Medicina (Kaunas) 2013;49(9):393-8

CTX-M-Producing *Escherichia coli* in Lithuania: Associations Between Sites of Infection, Coresistance, and Phylogenetic Groups

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Key Words: *phylogenetic groups; site of infection; multiresistance; E. coli isolates; CTX-M.*

Summary. *Increasing resistance of Escherichia coli (E. coli) to antibiotics, especially to the third-generation cephalosporins, has prompted studies on widespread resistance genes such as bla_{CTX-M} and differentiation of E. coli to phylogenetic groups. The aim of this study was to determine the associations between the CTX-M type and the phylogenetic group, the site of infection, and coresistance in Lithuanian E. coli isolates producing β-lactamases.*

Material and Methods. A total of 90 E. coli ESBL strains were recovered from the lower respiratory tract, the urinary tract, sterile body sites, wounds, and other body sites between 2008 and 2012. The E. coli isolates resistant to at least 2 antibiotics with different modes of action along with resistance to cefotaxime were considered as multiresistant. The $bla_{CTX-M,}$ $bla_{TEM,}$ bla_{OXA-1}, and bla_{SHV} genes, the phylogenetic groups, and the resistance profiles were analyzed.

Results. Of the 90 isolates, 84 (93.3%) were classified as multiresistant and 6 (6.6%) as resistant. The $bla_{CTX-M-15}$ gene was the most prevalent gene followed by the $bla_{CTX-M-14}$ and $bla_{CTX-M-92}$ genes. The logistic regression analysis revealed the associations between CTX-M-15 and resistance to ceftriaxone, between CTX-M-14 and resistance to cefoxitin, aztreonam, ampicillin/sulbactam, ticarcillin/clavulanic acid, and tobramycin, and between CTX-M-92 and resistance to cefepime, piperacillin/tazobactam, gentamicin, and tobramycin.

Conclusions. The results of this study showed a significant association between CTX-M-15, CTX-M-14, and CTX-M-92 β-lactamases and resistance to some antibiotics as well as CTX-M-14 β-lactamase and phylogenetic group A in the Lithuanian population. The associations between the CTX-M type and the site of infection were not determined.

Introduction

Escherichia coli (*E. coli*) is the most common microorganism isolated from the sites of extraintestinal, intra-abdominal, community-acquired urinary tract infections and bacteremia (1, 2). Increasing resistance of *E. coli* to antibiotics, especially to the third-generation cephalosporins, has prompted studies on widespread resistance genes such as bla_{CTX-M} (3) and differentiation of *E. coli* strains to phylogenetic groups (4). CTX-M β-lactamases encoded by bla_{CTX-M} genes have almost replaced classical TEM- and SHV-type extended-spectrum β-lactamases (ESBLs). There are more than 120 different types of CTX-M β-lactamases that can be divided into 5 groups: CTX-M-1, -2, -8, -9, and -25 (5).

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E. coli strains can be assigned to 4 main phylogenetic groups: A, B1, B2, and D. Phylogenetic group B2 is common among community-acquired isolates, whereas phylogenetic group D is associated with hospital-acquired isolates. Isolates recovered from the sites of extraintestinal infections most frequently belong to both of these groups (6, 7). Phylogenetic groups A and B1 are associated with the sites of infection other than the urinary tract (7).

Molecular epidemiological analyses of CTX-M ESBLs have been carried out in most European countries (6). Cefuroxime-resistant *E. coli* and *Klebsiella pneumoniae* isolates from Finland have been found to produce CTX-M-1 and CTX-M-9 β-lactamases alone and in combination with TEM-1 β-lactamase (2). During outbreaks of *Salmonella typhimurium*, the CTX-M-5 enzyme has been described and identified in Latvia (8), Belarus, and Russia (9). The CTX-M-3 and CTX-M-15 enzymes

have been identified among the isolates of the *Enterobacteriaceae* family from 21 Russian hospitals (10) and 17 Polish medical centers (11, 12). In Lithuania, *E. coli* strains collected during the global tigecycline phase 3 clinical trials were positive for the CTX-M-2, -3, -15, and SHV-12 type β-lactamases (13). Among Lithuanian *E. coli* strains producing ESBLs, CTX-M-15 β-lactamase and a new specific local variant of CTX-M-92 β-lactamase have been reported to be most prevalent; among *Klebsiella pneumoniae* strains, CTX-M-15 and SHV-12 β-lactamases (14). CTX-M-2 β-lactamases have also been identified in Lithuania (14), Norway (15), and Russia (16).

To date, few studies have been carried out to establish the associations between a clinical origin of strains, resistance-encoding phenotypes, and phylogenetic groups among *E. coli* isolates (7, 17, 18). Therefore, the aim of this study was to determine the associations between the CTX-M type and the phylogenetic group, the site of infection, and coresistance in Lithuanian *E. coli* isolates producing β-lactamases.

Material and Methods

E. coli Strains. A total of 90 ESBL-producing *E. coli* with reduced susceptibility to the third-generation cephalosporins were randomly selected from all the ESBL strains collected during the 5-year period from 2008 to 2012. The specimens were recovered from the urinary tract, the lower respiratory tract, wounds, sterile body sites, and other body sites. All the clinical isolates were collected in regional and local hospitals of Lithuania: the Hospital of Lithuanian University of Health Sciences (n=54, 60%), the Republican Panevėžys Hospital (n=28, 31.1%), the Republican Šiauliai Hospital (n=4, 4.5%), Marijampolė Hospital (n=3, 3.3%), and Alytus County Kudirka Hospital (n=1, 1.1%).

Laboratory Testing. The isolates were identified using standard microbiological methods, i.e., colony morphology, the API 20E test system (bioMerieux, Marcy l'Etoile, France), or amplification of the region of the 16SrRNA gene (19). The isolates were kept in a tryptic soya broth and 15% glycerol at –20°C until analysis.

Antimicrobial Susceptibility Testing. The initial susceptibility testing to β-lactams was done using the Kirby Bauer disc diffusion method on Muller-Hinton agar (Becton, Dickinson and Company, USA) with cefotaxime and ceftazidime discs (Oxoid, UK). The results were interpreted according to the guidelines of the Clinical Laboratory Standards Institute (CLSI) (20). Commercial broth microdilution panels (GN1F, GN3F, ESB1F, Sensititre; TREK Diagnostic Systems, USA) were used according to the manufacturer's instructions and were tested against the CLSI quality control strain *E. coli* ATCC 25922. The minimum inhibitory concentrations (MICs) of the following 17 antibiotics were determined with the Trek Sensititre GN1F and GN3F systems: cefoxitin, ceftriaxone, ceftazidime, cefotaxime, cefepime, aztreonam, piperacillin/tazobactam, ampicillin/sulbactam, ticarcillin/clavulanic acid, meropenem, imipenem, gentamicin, amikacin, tobramycin, ciprofloxacin, trimethoprim/sulfamethoxazole, and nitrofurantoin. Confirmation tests for ESBL production were performed by using Trek Sensititre ESB1F panels. The results were interpreted according to the criteria of the CLSI (20). The *E. coli* isolates resistant to at least 2 antibiotics with different modes of action along with resistance to cefotaxime were considered as multiresistant (MDR).

Detection of β-Lactamase Genes. All the 90 strains included in this study were tested for the $bla_{\text{CTX-M}}$ (CTX-M-1, CTX-M-2, and CTX-M-9), bla_{TEM} (21), bla_{SHV} (22), and $bla_{\text{OXA-1}}$ (23) genes by using the polymerase chain reaction (PCR) method. PCR was carried out with a GeneAmp PCR System 9700 thermocycler (Applied Biosystems, France) under the following conditions: initial denaturation at 94°C for 5 minutes, 35 cycles of denaturation at 94°C for 40 seconds, annealing at 55°C for 40 seconds, elongation at 72°C for 1 minute, and final elongation at 72°C for 5 minutes. PCR and the sequencing of amplicons were performed by using the specific primers as described previously (21, 23).

The PCR products were separated by agarose gel electrophoresis on the 1% gel stained with ethidium bromide (10 mg/mL). The length of DNA fragments was determined by using the 100-bp dsDNA fragment standard (GeneRuler 100-bp DNA ladder, New England BioSystems, USA) at a wavelength of 302 nm. Sequencing reactions were carried out with the specific primers used previously for genotyping. Sequencing was performed on an automated sequencer 3130xl (Applied Biosystems, USA). The DNA sequences of interest were checked using the basic local alignment search tool provided by the National Center for Biotechnology Information (24).

Phylogenetic Grouping. Three genetic markers – the *chuA* and *yjaA* genes as well as the DNA fragment TspE4.C2 – were used to determine phylogenetic groups by the triplex PCR method. The isolates were assigned to 4 main phylogenetic groups (A, B1, B2, and D) by using a dichotomous decision tree as described by Clermont et al. (4). The fragments after PCR amplification were separated by agarose gel electrophoresis on the 1.5% gel.

Statistical Analysis. Statistical analysis was conducted by using the SPSS (Statistical Package for the Social Sciences, Microsoft Inc., USA) software, version 21.0 for Windows. Categorical variables were compared using the Pearson square or Fisher

exact tests. The logistic regression analysis was used to determine whether a particular CTX-M type had associations with the phylogenetic group, the site of infection, and coresistance in ESBL-producing *E. coli* strains. The level of significance was at $P<0.05$.

Ethical Considerations. The study was approved by Kaunas Regional Ethics Committee for Biomedical Research (No. BE-2-10).

Results

Associations Between CTX-M Genotype and Antimicrobial Resistance. It was found that 51 *E. coli* isolates were positive by PCR identification for the $bla_{\text{CTX-M-15}}$ gene (56.7%), 12 for $bla_{\text{CTX-M-14}}$ (13.3%), 10 for $bla_{\text{CTX-M-92}}$ (11%), 3 for $bla_{\text{CTX-M-2}}$ (3.3%), 2 for $bla_{\text{CTX-M-3}}$ (2.2%), and 1 for $bla_{\text{CTX-M-1}}$ (1.1%). A combination of 2 $bla_{\text{CTX-M}}$ genes was identified in 11 isolates: $bla_{\text{CTX-2\&15}}$ in 3 isolates (3.3%); $bla_{\text{CTX-3\&14}}$ in 3 (3.3%); $bla_{\text{CTX-14\&15}}$ in 3 (3.3%); and $bla_{\text{CTX-1\&14}}$ and $bla_{\text{CTX-15\&92}}$ in 1 (each 1.1%). One-fourth (25%) of all the studied isolates were positive for non-ESBL enzymes of bla_{TEM} (n=23), 22.2% for $bla_{\text{OXA-1}}$ (n=20), and 7.7% for both bla_{TEM} and $bla_{\text{OXA-1}}$ (n=7). None of the isolates carried the bla_{SHV} gene.

All the 90 isolates were resistant to cefotaxime in vitro. The majority of *E. coli* isolates were resistant to ampicillin/sulbactam (96.7%), ceftriaxone (90%), and ticarcillin/clavulanic acid (88.9%). The percentages of *E. coli* isolates resistant to tobramycin, gentamicin, trimethoprim/sulfamethoxazole, aztreonam, and ciprofloxacin were 74.4%, 73.3%, 70%, 66.7%, and 61.1%, respectively. Half (51.5%) of the isolates were resistant to the fourth-generation cephalosporin cefepime. The percentages of *E. coli* isolates resistant to ceftazidime, cefoxitin, piperacillin/tazobactam, amikacin, and nitrofurantoin were 35.6%, 31.1%, 23.3%, 14.4%, and 13.3%, respectively. None of the tested isolates displayed resistance to imipenem or meropenem.

Of the 90 isolates, 84 (93.3%) were classified as MDR and 6 (6.6%) as resistant only to cephalosporins. Besides, 23 isolates (25.6%) were resistant to 3 different classes of antibiotics, 34 isolates (37.8%) to 4, 22 isolates (24.4%) to 5, and 5 isolates (5.6%) to 6. Multiresistance was most common among the CTX-M-92 isolates (100%, n=10) followed by the CTX-M-15 (94%, n=48) and CTX-M-14 isolates (75%, n=9) ($P>0.05$). Among nonmultiresistant isolates, 1 isolate was resistant to cefotaxime only, 1 exhibited additional resistance to aztreonam, and 4 isolates had resistance to gentamicin. The distribution of *E. coli* isolates producing different CTX-M enzymes by antimicrobial resistance is shown in Table 1. The percentage of the CTX-M-92-producing isolates resistant to cefepime was significantly greater as compared with the percentages of the isolates producing CTX-M-15 and CTX-M combinations (90% vs. 47.0% and 45.5%; $P=0.011$ and $P=0.043$, respectively). The percentage of the CTX-M-14-producing isolates resistant to aztreonam and tobramycin was significantly lower as compared with the percentages of the isolates producing CTX-M-15 and CTX-M-92 (33.3% vs. 70.6% and 80.0%; $P=0.020$ and $P=0.038$; 100% vs. 41.6% and 76.4%; $P=0.023$ and $P=0.005$, respectively). The CTX-M-92-producing isolates were more frequently resistant to gentamicin than those producing CTX-M combinations (100% vs. 54.5%, $P=0.023$).

Table 2 summarizes the results of the logistic regression analysis. The binary logistic regression analysis revealed significant associations between CTX-M-15 and resistance to ceftriaxone (OR, 1.2; 95% CI, 1.07–1.37). Moreover, CTX-M-14 was significantly associated with resistance to cefoxitin (OR, 3.8; 95% CI, 1.09–13.29), aztreonam (OR, 0.2; 95% CI, 0.06–0.73), ampicillin/sulbactam (OR, 0.7; 95% CI, 0.01–0.78), ticarcillin/clavulanic acid (OR, 0.2; 95% CI, 0.04–0.72), and tobramycin (OR, 0.2; 95% CI, 0.05–0.66). CTX-M-92 was significantly associated with resistance to cefepime (OR, 10.5; 95% CI, 1.27–86.46), piperacillin/tazobactam (OR, 4; 95% CI, 1.03–15.51), gentamicin (OR, 0.7;

Table 1. Distribution of *E. coli* Isolates Producing Different CTX-M Enzymes by Antimicrobial Resistance

Antibiotic	CTX-M-15 N=51	CTX-M-14 N=12	CTX-M-92 N=10	Other N=6	Combination N=11
Ceftriaxone	43 (84.3)	12 (100.0)	10 (100.0)	5 (83.4)	11 (100.0)
Cefoxitin	14 (27.5)	7 (58.4)	2 (20.0)	1 (16.7)	4 (36.4)
Ceftazidime	21 (41.2)	2 (16.7)	3 (30.0)	1 (16.7)	5 (45.5)
Cefepime	24 (47.0)	6 (50.0)	9 (90.0)	2 (33.3)	5 (45.5)
Aztreonam	36 (70.6)	4 (33.3)	8 (80.0)	4 (66.7)	8 (72.7)
Ampicillin/sulbactam	50 (98.0)	10 (83.4)	10 (100.0)	6 (100.0)	11 (100.0)
Ticarcillin/clavulanic acid	46 (90.2)	8 (66.7)	10 (100.0)	6 (100.0)	10 (91.0)
Piperacillin/tazobactam	11 (21.6)	1 (8.3)	5 (50.0)	1 (16.7)	3 (27.7)
Gentamicin	37 (72.5)	8 (66.7)	10 (100.0)	5 (83.4)	6 (54.5)
Tobramycin	39 (76.4)	5 (41.6)	10 (100.0)	5 (83.4)	8 (72.7)
Amikacin	6 (11.8)	1 (8.3)	3 (30.0)	2 (33.0)	1 (9.0)
Ciprofloxacin	33 (65.0)	6 (50.0)	6 (60.0)	3 (50.0)	7 (63.6)
Trimethoprim/sulfamethoxazole	35 (68.6)	7 (58.3)	6 (60.0)	6 (100.0)	9 (81.8)
Furantoin	7 (13.7)	1 (8.3)	1 (10.0)	1 (16.7)	2 (18.0)

Table 2. Association Between the Type of CTX-M and Antibiotic Resistance Among *E. coli* Isolates

Antibiotic Resistance	CTX-M-15		CTX-M-14		CTX-M-92		Other		Combination	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Ceftriaxone	1.2 (1.07–1.37)	0.005	NA	NA	NA	NA	NA	NA	NA	NA
Cefoxitin	0.6 (0.26–1.55)	NS	3.8 (1.09–13.29)	0.035	0.5 (0.10–2.62)	NS	0.5 (0.06–5.04)	NS	1.3 (0.35–4.89)	NS
Ceftazidime	1.7 (0.68–4.06)	NS	0.3 (0.67–1.56)	NS	0.8 (0.18–3.14)	NS	0.4 (0.05–4.07)	NS	1.6 (0.45–5.74)	NS
Cefepime	0.6 (0.27–1.45)	NS	0.9 (0.28–3.20)	NS	10.5 (1.27–86.46)	0.009	0.6 (0.09–3.91)	NS	0.8 (0.22–2.74)	NS
Aztreonam	1.57 (0.65–3.79)	NS	0.2 (0.06–0.73)	0.013	2.2 (0.44–11.06)	NS	0.8 (0.12–4.75)	NS	1.4 (0.35–5.76)	NS
Ampicillin/ sulbactam	2.8 (0.25–32.44)	NS	0.7 (0.01–0.78)	0.046	0.9 (0.92–1.01)	NS	0.9 (0.93–1.01)	NS	NA	NA
Ticarcillin/ clavulanic acid	1.4 (0.38–5.32)	NS	0.2 (0.04–0.72)	0.010	NA	NA	NA	NA	1.3 (0.15–11.26)	NS
Piperacillin/ tazobactam	0.8 (0.28–2.01)	NS	0.3 (0.32–2.17)	NS	4 (1.03–15.51)	0.034	0.8 (0.09–7.69)	NS	1.2 (0.30–5.29)	NS
Gentamicin	0.97 (0.38–2.49)	NS	0.7 (0.19–2.54)	NS	0.7 (0.60–0.80)	0.037	1.5 (0.16–13.98)	NS	0.4 (0.10–1.39)	NS
Tobramycin	1.4 (0.52–3.52)	NS	0.2 (0.05–0.66)	0.010	0.7 (0.62–0.82)	0.043	1.4 (0.15–13.18)	NS	0.9 (0.22–3.74)	NS
Amikacin	0.58 (0.18–1.88)	NS	0.5 (0.06–4.24)	NS	3 (0.67–13.53)	NS	4.5 (0.67–29.93)	NS	0.6 (0.06–4.77)	NS
Ciprofloxacin	1.2 (0.54–2.97)	NS	0.6 (0.18–2.00)	NS	0.9 (0.25–3.63)	NS	0.9 (0.15–6.00)	NS	1.1 (0.30–4.18)	NS
Trimethoprim/ sulfamethoxazole	0.9 (0.37–2.29)	NS	0.6 (0.16–1.92)	NS	0.6 (0.16–2.35)	NS	NA	NA	2.1 (0.42–10.36)	NS
Furantoin	1.0 (0.29–3.52)	NS	0.6 (0.07–4.73)	NS	0.6 (0.08–6.05)	NS	1.7 (0.17–16.46)	NS	1.5 (0.29–8.14)	NS

NS, not significant; NA, not applicable.

Table 3. Distribution of ESBL-producing *E. coli* Isolates Carrying Different $bla_{CTX\text{-}M}$ Genes According to the Phylogenetic Groups and Infection Sites

Characteristic	CTX-M-15 N=51	CTX-M-14 N=12	CTX-M-92 N=10	Other N=6	Combination N=11	Total
Phylogenetic group						
B2	20 (39.2)	6 (50.0)	7 (70.0)	1 (16.7)	5 (45.4)	39 (43.3)
D	13 (25.5)	6 (50.0)	2 (20.0)	1 (16.7)	3 (27.3)	25 (27.8)
A	18 (35.3)	0 (0.0)	1 (10.0)	4 (66.6)	3 (27.3)	26 (28.9)
Infection site						
Urinary tract	22 (43.1)	4 (33.4)	1 (10.0)	0 (0.0)	4 (36.4)	31 (34.4)
Lower respiratory tract	11 (21.6)	3 (25.0)	4 (40.0)	2 (33.3)	3 (27.3)	23 (25.6)
Wounds	10 (19.6)	1 (8.3)	1 (10.0)	2 (33.3)	3 (27.3)	17 (18.9)
Sterile body site	6 (11.8)	3 (25.0)	3 (30.0)	1 (16.7)	0 (0.0)	13 (14.4)
Other body site	2 (3.9)	1 (8.3)	1 (10.0)	1 (16.7)	1 (9.0)	6 (6.7)

95% CI, 0.60–0.80), and tobramycin (OR, 0.7; 95% CI, 0.62–0.82).

Distribution of E. coli Isolates Carrying $bla_{CTX\text{-}M}$ Genes According to Phylogenetic Groups and Infection Sites. The distribution of the ESBL-producing *E. coli* isolates carrying different $bla_{CTX\text{-}M}$ genes according to the phylogenetic groups and infection sites is shown in Table 3. The isolates investigated in our study were assigned to 3 main phylogenetic groups: A, B2, and D. The results showed that 39 isolates (43.3%) belonged to phylogenetic group B2, 26 isolates (28.9%) were assigned to group A, and 25 (27.8%) belonged to group D ($P>0.05$). None of the isolates were assigned to group B1. The binary logistic regression analysis showed a significant association only between CTX-M-14 and phylogenetic

group A (OR, 0.56; 95% CI, 0.45–0.70, P=0.039); no significant associations between other CTX-M and phylogenetic groups were documented.

The greatest percentage of the *E. coli* isolates producing CTX-M-type β-lactamases in our study were isolated from the urinary tract (34.4%) followed by the lower respiratory tract (25.6%), wounds (18.9%), sterile body sites (14.4%), and other body sites (6.7%) (P>0.05). The logistic regression analysis revealed no significant associations between a particular CTX-M type and infection sites.

Discussion

To our knowledge, this study was the first that was aimed at determining associations between the CTX-M type and the phylogenetic group, the site of infection, and coresistance in *E. coli* isolates-producing β-lactamases.

Our results showed that the most common CTX-M β-lactamase among the *E. coli* isolates, collected during the period of 5 years, was CTX-M-15 followed by CTX-M-14 and CTX-M-92. In 2010, the most prevalent CTX-M β-lactamase in the *E. coli* isolates was the same CTX-M-15 (36%) followed by CTX-M-92 (17%) and CTX-M-14 (13%) (14). The results of our study are consistent with the global distribution of CTX-M-15 and CTX-M-14 (6). In agreement to other studies (14, 25), our study showed that the *E. coli* isolates producing CTX-M also encoded narrow-spectrum β-lactamases TEM or OXA-1. Moreover, we determined that the *E. coli* isolates could carry both TEM and OXA-1 β-lactamases. None of our *E. coli* isolates were found to carry the bla_{SHV} gene, as in the study by Dahmen et al. (25).

The isolates producing CTX-M β-lactamases also exhibit coresistance to non-β-lactam antibiotics. According to the study by Östholm Balkhed et al. (26), 68% of the CTX-M-producing *E. coli* isolates were multiresistant. Our study showed a higher percentage of multiresistant strains (93.3%). This could be influenced by the fact that the isolates for analysis were sent to the Department of Microbiology from the biggest hospitals in Lithuania where patients with the most severe illnesses are treated.

This study demonstrated that the *E. coli* isolates producing CTX-M-14 were more susceptible to ciprofloxacin, gentamicin, and tobramycin than the isolates carrying CTX-M-15 and CTX-M-92 β-lactamases. These results are consistent with the results of the study done by Östholm Balkhed et al. (26). According to this study, the isolates belonging to CTX-M group 9 were more susceptible to ciprofloxacin, gentamicin, and tobramycin than those belonging to CTX-M group 1 (26). All our isolates carrying CTX-M-92 genes were resistant to ampicillin/sulbactam, ticarcillin/clavulanic acid, gentamicin, and tobramycin (100%). The majority of our isolates were susceptible to furantoin and amikacin, which confirms the results of the study by Östholm Balkhed et al. (26). One-third of the isolates producing CTX-M-92 and other β-lactamases (CTX-M-1, -2, and -3) were resistant to amikacin. The results of our study also demonstrated that CTX-M-92 was associated with 10-fold greater resistance to cefepime and nearly 1.5-fold lower resistance to tobramycin and gentamicin.

To our knowledge, this study was the first to report the distribution of Lithuanian ESBL-producing *E. coli* clinical isolates according to the phylogenetic groups. It was determined that the CTX-M *E. coli* isolates most frequently belonged to group B2 (43%). Interestingly, our results are similar to those obtained in the French studies by Branger et al. (17) and Brisse et al. (27), who reported the corresponding percentages of 39.4% and 42%, respectively. Nearly one-third of our isolates belonged to phylogenetic groups A and D (29% and 28%, respectively), whereas in the study by Brisse et al. (27), 29% of the studied *E. coli* isolates were assigned to phylogenetic group A and 16% to phylogenetic group D. Among ESBL-producing strains, none of the 4 groups were associated with one particular type of CTX-M (28). However, our study showed a significant association between the CTX-M-14 type and phylogenetic group A. According to the authors, the frequency of a phylogenetic group among isolates might be related to a geographical area, differences in the characteristics of the host population, and differences in sampling methods (18).

It has been reported that CTX-M *E. coli* strains are mainly isolated from the urinary tract (17), less frequently from the lower respiratory tract, sterile body sites, wounds, and other body sites (1). The greatest percentages of the strains producing CTX-M-type β-lactamases were isolated from the urinary tract except for the isolates producing CTX-M-92 and other CTX-M β-lactamases (CTX-M-1, CTX-M-2, and CTX-M-3). Finally, we failed to determine significant associations between the CTX-M type and infection sites.

Conclusions

A better understanding of the relationship between CTX-M β-lactamases and other associated factors would ease decisions regarding the empirical treatment of infections caused by ESBL *E. coli*. The results of this study showed a significant association between CTX-M-15, CTX-M-14, and CTX-M-92 β-lactamases and resistance to some antibiotics as well as CTX-M-14 β-lactamase and phylogenetic group A in the Lithuanian population. The associations between the CTX-M type and the site of infection were not determined.

Acknowledgments

The authors would like to thank Dr. V. Tatarūnas for reading the manuscript.

This work was supported by the Pierre and Marie Curie Faculty of Medicine, University of Paris 6, France, the Embassy of France in Lithuania, the French Institute in Lithuania, the Research Council of Lithuania, and the Open Foundation of the Lithuanian University of Health Sciences.

Statement of Conflict of Interest

The authors state no conflict of interest.

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Received 20 August 2013, accepted 30 September 2013