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Authors: Ewa Jurałowicz, Anna Bartoszko-Tyczkowska, Ewa Tyczkowska-Sieroń, Ilona Kurnatowska

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Short title: Bacterial susceptibility in recurrent lower urinary tract infections.

Ewa Jurałowicz¹, Anna Bartoszko-Tyczkowska², Ewa Tyczkowska-Sieroń³, Ilona Kurnatowska¹

¹Department of Internal Medicine and Transplant Nephrology, Medical University of Lodz, Lodz, Poland
²Department of Microbiology, Medical University Hospital No 1, Lodz, Poland
³Department of Biology and Parasitology, Medical University of Lodz, Lodz, Poland

Corresponding author: Ilona Kurnatowska, PhD, M.D.
Department of Internal Medicine and Transplant Nephrology; Medical University of Lodz, Poland
Kopcinskiego 22, 90-153 Lodz, Poland
tel. +48 42 2919557; fax +48 42 2919551; e-mail: ilona.kurnatowska@umed.lodz.pl

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What’s new?

Our study showed that fosfomycin, nitrofurantoin and cefuroxime should be recommended as a first line therapy in community-acquired lower urinary tract infection (UTI) including recurrent UTI. The bacteria that are the most common causes of lower UTIs are characterised by significant resistance to the antimicrobial therapy most commonly used and recommended as the first-line treatment (ciprofloxacin and trimethoprim/sulfamethoxazole). It seems reasonable to conduct local analyses of changing etiology and antibiotic susceptibility of microorganisms causing UTIs and to accordingly modify the treatment recommendations.
Abstract

Introduction: Recurrent urinary tract infections (rUTI) are a frequent health problem and a common reason for treatment resistance.

Objectives: The purpose of the study was to evaluate the etiology of community-acquired lower rUTI and bacterial antibiotic susceptibility.

Patients and methods: 796 microbiological urine cultures (UC) from 332 patients (280F, 52M) treated in one nephrology outpatient department in central Poland in years 2016-2018 were analyzed. The most frequent species responsible for lower rUTI were identified and the susceptibility of all the microbes to specific antibiotics was assessed. The patients’ kidney function and inflammation parameters were evaluated.

Results: The age of the patients was 65.0 (59.0-77.0) [F: 69.0 (57.0-78.0), M: 67.0 (62.0-77.0)], glomerular filtration rate was 56.6 (40.2-81.3) ml/min/1.73 m² with C-reactive protein: 3.2 (1.5-7.0) mg/l. 43 bacterial species were identified: 24 Gram-positive, 19 Gram-negative. The analyzed UCs contained 977 microbial samples (563 Gram-negative bacteria, 408 Gram-positive, 6 fungi). The most common bacteria was *Escherichia coli* 39.6% that showed 100.0% susceptibility to carbapenems, 98.9% to amikacin, 96.5% to piperacillin/tazobactam and 94.3% to gentamicin, among the oral antibiotics its highest susceptibility was to: fosfomycin 95.5%, nitrofurantoin 85.5% and cefuroxime 82.3%. In 39.9% of cases *E. coli* was resistant to fluoroquinolones and in 46.6% to trimethoprim/sulfamethoxazole.

Conclusions: The most frequently occurring bacteria causing lower rUTI are characterized by significant resistance to the antimicrobial therapy recommended as the first-line treatment: fluoroquinolones and trimethoprim/sulfamethoxazole. It seems that the first choice in treatment of lower UTIs should be: fosfomycin, nitrofurantoin or cefuroxime.

key words: antibiotic susceptibility, urinary tract infections,
Introduction

Urinary tract infections (UTIs) constitute the most common reason for the employees taking sick leave and attending General Practitioner (GP) appointments [1]. There is little statistical data available regarding the frequency of UTIs, however it is estimated that they are responsible for about 20% of hospital acquired infections and 40-50% infections acquired outside the hospital setting [2]. Moreover, 20 – 40% of patients with lower UTI experience recurrent infection [3].

The etiology of UTIs is predominantly bacterial, they are caused most frequently by Escherichia coli 70-95%, less often by: Staphylococcus saprophyticus 5-10%, Proteus mirabilis, Klebsiella spp., Enterococcus spp. ≤5% and occasionally Staphylococcus aureus [4].

The appearance of symptoms of lower UTI such as dysuria, frequent urination, pain in the suprapubic region or urinary incontinence is a common reason for antimicrobial empiric therapy which due to various etiology factors of UTIs and constantly increasing resistance of microorganisms, is ineffective in some patients [5,6]. In case of an uncomplicated UTI as the first line treatment are recommended: nitrofurantoin (in Poland unavailable – available furazidinum), trimethoprim/sulfamethoxazole (co-trimoxazole), trimethoprim or fosfomycin. Alternatively, if contraindications to the above substances are reported, treatment with an antibiotic belonging to the group of fluoroquinolones is recommended [4].

According to the guidelines, in an uncomplicated UTI, it is not necessary to perform microbiological urine examination, therefore information about the etiology, especially about antibiotic susceptibility of bacteria prevalent in specific populations is relevant in order to choose an antibiotic with the highest probability of effectiveness in the empiric treatment [7], in view of the treatment having become increasingly hindered by growing antibiotic
Resistance to trimethoprim has been reported as >20%, to co-trimoxazole is also widespread, particularly in developing countries, where it has been reported to be as high as 64%. Identification of resistant urinary isolates is often associated with previous exposure to antibiotics [8].

Although GP’s office is usually the first point of contact for the patients with lower UTI, the majority of microbiological urine examinations are carried out in the nephrology outpatient department, where the patients are referred to for the diagnosis of rUTIs and complicated infections.

The aim of this study was analysis of microbiological urine examinations carried out in patients referred for diagnosis and treatment to nephrology outpatient department in central Poland from 2016 to 2018, mostly due to lower rUTI, with particular emphasis on the bacteria antibiotic susceptibility.

**Patients and methods**

Retrospective analysis included all microbiological urine examinations done over three years: from 2016 to 2018 in adult Caucasian patients, diagnosed/treated mostly because of rUTIs in one nephrology outpatient department of a University Hospital in central Poland. All the samples came from the outpatients presenting with clinical symptoms of lower UTIs. The analysis did not include urine cultures (UCs) from patients with estimated glomerular filtration rate (eGFR) < 15 ml/min/1.73 m², with C-reactive protein (CRP) value > 20 mg/l and patients with Foley catheter. The type of microorganisms and their antibiotic susceptibility were analyzed. As a part of standard diagnostic process of rUTIs all the patients once underwent an ultrasound examination in the radiology department at the hospital, with the use of the same equipment, but carried out by different radiologists. On the basis of available medical documentation, including anthropometric data, patient’s history and the
results of ultrasound examination of the urinary system, UTI was classified as uncomplicated or complicated. As complicated was considered UTI occurring in a person with a urinary tract defect, reflux nephropathy, stasis within the pelvicalyceal system, nephrolithiasis, congenital nephropathy (polycystic kidney disease) or with functional changes in the form of neurogenic bladder. We also took into consideration concomitant disorders such as diabetes mellitus (DM) or treatment with immunosuppressive therapy. Information about the serum level of creatinine and CRP values obtained on the same appointment as UC, was taken from the patients’ medical history. The results of UC were also obtained from medical records. Kidney function was assessed by calculating eGFR using the CKD-epi formula [9].

The microbiological urine tests were done in the local hospital microbiological laboratory. The inoculations were performed according to EUCAST guidelines (European Committee on Antimicrobial Susceptibility Testing) [10]. Tested specimens were inoculated onto Columbia agar + 5% sheep blood (bioMérieux, Marcy l’Etoile, France) – the medium that supports growth of a variety of bacteria, MacConkey agar with crystal violet (bioMérieux, Marcy l’Etoile, France) – the agar that allows the growth of only Gram-negative bacteria, and Sabouraud gentamicin chloramphenicol 2 agar (bioMérieux, Marcy l’Etoile, France) which allows growth of fungi. The inoculations on Columbia agar and MacConkey agar were incubated (CO2-Incubtor model INC153med, Memmert GmbH, Heilbronn, Germany) at 35°C for up to 48 hours whereas the inoculations on Sabouraud agar were incubated at 35°C for up to 7 days. Bacterial and yeast species identification was performed using VITEC®2 Compact (bioMérieux, Inc. Hazelwood, MO, USA). Reference strains of *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922 and 35218, *K. pneumoniae* ATCC 700603, *P. aeruginosa* ATCC 27853, *C. albicans* ATCC 90028, and *C. parapsilosis* ATCC 22019 were tested for quality control. Susceptibility testing was performed using VITEC®2 Compact (bioMérieux, Inc. Hazelwood, MO, USA) with Vitec
card YS08 for yeast and Vitec 2 AST-PG43 and Vitec 2 AST - N330 for bacteria. The disk diffusion method was used to determine drug susceptibility to antibiotics not included in Vitek cards, e.g. fosfomycin, tetracycline, ofloxacin, levofloxacin. Susceptibility to a range of antibiotics was evaluated by the disk diffusion method on Mueller–Hinton agar (MHA; Bio-Rad, Marnes-la-Coquette, France) for Gram-negative rods, staphylococci, and enterococci, and MHA supplemented with 5% defibrinated horse blood and 20 mg/L NAD (Bio-Rad, Marnes-la-Coquette, France) for streptococci. Minimum inhibitory concentrations (MICs) were determined by VITEC®2 Compact (bioMérieux, Inc. Hazelwood, MO, USA) and, in addition, by antibiotic gradient strips, Etest (bioMérieux, Marcy l’Etoile, France). In addition, M.I.C.E (Oxoid Limited, Hampshire, United Kingdom) were used for extended-spectrum β-lactamase (ESBL)-producing strains.

For this type of a retrospective study, formal patient consent and the approval of an institutional review board were not required.

Statistical analyses
Nominal data are presented as numbers with percentages; numerical data are presented as medians with the values of upper and lower quartile, the lack of normality was assessed based on visual inspection of histograms. All calculations were done using the Microsoft Excel program.

Results

796 urine cultures from 332 patients (280F, 52M) were analyzed. 75 patients suffered from DM, 9 patients were diagnosed with autoimmune diseases (6 patients: systemic lupus erythematosus, 3 rheumatoid arthritis) and were treated with immunosuppressive therapy. Abdominal ultrasound detected nephrolithiasis without any signs of stasis in 41 of the
patients; 21 patients were diagnosed with chronic obstructive nephropathy and 10 patients with polycystic kidney disease. Complicated UTIs were diagnosed altogether in 72 (21.7%) patients. In other patients imaging examinations did not show significant deviations from normal, except for single simple cysts. The characteristics of the study group along with the number of UCs and the number of isolated bacteria is presented in Table 1.

According to all identified microorganisms in the analyzed UCs, infections in the examined group were caused most often by bacteria 99.2%, seldom by fungi 0.4% or mixed flora 0.4%. Among the bacteria 58.0% belonged to Gram-negative, 42.0% to Gram-positive. The most frequently identified Gram-negative bacteria were: *Escherichia coli* (39.6% of all microorganisms), *Klebsiella pneumoniae* 6.4% and *Proteus mirabilis* 5.1% and among Gram-positive bacteria: *Enterococcus faecalis* 11.3%, *Streptococcus mitis* 6.1% and *Staphylococcus aureus* 5.9%. The etiology of UTIs in the whole examined group and separately in females and in males is illustrated in Table 2.

All identified bacteria in the assessed UCs and the percentage distribution of individual species are depicted in Figures 1 and 2.

Among the identified bacteria the number of microorganisms belonging to particularly resistant strains was calculated: *E. coli* ESBL+ (extended-spectrum beta-lactamases) constituted 9.0% of all cases of a given species and respectively: *K. pneumoniae* ESBL+: 30.2%, *P. mirabilis* ESBL+: 6.0%, *E. faecalis* HLAR (high-level aminoglycoside resistance): 28.2%, MRSA (methicillin-resistant *Staphylococcus aureus*): 24.1%.

The most common bacteria found in UCs from patients with complicated UTI were: *E. coli* 33.6%, *E. faecalis* 11.4% and *S. aureus* 10.0%.
Patients ≥ 65 years old constituted 60.8% (n=202) of the examined population. Among those patients the etiology of rUTIs was similar to that of the entire group, the most often occurring microorganisms were: *E. coli* 44.2%, *E. faecalis* 10.5% and *K. pneumoniae* 8.1%.

*E. coli*, the most frequently occurring Gram-negative bacteria in the studied group, presented 100.0% susceptibility to intravenous antibiotics such as carbapenems: imipenem and meropenem, 98.9% to amikacin, 96.5% to piperacillin with tazobactam, 94.3% to gentamicin, while among oral antimicrobial drugs its highest susceptibility was to fosfomycin 95.5%, nitrofurantoin 85.5% and cefuroxime 82.3%. In 39.9% of cases *E. coli* was resistant to fluoroquinolones and in 46.6% to co-trimoxazole. The most frequently occurring Gram-positive bacteria, *E. faecalis*, was susceptible to imipenem, linezolid and vancomycin in 100.0%, and from among oral medications to ampicillin and amoxicillin in 100.0%, to nitrofurantoin in 97.3% and to amoxicillin with clavulanic acid in 80.0%. *E. faecalis* was resistant to ciprofloxacin in 93.2%, to co-trimoxazole in 98.9% and to cefuroxime and gentamicin in 100.0%.

Antibiotic susceptibility of the most often occurring Gram-negative and Gram-positive bacteria causing UTIs, is presented in detail in Tables 3 and 4.

Susceptibility of the most commonly identified bacteria (all cases from each species, including particularly resistant strains) to the most frequently used antibiotics, including those recommended as the first-line treatment in UTI [2] is summarized in Table 5.

The susceptibility of the most often occurring bacteria in the examined group (*E. coli, K. pneumoniae, P. mirabilis, E. faecalis, S. mitis, S. aureus*) constituting 74.5% of all identified microorganisms is presented in Figure 3.

**Discussion**
Our research confirmed that lower UTIs are diagnosed much more frequently in women than in men (84.3% F, 15.7% M), and in elderly people [11].

The most common pathogen identified in the examined population was E. coli, constituting 39.6% of all found microorganisms, which is less common than reported in other studies, however the analysed UCs were taken mainly from patients with recurrent UTI. Stefaniuk et al, in a multicentre analysis conducted among Polish population in 2013, found that E. coli was responsible for 71.4% of all UTIs [12]. In a California study, where the etiology of UTIs from 2008 to 2017 was analyzed, E. coli was the cause of UTIs acquired outside hospital in 70% [13], and in a research from Russia: 49.1% [14]. Other identified bacteria in our population were: E. faecalis 11.3%, K. pneumoniae 6.4%, S. mitis 6.1%, S. aureus 5.9% and P. mirabilis 5.1%, which are also mentioned in other reports as the common causes of UTIs [15,16,17], but with variable frequency. The percentage distribution of the most common occurring microorganisms causing UTIs differs depending on the studied population, however in all the studies a significant numerical superiority of Gram-negative over Gram-positive species is emphasized [12,16].

According to the guidelines, in case of an uncomplicated UTI, as a first-line treatment is recommended the use of chemotherapeutics such as: nitrofurantoin, co-trimoxazole, trimethoprim, fosfomycin or alternatively fluoroquinolones [4]. Our analysis showed that bacteria which are the most common etiological factors of rUTI demonstrate significant resistance to the above mentioned substances, which is also confirmed in other European analyses, for example in one conducted in Spain [18], and another in Switzerland [19]. In our study E. coli was characterised by as much as 39.9% resistance to ciprofloxacin and 46.6% to trimethoprim/sulfamethoxazole. Both of the above chemotherapeutics belong to the most often prescribed substances by GP in the treatment of UTI, including rUTI, not only in Poland [20]. A Polish research published in 2016 presents the susceptibility of E. coli to
ciprofloxacin in 65.8% and to trimethoprim/sulfamethoxazole in 65.1% [12], in Spain in years 2003-2004 it was shown to be as much as 81.4% and 74.1% [21] and in the earlier mentioned studies 73.8%, 76.1% [18] and 88.9%, 85.7% [19], respectively. Our observations confirm a constantly growing resistance of bacteria to the frequently used chemotherapeutics. Perhaps the higher percentage of resistance to fluoroquinolones noted in our population is due to the fact that the antibiotic susceptibility was assessed several years later than in the cited studies, and most of our population suffered specifically from recurrent UTI, having probably already undergone a course of antibiotic therapy [12,21]. It should be mentioned that ciprofloxacin and trimethoprim/sulfamethoxazole apart from amoxicillin, amoxicillin and enzyme inhibitor and cefuroxime are on the list of antibacterials with the highest consumption due to different indications including community-acquired respiratory tract infections in 2014 in Poland [22]. It may partly account for such a high resistance of bacteria to this chemotherapeutics causing UTI in our population. Noteworthy in our studied group is high susceptibility of E. coli to fosfomycin 95.5% and nitrofurantoin 85.5%, which is also highlighted in other publications [6,23,24].

Such high susceptibility of E. coli to nitrofurantoin in Poland may be due to the fact that in our country nitrofurantoin is not available and another substance, furazidinum, having similar properties and belonging to the group of nitrofurans, is in common use. However, the analysis made in Switzerland in years 2009-2015 also revealed significant effectiveness of nitrofurantoin in the treatment of lower UTI, including recurrent, although this substance is available and often prescribed in GP’s practice [25].

Despite high susceptibility of E. coli to nitrofurantoin and fosfomycin, these substances present low efficacy against other pathogens, especially Gram-positive bacteria, which cause UTIs (they were the cause of UTIs in our population in 42.0%). In our study, the
most often occurring Gram-positive bacteria (S. mitis, S. aureus), except E. faecalis that showed 97.3% susceptibility, were resistant to nitrofurantoin in every case, while resistance to fosfomycin was not estimated at all. An antibiotic available in oral form, highly effective both against Gram-negative and Gram-positive bacteria proved to be cefuroxime, which is not on the list of substances recommended as first-line treatment in uncomplicated UTI. Its effectiveness against six of the most often occurring bacterial species (constituting 74.5% of all identified bacteria) was estimated as 77.0%. E. coli showed 82.3% susceptibility to cefuroxime in our analysis and 90.1% in other authors’ research [12].

After analyzing all our microbiological UCs, high susceptibility of microorganisms to intravenous antibiotics was observed. E. coli showed 100.0% susceptibility to carbapenems (imipenem and meropenem), 98.9% to amikacin, 96.5% to piperacillin with tazobactam and 94.3% to gentamicin and E. faecalis showed 100.0% susceptibility to ampicillin, imipenem, linezolid and vancomycin. However, it is likely that such high susceptibility of bacteria causing lower rUTI may be due to the fact that in such infections intravenous antibiotic therapy is practically not used, remaining reserved for more severe systemic infections, and oral treatment is preferred. The high susceptibility of pathogens to aminoglycosides should be emphasized. It may result from the fact that due to their nephrotoxicity, it is currently a very rarely recommended class of drugs.

Another problem, signalled in many studies [26,27,28,29], is a growing prevalence of pathogens belonging to particularly resistant strains, which renders effective antibiotic therapy of UTI very difficult. As suggested in a research published in 2019, potential risk factors of infection with ESBL producing strains may be: antibiotic therapy or previous hospitalization during the last 3 months, history of recurrent UTIs or abnormalities in the structure and functioning of the kidneys [30]. In the analyzed UCs, E. coli ESBL+ represented 9.0% of all cases of a given species, K. pneumoniae ESBL+: 30.2%, P. mirabilis ESBL+: 6.0%. E. coli
ESBL+ showed lower susceptibility to nitrofurantoin: 77.1% and fosfomycin: 80.0% compared to ESBL-: 86.4% and 97.1%, respectively. *K. pneumoniae* ESBL+ was sensitive to nitrofurantoin only in 10.0% and to fosfomycin in 17.7%. That is not compatible with the results of the research conducted in England in years 2015-2017 where over 95% of Enterobacteriaceae ESBL+ were susceptible to nitrofurantoin and fosfomycin [26]. In another study, published in 2019, no significant difference was observed in the treatment of UTI caused by pathogens ESBL+ with antibiotics belonging to carbapenems or to other groups [27], however in our analysis those microorganisms showed 100.0% susceptibility especially to carbapenems (imipenem and meropenem). These bacteria were susceptible to an old antibiotic – amikacin (*E coli* ESBL+: 97.1%, *K. pneumoniae* ESBL+: 89.5%), less often were they sensitive to the oral preparations: amoxicillin with clavulanic acid (22.9% and 5.3%, respectively), co-trimoxazole (32.4% and 10.5%, respectively) and demonstrated no susceptibility to cefuroxime.

The kidney function in our patients was quite normal with median eGFR 56.6 (40.2-81.3) ml/min/1.73 m² and with median C-reactive protein value 3.2 (1.5-7.0) mg/l. slightly exceeding the upper limit of standards (the laboratory CRP norm < 5 mg/l).

The conducted research has some limitations. First of all, this is a retrospective study and the assessment was carried out based on medical documentation, including the patient’s medical history, laboratory results with UCs, results of imaging examinations, on the basis of which UTIs were qualified as complicated/uncomplicated. We cannot give reliable treatment results since the patients were treated by different nephrologists and outpatients check-ups were performed at different time schedules, and sometimes patients were recommended to have a check-up at GP’s.
In conclusion, the analysis showed that bacteria that are the most common causes of lower UTIs are characterised by significant resistance to the antimicrobial therapy most commonly used and recommended as the first-line treatment: fluoroquinolones and trimethoprim/sulfamethoxazole. It seems that the first choice in treatment of lower UTIs should be: fosfomycin, nitrofurantoin or cefuroxime. It is advisable to conduct local analyses of changing etiology and antibiotic susceptibility of microorganisms causing UTIs and to accordingly modify the recommendations regarding the implementation of empiric treatment depending on the results obtained in a given population.

Contribution statement

IK conceived the idea for the study. AB-T and ET-S collected microbiological data, EJ and IK collected data from the patients’ medical history. EJ analysed and described the data. All authors edited and approved the final version of the manuscript.
Table 1. The characteristic of the study group along with the number of urine cultures and the number of bacteria divided into Gram-negative and Gram-positive.

|                                      | The whole group of patients | Females  | Males   |
|--------------------------------------|----------------------------|----------|---------|
| Number of patients                   | 332 (100.0%)               | 280 (84.3%) | 52 (15.7%) |
| Age of patients, years               | 65.0 (59.0-77.0)           | 69.0 (57.0-78.0) | 67.0 (62.0-77.0) |
| Patients with diabetes               | 75 (22.6%)                 | 64 (22.9%) | 11 (21.2%) |
| Patients with complicated UTI        | 72 (21.7%)                 | 55 (19.6%) | 17 (32.7%) |
| Number of UCs                        | 796 (100.0%)               | 688 (86.4%) | 108 (13.6 %) |
| Number of UCs per patient            | 1 (1-3)                    | 1 (1-3)   | 1 (1-2.5) |
| eGFR, ml/min/1.73m²                  | 56.6 (40.2-81.3)           | 56.5 (40.1-82.2) | 57.7 (40.2-75.5) |
| CRP, mg/l                            | 3.2 (1.5-7.0)              | 3.3 (1.4-7.0) | 3.0 (1.8-7.1) |
| Number of bacterial samples          | 97                         | 845       | 126     |
| Number of Gram-negative bacterial samples | 563                      | 502       | 61      |
Nominal variables are presented as absolute and relative numbers and continuous data are presented as medians with the values of upper and lower quartile. Variables: number of UCs, number of UCs per patient, eGFR, CRP, number of bacteria, number of G-negative and G-positive bacteria are presented in regards to all UTI cases.

Abbreviations: CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; UC, urine culture; UTI, urinary tract infection
Table 2. Etiology of lower urinary tract infections in the whole examined group and separately in females and in males

| Bacterial Strain          | Number of bacterial samples in the whole group of patients | Number of bacterial samples in females | Number of bacterial samples in males |
|---------------------------|-----------------------------------------------------------|---------------------------------------|-------------------------------------|
| *Escherichia coli*        | 387 (39.6%)                                               | 359 (42.4%)                           | 28 (21.5%)                          |
| *Enterococcus faecalis*   | 110 (11.3%)                                               | 94 (11.1%)                            | 16 (12.3%)                          |
| *Klebsiella pneumoniae*   | 63 (6.4%)                                                 | 51 (6.0%)                             | 12 (9.2%)                           |
| *Streptococcus mitis*     | 60 (6.1%)                                                 | 54 (6.4%)                             | 6 (4.6%)                            |
| *Staphylococcus aureus*   | 58 (5.9%)                                                 | 46 (5.4%)                             | 12 (9.2%)                           |
| *Proteus mirabilis*       | 50 (5.1%)                                                 | 50 (5.9%)                             | 0 (0%)                              |

Percentage was calculated in respect to number of microbial samples.
Table 3. Antibiotic susceptibility of the most frequently occurring Gram-negative bacteria (expressed in %; x - susceptibility was not estimated)

|                    | Amikacin | Gentamicin | Amoxicillin/ clavulanic acid | Ampicillin | Piperacillin/ tazobactam | Cefuroxime | Ceftazidime | Cefepim | Ciprofloxacin | Fosfomycin | Nitrofurantoin | Imipenem | Meropenem | Ce-trimoxazole |
|--------------------|----------|------------|------------------------------|------------|---------------------------|------------|-------------|----------|---------------|------------|----------------|----------|-----------|----------------|
| **E. coli**         |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| all                | 98.9     | 94.3       | 70.5                         | 44.7       | 96.5                      | 82.3       | 90.7        | 60.1    | 95.5          | 85.5       | 100.0          | 100.0    | 100.0     | 53.4           |
| n = 387            |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| **E. coli** ESBL - | 99.1     | 96.6       | 75.3                         | 49.7       | 98.1                      | 90.5       | 99.6        | 65.2    | 97.1          | 86.4       | 100.0          | 100.0    | 100.0     | 55.5           |
| n = 352            |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| **E. coli** ESBL + | 97.1     | 70.6       | 22.9                         | 0          | 82.4                      | 0          | 17.9        | 8.6     | 80.0          | 77.1       | 100.0          | 100.0    | 100.0     | 32.4           |
| n = 35             |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| **K. pneumoniae**   | 95.2     | 90.5       | 54.0                         | 0          | 67.2                      | 59.7       | 72.2        | 45.2    | 23.8          | 2.3        | 100.0          | 100.0    | 100.0     | 50.8           |
| all                |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| n = 63             |          |            |                              |            |                           |            |             |          |               |            |                |          |           |                |
| Organism          | 97.7 | 95.5 | 75.0 | 0    | 81.0 | 86.1 | 100.0 | 65.1 | 26.2 | 0    | 100.0 | 100.0 | 68.2 |
|-------------------|------|------|------|------|------|------|-------|------|------|------|-------|-------|------|
| *K. pneumoniae*   |      |      |      |      |      |      |       |      |      |      |       |       |      |
| ESBL -            | 89.5 | 79.0 | 5.3  | 0    | 36.9 | 0    | 0     | 0    | 17.7 | 10.0 | 100.0 | 100.0 | 10.5 |
| ESBL +            | 100.0 | 67.4 | 88.0 | 46.9 | 100.0 | 94.0 | 92.3  | 50.0 | 35.9 | 0    | 100.0 | 100.0 | 36.0 |
| *P. mirabilis*    |      |      |      |      |      |      |       |      |      |      |       |       |      |
| All               | 100.0 | 72.1 | 93.6 | 51.7 | 100.0 | 100.0 | 100.0 | 53.2 | 36.8 | 0    | 100.0 | 100.0 | 38.3 |

Abbreviations: ESBL, extended-spectrum beta-lactamases
Table 4. Antibiotic susceptibility of the most frequently occurring Gram-positive bacteria

(expressed in %; x - susceptibility was not estimated)

|                     | Amikacin | Gentamicin | Amoxicillin | Amoxicillin/ | Ampicillin/ | Piperacillin/ | Cefuroxime | Ciprofloxacin | Levofloxacin | Nitrofurantoin | Co-trimoxazole | Imipenem | Linezolid | Vancomycin |
|---------------------|----------|------------|-------------|--------------|-------------|--------------|------------|--------------|--------------|----------------|----------------|-----------|-----------|------------|
| **E. faecalis**     |          |            |             |              |             |              |            |              |              |                |                |           |           |            |
| all n = 110         | 4.2      | 0          | 100.0       | 80.0         | 100.0       | 100.0        | 0          | 6.8          | 64.3         | 97.3           | 1.1             | 100.0     | 100.0     | 100.0      |
| **E. faecalis**     |          |            |             |              |             |              |            |              |              |                |                |           |           |            |
| HLAR - n = 79       | 5.9      | 0          | 100.0       | 80.0         | 100.0       | 100.0        | 0          | 8.2          | 77.8         | 100.0          | 0               | 100.0     | 100.0     | 100.0      |
| **E. faecalis**     |          |            |             |              |             |              |            |              |              |                |                |           |           |            |
| HLAR + n = 31       | 0        | 0          | 100.0       | x            | 100.0       | 100.0        | 0          | 3.7          | 40.0         | 90.3           | 4.0             | 100.0     | 100.0     | 100.0      |
| **S. mitis**        |          |            |             |              |             |              |            |              |              |                |                |           |           |            |
| all n = 60          | x        | 0          | 100.0       | x            | 96.8        | x            | 98.3       | 0            | 61.7         | 0               | 0               | x         | 100.0     | 100.0      |
| **S. aureus**       |          |            |             |              |             |              |            |              |              |                |                |           |           |            |
| all n = 58          | 80.0     | 82.1       | x           | 75.0         | x            | x            | 76.0       | 68.4         | 65.9         | 0               | 58.2           | x         | 100.0     | 100.0      |
| **MSSA**            |          |            |             |              |              |              |            |              |              |                |                |           |           |            |
| n = 44              | 91.3     | 90.7       | x           | 100.0        | x            | x            | 100.0      | 86.1         | 81.3         | 0               | 69.1           | x         | 100.0     | 100.0      |
| MRSA        | 42.9 | 53.9 | x   | 0   | x   | x   | 0   | 14.3 | 11.1 | 0   | 23.1 | x   | 100.0 | 100.0 |
|-------------|------|------|-----|-----|-----|-----|-----|------|------|-----|------|-----|--------|--------|

Abbreviations: HLAR, high-level aminoglycoside resistance; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*
Table 5. Susceptibility of the most common bacteria in recurrent lower urinary tract infections to the most frequently used antibiotics, including those recommended as the first-line treatment (x - susceptibility was not estimated)

|                 | Amoxicillin | Amoxicillin/ clavulanic acid | Cefuroxime | Ciprofloxacin | Fosfomycin | Nitrofurantoin | Co-trimoxazole |
|-----------------|-------------|------------------------------|------------|---------------|------------|----------------|----------------|
| **E. coli**     |             |                              |            |               |            |                |                |
| n = 387; 39.6%  | x           | 70.5%                        | 82.3%      | 60.1%         | 95.5%      | 85.5%          | 53.4%          |
| **E. faecalis** |             |                              |            |               |            |                |                |
| n = 110; 11.3%  | 100.0%      | 80.0%                        | 0%         | 6.8%          | x          | 97.3%          | 1.1%           |
| **K. pneumonia**|             |                              |            |               |            |                |                |
| n = 63; 6.4%    | x           | 54.0%                        | 59.7%      | 45.2%         | 23.7%      | 2.3%           | 50.8%          |
| **S. mitis**    |             |                              |            |               |            |                |                |
| n = 60; 6.1%    | 100.0%      | x                            | 98.3%      | 0%            | x          | 0%             | 0%             |
| **S. aureus**   |             |                              |            |               |            |                |                |
| n = 58; 5.9%    | x           | 75.0%                        | 75.9%      | 68.4%         | x          | 0%             | 58.2%          |
| **P. mirabilis**|             |                              |            |               |            |                |                |
| n = 50; 5.1%    | x           | 88.0%                        | 94.0%      | 50.0%         | 35.9%      | 0%             | 36.0%          |

In the first column are presented the most often occurring bacteria along with the number of identified samples and their percentage distribution.
Figure 1. Gram-negative bacterial species in the examined population (19 species)

- Escherichia coli - 387 (68.7%)
- Klebsiella pneumoniae - 63 (11.2%)
- Proteus mirabilis - 50 (8.9%)
- Pseudomonas aeruginosa - 15 (2.7%)
- Enterobacter cloacae - 10 (1.8%)
- Morganella morganii - 8 (1.4%)
- Klebsiella oxytoca - 6 (1.1%)
- Citrobacter koserii - 5 (0.9%)
- Providencia stuartii - 4 (0.7%)
- Acinetobacter baumannii - 3 (0.5%)
- Proteus hauseri - 2 (0.4%)
- Serratia marcescens - 2 (0.4%)
- Providencia rettgeri - 2 (0.4%)
- Citrobacter braakii - 1 (0.2%)
- Citrobacter freundii - 1 (0.2%)
- Acinetobacter calcoaceticus - 1 (0.2%)
- Pseudomonas putida - 1 (0.2%)
- Enterobacter aerogenes - 1 (0.2%)
- Pantoea agglomerans - 1 (0.2%)
Figure 2. Gram-positive bacterial species in the examined population (24 species)

- **Enterococcus faecalis** - 110 (27.0%)
- **Streptococcus mitis** - 60 (14.7%)
- **Staphylococcus aureus** - 58 (14.2%)
- **Staphylococcus epidermidis** - 38 (9.3%)
- **Corynebacterium urealyticum** - 36 (8.8%)
- **Streptococcus agalactiae** - 31 (7.6%)
- **Streptococcus anginosus** - 25 (6.1%)
- **Staphylococcus hominis** - 12 (2.9%)
- **Enterococcus faecium** - 6 (1.5%)
- **Staphylococcus haemolyticus** - 5 (1.2%)
- **Streptococcus sanguinis** - 4 (1.0%)
- **Staphylococcus saprophyticus** - 4 (1.0%)
- **Staphylococcus simulans** - 3 (0.7%)
- **Streptococcus parasanguinis** - 2 (0.5%)
- **Corynebacterium pseudodiphtheriticum** - 2 (0.5%)
- **Staphylococcus lindemansii** - 2 (0.5%)
- **Streptococcus constellatus** - 2 (0.5%)
- **Streptococcus gordonii** - 2 (0.5%)
- **Streptococcus galoliticus** - 1 (0.3%)
- **Streptococcus uberis** - 1 (0.3%)
- **Streptococcus intermedius** - 1 (0.3%)
- **Streptococcus bovis** - 1 (0.3%)
- **Streptococcus ovis** - 1 (0.3%)
- **Corynebacterium amycolatum** - 1 (0.3%)
Figure 3. Susceptibility of the most often occurring bacteria (constituting 74.5% of all identified microorganisms) to particular antibiotics.
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