High Rates of Intestinal Colonization With Extended-Spectrum Lactamase-Producing Enterobacteriaceae Among Healthy Individuals

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Background: Infections caused by extended-spectrum β-lactamase (ESBL)–producing bacteria become an emerging problem in the community setting in many parts of the world.

Objective: The objective of the study was to determine fecal carriage of ESBL-producing organisms in a community setting.

Methods: A total of 632 fecal specimens from healthy individuals were screened for ESBL using the agar screening test with MacConkey agar plates supplemented with 1 μg/mL of cefotaxime for selection of ESBL-producing strains and confirmed by the Clinical Laboratory Standards Institute combined disk method.

Results: Four hundred isolates (63.3%) were ESBL producers. Two hundred eighty-five isolates (71.25%) of them were *Escherichia coli* and 96 (24.0%) *Klebsiella pneumoniae*.

Conclusion: We concluded that the community could be a reservoir of these ESBL-producing bacteria and enzymes.

Key Words: extended-spectrum β-lactamases, MacConkey selective agars

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Resistance to β-lactam antimicrobial drugs among gram-negative bacteria is mainly the result of extended-spectrum β-lactamases (ESBLs), a major group of enzymes. These enzymes are typically plasmid mediated and have the ability to hydrolyze penicillins, third-generation cephalosporins, and monobactams.[1]

They are not active against cephamycins or carbapenems and are highly susceptible in vitro to inhibition by β-lactamase inhibitors, such as clavulanic acid.[1]

Infections due to such strains are associated with prolonged hospital stays, increased health care costs, and, in the setting of bloodstream involvement, increased mortality if appropriate therapy is delayed.[2]

Several articles have recently described the prevalence of ESBLs in the community, mainly in patients with urinary tract infections or ambulatory patients with chronic conditions.[2–4]

This marks a serious problem, as infections with ESBL-containing bacteria have mostly been described as nosocomially acquired or nursing-home related.

Although carriers of ESBL-producing organisms are assumed to exist in general practice, this condition has rarely been reported. The prevalence of ESBL production among clinical isolates of *Escherichia coli* and *Klebsiella pneumoniae* from our hospital is approximately 11%.[5]

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In our laboratory, all clinical isolates of the family Enterobacteriaceae that are resistant to ceftazidime and/or cefotaxime (CTX) are regularly screened for ESBL production. We do not routinely screen fecal specimens for ESBL-producing bacteria.

The current study was conducted to determine the rates of ESBL-mediated resistance in fecal isolates of *E. coli* and *K. pneumoniae* in asymptomatic individuals in the community.

MATERIALS AND METHODS

The study was performed from August 2010 to January 2011 at Cairo University hospitals, Cairo, Egypt. Six hundred thirty-two fecal samples were studied from healthy asymptomatic individuals attending the checkup clinic. The physician who examined the participants collected the patients' demographic data (age, sex, weight, and address) and clinical data concerning hospital stays and antibiotic intake in the past month, as well as any occupational activity in a health care setting.

Stool samples were spread onto MacConkey agar plates (Mast Diagnostics, Merseyside, UK) supplemented with 1 μg/mL of CTX and incubated in ambient air at 35°C for a minimum of 24 hours before initial examination.[6]

Samples yielding bacteria that grew on MacConkey agar were identified by standard biochemical procedures[7] and initially identified as suggestive of ESBL. The standard CLSI combined disk method involving CTX with and without the inhibitor clavulanic acid (30 μg) (Mast Diagnostics) was used to confirm the presence of ESBL.[6] Extended-spectrum β-lactamase production was indicated by an increase in zone size of more than 5 mm around CTX with clavulanic acid compared with CTX alone.

RESULTS

Cases with history of hospital stays and/or antibiotic intake in the past month, as well as any occupational activity in a health

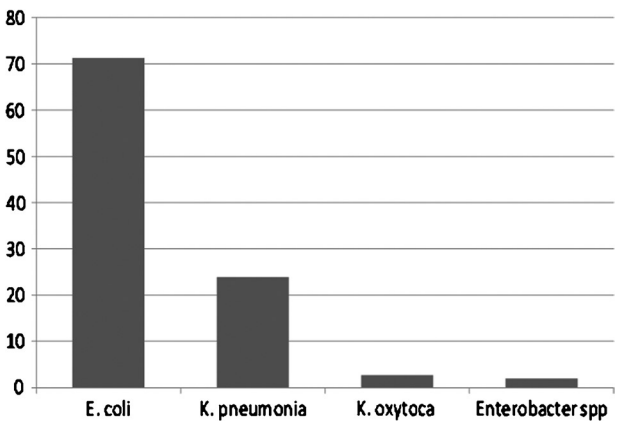

FIGURE 1. Distribution of ESBL-producing isolates in fecal samples from healthy persons.

TABLE 1. Antimicrobial Susceptibility of the ESBL-Producing Isolates of *E. coli* and *K. pneumonia*

Organism	Percentage (%) of Resistance to Antimicrobial Agent		
	Carbapenems	Amikacin	Fluoroquinolones
E. coli (n = 285)	0	11.9	39.4
K. pneumoniae (n = 96)	0	18.9	33.0

care setting, were excluded from the study. Our study was performed on 632 stool samples from 632 persons; their ages ranged from 20 to 85 years.

Of the 632 stool samples tested, isolates that were resistant to CTX were cultured from 411 samples (65.0%) and ESBL producers from 400 (63.3%). Of the 400 ESBL-producing isolates, 285 (71.25%) were *E. coli*, 96 (24.0%) were *K. pneumoniae*, 11 (%2.75) were *Klebsiella oxytoca*, and 8 (2.0%) were *Enterobacter* spp (Fig. 1).

The susceptibility data of the ESBL-producing *E. coli* and *K. pneumoniae* are summarized in Table 1. The antibiotics with the highest activity against the ESBL-producing isolates were carbapenems (imipenem/meropenem) and amikacin.

DISCUSSION

This study demonstrates the presence of ESBL in 63.3% of fecal strains of Enterobacteriaceae from healthy asymptomatic individuals attending the checkup clinic of Cairo University hospitals in Egypt. Previous studies in Israel[8] reported lower figures (35.5%), and 12.7% in a study done in Saudi Arabia.[9]

In our study, 71.25% of ESBL-producing isolates were *E. coli*, 24.0% were *K. pneumoniae*, 2.75% were *K. oxytoca*, and 2.0% were *Enterobacter* spp. Similarly, other authors reported that more than 95% of ESBL-producing fecal isolates were *E. coli* but reported lower figures (4.4%) for *K. pneumoniae*.[9] Other authors reported lower figures for *E. coli* (31.7%) but similar figures for *K. pneumoniae* (27.0%) and higher figures for *Enterobacter cloacae* (11.1%).[8]

Despite normally living harmlessly in the gut, *E. coli* can cause various types of infections, especially urinary tract infection. In a study done in our hospital, 17.1% of the uropathogens isolated from outpatients were ESBL-producing *E. coli*.[10]

Other studies in Saudi Arabia showed that 10% to 12% of the gram-negative uropathogens isolated from community patients were ESBL producers.[11,12] Some reports from Europe and Canada also suggest that infections caused by ESBL-producing organisms are emerging among community patients.[13,14]

The existence of ESBL-producing organisms in the gut of healthy individuals has clinical implications as intestinal tract colonization is a prerequisite for infection by ESBL producers.[15] The presence of ESBL-producing *E. coli* in the gut not only contributes to difficult-to-treat extraintestinal infections, but also can result in the transfer of antibiotic-resistant determinants to other strains of *E. coli* and other organisms within the gastrointestinal tract.[16] Their presence increases the risk of transmission to other individuals as a result of human-to-human transmission or through the environment.[17] In addition, the admission of carriers to hospitals increases the risk of infection for other hospitalized patients.[18]

Other authors stated that the spread of ESBL-producing organisms to the community could be related to previous hospital acquisition as some hospitalized patients continue to carry ESBL-producing bacteria over prolonged periods, which may contribute to their extrahospital propagation.[19] Their emergence in the community could also be caused by the overuse of antibiotics, especially β-lactams (eg, penicillins, cephalosporins) and quinolones in community patients. Antibiotic use creates a selective pressure on host bacteria in the large bowel, leading to the emergence of antimicrobial-resistant organisms, which in turn causes an increase in the number of carriers harboring resistant bacteria and enhances the opportunity for these bacteria to cause infections.[18–22]

Although our cases denied any history of recent hospitalization or antibiotic consumption in the preceding month among our subjects, many are likely to have been exposed to multiple courses of antibiotics because of the easy access to and unrestricted antibiotic use in developing countries.

Previous fluoroquinolone use has also been demonstrated to be a risk factor for the acquisition of ESBL-producing isolates.[3] In our study, the fluoroquinolone resistance rate among the ESBL-producing organisms was high (33%–39.4%). Other authors reported higher figures of fluoroquinolone resistance rate (61.5%) among the ESBL-producing organisms.[8]

Despite the high prevalence of ESBL-producing organisms among healthy individuals, the results are unlikely to represent the actual prevalence of ESBL producers in the community, and asymptomatic carriers may remain unnoticed for a long period.

Because of the significant public health implication, infectious disease physicians, microbiologists, and community doctors or general practitioners need to be aware that ESBL-producing strains of bacteria are circulating not only in hospital environments but also in the community, and they should deal with them accordingly. Confirmation of community-based transmission of ESBL requires further investigation, including molecular studies, to determine the reservoirs and vehicles for dissemination of ESBL within the community. Laboratory monitoring and detection of ESBL-producing bacteria are important steps in the appropriate treatment of patients and infection control efforts. It is also crucial in the tracking and monitoring of these resistant bacteria in community surveillance programs.

The limited availability of treatment options for infections caused by ESBL-producing organisms necessitates prevention of these infections by restricting the use of antimicrobial agents, along with implementation of prompt infection control measures. To control or reduce the high rate of carriage for these organisms, effective measures should be taken to prohibit the sale of antibiotics without prescription and to increase awareness among the population of the hazards of taking antibiotics without medical consultation. Finally, the scope of this study was limited to identifying ESBL producers by standard phenotypic methods.

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