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Risk Factors for Infection or Colonization with CTX-M Extended-Spectrum-β-Lactamase-Positive *Escherichia coli*

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There has been a significant increase in the prevalence of *Enterobacteriaceae* that produce CTX-M-type extended-spectrum β-lactamases. The objective of this study was to evaluate risk factors for infection or colonization with CTX-M-positive *Escherichia coli*. A case-control study was conducted within a university system from 1 January 2007 to 31 December 2008. All patients with clinical cultures with *E. coli* demonstrating resistance to extended-spectrum cephalosporins were included. Case patients were designated as those with cultures positive for CTX-M-positive *E. coli*, and control patients were designated as those with non-CTX-M-producing *E. coli*. Multivariable logistic regression analyses were performed to evaluate risk factors for CTX-M-positive isolates. A total of 83 (56.8%) of a total of 146 patients had cultures with CTX-M-positive *E. coli*. On multivariable analyses, there was a significant association between infection or colonization with CTX-M-type β-lactamase-positive *E. coli* and receipt of piperacillin-tazobactam in the 30 days prior to the culture date (odds ratio [OR], 7.36; 95% confidence interval [CI], 1.61 to 33.8; $P = 0.01$) and a urinary culture source (OR, 0.36; 95% CI, 0.17 to 0.77; $P = 0.008$). The rates of resistance to fluoroquinolones were significantly higher in isolates from case patients than in isolates from control patients (90.4 and 50.8%, respectively; $P < 0.001$). We found that nonurinary sources of clinical cultures and the recent use of piperacillin-tazobactam conferred an increased risk of colonization or infection with CTX-M-positive *E. coli*. Future studies will need to focus on outcomes associated with infections due to CTX-M-positive *E. coli*, as well as infection control strategies to limit the spread of these increasingly common organisms.

Since their initial description in 1983 (17), extended-spectrum-β-lactamase (ESBL)-producing Gram-negative organisms have emerged as a global problem (1, 3, 13, 28, 29). Infections with ESBL-producing *Enterobacteriaceae* are associated with increased morbidity, mortality, and health care costs (19, 42). In the past decade, there has been a significant increase in the prevalence of *Enterobacteriaceae* that produce CTX-M-type β-lactamases (6, 10, 45). CTX-M-type β-lactamases are predominantly found in *Escherichia coli* and have now surpassed the TEM and SHV types as the most common ESBL type in some geographic regions (22, 40, 43).

Given the increased mortality associated with delay in appropriate treatment for ESBL-associated infections (41), early recognition of patients who are at risk for infection with ESBL-producing *E. coli* is critical for selection of empirical antibiotic therapy and implementation of infection control measures to limit spread. Risk factors such as severity of illness, instrumentation, and prior antibiotic use have been identified for ESBL-producing *Enterobacteriaceae* in general (4, 5, 19). However, despite emerging data suggesting that the epidemiology of CTX-M-producing isolates is different from those producing other types of ESBLs (4, 38), there are few published studies specifically evaluating risk factors for CTX-M-producing *Enterobacteriaceae* (7, 20, 26, 37, 39, 46). Furthermore, these have been limited by small sample sizes (20, 26, 37, 46) and restricted to select patient populations or types of infections (7, 20, 26, 37, 39, 46). To our knowledge, there are no studies evaluating risk factors for CTX-M-producing *E. coli* in the United States, where the epidemiologies of infections associated with CTX-M-type β-lactamases may be different due to variation in antibiotic prescription and infection control practices. Finally, to our knowledge, our study is the first to investigate risk factors for CTX-M production in *E. coli* using a control group selected from non-CTX-M-producing *Enterobacteriaceae* demonstrating resistance, as opposed to susceptibility, to extended-spectrum cephalosporins. Elucidating risk factors for different resistance mechanisms (i.e., CTX-M versus other ESBLs) is critical, since prior work suggests that the epidemiologies of various resistance mechanisms among *Enterobacteriaceae*, including risk factors for isolation, may be different (18). Therefore, we conducted the present study to evaluate risk factors for infection or colonization with CTX-M-positive *E. coli*, with the hypothesis that prior antibiotic use is a significant risk factor for isolation of CTX-M-positive *E. coli*.

MATERIALS AND METHODS

Study design and setting. This case-control study was conducted at two hospitals in the University of Pennsylvania Health System (UPHS) in Philadelphia: the Hospital of the University of Pennsylvania (HUP), a 725-bed academic tertiary care medical center, and Penn Presbyterian Medical Center (PPMC), a 344-bed urban community hospital. The study was approved by the institutional review board of the University of Pennsylvania.

Study population. All adult inpatients and outpatients with clinical cultures positive for *E. coli* during the study period from 1 January 2007 to 31 December 2008 were identified through the HUP clinical microbiology

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laboratory, which processes all specimens obtained from patients at HUP and PPMC. Subsequently, patients with clinical cultures with *E. coli* resistant to ceftriaxone or ceftazidime were eligible for inclusion in the study. Each patient was included only once, using the first clinical culture with *E. coli* meeting the above criteria identified during the study period.

Microbiological identification and susceptibility testing. Standard susceptibility testing of *E. coli* was performed and interpreted according to standard methods (8, 9) using the Vitek2 semiautomated system or disk diffusion testing. Confirmatory ESBL testing was performed using the double-disk synergy test for nonurinary isolates, as well as for urinary isolates that exhibited a ceftazidime or ceftriaxone MIC that was >1 μg/ml but <64 μg/ml. Urinary isolates with a ceftazidime or ceftriaxone MIC of ≥64 μg/ml, as well as those with carbapenem resistance as determined by a positive modified Hodge test (9), did not have double-disk testing performed as these were assumed to be ESBL-producers. Finally, the presence of the bla_{CTX-M} gene was detected by PCR as previously reported (31). Therefore, cases and controls were defined solely on the basis of CTX-M production, with case patients designated as those with cultures positive for CTX-M-positive *E. coli*, and control patients designated as those who had non-CTX-M-producing, extended-spectrum cephalosporin-resistant *E. coli* isolated. A previous study of the CTX-M-positive *E. coli* isolated in 2007 showed that the isolates were not clonal based on pulsed-field gel electrophoresis analysis and that multiple CTX-M types were represented (25).

Data collection. Data were abstracted from the Pennsylvania Integrated Clinical and Administrative Research Database (PICARD), which includes demographic, laboratory, pharmacy, and billing information and has been used successfully in prior studies of antibiotic utilization and resistance (2, 12, 21). The following data were collected for all subjects: baseline demographics, inpatient or outpatient status in relation to the culture date, origin at the time of hospital admission for inpatients (i.e., physician referral, transfer from another facility, or admission through the Emergency Department), hospital location at the time of infection (i.e., intensive care unit or medical floor), prior admission to UPHS in the 30 days prior to the culture date, time of onset of nosocomial infection (date of the first positive culture ≥48 h from the date of admission), health care-associated infection (date of the first positive culture ≥48 h from the date of admission or admission as a transfer from another institution), and culture site (i.e., blood, urine, respiratory tract, or wound). The presence of the following comorbid conditions was documented in relation to the culture date: diabetes mellitus, malignancy, renal insufficiency (creatinine of ≥2.0 mg/dl or the requirement of dialysis), chronic liver disease (i.e., cirrhosis or chronic hepatitis), chronic pulmonary disease (i.e., chronic obstructive pulmonary disease, asthma, or interstitial lung disease), congestive heart failure, solid organ or hematopoietic stem cell transplantation, HIV infection, neutropenia (absolute neutrophil count $< 500/mm^3$), and receipt of an immunosuppressive agent, including corticosteroids, in the prior 30 days. In addition, the Charlson comorbidity index was calculated for each subject (34). Furthermore, chart review was performed to collect data on the presence of indwelling devices, including central venous catheters, urinary catheterization, and mechanical ventilation prior to the culture date.

All antimicrobial therapy administered during the 30 days prior to the clinical culture date was documented. Antimicrobial therapy was categorized by agent or class, including vancomycin, aminoglycosides, extended-spectrum penicillins (e.g., piperacillin-tazobactam), antistaphylococcal penicillins (e.g., nafcillin), other penicillins (e.g., ampicillin and ampicillin-sulbactam), extended-spectrum cephalosporins (e.g., ceftriaxone, ceftazidime, and cefepime), other cephalosporins (e.g., cefazolin), trimethoprim-sulfamethoxazole, fluoroquinolones, tetracyclines (e.g., doxycycline), metronidazole, aztreonam, tigecycline, and daptomycin (11, 23).

Statistical analysis. Cases and controls were characterized by potential risk factors, including demographic variables, comorbid conditions, and prior antibiotic use. Continuous variables were compared using the Student *t* test or Wilcoxon rank-sum test, and categorical variables were compared using the χ^2 or Fisher exact test. Bivariable analyses were then performed to determine the association between potential risk factors and isolation of CTX-M-positive *E. coli*, focusing on prior antibiotic use as the primary risk factor of interest. The odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of any association.

Stratified analyses were conducted to elucidate where confounding and interaction were likely to exist in multivariable analyses, using the Mantel-Haenszel test for summary statistics (24). In particular, inpatient versus outpatient status at the time of the culture date, as well as culture site (e.g., bacteremia or urinary source), were *a priori* designated as potential effect modifiers of the association of interest. Interaction was determined to be present when the test for heterogeneity between the ORs for different strata yielded a *P* value of ≤0.05. Multivariable analyses were subsequently performed using multiple logistic regression (15), with calculation of adjusted ORs with 95% CIs. A stepwise (forward-backward) selection procedure was used, with variables with *P* values <0.20 in bivariable analyses or noted to be confounders in stratified analyses considered candidate variables and maintained in the final explanatory model if their inclusion resulted in a ≥15% change in the effect measure for the primary association of interest or if they were statistically significant on likelihood ratio testing (27). For all calculations, a two-tailed *P* value of <0.05 was considered significant.

All statistical calculations were performed using commercially available software (STATA version 11.0; StataCorp LP, College Station, TX).

RESULTS

Study population. A total of 146 unique patients with clinical cultures with *E. coli* resistant to extended-spectrum cephalosporins were identified during the 2 year study period. The mean age of patients was 63 years (standard deviation [SD], 17.3), and 61 (41.8%) of them were male. Of the 146 patients, 81 (55.5%) were white, 47 (32.2%) were African-American, 6 (4.1%) were Asian, 5 (3.4%) were Hispanic, and the remainder were self-identified as "other." Furthermore, among all patients, 108 (74.0%) were hospitalized at the time of the clinical culture, while 38 (26.0%) were outpatients. Finally, the distribution of culture sources was as follows: 88 (60.3%) of the cultures were from urine, 29 (19.9%) blood, 18 (12.3%) wound, and 11 (7.5%) respiratory tract.

Microbiological results. Of the 146 unique isolates, 83 (56.8%) were positive for CTX-M-type β-lactamases by PCR testing and were designated as from case patients. Control patients, of which there were 63 (43.2%), were negative for CTX-M-type β-lactamase. The distribution of CTX-M groups among the isolates was as follows: 52 (62.6%) belonged to group I, 30 (36.1%) belonged to group IV, and 1 (1.2%) belonged to group II. Two unique isolates among the control group were *Klebsiella pneumoniae* carbapenemase-producing *E. coli*.

Antibiotic susceptibility patterns of isolates from case and control patients are shown in Table 1. Coresistance to antibiotics was notable for a significant association between CTX-M positivity and fluoroquinolone ($P < 0.001$) and tobramycin ($P = 0.004$) resistance.

Risk factors for CTX-M isolation. In bivariable analyses, several variables were noted to be significantly associated with CTX-M-type β-lactamase positivity (Table 2), including hospitalization at the time of the clinical culture (OR, 2.25; 95% CI, 1.06 to 4.77; $P = 0.03$) and mean Charlson comorbidity score ($P = 0.01$). The culture site was also significantly associated with CTX-M production, whereby bacteremia demonstrated an OR of 2.89 (95% CI, 1.14 to 7.27; $P = 0.02$) and a urinary source was associated with an OR of 0.29 (95% CI, 0.13 to 0.60; $P = 0.001$). Finally, receipt of

TABLE 1 Antibiotic susceptibility rates of *E. coli* resistant to extended-spectrum cephalosporins among case and control patients

Antibiotic	No. (%)[a] with resistance among: Cases ($n = 83$)	Controls ($n = 63$)	P
Levofloxacin	75 (90.4)	32 (50.8)	<0.001
Piperacillin-tazobactam[b]	8 (18.6)	2 (13.3)	0.99
Trimethoprim-sulfamethoxazole	51 (61.5)	30 (47.6)	0.13
Gentamicin	31 (37.4)	19 (30.2)	0.38
Tobramycin	45 (54.2)	19 (30.2)	0.004
Amikacin[c]	8 (10.8)	2 (3.9)	0.20
Tetracycline[d]	25 (62.5)	27 (57.5)	0.67
Ertapenem	1 (1.2)	3 (4.8)	0.32

[a] Includes intermediate and resistant isolates.
[b] Susceptibility testing was performed only for nonurinary isolates.
[c] Susceptibility information was unavailable for 21 patients (12 control patients, 9 case patients).
[d] Susceptibility testing was performed only for urinary isolates.

an extended-spectrum penicillin (i.e., piperacillin-tazobactam) was significantly associated with CTX-M positivity (OR, 9.05; 95% CI, 2.02 to 40.5; $P = 0.001$).

On multivariable analyses of risk factors for infection or colonization with CTX-M-type β-lactamase-positive *E. coli* (Table 3), there was no significant effect modification by inpatient status ($P = 0.43$), health care association ($P = 0.13$), bacteremia ($P = 0.99$), or urinary source ($P = 0.98$). The unadjusted OR between receipt of any antibiotic in the 30 days prior to the culture date and CTX-M-type β-lactamase production was 1.62 (95% CI, 0.83 to 3.16; $P = 0.16$). In multivariable analyses, receipt of an extended-spectrum penicillin (i.e., piperacillin-tazobactam) in the 30 days prior to the culture date was an independent risk factor for CTX-M-type β-lactamase production (OR, 7.36; 95% CI, 1.61 to 33.8; $P = 0.01$). After controlling for confounders, a urinary clinical culture was significantly associated with a reduced risk of infection or colonization with CTX-M-positive *E. coli* (OR, 0.36; 95% CI, 0.17 to 0.77; $P = 0.008$).

DISCUSSION

In this cohort study of 146 patients with both nosocomial and community-acquired cultures with *E. coli* demonstrating resistance to extended-spectrum cephalosporins, we found that 83 (56.8%) isolates were positive for CTX-M-type ESBLs. Furthermore, isolation of CTX-M positive *E. coli* was significantly associated with the recent use of an extended-spectrum penicillin and a nonurinary source of infection or colonization.

The risk factors for the isolation of ESBL-producing *Enterobacteriaceae* from clinical specimens have been well described, including previous antibiotic use (19, 30, 44). However, despite emerging data suggesting that the epidemiology of CTX-M-positive isolates is different from those producing other types of ESBLs (4, 38), only a few studies to our knowledge have evaluated risk factors specifically for CTX-M production among *Enterobacteriaceae* (7, 20, 26, 35, 37, 39, 46). These studies have been limited by small sample sizes (20, 26, 37, 46), lack of multivariable analyses (26), and evaluation restricted to select populations such as hospitalized patients (7, 20, 26, 37) or specific types of infections such as bacteremia (46). In addition, the majority of studies selected control groups for comparison from non-CTX-M-positive *Enterobacteriaceae* with susceptibility to extended-spectrum cephalosporins; however, this method of control group selection may lead to overestimation of the ORs for prior exposure to antibiotics, particularly the antibiotic to which the organism associated with infections in control but not case patients is susceptible (14). To our knowledge, the present study is the first in the literature to evaluate risk factors for CTX-M production in *E. coli* associated with both the health care and community settings in the United States and to utilize a control group comprised of patients with cultures with *E. coli* demonstrating resistance to extended-spectrum cephalosporins.

A novel finding of our study is that isolation of CTX-M positive *E. coli* from clinical specimens was associated with prior use of an extended-spectrum penicillin in the 30 days prior to the culture date. Prior antibiotic use has been well described as a risk factor for infections due to ESBL-producing *Enterobacteriaceae* (4). Among studies evaluating risk factors specifically for CTX-M-positive isolates, recent receipt of extended-spectrum cephalosporins, fluoroquinolones, or a combination of the above has been implicated (7, 37). In addition, a study of 45 patients with cultures positive for CTX-M-producing *E. coli* reported a significant association between the prior use of antibiotics from the β-lactam/β-lactamase inhibitor class and CTX-M production (26), but that study was limited to bivariable analyses and lacked a control group.

Why piperacillin-tazobactam use was a risk factor for CTX-M colonization or infection is not clear, since there appeared to be no selective disadvantage for CTX-M-negative *E. coli*, based on nearly identical piperacillin-tazobactam susceptibility frequencies between case and control isolates. Nevertheless, consideration of this finding will be important in the implementation of antibiotic stewardship measures, particularly in institutions with high rates of extended-spectrum penicillin use. Ultimately, further work is needed to elucidate outcomes associated with infections due to *E. coli* with CTX-M-type β-lactamases compared to other ESBLs to help guide development of effective antimicrobial stewardship and restriction policies.

One potential explanation for CTX-M infection or colonization not involving antibiotic selection is that the use of extended-spectrum penicillins, specifically piperacillin-tazobactam, may be a marker for disease severity in patients with clinical cultures with CTX-M-positive *E. coli*. Along these lines, on bivariable analyses, case patients were more likely to be hospitalized ($P = 0.03$) and had a higher mean Charlson comorbidity score ($P = 0.01$) at the time of the culture date.

The results of our study also demonstrated an increased risk of CTX-M production with nonurinary sources of colonization or infection, and to our knowledge, this study is the first to demonstrate such an association. Furthermore, this association remained significant on *post hoc* subanalyses restricted to inpatients (OR for urinary source, 0.37; 95% CI, 0.16 to 0.87; $P = 0.02$). Although CTX-M-producing *Enterobacteriaceae* have typically been associated with community onset infections (20, 32, 36), and most notably urinary tract infections, the results of our study suggest that CTX-M-type β-lactamases may play an important role in the hospital setting and in particular in nonurinary infections such as bacteremia. Differences in control group selection may have, in part, explained the novel association with a nonurinary source demonstrated in our study. Furthermore, studies suggest that CTX-M-type β-lactamases may be associated with virulence fac-

TABLE 2 Characteristics of patients with clinical cultures with *E. coli* resistant to extended-spectrum cephalosporins

Patient characteristic	No. (%)[a]		*P*	OR (95% CI)[b]
	With CTX-M ($n = 83$)	Without CTX-M ($n = 63$)		
Mean age in yrs (SD)	64.8 (15.3)	61.1 (19.6)	0.32	NA
Female	45 (54.2)	40 (63.5)	0.26	0.68 (0.35–1.33)
Nonwhite race	38 (45.8)	27 (42.9)	0.72	1.13 (0.58–2.18)
Inpatient status	67 (80.7)	41 (65.1)	0.03	2.25 (1.06–4.77)
Emergency department admission	38 (45.8)	23 (36.5)	0.26	1.47 (0.75–2.87)
Physician referral on admission	14 (16.9)	6 (9.5)	0.23	1.93 (0.70–5.33)
Nosocomial onset	35 (42.2)	20 (31.8)	0.20	1.57 (0.79–3.11)
Duration of hospitalization prior to the culture date, mean days (SD)	10.2 (30.1)	13.0 (33.0)	0.86	NA
Health care-associated infection	40 (48.2)	24 (38.1)	0.22	1.51 (0.78–2.94)
Prior admission to UPHS ≤ 30 days before the culture date	10 (12.1)	5 (7.9)	0.76	1.59 (0.51–4.91)
Bacteremia	22 (26.5)	7 (11.1)	0.02	2.89 (1.14–7.27)
Urinary source	40 (48.2)	48 (76.1)	0.001	0.29 (0.13–0.60)
Mean white blood cell count × 10^9/liter (SD)[c]	11.5 (7.4)	10.5 (7.1)	0.21	NA
Indwelling device	36 (43.4)	19 (30.2)	0.10	1.77 (0.89–3.54)
Central venous catheter	22 (26.5)	11 (17.5)	0.23	1.70 (0.76–3.84)
Mechanical ventilation	9 (10.8)	3 (4.8)	0.23	2.43 (0.63–9.39)
Urinary catheter	17 (20.5)	9 (14.3)	0.39	1.55 (0.64–3.74)
Diabetes mellitus	36 (26.9)	84 (32.6)	0.25	1.44 (0.65–3.20)
HIV	2 (2.4)	1 (1.6)	0.99	1.53 (0.14–17.3)
Malignancy	18 (21.7)	9 (14.3)	0.29	1.66 (0.69–4.00)
Renal insufficiency	25 (30.1)	10 (15.9)	0.05	2.28 (1.00–5.20)
Neutropenia	3 (3.6)	0 (0.0)	0.26	NA
Transplant (solid organ or hematopoietic stem cell)	8 (9.6)	8 (12.7)	0.60	0.73 (0.26–2.07)
Chronic liver disease	8 (9.6)	3 (4.8)	0.35	2.13 (0.54–8.39)
Chronic pulmonary disease	8 (9.6)	5 (7.9)	0.78	1.24 (0.38–3.98)
Congestive heart failure	15 (18.1)	11 (17.5)	0.92	1.04 (0.44–2.46)
Mean Charlson comorbidity score (SD)	2.5 (2.4)	1.7 (2.3)	0.01	NA
Receipt of any immunosuppression ≤ 30 days prior to the culture date	30 (36.1)	20 (31.8)	0.58	1.22 (0.61–2.44)
Receipt of corticosteroids ≤30 days prior to the culture date	25 (30.1)	19 (30.2)	0.99	1.00 (0.49–2.04)
ICU location on culture date	22 (26.5)	9 (14.3)	0.10	2.16 (0.92–5.10)
Receipt of antibiotics ≤30 days prior to the culture date[d]				
Any antibiotic	40 (48.2)	23 (36.5)	0.16	1.62 (0.83–3.16)
Vancomycin	30 (36.1)	14 (22.2)	0.07	1.98 (0.94–4.17)
Antistaphylococcal penicillin	0 (0.0)	2 (3.2)	0.19	NA
Extended-spectrum penicillin	19 (22.9)	2 (3.2)	0.001	9.05 (2.02–40.5)

[a] Data are presented as numbers (percentages) except as noted otherwise in column 1. NA, not applicable.
[b] ORs were unavailable for continuous variables or categorical variables with no events in one or more cells.
[c] Data were unavailable for 24 patients (16 control patients, 8 case patients).
[d] All other agents and classes of antimicrobials not shown due to $P > 0.20$ on bivariable analyses.

tors different from those of other ESBL types (16, 33), and it is possible that specific factors may predispose toward bacteremia as opposed to low-inoculum infections such as urinary tract infections. However, further work is needed to elucidate the epidemiology of CTX-M-positive *Enterobacteriaceae* as a cause of non-urinary tract infections, including in the hospital as opposed to the community setting. Nevertheless, this finding has important implications for empirical treatment of associated infections in the hospital setting, as the antibiotic susceptibility patterns of CTX-M-positive *E. coli* strains appear to differ significantly from those of *E. coli* strains with production of other ESBL types (7, 20, 38).

TABLE 3 Final multivariable model of risk factors associated with CTX-M-type β-lactamase positivity in patients with clinical cultures with *E. coli*

Variable	OR (95% CI)	*P*
Urinary source	0.36 (0.17–0.77)	0.008
Charlson comorbidity score	1.11 (0.95–1.30)	0.20
Receipt of an extended-spectrum penicillin ≤30 days prior to the culture date	7.36 (1.61–33.8)	0.01

As in previous studies (7, 20), we observed high rates of coresistance to fluoroquinolones in isolates from case as opposed to control patients, with 90.4% of CTX-M-positive *E. coli* isolates demonstrating resistance to levofloxacin. Resistance rates to other antibiotics, including trimethoprim-sulfamethoxazole and tobramycin, were relatively high and may reflect geographic variation. Finally, the results of our study confirm that carbapenems remain active against *E. coli* with CTX-M-type β-lactamases, and these antibiotics should be considered first-line treatment for serious infections due to these organisms.

There are several potential limitations of the present study. We

were unable to differentiate colonization from infection in regard to clinical cultures, although a substantial proportion of patients in our study had bacteremia as the culture source. The selection bias is likely small, since subjects were identified through the clinical microbiology laboratory which processed and cultured all specimens obtained at HUP and PPMC during the study period. Similarly, misclassification bias is a concern in case-control studies, but case and control patients were identified based solely on antibiotic susceptibility testing. Of note, our control group included two patients with isolates that were carbapenem resistant as determined by a positive modified Hodge test. However, exclusion of these patients from the control group did not affect the results of final multivariable analyses. Finally, the present study was conducted in a single health care system, and these results may not be generalizable to other institutions with differing characteristics or to other geographical locations.

In conclusion, we found that nonurinary sources of clinical cultures, as well as the recent use of extended-spectrum penicillins, conferred an increased risk of colonization or infection with *E. coli* strains producing CTX-M-type β-lactamases as opposed to other ESBL types. Future studies will need to focus on outcomes associated with infections due to CTX-M-producing *E. coli*, including mortality, as well as elucidation of optimal infection control strategies designed to limit the spread of these increasingly prevalent organisms.

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