four patients in our cohort acquired infections in the community, and three survived for 30 days after bacteremia onset even under inappropriate empirical therapy. Peralta et al[28] reported that nosocomial ESBL-producer infections had a worse outcome. However, our case number of community-acquired pneumonia is limited and more clinical studies are warranted to define the prognostic implication of community-acquired pneumonia due to ESBL producers. In Taiwan, *K. pneumoniae* is a common pathogen of pneumonia and causes a high mortality rate, up to 55%, even in the cases of community-acquired pneumonia.[37] Moreover in our study, like *K. pneumoniae*, *E. coli* also caused severe and fatal pneumonia.

Our study had some limitations. First, it was a retrospective study and conducted at two medical centers, and therefore, there may be selection bias, which limits the general application of the study results to other areas.

Second, our study included only patients with bacteremia, and thus, our findings may not be applicable to the cases of ESBL-producer pneumonia without bacteremia.

In conclusion, our study highlights the poor prognosis of bacteremic pneumonia caused by ESBL-producing *E. coli* and *K. pneumoniae*. Early identification and initiation of appropriate antimicrobial therapy will improve the clinical outcome of these patients.

Conflicts of interest

No reported conflicts.

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