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ARTICLE

Prevalence of faecal ESBL carriage in the community and in a hospital setting in a county of Southern Sweden

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Abstract The aim of this study was to investigate the prevalence of extended-spectrum beta-lactamase (ESBL)-producing bacteria in patients at various hospital wards and in a group of relatively healthy volunteers, in order to obtain greater knowledge on how common these bacterial strains are in hospital settings and in the general community. Participants (n=427) were enrolled at a University Hospital and at Primary Health Care Units (PHCUs) in Sweden in 2008 and 2010. The participants provided rectal swabs, which were tested for the occurrence of ESBL-producing bacteria. Positive samples were analysed with polymerase chain reaction (PCR) methods for bacterial strain typing and ESBL phylogroups. In 2008, the prevalence was 2.1% (2/96) in PHCU subjects and 1.8% (2/113) in hospital patients. In 2010, the prevalence was 3.0% (3/100) in PHCU subjects and 6.8% (8/118) in hospital patients. The dominating phylogroups were CTX-M-1 and CTX-M-9. All ESBL-positive isolates were *Escherichia coli*. We found a higher prevalence of ESBL faecal carriage than expected, both in the hospital setting and in the PHCU group.

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Introduction

The occurrence of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae has developed into a pandemic, especially over the last decade, and poses a great challenge and threat to health care worldwide [1–4]. Commonly-reported risk factors for infection or colonisation with ESBL-producing bacteria are antibiotic use, severe illness, prolonged hospital stay, recent surgery, travels to foreign countries, residence in a long-term care facility, recent hospitalisation and age ≥65 years [5–7].

The use of antibiotics in Sweden, especially broad-spectrum antibiotics, is low from an international perspective [8]. Although the ESBL prevalence in blood isolates in Sweden has long remained relatively low compared to other European countries(<5% of *Escherichia coli* and *Klebsiella pneumoniae* strains), there is a tendency of an increase [4, 9]. Furthermore, the prevalence of ESBL-producing Enterobacteriaceae in the population is not known.

The aim of this study was to investigate the frequency of ESBL-producing bacteria in patients at various hospital wards, where the use of antibiotics is known to be high, and in a group of relatively healthy volunteers without risk factors for ESBL carriage enrolled at Primary Health Care Units (PHCUs), in order to obtain greater knowledge on

how common these bacterial strains are in hospital settings and in the general community. We also carried out an identical follow-up study two years after the initial study, to see if the prevalence had changed within this time span.

Materials and methods

The study was set out as a cross-sectional comparison study in two parts performed at Malmö University Hospital and at different PHCUs in March to April 2008 and April to June 2010. Wards at departments with high proportions of patients treated with antibiotics were selected for the study. These were at the Departments of Infectious Diseases, Surgery, Urology, Oncology and Haematology, and the Intensive Care Unit (ICU). The latter two were not included in the follow-up study in 2010, since the Department of Haematology had moved to another hospital, and the patient number at the ICU was considered to be too low at the time of the study.

All participants in the study had to be at least 18 years old. In addition, they had to give a written consent after being provided with verbal and/or written standardised information about the study. In those cases where the patient could not give written consent or be supplied with information, such as patients with dementia or some patients at the ICU, this was mediated by a relative. No patient was included more than once.

For participants at the PHCUs, the exclusion criteria were admission to a hospital during the last 3 months, recent antibiotic use within the last 3 months and patients consulting for infection. The participants were individually given standardised verbal and written information about the study and the sample procedure by the author. At each PHCU, enrolment for the study was carried on for 2 days in 2008 and 2 days in 2010.

Rectal bacterial samples were acquired by using Amies agar gel swabs with charcoal (Copan, Brescia, Italy).

All samples were sent to the Laboratory of Microbiology at Malmö University Hospital, where they were incubated at 35°C overnight on agar plates with medium selective for cephalosporin resistance (chromID ESBL, bioMérieux, Marcy l'Etoile, France). Any growth on these plates was further examined for ESBL production through synergy testing with disks prepared with ceftazidime and cefotaxime and amoxicillin/clavulanic acid (AmpC and ESBL Detection Set, Mast, Merseyside, UK). Antibiotic susceptibility testing was performed according to the Swedish Reference Group of Antibiotics (SRGA) method [10]. MIC determination was performed by using E-test strips (AB Biodisk, Solna, Sweden). The species determination of the ESBL-producing strains was performed with phenotypic tests according to national guidelines [11, 12].

A multiplex, real-time TaqMan polymerase chain reaction (PCR) method was used to detect and characterise the CTX-M phylogroups. Conventional PCR was conducted with general primers for SHV and TEM enzymes [13]. Repetitive sequence-based PCR (rep-PCR) was performed for bacterial strain typing. The extracted DNA was amplified using the appropriate DiversiLab DNA Fingerprinting Kit (Spectral Genomics, Inc., Houston, TX, USA) according to the manufacturer's instructions. A difference between the strains was defined as more than three bands difference in the lane. An allele-specific *pabB* PCR was performed for the detection of O25b-ST131 according to Clermont et al. Ethical approval for the study was obtained from the Research Ethics Committee of the University of Lund.

Results and discussion

There were, as expected, disparities in the demographic data between the hospital patients and the patients from PHCUs. The mean and median ages were higher in participating hospital patients than outpatients. At the

Table 1 Demographic data from the 2008 and 2010 studies on participating subjects and response rates

	2008 study			2010 study		
	Hospital wards	PHCUs	Total	Hospital wards	PHCUs	Total
Sex						
Female, *n* (%)	57 (50)	64 (67)	121 (58)	48 (41)	64 (64)	112 (51)
Male, *n* (%)	56 (50)	32 (33)	88 (42)	70 (59)	36 (36)	106 (49)
Total, *n* (%)	113 (54)	96 (46)	209 (100)	118 (54)	100 (46)	218 (100)
Age						
Median, years (range)	71 (21–98)	46 (21–87)	60 (21–98)	68 (19–94)	55 (20–90)	64 (19–94)
Response rate, % (*n*)	59 (113/192)	81 (96/118)	67 (209/310)	61 (118/195)	89 (100/112)	71 (218/307)

PHCUs, Primary Health Care Units

PHCUs, younger staff members and relatives were often enrolled in the study. This also partly explained the greater percentage of female participants at the PHCUs (Table 1).

Four subjects, or 1.9%, in the 2008 study were tested positive for the faecal carriage of ESBL-producing bacteria. Two were hospital patients (1.8% of all participating hospital patients) and two were PHCU subjects (2.1% of all PHCU subjects). None of these four positive subjects were previously known carriers of ESBL. In the follow-up study from 2010, 11 subjects (5.0%) were found to be ESBL carriers. Eight of these were hospital patients (6.8% of all participating hospital patients) and three were PHCU subjects (3% of all PHCU subjects). Three of the 11 positive participants in the 2010 study were previously known ESBL carriers. The total prevalence of faecal carriage of ESBL-producing bacteria in our study population was 1.9% in 2008 and 5.0% in 2010. The prevalence among hospital patient participants increased from 1.8% to 6.8%, and among the PHCUs, the increase was 2.1% to 3.0%. The study shows a clear tendency, although not statistically significant, for a growing problem with ESBL-producing bacteria in the community, and especially in the hospital setting.

A majority of ESBL-positive hospital patients in 2008 and 2010 were found at the ward for Infectious Diseases. Fourteen of the 15 positive subjects from both years had at least one risk factor for ESBL carriage. All of the isolates of the ESBL-producing bacteria were *E. coli*.

The phylotyping of the found ESBL enzymes showed that CTX-M-1 was the dominating phylogroup in our study population, with 11 out of 16 bacterial strains harbouring this enzyme group. Four strains carried the gene coding for the CTX-M-9 phylogroup, one ESBL strain harboured the SHV enzyme, but no TEM enzyme was found.

The resistance patterns of the ESBL-producing bacterial strains ($n=16$) showed that all were susceptible to imipenem. The resistance patterns showed great variability for tobramycin (seven isolates were resistant), trimetoprim–sulfametoxazol and ciprofloxacin (ten of the isolates were resistant in both groups and one respectively three were classified as intermediate). Eleven of 16 strains were susceptible to piperacillin–tazobactam, four were intermediate and one was resistant.

The epidemiological typing with DiversiLab of the ESBL-producing bacteria showed that none of the bacterial strains were genetically identical. Five of the 16 (31%) ESBL-producing isolates were O25b-ST131 allele-specific *pabB*-positive and all of them carried the gene coding for the CTX-M-1 phylogroup. The five isolates belonging to O25b-ST131 were related by ≥85% similarity, as confirmed by DiversiLab. This should, presumably, not be interpreted as clonal spread, since the *E. coli* ST131 is a widespread genetically stable lineage that is strongly associated with ESBL-producing strains of the CTX-M-1 phylogroup and multi-resistance.

Other recent studies on ESBL prevalence and spread in Sweden also conclude that ESBL-producing bacteria is an increasing problem.

Of the ESBL-positive PHCU subjects, 3 out of 5 had recently travelled outside Northern Europe. In total, 14 out of 15 positive subjects had at least one risk factor for ESBL carriage, but 12 were previously unknown ESBL carriers. This shows the complexity of the most often asymptomatic faecal ESBL colonisation and the potential clinical consequences [5, 6].

There are some limitations to our study. Most apparent, the study population would have ideally been larger and with a greater coverage of different hospital wards. Also, there are a few noticeable disparities between the 2008 and 2010 studies regarding participating wards and PHCUs, and their response rates in all; no statistically confirmed conclusions can be drawn from our study when comparing the 2008 study with the follow-up study, but, on the whole, the two study populations are comparable demographically and we believe that the observed increase in ESBL prevalence reflects the real situation accurately.

In summary, we found a higher prevalence of ESBL faecal carriage than expected, both in the hospital setting and in the PHCU group. Our study showed that, in 2010, 1 of 15 patients carried ESBL-producing *E. coli* at our hospital, which questions the current empiric antibiotic treatment of patients with certain risk factors.

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Declaration of interest None to declare.

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