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Extended-spectrum β-Lactamase-producing Flora in Healthy Persons

To the Editor: Extended-spectrum β-lactamase (ESBL)–producing gram-negative bacilli are endemic in hospitals. In intensive care units, 2% prevalence of ESBL-producing organisms has been reported (1). Exceedingly high rates of ESBL-producing bacteria in Indian hospitals prompted us to look at the fecal carriage of ESBL in the community (2).

One hundred healthy executives received a comprehensive health check at our tertiary care center in central Mumbai from August to September 2004. The predominant isolates from stool samples obtained for routine examination were cultured, and initial screening for ESBL production was conducted by using the disk diffusion method according to NCCLS guidelines (3). For these isolates, the ESBL phenotypic confirmation was performed with ceftazidime-clavulanate for an increase in zone diameter by 5 mm (disk potentiation). In addition, the ATB BLSE strip (bioMérieux, Lyon, France) was used to confirm the presence of inhibitor (sulbactam)-susceptible enzymes and to differentiate the strains from those that were either inhibitor resistant or harboring other β-lactamases, such as those of AmpC derivation. The ATB BLSE strip consists of a varying concentration of ceftazidime, 0.5–32 mg/L, and aztreonam, 0.5–8 mg/L, with varying combinations of these agents with a β-lactamase inhibitor, i.e., + sulbactam, 0.06–1 mg/L. Cefotetan (4 and 32 mg/L) and imipenem (4 and 8 mg/L) were also included in the strip. The test was considered positive when a variation of ≥4 dilutions was observed between the antimicrobial agent tested alone and the agent combined with the inhibitor. Eleven of the 100 samples screened were positive for ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*. Seven of the 11 were confirmed by using the ATB BLSE strip. The MIC of ceftazidime and aztreonam in all 7 isolates was 8 μg/mL. We might be underreporting ESBL producers in these cases by not including the cefotaxime-clavulanate combination in addition to the ceftazidime-clavulanate concentration. The percentage resistance to ciprofloxacin was 45%. All isolates were susceptible to amikacin and the carbapenems. None of the executives gave a history of hospitalization in the last year or history of antimicrobial drug consumption in the last 6 months.

This trend in patients with no apparent risk factors for ESBL carriage calls for urgent attention. Unknown environmental factors are likely playing a key role in maintaining this selective pressure. Larger studies are required to substantiate these findings.

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Measuring Impact of Antimicrobial Resistance

To the Editor: *Staphylococcus aureus* and *Enterococcus faecium* commonly cause healthcare-associated bloodstream infections (BSI) in the intensive care unit (ICU). Antimicrobial resistance is increasing in both organisms. The impact of antimicrobial resistance on dying of BSI has been studied extensively (1,2). Many studies have concluded that BSI caused by an antimicrobial-resistant organism results in higher death rates (1,3–8). However, as discussed in a recent report by Kaye et al., "outcome studies of antimicrobial drug resistance are notoriously hard to perform because of confounding variables related to coexisting conditions" (9). Indeed, almost all studies have shown that infections with antimicrobial-resistant organisms occur later in hospitalization than infections with antimicrobial-susceptible organisms, which suggests that differences in death rates may be, at least in part, caused by a difference in the patients' underlying illnesses and protracted hospital course. We report 2 additional methodologic issues that can affect estimates of the impact of antimicrobial resistance: combining different organisms and combining populations from different types of ICUs.

The original objective of our multicenter observational study was to quantify the clinical impact of antimicrobial resistance in *S. aureus* and *E. faecium* infections when these bacteria cause a specific type of infection: a monomicrobial, ICU-attributable, central vascular catheter–associated bloodstream infection (CVC-BSI). We studied 187 adult ICU patients with BSI caused by *S. aureus* and *E. faecium* at 3 tertiary care institutions from 1994 to 1999. The institutional review boards of each institution and the Centers for Disease Control and Prevention approved this study. Severity of illness was measured with an APACHE II score at ICU admission and on day 7 in the ICU (if applicable). The score would indicate the patient's risk of dying in the hospital before a BSI developed by using a measure validated for predicting in-hospital deaths in ICU patients (10).

The study population stratified by organism is shown in the Table. Fifty-eight percent of patients had CVC-BSI with *S. aureus*, and 42% had CVC-BSI with *E. faecium.* Overall, 58% of the organisms causing CVC-BSI were resistant to oxacillin if *S. aureus* or to vancomycin if *E. faecium*. However, patients with *E. faecium* CVC-BSI were more likely to be infected with antimicrobial-resistant bacteria (69% versus 50%, p<0.01), and had a higher mortality rate (54% versus 34%, p<0.01) than patients with *S. aureus* CVC-BSI. This finding indicates that the type of organism (*E. faecium* versus *S. aureus*) confounds the association between resistance and death. In addition, the distribution of ICU type by organism varies, which suggests that patient populations infected with these 2 different organisms were different in other

Table. Description of 187 adult patients with central vascular catheter-associated bloodstream infections with *Staphylococcus aureus* or *Enterococcus faecium* attributable to the intensive care unit*

Characteristics	*S. aureus* (n = 109)	*E. faecium* (n = 78)	p value
Patient demographics			
Male (%)	74	56	0.02
Mean age, y (SD)	58 (17)	56 (16)	0.32
Type of ICU			<0.01
Cardiac (%)	20	10	
Cardiothoracic surgery (%)	6	6	
Medical (%)	20	40	
Neurologic/neurosurgical (%)	6	0	
Surgical (%)	20	37	
Trauma (%)	28	6	
Severity of illness			
Mean APACHE II score at ICU admission (SD)	19 (8)	21 (9)	0.12
Mean APACHE II score within 7 days of BSI (SD)	17 (8)	20 (8)	0.05
Resistant infections (%)	50	69	0.01
In-hospital death rate (%)	34	54	<0.01

*SD, standard deviation; ICU, intensive care unit.