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Prevalence of extended-spectrum beta-lactamase producing *Escherichia coli* in community-onset urinary tract infections in France in 2013

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Summary *Objectives:* We sought to assess the importance of extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae in urinary tract infections in outpatients in France.
Methods: Retrospective laboratory based survey analysing susceptibility patterns of *Escherichia coli* and *Klebsiella pneumoniae* isolates providing from urines collected from outpatients during three months in 2013.
Results: Four hundred and ninety-nine laboratories collected data on 51,643 *E. coli* and 3495 *K. pneumoniae* isolates. The overall proportion of ESBL-producing *E. coli* was 3.3%. The proportion was higher for males (4.8%) than for females (3.0%) and increased with age: 2% for patients <20 years to 5.4% for those aged >80 years. More than 95% of isolates we susceptible to cefixime, fosfomycin, and nitrofurantoin. In nursing homes, the ESBL-producing *E. coli* proportion

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was 12.1%. For *K. pneumoniae*, the proportion of ESBL-positive isolates was 6.6%, and this proportion increased with age. Data from 2010 collected from a subset of the network showed that the ESBL-producing *E. coli* proportion was 2.0%.

Conclusion: ESBL-producing isolates were rather frequent in urines in French outpatients in 2013. Males and persons residing in nursing homes were at higher risk of ESBL-positive infection. Despite the increase in ESBL-positive isolates, the susceptibility to antibiotics used to treat cystitis remains high.

Introduction

The worldwide rise of antimicrobial resistance conducted many countries to develop national plans to control this public health threat.[1,2] After promising results of its first plans, France is currently in the middle of its third antibiotic sparing plan.[3] In a majority of these plans, surveillance of antibiotic resistance is recognised as a core issue. The goals for such surveillance have been listed elsewhere.[4] In particular, surveillance data should help in establishing guidelines for empirical treatment when antibiotic susceptibility tests results are not yet available or will not be performed. In addition, up-to-date data are of interest to assess the accuracy of already published guidelines.

Urinary tract infections (UTI) are among the most common bacterial infections that are treated in the community by an empirical antibiotic treatment regimen. In many countries, it is currently not recommended to perform urinalysis for cystitis before treatment, and the choice of the antibiotic regimen relies on the epidemiology of antibiotic resistance. *Escherichia coli*, which is a commensal species of the digestive tract, is the most common bacterial species isolated in UTI. The increase in resistance of *E. coli* to extended-spectrum cephalosporins (ESC) is now well documented, and is mainly due to the production of extended-spectrum beta-lactamase (ESBL) in the hospital setting as well as in the community.[1,5] In France for instance, there has been a 10-fold increase in the digestive carriage of ESBL-producing *E. coli* in the community in the last years.[6] The increase in ESBL-producing *E. coli* makes the treatment of community-onset UTI more complex because such isolates are usually multidrug-resistant, which increases the risk of treatment failure.[1,2,7] In addition, treating ESBL-positive infection is more costly that treating their susceptible counterpart.[7] Therefore, it is of interest to gather up-to-date data on the prevalence of antibiotic resistance of *E. coli* isolated from UTIs in the community.

Our main objective was to assess the prevalence of ESBL-producing *E. coli* amongst all *E. coli* isolated from urine samples in the community in ambulatory care in 2013. Data on *Klebsiella pneumoniae* the second most frequent Enterobacteriaceae isolated in community-acquired UTIs and data from patients in nursing homes were also collected for comparison purposes.

Materials and methods

Laboratories

Private practice laboratories participating in one of the three pre-existing networks (Epiville, MedQual-ville, Aforcopi-Bio) of the national observatory for epidemiology of bacterial resistance to antibiotics (ONERBA), and to a fourth network previously set-up for other purposes than surveillance of bacterial resistance (BPR network) were asked to participate on a voluntary basis. A special attention has been paid to national coverage of the network. A total of 499 private practice laboratories distributed throughout metropolitan France, and that referred urines clinical samples to 43 bacteriological centres participated into the network.

Bacteriology

Laboratories participating in this new network called «ONERBA-Ville» complied with national recommendations regarding antibiotic susceptibility testing (www.sfm-microbiologie.org), which are very similar to EUCAST recommendations (http://www.eucast.org/ast_of_bacteria), derived from ONERBA's recommendations for surveillance of bacterial resistance.[4,8]

Antibiotic susceptibility test methods were chosen locally and included liquid media automated systems (n = 35 for Vitek-2, BioMérieux; n = 4 for BD Phoenix system, BD Biosciences; n = 4 for Microscan WalkAway, Siemens Healthcare diagnostics) and the disk diffusion method (n = 6). ESBL-production was determined according to national recommendations as described elsewhere.[9]

Isolates were considered susceptible to tested antibiotics by using the following breakpoints: $\leq$4/2 mg/L for amocicilline/clavulanate, $\leq$1 mg/L for cefixime, $\leq$0.5 mg/L for ciprofloxacin, $\leq$32 mg/L for fosfomycin, $\leq$64 mg/L for nitrofurantoin, and $\leq$2/38 mg/L for cotrimoxazole.

Database

Data were retrospectively collected for each *E. coli* or *K. pneumoniae* strain isolated from urines routinely collected for diagnosis of community-onset urinary tract infections in outpatients or those in nursing home during September—November 2013. Data included patient's age, gender, and susceptibility tests results including ESBL production. In case of duplicates, only the first isolate was retained for the study. Whenever possible and for comparison purpose, similar data were collected for 2010.

Data analysis

Data have been analysed by using STATA 11 (StataCorp, College Station, TX, USA). Fisher's exact test was used to compare proportions. The Chi-square test for trend has been used to assess the impact of age on the proportion of

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