Prevalence, Treatment, and Outcome of Infection Due to Extended-Spectrum β-Lactamase–Producing Microorganisms

TO THE EDITOR—We read with interest the article by Kang et al.[1] and would like to report the prevalence, treatment, and outcome of nosocomial infections caused by extended-spectrum β-lactamase (ESBL)–producing *Escherichia coli* and *Klebsiella pneumoniae* at a tertiary care center in Thailand. At Thammasart University Hospital (Pratumthani, Thailand), routine laboratory-based detection and confirmation of ESBL-producing *E. coli* and *K. pneumoniae* began on October 1, 2003. All microbiological detection and confirmation methods were performed according to criteria of the Clinical and Laboratory Standards Institute (formerly, the NCCLS).[2] To evaluate the baseline prevalence, treatment, and outcomes among hospitalized adults with ESBL-producing *E. coli* or *K. pneumoniae* nosocomial infections, a retrospective study was conducted from October 1, 2003 through July 31, 2004. Centers for Disease Control and Prevention definitions for nosocomial infections were used in the diagnosis of all infections.[3] The primary outcome was 30-day mortality. Available exposure data included patients' demographic characteristics, comorbidities, severity of illness (based on the Acute Physiology and Chronic Health Evaluation II score), sources of nosocomial infections, empirical antimicrobial regimens received, and the time to initiation of effective antimicrobial therapy (ie, the interval between the first positive culture result and the initiation of carbapenem therapy).

During the 9-month study period, ESBL production was confirmed in 160 (26.3%) of 448 *E. coli* culture isolates and 50 (21%) of 240 *K. pneumoniae* culture isolates. A total of 100% of the ESBL-producing clinical isolates were susceptible to imipenem, 60% to amikacin, and 43% to ciprofloxacin. Clinically, 110 patients had a nosocomial infection with ESBL-producing *E. coli* or *K. pneumoniae*; 90 (81.8%) had medical records available for further clinical evaluation. Twenty-four (27%) of these 90 patients developed nosocomial bloodstream infection (BSI) due to ESBL-producing *E. coli* or *K. pneumoniae*. Of these patients, 21 (87%) developed secondary nosocomial BSI, including urinary tract infection (in 15 patients), pneumonia (in 5), and surgical site infection (in 1),

TABLE. Demographic and Clinical Characteristics of 90 Patients With Extended-Spectrum β-Lactamase–Producing *Escherichia coli* or *Klebsiella pneumonia* Nosocomial Bloodstream Infection (BSI) at a Tertiary Care Center in Thailand

Characteristic	Total cohort (n = 90)	Survivors of BSI (n = 12)	Nonsurvivors of BSI (n = 12)	P
Male sex	34 (38)	5 (42)	7 (58)	.68
Age, median years (range)	63 (17-97)	61 (30-93)	65 (23-89)	.85
Underlying disease				
Liver cirrhosis	7 (8)	2 (17)	1 (8)	1.0
End-stage renal disease	10 (11)	2 (17)	2 (17)	1.0
Diabetes	28 (31)	3 (25)	2 (17)	1.0
Any immunocompromised state[a]	8 (8)	2 (17)	2 (17)	1.0
APACHE II score, median (range)	10 (2-22)	11 (3-15)	12 (3-18)	.82
Type of nosocomial infection				
Bloodstream infection	24 (26.7)	12 (50)	12 (50)	1.0
Urinary tract infection only	49 (54)	NA	NA	NA
Pneumonia only	14 (16)	NA	NA	NA
Wound infection only	3 (3.3)	NA	NA	NA
Other types only	0 (0)	NA	NA	NA
Empirical antimicrobial therapy received				
Carbapenems	14 (17)	4 (33)	2 (18)	.67
Quinolones	8 (9)	2 (18)	1 (8)	1.0
Third- or fourth-generation cephalosporins	38 (42)	4 (33)	5 (40)	1.0
β-Lactam or β-lactamase inhibitor	12 (13)	1 (8)	1 (8)	1.0
Aminoglycosides	6 (6)	1 (8)	2 (18)	1.0
Other	12 (13)	0 (0)	1 (8)	1.0
Received effective initial antimicrobial therapy	37 (41)	8 (67)	5 (42)	0.41
30-day mortality	26 (29)	NA	12 (100)	NA

NOTE. Data are no. (%) of subjects, unless otherwise indicated. APACHE = Acute Physiology and Chronic Health Evaluation; NA = not applicable; NS = not significant.

[a] Includes subjects with any type of currently active malignancy, human immunodeficiency virus type 1 infection, or neutropenia and subjects who were currently receiving steroids or immunosuppressive agents.

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whereas 4 patients developed primary BSI due to ESBL-producing *E. coli* or *K. pneumoniae*. Demographic and clinical data, including empirical antimicrobial treatment regimens received and outcomes, are summarized in the Table. The overall 30-day mortality rate was 29% (26 of 90 patients).

Patients with nosocomial BSI due to ESBL-producing *E. coli* or *K. pneumoniae* were more likely to die than patients without BSI (50% vs 21%; $P = .01$). There were no significant differences in survival according to baseline demographic or clinical characteristics (Table). Adjustment for severity of illness revealed that mortality was higher among patients who did not receive a carbapenem for at least 2 days during the 5-day period after the first positive blood culture result than among patients who did (adjusted odds ratio, 2.12; 95% confidence interval, 1.15-61; $P = .03$). There was no significant difference in mortality among patients who received initial antimicrobial therapy that was effective, compared with patients who received initial antimicrobial therapy that was not effective (42% vs 58%; $P = .41$), nor was there a significant difference in mortality for patients who received empirical antimicrobial therapy with a carbapenem, compared with patients who received a noncarbapenem regimen (33% vs 55%; $P = .67$). There was also no difference with respect to patient characteristics, empirical antimicrobial regimens received, or 30-day mortality between patients infected with ESBL-producing *E. coli* and patients infected with ESBL-producing *K. pneumoniae*.

Debate continues on the role of screening clinically relevant gram-negative bacteria for ESBL production, and there are varied interpretations of the impact of this laboratory-based practice on health outcomes and resource use.[4] Recent studies of treatment failure have called into question the usefulness of screening patients for pathogens with susceptibility to extended-spectrum cephalosporins and the use of carbapenems for treatment of serious infections due to ESBL-producing pathogens.[1,5-7] Given the high prevalence and associated crude mortality rate associated with ESBL-producing *E. coli* and *K. pneumoniae* BSIs in our study, tertiary care centers in Thailand should consider routine screening of *E. coli* and *K. pneumoniae* isolates for ESBL production. Although the small sample size limits our ability to quantify the true risk associated with ineffective antimicrobial therapy or to identify additional factors that may be associated with mortality, our data further substantiate the findings by Kang et al.[1] and suggest that initial empirical antimicrobial therapy that is ineffective may not be associated with higher mortality rates for nosocomial BSI caused by ESBL-producing *E. coli* or *K. pneumoniae*. Additional studies on the prevalence, treatment, and role of ineffective antimicrobial therapy on the outcomes for persons infected with ESBL-producing *E. coli* or *K. pneumoniae* in Asian-Pacific countries are needed.

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