ORIGINAL ARTICLE

Prospective Evaluation of Colonization with Extended-Spectrum β-Lactamase (ESBL)–Producing Enterobacteriaceae Among Patients at Hospital Admission and of Subsequent Colonization with ESBL-Producing Enterobacteriaceae Among Patients During Hospitalization

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OBJECTIVE. To determine the rates of and risk factors for carriage and acquisition of extended-spectrum β-lactamase (ESBL)–producing Enterobacteriaceae during hospitalization.

DESIGN. Cohort study.

SETTING. Shaare Zedek Medical Center, a 550-bed teaching hospital.

METHODS. During a 5-month period (February 1–June 30, 2004), 167 (8%) of 1,985 newly admitted general medical patients were enrolled in our study. Nasal, oropharyngeal, and rectal swab specimens were obtained at admission and every 2–3 days until hospital discharge or death. Enterobacteriaceae isolates were tested for ESBL, and *Staphylococcus aureus* isolates were tested for methicillin resistance.

RESULTS. Of the 167 patients enrolled in our study, 15 (9%) were identified as nasal carriers of methicillin-resistant *S. aureus* (MRSA) at admission, and 13 (8%) were rectal carriers of ESBL-producing Enterobacteriaceae at admission. Univariate risk factors for rectal carriage of ESBL-producing Enterobacteriaceae included female sex (odds ratio [OR], 11 [95% confidence interval {CI}, 1.4–238]; $P < .05$), nursing home residence (OR, 6.9 [95% CI, 1.8–27]; $P < .01$), recent antibiotic treatment (OR, 9.8 [95% CI, 1.7–74]; $P < .05$), and concomitant nasal carriage of MRSA and/or ESBL-producing Enterobacteriaceae (OR, 5.8 [95% CI, 1.2–26]; $P < .01$). Multivariate risk factors were female sex and recent antibiotic treatment. During hospitalization, 35 (21%) of 167 patients had acquired rectal carriage of ESBL-producing Enterobacteriaceae ($P = .002$, for trend analysis). Of the 12 patients who were still in the hospital 2 weeks after admission, 4 (33%) were carriers of ESBL-producing Enterobacteriaceae. Univariate risk factors for acquisition included an age of older than 65 years ($P < .005$), nursing home residence (OR 2.6, [95% CI, 0.98–2.6]), impaired cognition (OR, 4.8 [95% CI, 1.9–12]), recent antibiotic treatment (OR, 2.7 [95% CI, 0.9–8.3]), respiratory assistance (OR, 4.2 [95% CI, 1.2–14]), and prolonged hospitalization. Multivariate risk factors were an age of older than 65 years and broad-spectrum antibiotic therapy.

CONCLUSIONS. Rectal carriage of ESBL-producing Enterobacteriaceae occurred in 13 (8%) of 167 patients at admission to the medical departments of our hospital and in 4 (33%) of 12 patients still remaining in our hospital after 2 weeks.

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In gram-negative pathogens, β-lactamase production remains the most important contributing factor to β-lactam resistance.[1] Cases of infection with extended-spectrum β-lactamase (ESBL)–producing Enterobacteriaceae were first reported during the late 1980s and have subsequently spread worldwide.[2] Many clinical laboratories have reported that significant percentages of *Klebsiella* species and *Escherichia coli* infections acquired in the hospital setting are caused by strains that produce ESBL.[3-5] As expected, these organisms have spread to long-term care facilities.[6] In the last decade, several studies have reported their spread to the community as well,[7-13] giving rise to considerable concern and accentuating the need to amend guidelines for empirical therapy of infections suspected to be caused by gram-negative bacilli.

The medical departments of our community-based teaching hospital admit many elderly patients, including many from nursing homes.[14,15] In multiple studies, we have reported high drug resistance rates among both gram-positive and

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TABLE 1. Demographic and Clinical Characteristics of Study Cohort and of the Entire Patient Population Admitted to Shaare Zedek Medical Center in Jerusalem, Israel, During the 5-Month Study Period, February 1–June 30, 2004

Characteristic	Study cohort ($n = 167$)	Entire patient population ($n = 1,985$)	P
Male sex	75 (45)	907 (46)	.96
Age, years			.32
Mean ± SD (range)	76 ± 13 (20–100)	77 ± 15 (16–104)	
Median	78	80	
Nursing home residence	25 (15)	246 (12)	.26
Source of referral			.92
Arrival by ambulance	80 (48)	981 (49)	
Family physician	32 (19)	417 (21)	
Institution	25 (15)	246 (12)	
Self-referral	23 (14)	296 (15)	
Hospital clinic	5 (3)	28 (1)	
Private physician	2 (1)	17 (1)	
Admitting department			.97
Geriatrics	38 (23)	377 (19)	
Hematology-oncology	14 (8)	163 (8)	
Medicine A	41 (25)	529 (27)	
Medicine B	55 (33)	649 (33)	
Short observation unit	19 (11)	267 (13)	

NOTE. Data are no. (%) of patients, unless otherwise indicated. All P values were statistically nonsignificant. SD, standard deviation.

gram-negative organisms,[16-20] and we and many others have therefore devised protocols for empirical treatment on the basis of risk stratification.[21-24] To update these protocols, annual summarized results from the clinical microbiology department are supplemented by additional surveillance of well-defined patient populations. The surveillance studies facilitate determination of clinical risk factors for colonization or infection with certain pathogens. It is within this context that the current study was undertaken, with the following aims: to determine the rate of rectal carriage of ESBL-producing Enterobacteriaceae in newly admitted patients at our medical departments, to determine the rate of acquisition of such organisms during their ensuing hospitalization, and to determine risk factors for both carriage and acquisition.

METHODS

Setting

Our study was conducted at the Shaare Zedek Medical Center, a 550-bed general and university-affiliated hospital. The division of internal medicine consists of 5 departments, consisting of a total of 150 beds. Our study was conducted during a 5-month period (February 1–June 30, 2004) and was prospective, descriptive, and noninterventional. Every 10th patient admitted to the hospital during this period (except for those admitted during weekends) had culture samples obtained at admission and every second or third day thereafter, until the conclusion of their hospitalization (defined as either hospital discharge, death, or the end of our study, which was defined as 2 weeks after enrollment of the last patient). Our study was a pilot study: although ESBL-producing organisms are frequently isolated in the clinical laboratory and although studies of special cohorts (such as intensive care unit patients) have indicated a high rate of ESBL carriage, no preexisting data regarding the general patient population admitted to our medical departments allowed us to calculate a sample size. Furthermore, for each patient enrolled in our study, we intended to obtain culture samples every second or third day of hospitalization and to collect demographic, clinical, and laboratory data to determine risk factors for the carriage of ESBL-producing organisms. Accordingly, rather than focus on a small cohort during a brief period, we decided to enroll a larger group of patients during an extended period. Demographic and clinical data were used to rule out selection bias and determine whether the study group represented the entire patient population. Standard infection control measures were implemented throughout the entire study period. In brief, these measures included universal contact precautions; isolation in single-bed rooms or cohorting of patients from whom vancomycin-resistant organisms, carbapenem-resistant Enterobacteriaceae, or *Pseudomonas* species were isolated; and daily rounds by infection control nurses to detect nonadherence with Centers for Disease Control and Prevention guidelines and to educate patients.

Sampling and Screening

Each enrolled patient was screened at hospital admission for carriage of methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), and ESBL-producing En-

TABLE 2. Baseline Demographic and Clinical Characteristics of Study Patients Admitted to Shaare Zedek Medical Center in Jerusalem, Israel, During the 5-Month Study Period, February 1–June 30, 2004

Characteristic	Study patients (n = 167)
Sex	
Male	75 (45)
Female	92 (55)
Age, mean ± SD (range), years	76 ± 13 (20–100)
Department	
Geriatrics A and B	42 (25)
Hematology	13 (8)
Internal medicine A	40 (24)
Internal medicine B	53 (32)
Internal medicine C	19 (11)
Residence	
Home	130 (78)
Assisted living facility	4 (2)
Nursing home	7 (4)
Skilled nursing home[a]	24 (14)
Other	2 (1)
Functional status	
Independent	78 (47)
Requires nursing care	52 (31)
Frail	37 (22)
Cognitive state	
Normal	92 (55)
Mild dementia	36 (22)
Severe dementia	39 (23)
Diagnosis of infection at hospital admission	91 (54)
Diagnosis of infection with clinical specimen positive for MRSA and/or ESBL at hospital admission	14 (8)

NOTE. Data are no. (%) of patients, unless otherwise indicated. ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus;* SD, standard deviation.

[a] Providing intravenous antibiotics.

terobacteriaceae. Nasal swab specimens were obtained for testing for *S. aureus*, and oropharyngeal and rectal swab specimens were obtained for testing for ESBL-producing bacteria. Identical follow-up specimens were obtained every 2–3 days. Relevant culture samples were obtained from patients infected with these organisms.

Demographic, Clinical, and Laboratory Data

A detailed profile of each patient was created. Sources of information included the patient's medical record, referral documents (eg, from the family physician and nursing home), an interview with each patient and his or her family, and documents from previous hospital admissions. The following data were collected: (1) demographic characteristics, which included sex, age, department of admission, and residence (home, assisted living facility, nursing home, or skilled nursing home); functional status (independent, requires nursing care, and/or frail); cognitive state (normal, mild dementia, or severe dementia); and admission in the previous 30–90 days; and (2) clinical parameters, which included whether there was a diagnosis of infection at hospital admission and, if so, whether the relevant clinical (as opposed to surveillance) specimen was positive for MRSA or ESBL-producing organisms; whether the patient received antimicrobials 30–90 days prior to admission; whether antimicrobials active against MRSA or ESBL-producing organisms were prescribed during the current hospitalization; whether any indwelling tubes (ie, a urinary catheter or a gastrostomy or nasogastric feeding tube) were in place at admission or subsequently inserted; presence of underlying diseases; development of nosocomial infection; duration of stay; and outcome. Parenteral broad-spectrum antimicrobials were defined as follows: all penicillins and cephalosporins active against *Pseudomonas* species, all carbapenems, colistin, ciprofloxacin, amikacin, and vancomycin.

Microbiological Evaluation

For a diagnosis of *S. aureus* infection, nasal swab specimens had to be obtained from both nares and inoculated immediately onto mannitol salt agar and also tryptic soy broth containing 128 μg/mL of aztreonam. Broth samples showing evidence of growth of *S. aureus* were plated once again onto mannitol salt agar. Colonies suggestive of *S. aureus* were identified by use of Pastorex Staph Plus (Bio-Rad). Methicillin resistance was determined by growth of *S. aureus* on Mueller-Hinton agar plates containing 4% sodium chloride and 6 μg/mL of oxacillin, as recommended by the Clinical and Laboratory Standards Institute.[25]

Since 2000, for a diagnosis of infection with an ESBL-producing organism, it is recommended that all Enterobacteriaceae isolates be screened for possible ESBL production by use of the double disk diffusion method, according to Clinical and Laboratory Standards Institute criteria, and this method was used for all of the Enterobacteriaceae isolates recovered from patients in our surveillance study.[25,26] In brief, Enterobacteriaceae isolates were tested for susceptibility to cefotaxime with or without clavulanate and to ceftazidime with or without clavulanate. Results were confirmed by use of the Etest (AB Biodisk) with strips containing ceftazidime or cefotaxime, with and without clavulanic acid. ESBL-producing Enterobacteriaceae isolates were further identified.

Three end points were used to evaluate results. First, we determined the prevalence of carriage (ie, colonization with) MRSA and ESBL-producing Enterobacteriaceae among patients at hospital admission. Second, we determined the rate at which carriers became noncarriers during their hospital stay (ie, noncarriers were those patients whose subsequently obtained specimens tested negative for the originally isolated pathogen) and the number of patients who were not colonized with or who did not acquire the target organisms. Third, we determined the rate of acquisition of these organisms.

TABLE 3. Additional Clinical Characteristics of Study Patients Admitted to Shaare Zedek Medical Center in Jerusalem, Israel, During the 5-Month Study Period, February 1–June 30, 2004

Characteristic	No. (%) of patients ($n = 167$)
Previously hospitalized	
During past 30 days	34 (20)
During past 3 months	22 (13)
Antibiotic treatment	
At admission	94 (56)
During past 30 days	19 (11)
During past 3 months	14 (8)
Antibiotic treatment during current hospitalization	
For MSSA colonization or infection	94 (56)
For MRSA colonization or infection	77 (46)
For colonization or infection with ESBL-producing Enterobacteriaceae	60 (36)
Any antibiotic treatment during current hospitalization	94 (56)
Presence of indwelling device at admission	
Indwelling urinary catheter	2 (1)
Percutaneous, endoscopically inserted gastrostomy tube	2 (1)
Nasogastric feeding tube	4 (2)
Tracheostomy tube	2 (1)
Other	9 (5)
Underlying medical condition or receipt of therapy	
Diabetes mellitus	51 (31)
Corticosteroid therapy	21 (13)
Chemotherapy	14 (8)
Presence of indwelling device during current hospitalization	
Urinary catheter	2 (1)
Percutaneous, endoscopically inserted gastrostomy tube	0 (0)
Nasogastric tube	22 (13)
Tracheostomy tube	0 (0)
Respiratory device	17 (10)
Other	7 (4)
Any nosocomial infection	7 (4)
Patient outcome	
Discharged from hospital	121 (72)
Still in hospital at conclusion of study	32 (19)
Died	17 (10)

NOTE. ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *S. aureus.*

Finally, we attempted to determine risk factors for carriage or acquisition of ESBL-producing Enterobacteriaceae.

Statistical Analysis

The data were entered into a computer program written in EpiInfo, version 6.04d (Centers for Disease Control and Prevention), and analyzed by this program and by EpiInfo, version 3.4.3. Comparison between groups and evaluation of risk factors were done by use of the χ^2 test (and the Fisher exact test whenever applicable) and the Student t test. Multivariate regression analysis was done by use of SPSS, version 11.0 (SPSS).

Permission from the local internal review board was requested to conduct our study. The board allowed us to conduct this study with the provision that oral consent was requested and provided by the patients and/or their next of kin prior to obtainment of culture samples.

RESULTS

During the study period, 1,985 patients were hospitalized in the medical departments of our hospital. Of these, 167 (8%) were screened. The study sample reflected the overall patient population by sex, age, source of referral, residence, mode of transfer to hospital, and admitting department. However, there were more geriatric patients than short-stay patients included in our study (Table 1). Baseline data regarding demographic characteristics and functional status are shown in Table 2; clinical characteristics are shown in Table 3. The mean age ($\pm$ standard deviation [SD]) of the patients was

76 ± 13 years. Of the 167 patients in our study, 130 (78%) lived at home, 92 (55%) were cognitively intact, and 78 (47%) were functionally independent. Antimicrobial treatment had been prescribed to 19 (11%) of 167 patients within 1 month before admission, to an additional 14 patients (8%) 2–3 months before admission, and to 94 patients (56%) during the current hospitalization. The mean duration of hospitalization (±SD) for the study population was 9.8 ± 10.5 days (median duration, 8.0 days; range, 0–83 days).

A total of 490 rectal swab specimens, 490 nasal swab specimens, and 490 throat swab specimens were obtained for culture from the 167 enrolled patients. All 167 patients' specimens were cultured at admission, as previously described, and every 2–3 days thereafter. As expected, the number of patients remaining in the hospital decreased to 138 during the first screening period, to 87 during the second screening period, to 41 during the third screening period, to 24 during the fourth screening period, and to 12 during the fifth screening period (Figure). We continued to obtain samples for a total of 15 screening periods. However, during the sixth screening period, only 9 patients remained in the hospital; during the seventh screening period, only 4 patients remained; and during all subsequent screening periods, only 1 patient remained. Table 4 shows the proportion of patients who were found to be carriers of *S. aureus* and ESBL-producing Enterobacteriaceae at admission, patients who acquired these organisms during their hospital stay, and patients who became noncarriers during their hospital stay. At hospital admission, 39 (23%) of 167 patients were found to be nasal carriers of *S. aureus:* 24 (14%) were carriers of MSSA, and 15 (9%) were carriers of MRSA. The number of patients who were carriers of MRSA decreased during hospitalization (ie, these patients became noncarriers), but the trend was not statistically significant. Rectal carriage of ESBL-producing Enterobacteriaceae was detected in 13 (8%) of 167 patients at hospital admission; 35 additional patients (21%) acquired these organisms during hospitalization, and 6 carriers (4%) became noncarriers. Therefore, of the original cohort of 167 newly admitted patients, ultimately 42 (25%) were carriers

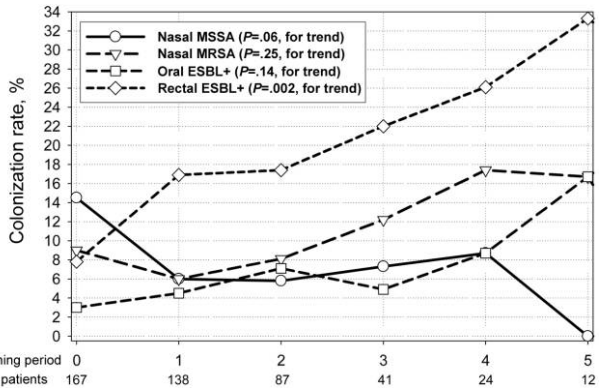

FIGURE. Colonization rate among 167 patients who were screened for nasal carriage of methicillin-susceptible *Staphylococcus aureus* (MSSA; nasal MSSA) and methicillin-resistant *S. aureus* (MRSA; nasal MRSA) and for oropharyngeal and rectal carriage of extended-spectrum β-lactamase (ESBL)–producing Enterobacteriaceae (oral and rectal ESBL+, respectively), at hospital admission (day 0) and subsequently every 2–3 days, for a total of 5 screening periods.

of ESBL-producing Enterobacteriaceae. Of the 12 patients remaining in the hospital during the fifth screening period (more than 2 weeks after admission), 4 (33%) were carriers of ESBL-producing Enterobacteriaceae. Of the 48 patients from whom ESBL-producing Enterobacteriaceae isolates were recovered, 1 patient (2%) had previously been admitted to our hospital, whereas, of the entire group of 1,985 patients admitted to the medical departments of our hospital, 59 patients (3%) had previously been admitted to our hospital. A total of 59 ESBL-producing Enterobacteriaceae isolates were recovered from rectal swab specimens: 25 *E. coli* isolates, 20 *Klebsiella pneumoniae* isolates, 6 *Proteus mirabilis* isolates, 6 *Enterobacter cloacae* isolates, and 2 *Citrobacter* isolates.

The Figure shows the rate of carriage at hospital admission and the rate of subsequent acquisition of nasal carriage of MSSA and MRSA and oropharyngeal and rectal carriage of ESBL-producing Enterobacteriaceae among all samples ob-

TABLE 4. Carriage Status of 167 Patients Admitted to Shaare Zedek Medical Center in Jerusalem, Israel, During the 5-Month Study Period, February 1–June 30, 2004

	No. (%) of patients who			
Organism, carriage status	Were carriers at admission	Became carriers during hospital stay	Became noncarriers during hospital stay	Were never carriers
Staphylococcus aureus				
Nasal carriage of MSSA	24 (14)	5 (3)	15 (9)	138 (83)
Nasal carriage of MRSA	15 (9)	12 (7)	5 (3)	140 (84)
ESBL-producing Enterobacteriaceae				
Oropharyngeal carriage	3 (2)	8 (5)	1 (1)	154 (92)
Rectal carriage	13 (8)	35 (21)	6 (4)	119 (71)

NOTE. ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *S. aureus;* MSSA, methicillin-susceptible *S. aureus.*

tained for each screening period. The Figure demonstrates that the more prolonged the hospitalization, the higher the rate of rectal carriage of ESBL-producing Enterobacteriaceae ($P = .002$, for trend analysis). Although modest changes in the rate of nasal carriage of MSSA and MRSA and in the rate of oropharyngeal carriage of ESBL-producing Enterobacteriaceae were noted, these changes were not statistically significant.

We detected several univariate risk factors for MRSA carriage at hospital admission: female sex ($P < .05$), nursing home residence ($P < .005$), and concomitant nasopharyngeal or rectal carriage of ESBL-producing Enterobacteriaceae ($P < .01$ and $P < .05$, respectively). On multivariate regression analysis, only concomitant oropharyngeal carriage of ESBL-producing Enterobacteriaceae was found to be statistically significant ($P < .01$). Univariate risk factors for carriage of nasopharyngeal ESBL-producing Enterobacteriaceae at hospital admission were as follows: residence at a nursing home ($P < .01$) or a skilled nursing home (with the latter providing intravenous antimicrobial treatment; $P < .005$), dementia ($P < .001$), receipt of antimicrobials during the month prior to admission ($P < .05$), presence of a nasogastric tube ($P < .005$) or a tracheostomy tube ($P < .05$), and concomitant nasal carriage of MRSA ($P < .01$) or rectal carriage of ESBL-producing Enterobacteriaceae ($P < .01$). On multivariate analysis, only concomitant nasal carriage of MRSA was found to be an independent risk factor. Table 5 shows the univariate and multivariate risk factors for rectal carriage and subsequent acquisition of rectal carriage of ESBL-producing Enterobacteriaceae. The multivariate risk factors for rectal carriage of ESBL-producing Enterobacteriaceae at hospital admission were as follows: female sex and recent broad-spectrum antimicrobial treatment. The multivariate risk factors for subsequent acquisition of rectal carriage of ESBL-producing Enterobacteriaceae were as follows: older than 65 years of age and recent broad-spectrum antimicrobial treatment.

DISCUSSION

In this 5-month study, 167 patients were enrolled for screening for presence on admission and subsequent acquisition of MRSA and ESBL-producing Enterobacteriaceae. The rate of nasal carriage of MSSA at admission was 14% (24 of 167 patients), similar to that reported by others.[27,28] However, the rate of nasal carriage of MRSA at hospital admission was 9% (15 of 167 patients), which underlies the fact that many of the patients admitted to our medical departments during the 5-month study period were either nursing home residents or chronically ill and/or patients who were readmitted to the hospital. The rate of rectal carriage of ESBL-producing bacteria at admission was 8% (13 of 167 patients); the rate of nosocomial acquisition with these ESBL-producing bacteria increased with the increased duration of hospitalization, doubling to 17% (15 of 87 patients) by day 4 or 5 after admission and gradually increasing to 33% (4 of 12 patients) after 10 or more days of hospitalization ($P = .002$).

Most studies report an increase in the number of ESBL-producing Enterobacteriaceae isolates recovered from both clinical and surveillance samples for culture. However, the differing study designs do not allow for easy comparison. Valverde et al.[29] reported that, from 1991 to 2003, the rate of carriage of these organisms increased from 0.3% to 5.5% among ambulatory patients and from 0.7% to 11.8% among hospitalized patients. In Buke et al.,[30] there were 439 patients who were still hospitalized 30 days after hospital admission; of these, 87 (20%) were colonized with multidrug-resistant organisms, 32 (37%) of whom were colonized with ESBL-producing Enterobacteriaceae. In Martins et al.,[31] intensive

TABLE 5. Univariate and Multivariate Risk Factors for Rectal Carriage of Extended-Spectrum β-Lactamase (ESBL)–Producing Enterobacteriaceae at Hospital Admission and Acquisition During Hospitalization at Shaare Zedek Medical Center in Jerusalem, Israel, During the 5-Month Study Period, February 1–June 30, 2004

	Carriage at admission[a]		Carriage during hospitalization[b]	
Risk factor	OR (95% CI)	*P*	OR (95% CI)	*P*
Female sex	11.0 (1.4–238)	<.005[c]	…	.28
>65 years of age	…	.24	…	<.005[c]
Residence in nursing home or lives at home	6.9 (1.8–27)	<.005	2.6 (0.98–2.6)	<.05
Normal cognitive state or dementia	…	.07	4.8 (1.9–12)	<.001
Prior anti-ESBL antimicrobial therapy	9.8 (1.7–74)	<.005[c]	2.7 (0.89–8.3)	<.05[c]
Respiratory assistance (with mechanical ventilation)	…	.7	4.2 (1.2–14)	<.05
MRSA carriage	5.8 (1.2–26)	<.05	…	.07
Nasal carriage of ESBL-producing organism	9.1 (0.9–80)	.049	…	.54
Duration of hospitalization, days	NA		…	<.001

NOTE. CI, confidence interval; MRSA, methicillin-resistant *Staphylococcus aureus;* NA, not available; OR, odds ratio;

[a] For 13 (8%) of 167 patients.

[b] For 35 (24%) of 144 patients.

[c] $P < .05$ in multivariate analysis.

care unit patients were screened at hospital admission and then weekly for ESBL-producing *K. pneumoniae;* the incidence rate for rectal colonization was 5.8 cases per 1,000 patient-days, and the incidence rate for infection with these organisms was 1.7 case per 1,000 patient-days. Of importance, colonization was found to be an independent risk factor for subsequent infection. In a 6-year study by Troché et al.,[32] nasal and rectal swab specimens were obtained for culture from 2,235 intensive care unit patients at hospital admission and then weekly during hospitalization. The incidence rate of colonization with ESBL-producing Enterobacteriaceae was 0.4 cases per 100 admissions, and the incidence rate of infection with ESBL-producing Enterobacteriaceae was 3.9 cases per 1,000 patient-days. Nasal mupirocin ointment was prescribed for nasal carriers of MRSA, and selective digestive decontamination with topical antibiotics was prescribed for carriers of ESBL-producing Enterobacteriaceae; although these treatments were not very effective at eradicating carriage, the authors reported a decrease in the acquisition of carriage of ESBL-producing Enterobacteriaceae from 5.5 cases per 1,000 patient-days during the first 3 years of the study to 1.9 cases per 1,000 patient-day during the last 3 years. Esposito et al.[33] conducted an 8-month study in surgical wards in Italy. Nasal, pharyngeal, and rectal specimens were obtained for culture at hospital admission and during hospitalization. ESBL-producing Enterobacteriaceae were isolated in 5% of patients at admission, and this percentage rate did not change during the course of the study (ie, during the hospitalization of the study patients). The striking difference between the results of the study by Esposito et al.[33] and the results of our study is probably because of the difference between surgical patients and general medical patients; for surgical patients, the mean age was lower than that for our general medical patients, and a significant percentage of surgical patients were admitted for elective surgery. Peña et al.[34] conducted a study in an intensive care unit; this study had a design that was quite similar to ours. Rectal specimens were obtained weekly from all patients during a 4-month period: 72 (38%) of 188 patients tested positive for ESBL-producing *K. pneumoniae,* and 42 (58%) of these 72 patients were colonized during the first week of hospitalization. Thirty days after admission, more than 150 (80%) of the 188 patients had become rectal carriers of ESBL-producing *K. pneumoniae.* In conclusion, the incidence and prevalence reported from various studies differed because of the different study designs that were used and because of the different patient populations studied. We were unable to find a study that was similar to ours (ie, that prospectively assessed patients in medical departments).

In our study, the multivariate analysis risk factors for acquisition of ESBL-producing Enterobacteriaceae were an age of older than 65 years and prior use of broad-spectrum antimicrobials. It is not unlikely that these factors flag persons at risk rather than being the cause of carriage of ESBL-producing Enterobacteriaceae. A study from an Israeli hospital[12] examined urine samples from 311 nonhospitalized patients; of these patients, 128 (41%) had urine samples from which isolates of ESBL-producing bacteria were recovered. The independent risk factors for ESBL-producing bacteria were hospitalization within the previous 3 months, antibiotic treatment within the previous 3 months (particularly with second- and third-generation cephalosporins and quinolones), age of more than 65 years, diabetes mellitus, male sex, and infection with *K. pneumoniae.* The conclusion of the study[12] was that colonization with ESBL-producing bacteria was endemic in the community, even though the community was in a relatively rural area.

Quite a few studies have assessed the clinical significance of infections caused by ESBL-producing bacteria. Some of these studies have shown that patients who were infected with ESBL-producing bacteria have clinical characteristics that can be identified, such as being elderly and/or a nursing home resident or having an indwelling device (ie, nasogastric or gastrostomy feeding tubes and/or urinary catheters).[5,21,35,36] The severity of illness and crude mortality rate among patients with sepsis due to an ESBL-producing organism may be higher than those among patients with sepsis due to non–ESBL-producing bacteria. Several studies have demonstrated the adverse effects of inappropriate empirical antibiotic treatment,[37,38] although our 2 previous studies did not.[10,21] We believe that improved implementation of infection control measures—such as isolation in single-bed rooms or cohorting of patients, improved nursing staff–to–patient ratios, and strict observance of contact precautions—could contribute to a decrease in the rates of colonization or infection with ESBL-producing organisms.[39] Unfortunately, the costs associated with these measures may pose a challenge to hospital administrators.

Our study has several limitations. First, we are not sure how well our study cohort was representative of the entire patient population of the medical departments in our hospital. The sample included 167 (8%) of 1,985 patients hospitalized in the medical departments during the 5-month study period. Various demographic and general clinical data suggest adequate representation, but we did not collect detailed clinical or laboratory data for further evidence. A second limitation of our study sample was the very high rate of elderly patients, which is representative of our patient population but not necessarily representative of medical departments in all hospitals. Most hospitals, however, do report an increasing elderly patient population. Finally, we did not evaluate our patients for evidence of clinical infection, but a substantial proportion of carriers of virulent and drug-resistant organisms will eventually develop clinical infection.[30,40]

In conclusion, 167 (8%) of the 1,985 patients newly admitted to our medical departments were rectal carriers of ESBL-producing Enterobacteriaceae. During their hospitalization, the rate of colonization increased rapidly, and of the 12 patients remaining in the hospital during the fifth screening period (more than 2 weeks after admission), 4 (33%)

were carriers of ESBL-producing Enterobacteriaceae. The risk factors that were identified in our study and in others allow for refinement of protocols for empirical treatment based on risk stratification, ideally leading to appropriate treatment for most patients and a reduction in the use of broad-spectrum antimicrobial treatment for patients without such risk factors.

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