Risk factors for community-onset urinary tract infections caused by extended-spectrum β-lactamase-producing Escherichia coli

Türkan TÜZÜN1, Selda SAYIN KUTLU2,* Murat KUTLU3, Ilknur KALELİ3
1Department of Infectious Diseases and Clinical Microbiology, Denizli Surgery Hospital, Denizli, Turkey
2Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Pamukkale University, Denizli, Turkey
3Department of Medical Microbiology, Faculty of Medicine, Pamukkale University, Denizli, Turkey

Background/aim: Community-onset urinary tract infections (UTIs) caused by extended-spectrum β-lactamase (ESBL)-producing Escherichia coli have increased in many parts of the world. This study aimed to determine the prevalence and risk factors for community-onset UTI caused by ESBL-producing E. coli.

Materials and methods: This prospective cohort study was conducted between January 2012 and March 2014 in cases of community-onset UTI caused by E. coli. Patients with UTI due to ESBL-producing E. coli and patients with UTI due to non-ESBL-producing E. coli were compared to identify risk factors for ESBL-producing E. coli in the community.

Results: A total of 305 patients (116 males [46.4%]; mean age: 57.76 ± 18.06 years) were included in the study. Among these patients, 154 (50.5%) were infected with ESBL-producing E. coli. In multivariate analysis, the healthcare-associated UTI (odds ratio [OR]: 1.80; 95% confidence interval [CI]: 1.02–3.18; P = 0.041), upper urinary tract infection (OR: 3.05; 95% CI: 1.76–5.29; P < 0.0001), use of antibiotics in the preceding 6 months (OR: 2.28; 95% CI: 1.21–4.30; P = 0.011), and having two or more risk factors (OR: 4.03; 95% CI: 1.73–9.35; P = 0.001) were the significant factors associated with increased risk of community-onset UTIs due to ESBL-producing E. coli.

Conclusion: The increasing prevalence of ESBL-producing E. coli makes it difficult to decide the empirical therapy in UTIs, especially in patients with two or more of the risk factors. A better understanding of the epidemiology and risk factors associated with community-onset UTIs due to ESBL-producing E. coli may have significant implications in decision-making for empirical antimicrobial treatment.

Key words: Community-onset, epidemiology, extended-spectrum β-lactamase, risk factors, urinary tract infections
underlying diseases, and clinical signs and symptoms of the patients, as well as microbiological data, were recorded. This study was conducted with the approval of the Medical Ethics Committee of Pamukkale University (date: 17 January 2012; resolution number: 02) and adhered to the principles of the Declaration of Helsinki. Individual informed consent was obtained from all study participants.

Patients admitted with clinical signs and/or symptoms of UTIs (e.g., fever >38°C, urgency, frequency, dysuria, or suprapubic tenderness) with no other recognized cause, pyuria (i.e. urine specimen with ≥10 white blood cells/mm³), and a positive urine culture were enrolled in the study [7].

UTI was defined as “community-onset” when the infection occurred among nonhospitalized patients or <48 h after hospitalization. Community-onset UTIs include community-acquired UTIs and healthcare-associated UTIs [7]. Therefore, we included healthcare-associated UTIs according to previously published criteria: hospitalization in an acute care hospital for two or more days in the previous 90 days; residence in a nursing home or a long-term care facility; received intravenous therapy at home or in a day hospital; hemodialysis treatment; intravenous chemotherapy 30 days before the infection; received wound care or specialized nursing care in the preceding 30 days; presence of long-term indwelling urethral catheters or an invasive urinary tract procedure in the previous 30 days [8].

2.2. Microbiological analysis

Urine specimens were obtained from either first clean-catch midstream urine or urinary catheters. The isolated bacteria were identified by conventional methods in the microbiology laboratory. Positive urine cultures were defined when the bacterial growth was ≥10⁵ colony forming units (CFU)/mL [9]. ESBL determination was performed phenotypically with ceftazidime/cefotaxime clavulanate and cefotaxime/cefotaxime clavulanate disks, as recommended by the Clinical and Laboratory Standards Institute (CLSI) [10]. Antimicrobial susceptibility testing was performed using the disk diffusion method, according to the CLSI standards. Patients with UTI due to ESBL-producing E. coli and non-ESBL-producing E. coli were compared in terms of demographic characteristics, underlying diseases, and microbiological data to identify risk factors for ESBL-producing E. coli in the community.

2.3. Statistical analysis

Continuous variables were compared by independent samples t-test, and categorical variables were compared by chi-square test or Fisher’s exact test for association. Differences were considered statistically significant at P < 0.05. Statistical calculations were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). In order to analyze the effect of the number of risk factors on ESBL-producing E. coli, we separated the patients based on existing risk factors. Patients with no risk factor, one risk factor, and two or more risk factors were analyzed.

Backward stepwise multiple logistic regression was performed to identify the risk factors for community-onset UTI caused by ESBL-producing E. coli as the dependent variable. However, we did not include the risk factors that were also in the definition of healthcare-associated UTIs in the multivariate analysis.

3. Results

A total of 305 patients (116 males (46.4%); mean age: 57.76 ± 18.06 years; range: 16–87 years) were included in the study. Among these patients, 154 (50.5%) were infected with ESBL-producing E. coli.

Being male, old age (≥55 years), hospitalization within 3 months, use of antibiotics within the previous 6 months, healthcare-associated UTI, upper UTI, frequent UTIs (>3 times/year), presence of indwelling urethral catheter, renal failure, and neoplasia were significant risk factors for ESBL-producing E. coli among community-onset UTI cases in univariate analysis (P < 0.05). Moreover, patients with two or more risk factors were more likely to have ESBL-producing E. coli. ESBL positivity was lower in patients with one risk factor or no risk factors (P < 0.05) (Table 1). Healthcare-associated UTI was seen in 142/305 (46.6%) patients; indwelling urethral catheter use was the most common reason, with a rate of 102/142 (71.8%) patients.

In multivariate analysis, factors associated with an increased risk of community-onset UTIs due to ESBL-producing E. coli included healthcare-associated UTI (odds ratio [OR]: 1.80; 95% confidence interval [CI]: 1.02–3.18; P = 0.041), upper urinary tract infection (OR: 3.05; 95% CI: 1.76–5.29; P < 0.0001), use of antibiotics in the preceding 6 months (OR: 2.28; 95% CI: 1.21–4.30; P = 0.011), and having two or more risk factors (OR: 4.03; 95% CI: 1.76–9.35; P = 0.001) (Table 2). Regarding antibiotic class, previous use of cephalosporin and fluoroquinolones was associated with ESBL-producing E. coli (respectively P < 0.001, P = 0.019). There was no correlation between the use of beta-lactam-beta-lactamase inhibitors and ESBL positivity (P = 0.16) (Table 1).

ESBL-producing E. coli isolates had more non-beta-lactam antibiotic resistance than non-ESBL-producing E. coli isolates. The resistance rates for ciprofloxacin were 91.6% and 30.5% (P < 0.0001), for TMP-SMX were 65.4% and 35.8% (P < 0.0001), for gentamicin were 64.3% and 7.3% (P < 0.0001), for amoxicillin–clavulanate were 99.4% and 23.8% (P < 0.0001), for piperacillin-tazobactam were 19.5% and 4% (P < 0.0001), and for nitrofurantoin were
9.7% and 5.3% (P = 0.193), respectively. Fosfomycin resistance was found only in one ESBL-producing E. coli isolate, and there was no resistance to fosfomycin in non-ESBL-producing E. coli isolates (Figure).

4. Discussion
ESBL-producing E. coli is a precariously increasing pathogen among community-onset UTIs. The ESBL prevalence rate is variable in different geographical regions. For instance, in Norway, it is lower than 2%, but it can also be very high, over 74%, like in Iran [11,12]. ESBL-producing E. coli is responsible not only for healthcare-associated but also for community-acquired UTI even in countries with low antibiotic use [5,11,13], and multidrug resistance makes it more difficult to decide the appropriate antibiotic treatment.

Table 1. Characteristics of community-onset UTI caused by ESBL-producing Escherichia coli.

|                                      | ESBL-positive E. coli, n=154 (%) | ESBL-negative E. coli, n=151 (%) | P-value |
|--------------------------------------|----------------------------------|----------------------------------|---------|
| Sex, male, n = 116 (%)               | 73 (47.4)                        | 43 (28.5)                        | 0.01    |
| Age ≥55 years                        | 101 (65.6)                       | 78 (51.7)                        | 0.014   |
| Hospitalization within 6 months      | 73 (47.4)                        | 22 (14.6)                        | <0.0001 |
| Length of hospital stay, days, mean ± SD | 16.86 ± 18.07                  | 15.95 ± 15.71                    | 0.83    |
| Use of antibiotics within previous 6 months |                    |                                  |         |
| Fluoroquinolones                     | 62 (40.3)                        | 20 (13.2)                        | <0.0001 |
| Cephalosporins                       | 24 (16.0)                        | 11 (7.3)                         | 0.019   |
| Beta-lactam-beta-lactamase inhibitors | 28 (18.3)                        | 6 (4.0)                          | <0.001  |
|                                     | 6 (3.9)                          | 2 (1.3)                          | 0.16    |
| Healthcare-associated UTI            | 98 (63.6)                        | 44 (29.1)                        | <0.0001 |
| Upper UTI                            | 94 (61.0)                        | 36 (23.8)                        | <0.0001 |
| Frequent UTIs (>3 times/year)        | 45 (29.2)                        | 16 (10.6)                        | <0.0001 |
| Indwelling urethral catheter         | 75 (48.7)                        | 30 (19.9)                        | <0.0001 |
| Diabetes mellitus                    | 41 (26.6)                        | 45 (29.8)                        | 0.53    |
| Renal failure                        | 54 (35.1)                        | 23 (15.2)                        | <0.0001 |
| Nephrolithiasis                      | 28 (18.2)                        | 25 (16.6)                        | 0.708   |
| Renal transplantation                | 6 (3.9)                          | 2 (1.3)                          | 0.160   |
| Use of corticosteroid                | 11 (7.1)                         | 10 (6.6)                         | 0.858   |
| Chronic obstructive lung disease     | 13 (8.4)                         | 9 (6.0)                          | 0.402   |
| Neoplasia                            | 37 (24.0)                        | 19 (12.6)                        | 0.01    |
| Chemotherapy                         | 6 (3.9)                          | 5 (3.3)                          | 0.784   |
| Menopause, n = 189 (%)               | 57 (70.4)                        | 72 (66.7)                        | 0.588   |
| Prostate benign hypertrophy, n = 116 (%) | 48 (64.9)                     | 27 (62.8)                        | 0.822   |
| No risk factor                       | 7 (4.5)                          | 20 (13.2)                        | 0.007   |
| One risk factor                      | 4 (2.6)                          | 24 (15.9)                        | <0.0001 |
| Two or more risk factors             | 146 (94.8)                       | 106 (70.2)                       | <0.0001 |

*: Univariate analysis was performed in women.
#: Univariate analysis was performed in men.

Table 2. Multivariate analysis of risk factors for community-onset UTI caused by ESBL-producing Escherichia coli.

|                                      | Odds ratio | 95% Confidence interval | P-value |
|--------------------------------------|------------|-------------------------|---------|
| Use of antibiotics within previous 6 months | 2.28       | 1.21–4.3                | 0.011   |
| Healthcare-associated UTI            | 1.80       | 1.02–3.18               | 0.041   |
| Upper UTI                            | 3.05       | 1.76–5.29               | <0.0001 |
| Two or more risk factors             | 4.03       | 1.73–9.35               | 0.001   |
Our results revealed that the ESBL-producing *E. coli* rate was 50.5% in patients with community-onset UTI, and 63.6% of ESBL (+) patients were diagnosed as having healthcare-associated UTIs, while only 29% of ESBL (-) patients had healthcare-associated UTIs. This prevalence seems to be higher than in previous studies [3,14]. In a study from Turkey, the SMART study, the rate of ESBL-positive *E. coli* was much higher in healthcare-associated than community-acquired UTIs during 2011 and 2012, at 50% and 38%, respectively [14]. Another study from Turkey reported a similar ESBL-producing *E. coli* rate in 2006, as 36.7%, among patients with community-acquired UTIs, but ESBL-producing *E. coli* rates were not given for healthcare-associated UTIs [3]. The higher rates of ESBL-producing *E. coli* in community-onset UTIs in our study can be related to higher rates of healthcare-associated UTIs and also a different study period.

The major independent risk factors for ESBL positivity in our series were the presence of healthcare-associated UTIs, upper urinary tract infection, use of antibiotics in the preceding 6 months, and having two or more risk factors. Healthcare-associated UTIs were associated with an increased risk for ESBL positivity in our analysis. Similarly, previous studies showed that ESBL-producing *E. coli* was more frequent in patients with several healthcare-associated infections including UTIs [15–18]. Indwelling urethral catheter use was the most common reason for healthcare-associated UTI [19,20]. Similarly, the rate of indwelling urethral catheter use was as high as 71.8% in healthcare-associated UTIs in our series.

Our results revealed that there is a threefold increased risk of ESBL-producing *E. coli* in upper UTI cases. We did not come across a study that showed a relationship between upper UTIs and ESBL positivity in our literature review. However, it may be suggested that ESBL-producing *E. coli* is a frequent causative agent in upper UTIs due to a requirement for more frequent hospitalizations, more complications, and the presence of different underlying risk factors in this patient group.

We also found the number of risk factors for ESBL-positive *E. coli* to be important. ESBL positivity was lower in patients with no risk factors or one risk factor, which included being male, old age (≥55 years), use of antibiotics within the previous 6 months, healthcare-associated UTI, upper UTI, frequent UTIs (>3 times/year), renal failure, and neoplasia. In contrast, patients with two or more risk factors were more likely to have ESBL-producing *E. coli*.

When we did not include the presence of two or more risk factors in multivariate analysis, we found that being 55 years of age or older was an independent risk factor. In elderly patients, additional comorbid issues, hospital admission rates, and infectious diseases are more frequent. Antimicrobial drug use, and therefore a greater risk of acquiring antibiotic-resistant bacterial infections, is more frequent among older patients [21]. As in our study, older age and previous use of antibiotics
were reported as risk factors for ESBL-positive *E. coli* in previous studies [15,22–25]. In terms of antibiotic class, previous use of cephalosporin and fluoroquinolones was associated with ESBL-producing *E. coli*. Although the use of fluoroquinolone and cephalosporin was reported to be an independent risk factor in many studies [11,18,26,27], the use of fluoroquinolone was not associated with ESBL positivity in some studies [2,25].

Extended-spectrum beta-lactamase-producing *E. coli* is not only resistant to beta-lactam antibiotics; there is also a higher rate of coresistance to many antibiotic groups, particularly quinolones, TMP-SMX, and aminoglycosides [24]. Similar to previous reports [12,26,28], our results showed that ESBL-producing *E. coli* isolates had more antibiotic resistance than did non-ESBL-producing *E. coli* isolates. Particularly, amoxicillin-clavulanate, ciprofloxacin, TMP-SMX, and gentamicin resistance was very significant in ESBL-producing *E. coli* isolates. Both ESBL-positive and ESBL-negative *E. coli* isolates remain highly susceptible to carbapenems, fosfomycin, and nitrofurantoin. However, the amoxicillin-clavulanate resistance was higher in the ESBL-positive group than in the studies mentioned above. In a multinational survey, ESBL-producing Enterobacteriaceae isolates from Turkey were more likely to be resistant to amoxicillin-clavulanate than isolates from other regions [23].

A limitation of the present study is the absence of molecular strain typing of ESBL-positive *E. coli* isolates. However, the most prevalent type was CTXM-15 among these isolates, also reported in previous studies from Turkey [3,29].

This study revealed that the ESBL rate of *E. coli* isolated from community-onset UTI cases was high in Turkey. The major risk factors for ESBL-producing *E. coli* were the presence of a healthcare-associated UTI, upper urinary tract infection, use of antibiotics in the preceding 6 months, and having two or more risk factors. The increasing prevalence of ESBL-producing *E. coli* makes it difficult to decide the empiric therapy in UTI cases, especially in patients with two or more of the risk factors. Therefore, a better understanding of the epidemiology and risk factors of community-onset UTIs caused by ESBL-producing *E. coli* may have significant implications for the choice of empiric antimicrobial treatment. Considering the risk factors in this patient group can increase treatment success.

References

1. Fan NC, Chen HH, Chen CL, Ou LS, Lin TY et al. Risk of community-onset urinary tract infection caused by extended-spectrum β-lactamase-producing *Escherichia coli* in children. Journal of Microbiology, Immunology and Infection 2014; 47 (5): 399-405. doi: 10.1016/j.jmi.2013.05.006
2. Calbo E, Romaní V, Xercavins M, Gómez L, Vidal CG et al. Risk factors for community-onset urinary tract infections due to *Escherichia coli* harbouring extended-spectrum beta-lactamases. Journal of Antimicrobial Chemotherapy 2006; 57 (4): 780-783.
3. Celik AD, Yulgukral Z, Kuloglu F, Eroglu C, Torol S et al. CTX-M type extended spectrum-lactamasises in *Escherichia coli* isolates from community acquired upper urinary tract infections at a university in the European part of Turkey. Journal of Microbiology, Immunology and Infection 2010; 43 (2): 163-167. doi: 10.1016/S1684-1182(10)60026-6
4. Martin D, Fougnot S, Grobost F, Thibaut-Jovelin S, Ballereau F et al. Prevalence of extended-spectrum beta-lactamase producing *Escherichia coli* in community-onset urinary tract infections in France in 2013. Journal of Infection 2016; 72 (2): 201-206. doi: 10.1016/j.jinf.2015.11.009
5. Meier S, Weber R, Zbinden R, Ruef C, Hasse B. Extended-spectrum β-lactamase-producing Gram-negative pathogens in community-acquired urinary tract infections: an increasing challenge for antimicrobial therapy. Infection 2011; 39 (4): 333-340. doi: 10.1007/s15010-011-0132-6
6. Lee SS, Kim Y, Chung DR. Impact of discordant empirical therapy on outcome of community-acquired bacteremic acute pyelonephritis. Journal of Infection 2011; 62 (2): 159-164. doi: 10.1016/j.jinf.2010.10.009
7. Kung CH, Ku WW, Lee CH, Fung CP, Kuo SC et al. Epidemiology and risk factors of community-onset urinary tract infection caused by extended-spectrum β-lactamase-producing Enterobacteriaceae in a medical center in Taiwan: a prospective cohort study. Journal of Microbiology, Immunology and Infection 2015; 48 (2): 168-174. doi: 10.1016/j.jmi.2013.08.006
8. Smithson A, Chico C, Ramos J, Netto C, Sanchez M et al. Prevalence and risk factors for quinolone resistance among *Escherichia coli* strains isolated from males with community febrile urinary tract infection. European Journal of Clinical Microbiology & Infectious Diseases 2012; 31 (4): 423-430. doi: 10.1007/s10096-011-1322-y
9. Sobel JD, Kaye D. Urinary tract infections. In: Bennett JE, Dolin R, Blaser MJ (editors). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8th ed. Philadelphia, PA, USA: Elsevier; 2015. pp. 886-913.
10. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Eighteenth Informational Supplement, M100-S18. Wayne, PA, USA: CLSI; 2009.
11. Søraas A, Sundsfjord A, Sandven I, Brunborg C, Jenum PA. Risk factors for community-acquired urinary tract infections caused by ESBL-producing Enterobacteriaceae—a case-control study in a low prevalence country. PLoS One 2013; 8 (7): e69581. doi: 10.1371/journal.pone.0069581

12. Al-Mayahie S, Al Kuriashy JJ. Distribution of ESBLs among *Escherichia coli* isolates from outpatients with recurrent UTIs and their antimicrobial resistance. Journal of Infection in Developing Countries 2016; 10 (6): 575-583. doi: 10.3855/jidc.6661

13. Den Heijer CD, Donker GA, Maes J, Stobberingh EE. Antibiotic susceptibility of unselected uropathogenic *Escherichia coli* from female Dutch general practice patients: a comparison of two surveys with a 5 year interval. Journal of Antimicrobial Chemotherapy 2010; 65 (10): 2128-2133. doi: 10.1093/jac/dkq286

14. Koksal I, Yilmaz G, Unal S, Zarakoju P, Korten V et al. Epidemiology and susceptibility of pathogens from SMART 2011-12 Turkey: evaluation of hospital-acquired versus community-acquired urinary tract infections and ICU- versus non-ICU-associated intra-abdominal infections. Journal of Antimicrobial Chemotherapy 2017; 72 (5): 1364-1372. doi: 10.1093/jac/dkw574

15. Rodríguez-Baño J, Alcalá JC, Cisneros JM, Grill F, Oliver A et al. Community infections caused by extended-spectrum beta-lactamase-producing *Escherichia coli*. Archives of Internal Medicine 2008; 168 (17): 1897-1902. doi: 10.1001/archinte.168.17.1897

16. Park YS, Bae IK, Kim J, Jeong SH, Hwang SS et al. Risk factors and molecular epidemiology of community-onset extended-spectrum β-lactamase-producing *Escherichia coli* bacteremia. Yonsei Medical Journal 2014; 55 (2): 467-475. doi: 10.3349/jymj.2014.55.2.467

17. Kang CI, Wi YM, Lee MY, Ko KS, Chung DR et al. Epidemiology and risk factors of community onset infections caused by extended-spectrum β-lactamase-producing *Escherichia coli* strains. Journal of Clinical Microbiology 2012; 50 (2): 312-317. doi: 10.1128/JCM.06002-11

18. Rodríguez-Baño J, Picón E, Gijón P, Hernández JR, Ruiz M et al. Community-onset bacteremia due to extended-spectrum beta-lactamase-producing *Escherichia coli* risk factors and prognosis. Clinical Infectious Diseases 2010; 50 (1): 40-48. doi: 10.1086/649537

19. Chenoweth CE, Saint S. Urinary tract infections. Infectious Disease Clinics of North America 2011; 25 (1): 103-115. doi: 10.1016/j.idc.2010.11.005

20. Parker V, Giles M, Graham L, Suthers B, Watts W et al. Avoiding inappropriate urinary catheter use and catheter-associated urinary tract infection (CAUTI): a pre-post control intervention study. BMC Health Services Research 2017; 17 (1): 314. doi: 10.1186/s12913-017-2268-2

21. Yoshikawa TT, Norman DC. Geriatric infectious diseases: current concepts on diagnosis and management. Journal of the American Geriatrics Society 2017; 65 (3): 631-641. doi: 10.1111/jgs.14731

22. Qiao LD, Chen S, Yang Y, Zhang K, Zheng B et al. Characteristics of urinary tract infection pathogens and their in vitro susceptibility to antimicrobial agents in China: data from a multicenter study. BMJ Open 2013; 3 (12): e004152. doi: 10.1136/bmjopen-2013-004152

23. Ben-Ami R, Rodríguez-Baño J, Arslan H, Pitout JD, Quentin C et al. A multinational survey of risk factors for infection with extended-spectrum beta-lactamase-producing Enterobacteriaceae in non-hospitalized patients. Clinical Infectious Diseases 2009; 49 (5): 682-690. doi: 10.1086/604713

24. Rodríguez-Baño J, Navarro MD, Romero L, Martínez-Martínez L, Muniaín MA et al. Epidemiology and clinical features of infections caused by extended-spectrum beta-lactamase producing *Escherichia coli* isolated from non-hospitalized patients. Journal of Clinical Microbiology 2004; 42 (3): 1089-1094.

25. Azap OK, Arslan H, Serefhanoğlu K, Colakoğlu S, Erdoğan H et al. Risk factors for extended-spectrum beta-lactamase positivity in uropathogenic *Escherichia coli* isolated from community-acquired urinary tract infections. Clinical Microbiology and Infection 2010; 16 (2): 147-151. doi: 10.1111/j.1469-0691.2009.02941.x

26. Yilmaz E, Akalin H, Oz bey S, Kordan Y, Sınirtaş M et al. Risk factors in community-acquired/sonry urinary tract infections due to extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*. Journal of Chemotherapy 2008; 20 (5): 581-585.

27. Colodner R, Rock W, Chazan B, Keller N, Guy N et al. Risk factors for the development of extended-spectrum beta-lactamase producing bacteria in nonhospitalized patients. European Journal of Clinical Microbiology & Infectious Diseases 2004; 23 (3): 163-167.

28. Chervet D, Lortholary O, Zahar JR, Dufougeray A, Pilims B et al. Antimicrobial resistance in community-acquired urinary tract infections in Paris in 2015. Médecine et Maladies Infectieuses 2018; 48 (3): 188-192. doi: 10.1016/j.medim.2017.09.013

29. Can F, Azap OK, Seref C, Isipir P, Arslan H et al. Emerging *Escherichia coli* O25b/ST131 clone predicts treatment failure in urinary tract infections. Clinical Infectious Diseases 2015; 60 (4): 523-527. doi: 10.1093/cid/ciu864