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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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KEYWORDS
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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.