

STUDY ON URINARY TRACT INFECTIONS IN PREDISPOSED PATIENTS

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INTRODUCTION: The increasing number of patients suffering from urinary tract infections (UTI) especially those predisposed for this pathology require special attention in treatment, taking into consideration also the incidence of multidrug resistant strains [1], [2]. Treatment with improper antibiotics can lead to recurrence of the infection and facilitates drug resistance. Patients presenting urinary tract disorders, urolithiasis, pregnancy and diabetes are predisposed for this kind of pathology [3], [4].

THE AIM of this study was to reveal the frequency of bacteria causing urinary tract infections and their antibiotic resistance in different patient groups presenting risk factors for this pathology.

MATERIAL AND METHODS: The study was carried out between January 2011 – March 2015 on diabetic and non-diabetic patients of the SC Marmed SRL and SCM Procardia Laboratories in Tîrgu Mureș. The study group also included patients presenting urolithiasis and other urinary tract disorders (urethral fistula, stenosis or hypoplasia, hydronephrosis, pyelectasia, nephrotic syndrome) admitted to the Urology Clinical Hospital in Tîrgu Mureș in this period. We also studied a group of pregnant women, patients of the mentioned medical laboratories and pregnant presenting imminent preterm labor admitted to the Clinical Emergency County Hospital in Tîrgu

INTRODUCTION: Urinary tract infections (UTIs) are more common in people presenting predisposing factors (urinary stones, malformations, diabetes, pregnancy). Choosing the proper medication is very important for an efficient treatment and to prevent recurrences.

MATERIAL AND METHODS: We selected 566 hospitalized and outpatients in the high risk group and 1265 patients in the control group. Urine samples were collected in sterile recipients and cultivated on proper culture media. Antibiotic susceptibility testing (AST) was performed for all significant isolates.

RESULTS: Amongst the patients with predisposing factors we found the following proportions of UTI: diabetic patients - 38.5%, urolithiasis - 25.2%, urinary tract malformations - 23.85%, and pregnancy - 18.5% of the cases. The most frequent isolated strain was *Escherichia coli* in each group. Positive cultivation results were more frequent in women. We found multidrug resistant bacteria in every patient group (except the pregnant women), especially ESBL-producing *E. coli*. In the majority of cases enterobacteria presented good susceptibility to fluoroquinolones, cephalosporins and gentamycin.

CONCLUSIONS: In high-risk group patients the UTI are common and resistant strains are often present. Positive results were more frequent in women. The optimal treatment requires the antibiotic susceptibility testing for all isolates.

Keywords: antibiotics, bacteria, urinary tract infection

Mureș. The inclusion criteria were presence of risk factors for urinary tract infections in the study group (urolithiasis, urinary tract malformations, pregnancy or diabetes) and evidence of urine cultivation results. The exclusion criteria were recent treatment with antibiotics in the medical records. The control group included patients presenting symptoms of urinary tract infections, but no obvious risk factors for this disease.

Urine samples were collected in sterile recipients and were cultivated on proper culture media. In positive cases, when necessary, antibiotic susceptibility tests (AST) were performed.

Descriptive and comparative statistical analysis was performed using the Graph Pad InStat software. The values are expressed in percentage and mean +/- SD (standard deviation). We considered the p value significant under 0.05.

We obtained the approval of our study from the managers of all medical units and sections involved, and all the patients expressed their informed consent for performing urine analysis from their collected sample.

RESULTS: UTI were found in 143 patients (25.3%) from the study group and in 261 patients (20,6%) from the control group.

The average age of the studied patients in the high risk group without the pregnant women (n = 484) was 50.2 ± 21.3 (SD) years. The gender distribution of the patients presenting positive cultivation results showed that →

76.9% of the diabetic patients, 58.3% of the patients presenting urinary stones, 54.3% of the patients exhibiting urinary tract abnormalities and 68.1% of the control group were women. In the pregnant women's group (n = 82) the mean age was 28.9 ± 6.3 years (SD), minimum 14, maximum 39 years.

The average age of the patients in the control group (n = 1265) was 49.5 ± 13.8 (SD).

Following the urine cultures, we obtained positive results in 20.6% of the control cases. The most frequent isolate was *Escherichia coli* (174 cases), from which 33 were ESBL-producing strains (18.9% of the *E. coli* bacteria). We identified *Klebsiella spp.* in 23 patients, *Proteus spp.* in 16 cases, followed by the presence of *Enterococcus spp.* in 21 patients (every isolated *Enterococcus* strain proved to be vancomycin sensitive). *Proteus* strains were causing agents of UTI in 16 cases, *Streptococcus agalactiae* was identified in the urine of 13 patients. ESBL was found also in *Klebsiella* (5 isolates, 21.7% of the *Klebsiella* bacteria) and *Proteus* (2 isolates, 12.5% of the *Proteus* bacteria). In 12 patients the urinary infection was caused by *Staphylococcus spp.* (including 3 cases of *Staphylococcus saprophyticus*), and the urine of two patients showed *Pseudomonas aeruginosa*.

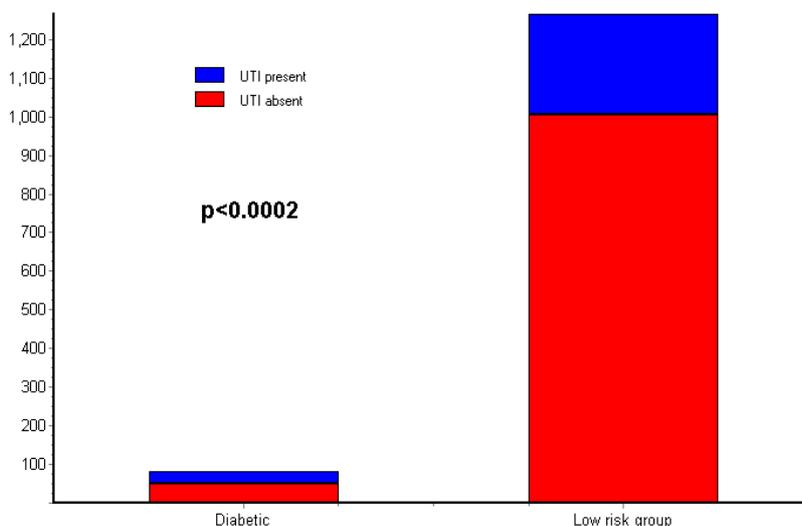
Amongst diabetic patients (n = 80) we found 38.5% UTIs, the proportion being significantly higher compared to the control group (fig.1). In 23.5% of the diabetic patients UTI were caused by *Escherichia coli*, including one ESBL-producing strain. In 9% of the cases we detected *Enterococcus spp.* Beta hemolytic *Streptococcus (agalactiae)* and ESBL producing *Klebsiella pneumonia* were present in 3% each.

The majority of the diabetic patients had a proper metabolic balance, the average glyated hemoglobin level of the patients was $6.57\% \pm 1.43$ (SD).

In patients presenting urolithiasis (n = 266) urinary tract infection was found in 25.2% of the cases. *Escherichia coli*, the most frequent uropathogen, was diagnosed in 22 cases (8.3%), *Staphylococcus spp.* in 15 cases (5.6%), *Pseudomonas aeruginosa* in 11 cases (4.1%), *Klebsiella pneumoniae* in 4 cases (1.5%), *Proteus mirabilis* in 4 cases (1.5%), beta hemolytic *Streptococcus* in 3 cases (1.1%), *Enterococcus spp.* in 3 cases (1.1%), and in 1-1 cases the detected bacteria were *Serratia marcescens* and *Citrobacter spp.*, respectively, etc.

In patients with urinary tract disorders (n = 138), positive urocultures were found in 33 patients (23.9% of the cases). *E.coli* was present in 23 cases (16.7%), including two extended-spectrum beta-lactamase (ESBL)-producing strains, 3 strains resistant to trimethoprim/ sulfamethoxazol and one resistant to fluoroquinolone derivatives. We also detected *Staphylococcus aureus*, *Pseudomonas aeruginosa* and beta hemolytic *Streptococcus*, 2 cases each, represent-

Figure 1 - Incidence of UTI in diabetic patients and in the low risk group



ing 1.5%. *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Proteus mirabilis* and *Morganella morgani* were diagnosed as causing agents of the UTI in one case each (0.8%). In one case *Pseudomonas aeruginosa* was resistant to cefotaxime, tobramycin, netilmicine and piperacillin+tazobactam, in another case the *Staphylococcus aureus* was meticillin-resistant (MRSA).

In cases of complicated urinary tract infections caused by *Klebsiella pneumoniae* and *Escherichia coli* various fluoroquinolone derivatives (norfloxacin, ciprofloxacin, levofloxacin), cephalosporins and gentamycin are the best options. According to our data trimethoprim+sulfamethoxazol-resistant *Escherichia coli* strains presented sensitivity to these drugs. UTI caused by ESBL-producing strains need to be treated after antibiotic susceptibility tests (AST) are performed. Usually these strains are sensitive to amikacin and imipenem. All of the detected *Enterococcus faecalis* showed sensitivity to ampicillin, nitrofurantoin and vancomycin. The beta hemolytic *Streptococcus* strains are usually sensitive to beta-lactams. Amikacin, colistin and imipenem sensitivity was present even in multidrug-resistant *Pseudomonas aeruginosa* infections.

The meticillin-resistant *Staphylococcus aureus* showed sensitivity to gentamycin, kanamycin, vancomycin, trimethoprim/sulfamethoxazol and norfloxacin. In UTI caused by *Morganella morgani* a highly sensitive strain was detected, showed no resistance to any of the tested antibiotics.

In the pregnant women's group the cultivation showed the presence of *E. coli* in 3.6% of the cases (3 patients), we also found one patient (1.2%) with *Streptococcus beta hemolyticus group F* infection, one presented *Staphylococcus saprophyticus* colonization, one pregnant woman was infected with *Enterococcus spp.* and one with *Klebsiella oxytoca*. In other cases we obtained

mixed culture (1,2%) and in 5 patients (6.1%) saprophytic flora was present.

DISCUSSION: A limitation of the study is that in some patients presenting pathological elements in the urine at the routine test, no cultivation was performed; in diabetic patients the percentage of these cases was 11.2%.

According to the literature, UTI caused by resistant bacteria is becoming more prevalent, especially ESBL-producing *E. coli* strains. Hospitalisation, institutionalisation, diabetes, recurrent UTI, comorbidity, long duration of prophylaxis and use of cephalosporins for prophylaxis were risk factors [5], [6], [7].

Many patients follow empirical treatment which can be often incorrect, and only a part of these patients will benefit of treatment correction according to AST. In other cases the doses might be less than efficient, the duration of the treatment sometimes is too short, and all these can allow the adaptation of bacteria to the regular antibiotics, enhancing occurrence of resistant strains [8].

In diabetic patients specialists recommend a minimum of 2 weeks of antibiotic therapy, because the eradication of the microorganism in diabetic patients is difficult, and improper duration of antibiotic treatment will encourage resistance [9], [10].

Sometimes the result of the sediment does not correspond to the uroculture, so in case that the patients present symptoms of UTI, cultivation is recommended, even if the sediment is negative [11].

Our data regarding the frequency of microorganisms in UTI is similar to those obtained by other studies, *Escherichia coli* being the most frequent pathogen in all groups of patients [12].

The presence of urinary infections in the group of pregnant women enhances premature delivery, so the proper treatment of these has a special importance [13]. In this group the treatment has to take into consideration the safety of the fetus, so cephalosporines and trimethoprim+sulfamethoxazol are more frequently used compared to antibiotherapy in case of other patients, the strains obtained showed sensibility to these drugs.

CONCLUSIONS: In high-risk group patients, UTI were common, resistant strains were often present, and the positive urocultures were more frequent in women. The most frequent strain causing urinary infections was *Escherichia coli* in all the studied groups, 18.6% of them being ESBL-producers. Therefore, the correct treatment can only be chosen after an AST is performed.

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