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Colonization with Extended-Spectrum β-Lactamase-Producing *Escherichia coli* and *Klebsiella* Species in Long-Term Care Facility Residents

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Abstract

We describe the prevalence of and risk factors for colonization with extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-EB) in the long-term care facility (LTCF) setting. Colonization prevalence differed significantly across the 3 LTCFs evaluated in the study, with recent use of levofloxacin and fecal incontinence demonstrating borderline significant associations with ESBL-EB colonization.

Infections due to extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-EB) are associated with increased morbidity, mortality, and healthcare costs.[1] Numerous studies have focused on ESBL-EB colonization and infection in the hospital setting.[1-3] However, despite the dramatic increase in the use of long-term care facilities (LTCFs) in the United States as well as their role as a reservoir for multidrug-resistant gram-negative bacteria,[4] very little is known regarding the epidemiology of ESBL-EB in LTCFs. We conducted the present study to characterize the prevalence of and risk factors for gastrointestinal tract colonization with ESBL-EB in 3 LTCFs.

Methods

We conducted a cross-sectional study within the Academic Long Term Care Network (ALTCN) of the University of Pennsylvania (Philadelphia, PA) during the period March 7, 2006, through October 2, 2008. Study subjects were enrolled at 3 primary LTCFs of the ALTCN: (1) LTCF-1, a 124-bed urban facility comprising 4 distinct units (each with ~30 beds), with a total of 17 skilled nursing beds; (2) LTCF-2, a 240-bed urban facility comprising four 60-bed units, with a total of 20 skilled nursing beds; and (3) LTCF-3, a 200-bed suburban facility comprising five 40-bed units, with a total of 20 skilled nursing beds.

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All subjects who provided informed consent were eligible for inclusion and subsequent fecal sampling via perirectal swabs, with each subject included only once in the study. If a study subject was unable to provide informed consent, the family member acting as the medical proxy or legally authorized representative was contacted to obtain consent, with a total of 3 attempts made.

Identification of *Escherichia coli* and *Klebsiella* species and antimicrobial susceptibility testing were performed and interpreted in accordance with Clinical and Laboratory Standards Institute (CLSI) criteria,[5] using the semi-automated Microscan identification and susceptibility system (Giles Scientific). Confirmatory testing for ESBL production was performed using the double disk confirmation test method.[5] The genetic relatedness of ESBL-EB isolates was determined by molecular typing using pulsed-field gel electrophoresis (PFGE; CHEF Mapper XA System [Bio-Rad]), with clonal relatedness determined according to established criteria.[6]

A case-control study was performed to assess risk factors associated with ESBL-EB colonization. Case patients were those patients colonized with ESBL-EB, and control patients were those patients without ESBL-EB colonization. Case patients and control subjects were drawn from the same population, with the case and control status of each subject determined solely by the results of ESBL testing. Potential risk factors were ascertained by medical record review, including baseline demographic characteristics, LTCF of residence, duration of stay before sampling, recent hospitalization (defined as hospitalization 30 days or less before sampling), and skilled nursing requirement. Comorbid conditions were documented, including dementia, coronary artery disease, pulmonary disease, cirrhosis, human immunodeficiency virus infection, diabetes, fecal incontinence, and renal insufficiency. Finally, antimicrobial use within the 30 days preceding sampling was assessed.

Bivariable analyses were conducted to determine the association between potential risk factors and ESBL-EB colonization. Categorical variables were compared using Fisher's exact test, with calculation of an odds ratio (OR) and 95% confidence interval (CI) to evaluate the strength of any association. Continuous variables were compared using the Wilcoxon rank-sum test. Because of the small number of cases, multivariable analyses were not performed. For all calculations, a 2-tailed P value of $<.05$ was considered significant. All statistical calculations were performed using Stata software, version 11.0 (StataCorp). This study was reviewed and approved by the institutional review board for all 3 facilities.

Results

A total of 1,283 subjects were screened across all 3 LTCF sites. Of the 725 subjects whom study personnel were able to approach, 307 consented and had perirectal swab samples obtained, and 418 refused. Subsequently, a total of 239 plates demonstrated growth with *E. coli* or *Klebsiella* species. There were 86 subjects (36.0%) at LTCF-1, 125 (52.3%) at LTCF-2, and 28 (11.7%) at LTCF-3. The mean age of subjects was 74 years (range, 35–100 years), and 60 subjects (25.1%) were female. Of the 217 subjects for which race was indicated, 106 (48.9%) were white and 109 (50.2%) were black. The median duration of stay before sampling was 164 days (interquartile range, 51–917 days). Fifty-seven subjects (23.8%) had received at least 1 antibiotic in the 3 days before sampling.

Among the 239 subjects, 8 (3.4%) were colonized with ESBL-EB. Twelve isolates demonstrated resistance to ceftriaxone, and 8 of these isolates were ESBL-producing *Enterobacteriaceae*. Seven isolates were *E. coli*, and 1 was *Klebsiella pneumoniae*. No isolates were determined to be clonally related by PFGE analysis. A comparison of the

characteristics of patients with and patients without ESBL-EB colonization is shown in Table 1. There were no significant differences between case patients and control subjects with regard to demographic characteristics, previous use of antibiotics, or comorbidities except for fecal incontinence, for which there was a borderline significant association with ESBL-EB colonization ($P = .05$). Finally, there were significant differences in the proportion of subjects with ESBL-EB colonization across study sites: 4.7% (4 of 86 total patients) at LTCF-1, 0.8% (1 of 125 total patients) at LTCF-2, and 10.7% (3 of 28 total patients) at LTCF-3 ($P = .02$).

Discussion

In this multicenter study, we found that 3.4% of LTCF residents were colonized with ESBL-EB, with prevalence rates differing significantly across sites. To our knowledge, only a few studies have previously assessed ESBL-EBs in LTCFs, and the majority of these have focused on clinical cultures as opposed to colonization.[7-10] These studies have reported varying results, with ESBL-EB prevalence ranging from ~20% in clinical urine cultures in a single LTCF[7] to as high as ~65% in a single LTCF using comprehensive surveillance methods.[9] Our prevalence of ESBL-EL colonization was significantly lower, and reasons for this difference may include (1) the use of a single perirectal swab sample, rather than swab samples obtained from multiple body sites or clinical cultures, to determine prevalence and (2) the fact that the majority of subjects in our study were enrolled from the LTCF with the lowest prevalence of ESBL-EL.

We noted that the prevalence of ESBL-EB colonization differed significantly across LTCFs. This may be attributable to differences in patient populations, antibiotic use patterns, or infection control procedures across the institutions. For example, spread within an LTCF may be particularly important in the epidemiology of ESBL-EB, and indeed, the association between fecal incontinence and ESBL-EB colonization in our study suggests a potential role for person-to-person spread. Regardless of the mechanism(s) underlying these differences, the implications of this finding are important. Selection of empirical antimicrobial therapy at a given LTCF should be based, at least in part, on the prevalent organisms colonizing residents. Furthermore, optimal empirical therapy for suspected infection may be different across LTCF sites.

The study had several potential limitations. Selection bias is likely to be minimal, because all residents of the participating LTCFs were eligible and were enrolled if they provided informed consent. Although misclassification bias may be of concern, case patients and control subjects were identified solely on the basis of ESBL-EB characterization without prior knowledge of the status of the patients with regard to possible risk factors of interest. Finally, results will be generalizable only to LTCFs with characteristics similar to those of the 3 LTCFs in our study.

In summary, we found that 3.4% of LTCF residents were colonized with ESBL-EB and that the prevalence of ESBL-EB colonization differed significantly across sites. Future work should focus on elucidating the reasons for differences in ESBL-EB prevalence across sites and the potential clinical implications of empirical antimicrobial therapy.

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Table 1

Bivariable Analysis of Risk Factors for Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae Colonization

Variable	Case patients (*n* = 8)	Control subjects (*n* = 231)	OR (95% CI)	*P*
LTCF-2[a]	1 (12.5)	124 (53.7)	0.12 (0.01–0.99)	.03
LCTF-3[a]	3 (37.5)	25 (10.8)	4.94 (0.72–26.92)	.05
Recent use of levofloxacin	1 (12.5)	6 (2.6)	5.36 (0.11–54.38)	.21
Dialysis	1 (12.5)	9 (4.3)	3.52 (0.07–32.61)	.28
Fecal incontinence	6 (75)	82 (36.8)	5.45 (0.94–56.00)	.05

NOTE. Only those variables with a *P* value ≤.30 are shown. CI, confidence interval; LTCF, long-term care facility; OR, odds ratio.

[a]Reference category, LTCF-1.