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Community-onset Bacteremic Urinary Tract Infections Caused by Extended-spectrum Beta-lactamase-producing *Escherichia coli and Klebsiella pneumoniae*

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Background: There is an in increase in community-onset bacteremic urinary tract infections (UTIs) caused by *Escherichia coli* and *Klebsiella pneumoniae*. Among these, extended-spectrum beta-lactamase (ESBL)-producing *E. coli* and *K. pneumoniae* (ESBL-EK) are the most prevalent in Taiwan. **Methods:** This study was conducted retrospectively from January 2003–June 2008 and 22 patients were enrolled. Diagnosis was based on the findings of at least one positive blood culture disclosing the same pathogen as urine culture on admission. **Results:** The proportion of patients with indwelling urinary catheters was 41.0% and the proportion for patients from healthcare facilities was 50%. Mean Acute Physiology and Chronic Health Evaluation II scores were 22.1±6.3. The rate of intensive care unit (ICU) admission was 27.3%. The mortality rate was 4.5%. The mean hospital stay was 14.5±7.9 days. Up to 72.7% of 22 patients received inappropriate antibiotic therapy. The mean expenditure on antibiotics was 533.2±370.2 USDs. **Conclusions:** Among the patients, the proportions of male gender patients, patients with urinary catheter indwelling and residents from healthcare facilities were high. Though the majority of them received inappropriate antibiotic treatment, the mortality rate was low.

Key words: bacteremia, extended-spectrum beta-lactamase, urinary tract infection, community

INTRODUCTION

Extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* (ESBLEs) were identified in the early 1980s following the introduction of oxyimino beta-lactam agents. *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) (ESBL-EK) have been regarded as the most predominant ESBLEs.[1,2] *E. coli* and *K. pneumoniae* are major nosocomial pathogens that cause urinary tract infections (UTIs), intra-abdominal infections, and bacteremia.[3] The Clinical and Laboratory Standards Institute (CLSI) has reported ESBL-producing isolates of *E. coli* or *K. pneumoniae* to be resistant to all penicillins and cephalosporins as well as to aztreonam by.[4-6] UTIs are the most common infections in adults, and they are treated by antibiotics. Some studies have regarded bacteremic incidence to be a marker of the disease severity of UTIs.[7,8] Most studies on ESBLEs have been performed in hospital settings, and the number of studies involving a community setting are limited.[9-11] The aim of this study is to evaluate the clinical characteristics of UTIs with bacteremia due to ESBL-EK.

METHODS

Patients

This study was undertaken retrospectively by chart review and approved by the Institutional Review Board (TSGHIRB Approval Number: 097-05-28) at the Tri-Service General Hospital, which is a 2000-bed medical center in Taipei, Taiwan.

The inclusion criteria included ages greater than 18 years and at least one positive blood culture result, with a positive urine culture that yielded both either *E. coli* or *K. pneumoniae* on the day of admission. The period of data collection was from January 2003 to June 2008. Data were collected from medical charts with the following demographic characteristics: Comorbid illnesses, clinical features, laboratory data, Acute Physiology and Chronic

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Health Evaluation (APACHE) II scores, presentation of ICU admission, duration of hospital stay, prior invasive procedures, prior urinary catheterizations, and responses to treatment.

Community-onset infection was defined as an infection diagnosed within 48 hours after admission. Community-onset infections were further classified as healthcare-associated, if any of the following criteria were present[12]: more than 48 hours of hospital admission within the past 90 days, reception of hemodialysis, administration of intravenous medication or home wound care in the past 30 days, and residence in a nursing home or long-term care facility. If these criteria were not met, the cases were recognized as strictly community acquired. Antimicrobial therapy was defined as inappropriate if an active antimicrobial agent (as determined by *in vitro* susceptibility testing) at the usual recommended dose was not administered within the first 48 hours. Oxyimino-beta-lactams (cefuroxime, cefotaxime, ceftriaxone, ceftazidime, cefepime, and atreonam) were considered inappropriate agents for ESBL-EK regardless of susceptibility.

Antibiotic expenditures included antibiotics consumed during hospitalization. Expenditures were calculated in United States dollars (USDs).

The most notable outcomes were based on the mortality rates 21 days after admission (calculated as the total number of deaths/total number of cases).

Microbiologic methods

Antimicrobial susceptibility was determined by the disk diffusion method and ESBL was confirmed using CLIS criteria.[4-6]

RESULTS

From January 2003 to June 2008, 123 patients were diagnosed with community-onset bacteremic UTIs caused by *E.coli* or *K. pneumonia*. Among them, 22 cases were caused by ESBLs. The incidence of ESBLs among community-onset bacteremic UTIs caused by *E. coli* and *K. pneumoniae* in this period was 17.9% (22/123).

The demographic and clinical characteristics of the patients are shown in Table 1. The most common underlying disease was diabetes (22.7% [5/22]). The proportion of males was 54.5% (12/22).

Among clinical presentations, most of the patients had fevers: 77.3% (17/22). The rate of indwelling urinary catheters was 41.0% (9/22) and patients from healthcare facilities made up 50% (11/22). Mean APACHE II scores were 22.1±6.3. The rate of intensive care unit (ICU) admission was 27.3% (6/22).

Table 1 Demographic and clinical characteristics of patients with bacteremic urinary tract infections caused by ESBL-EK.

Variables	n = 22 (%)
Age, mean yr (range)	75.3±11.4 (46-90)
Male	12(54.5)
Underlying disease	
Diabetes	5(22.7)
Malignancy	1(4.5)
Chronic liver disease	1(4.5)
Heart failure	2(9.1)
COPD	3(13.6)
Renal disease	3(13.6)
Prior antibiotic use in 30 days	2(9.1)
Invasive procedure in 30 days (Surgery or central catheter intervention)	0(0)
Indwelling urinary catheter	9(41.0)
Healthcare-associated	11(50)
APACHE II score, mean (range)	22.1±6.3
Clinical presentation	
Fever	17(77.3)
Chill	7(31.8)
Dysuria	2(9.1)
Frequency	2(9.1)
Flank pain	0(0)
ICU admission	6(27.3)
Bacteria	
E.coli	15(68.2)
K. pneumoniae	7(31.8)

Abbreviations: ESBL= extended-spectrum beta-lactamase; *E. coli* = *Escherichia coli*; *K. pneumoniae* = *Klebsiella pneumoniae*; COPD = chronic obstructive pulmonary disease; APACHE II = Acute Physiology and Chronic Health Evaluation II; ICU = intensive care unit.

Though there was a high percentage inappropriate antibiotic treatment: 72.7% (16/22), the mortality was only 4.5% (1/22). The mean time of defervescence after admission was 4.0±3.1 days. The mean hospital stay was 14.5±7.9 days and the mean expenditure on antibiotics was 533.2±370.2 USDs (Table 2).

DISCUSSION

In our study, the incidence of ESBLs among community-onset bacteremic UTIs caused by *E. coli* and *K. pneumoniae* between January 2003 and June 2008 was 17.9%. Indeed, the community may be a reservoir for

Table 2 Clinical outcomes of patients with bacteremic urinary tract infections caused by ESBL-EK.

	n = 22 (%)
Days in hospital, mean	14.5±7.9
Defervescence (days), mean	4.0±3.1
Inappropriate antibiotic treatment	16(72.7)
Mortality	1(4.5)
Antibiotics cost (USDs)	533.2±370.2

Abbreviations: USDs = United States Dollars

ESBL.[10,13,14] In a survey conducted from 2001 to 2002 to determine the incidence of ESBLEs in the stools of outpatients, the prevalence of ESBL carriers was found to have increased from 2.1% to 7.5%.[14] In another study, the incidence of ESBL-E bacteremia from the community was 4.1%.[11] The spread of multidrug-resistant gram-negative bacteria in the community is a serious problem in public health control. Recently, fecal carriage, intestinal colonization, international travel and household member transmission have also been considered to contribute to the spread of ESBL-producing organisms.[15-18]

Rodríguez-Baño et al. have demonstrated that diabetes, previous antibiotic use, recurrent UTIs, previous hospital admission, old age, and male gender are potential risk factors for infection with ESBL-producing organisms in the community.[9] In our study, the rates of patients with urinary catheter indwelling and health care facility residents were high. Our study also showed that male was the predominant gender. Whereas, female was the predominate gender in the general population of UTIs. Moor et al. indicated that health care facilities are important reservoirs of ESBL in the community; indeed, 45% (42/98) of cases they found were residents of health care facilities.[19] In our study, 50% of the patients were from health care facilities.

In choosing antibiotics for UTI patients, cephalosporins, fluoroquinolones, and penicillins are more frequently used than carbapenams. The clinicians should prescribe antibiotics that are appropriate depending on the local prevalence of ESBLs.

However, our study does have limitations. First, the sample size is relatively small. Secondly, this observational study cannot provide risk factor data. Further investigation with prospectively large sample size study should be conducted to overcome the above mentioned limitation .

In conclusion, ESBL-EK is not uncommon in patients with community-onset bacteremic UTIs. On the basis of the findings of our study, the proportions of male gender, patients with urinary catheter indwelling and residents from healthcare facilities are high. Though the majority of patients received inappropriate antibiotic treatment, the mortality rate was low. However, clinical practitioners should be well informed of the characteristics of such patients and should be cautious about the antimicrobial agents administered according to the local prevalence of ESBLs.

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