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Original Article

Propensity-matched analysis of the impact of extended-spectrum β-lactamase production on adults with community-onset *Escherichia coli*, *Klebsiella* species, and *Proteus mirabilis* bacteremia

Ching-Chi Lee [a,b,c], Chung-Hsun Lee [d,e], Ming-Yuan Hong [d,e], Chih-Chia Hsieh [e], Hung-Jen Tang [f,g,], Wen-Chien Ko [c,d,*]**

[a] *Division of Critical Care Medicine, Department of Internal Medicine, Madou Sin-Lau Hospital, Tainan 72152, Taiwan*
[b] *Graduate Institute of Medical Sciences, College of Health Sciences, Chang Jung Christian University, Tainan 71101, Taiwan*
[c] *Department of Internal Medicine, National Cheng Kung University Hospital, Tainan 70403, Taiwan*
[d] *Department of Medicine, National Cheng Kung University Medical College, Tainan 70403, Taiwan*
[e] *Department of Emergency Medicine, National Cheng Kung University Hospital, Tainan 70403, Taiwan*
[f] *Department of Medicine, Chi-Mei Medical Center, Tainan 71004, Taiwan*
[g] *Department of Health and Nutrition, Chia Nan University of Pharmacy and Science, Tainan 71710, Taiwan*

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Abstract *Background:* The presence of extended-spectrum β-lactamase (ESBL) in *Escherichia coli*, *Klebsiella* species, and *Proteus mirabilis* (EKP) is of great microbiological and clinical importance. The study dealing with the direct impact of ESBL producers on the outcome of patients with community-onset bacteremia is lacking.
Methods: Adults with community-onset EKP bacteremia were recruited retrospectively during a 6-year period. ESBL producers were determined according to ESBL phenotype. ESBL patients were compared on a 1:2 basis with non-ESBL patients by using propensity-score matching (PSM) calculated based on independent predictors of 28-day mortality.

* Corresponding author. Department of Internal Medicine, National Cheng Kung University Hospital, No. 138, Sheng Li Road, Tainan 70403, Taiwan. Fax: +886 6 2752038.
** Corresponding author. Division of Infectious Disease, Department of Medicine, Chi-Mei Medical Center, No. 901, Chung-Hwa Road, Yung-Kang City, Tainan 71004, Taiwan. Fax: +886 6 2833351.
E-mail addresses: 8409d1@gmail.com (H.-J. Tang), winston3415@gmail.com (W.-C. Ko).

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Results: Of the 1141 eligible adult patients, 65 (5.7%) caused by ESBL producers. Significant differences between the two groups were discovered in the proportions of patients with critical illness (a Pitt bacteremia score $\geq$ 4) at bacteremia onset, inappropriate empirical antibiotic therapy, bacteremia because of urosepsis and pneumonia, and several comorbidities. In a PSM analysis after controlling for six independent predictors—critical illness at bacteremia onset, underlying fatal comorbidities (McCabe classification), inappropriate empirical antibiotic therapy, comorbidities with liver cirrhosis, bacteremia because of urosepsis and pneumonia—a appropriate matching between two groups (ESBL group, 60 patients; non-ESBL group, 120) were observed in age, causative microorganism, bacteremia severity, major comorbidities, comorbidity severity, and major bacteremia source. Consequently, a strong relationship between ESBL producers and poor prognosis was highlighted.
Conclusions: The adverse influence of ESBL producers on clinical outcomes was presented with respect to adults with community-onset EKP bacteremia. Establishing a predictive scoring algorithm for identifying patients at risk of ESBL-producer infections is crucial.

Introduction

Bacteremia is a life-threatening condition that is associated with significant healthcare costs and high mortality rates.[1] Enterobacteriaceae, particularly *Klebsiella pneumoniae* and *Escherichia coli*, are the leading cause of community-onset bacteremia.[2,3] The presence of extended-spectrum β-lactamase (ESBL) in the Enterobacteriaceae family is of great microbiological and clinical importance.[4] In past years, ESBL enzymes have spread from hospital to community environments, and infections caused by ESBL-producing microorganisms are an important public health issue.[4–6] Additionally, the incidence of community-onset bacteremia caused by ESBL producers has increased worldwide.[5,6]

The adverse impact of ESBL producers on patients with hospital- or healthcare facility-onset bacteremia has been documented.[4,7] Research has investigated and compared community-onset bacteremia caused by non-ESBL producers, despite findings indicating the dissimilar clinical characteristics and outcomes of patients with community-onset bacteremia caused by ESBL producers.[8,9] Although previous reports have found the difference of bacteremia severity and patient demography between the patients infected by ESBL producers and those by non-ESBL producers to be significant, demonstrating the direct influence of ESBL producers on patient prognosis is difficult. Therefore, we analyzed the impact of ESBL-producing isolates on the outcome of bacteremic patient after controlling for baseline patient characteristics and bacteremia severity by using a propensity-matched analysis (PSM).

Methods

Study design and population

A retrospective, cohort study was conducted at an emergency department (ED) of medical center in southern Taiwan, between January 2008 and December 2013. The study hospital, National Cheng Kung University Hospital, is a 1200-bed, university-affiliated medical center with an annual ED census of approximate 70,000 patients. The hospital institutional review board approved the study, which was reported by the format recommended by STROBE (Strengthening the Reporting of Observational Studies in Epidemiology), and partial clinical information in this study cohort has been published.[10,11]

Study protocol

Bacterial growth in blood cultures from adults sampled in the ED during the study period was screened in a computer database. Patients caused by bacteremic isolates of *E. coli*, *Klebsiella* species, and *Proteus mirabilis* (EKP) were included. Clinical information on eligible adults was retrieved from medical records by using a predetermined case record form including demographic data, initial syndromes, vital signs, bacteremia severity, comorbidities, comorbidity severity, duration and type of antimicrobial agents, bacteremia source, length of hospitalization, and clinical outcome. The study excluded any patients with hospital-onset bacteremia, those with polymicrobial bacteremia, those lacking clinical information from chart records, and those diagnosed with bacteremia prior to visiting the ED. The medical records of eligible patients were reviewed for the preceding clinical information by two of the authors. If any discrepancies were found, both authors examined the medical records together. In cases with multiple bacteremic episodes, only the patient's first episode was included. Adults with bacteremia caused by ESBL producers were assigned to the ESBL group; otherwise, they were assigned to the non-ESBL group.

The overall mortality during the 28 days after ED arrival (bacteremia onset) was referred to as the primary outcome. If patients were discharged within 28 days after ED arrival and were not followed up at our hospital, the required information was retrieved by telephone. Any patients who could not be reached by telephone were excluded.

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