Journal of Neonatal Surgery
ISSN(Online):2226-0439
Vol.15 , Issue 1s (2026)
https://www.jneonatalsurg.com

OPEN ACCESS

Microbiological profile and antibiotic sensitivity in patients with urolithiasis complicated by diabetes mellitus..

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Cite this paper as: Omarova Zahraula Habirahmanovna, Gadzhiev Dzhabrail Dzhamalovich, Gamzatova Saida Zairkhanovna, Aliev Batyr Shamilovich , Ibragimova Uza Eldarovna , Koichueva Asil Rasulovna , Koichuev Tabiin Rashidovich , Mirzakhanov Said Madridovich (2026) Microbiological profile and antibiotic sensitivity in patients with urolithiasis complicated by diabetes mellitus... Journal of Neonatal Surgery, 15, (1s) 305-310

ABSTRACT

The combination of urolithiasis and diabetes mellitus is accompanied by an increased risk of urinary tract infections, changes in the microbiological spectrum of pathogens and an increase in antibiotic resistance. Studying the characteristics of antibiotic sensitivity in this category of patients is important for optimizing empirical antibacterial therapy.

To study the microbiological profile of urinary tract infections and determine their sensitivity to antibacterial drugs in patients with urolithiasis complicated by diabetes mellitus. A retrospective study of 120 patients with urolithiasis was conducted, of which 60 patients had concomitant type 2 diabetes mellitus, and 60 formed a comparison group. All patients underwent bacteriological examination of urine with identification of pathogens and determination of sensitivity to antibacterial drugs in accordance with the recommendations of EUCAST. Statistical data processing was performed using the IBM SPSS Statistics 27.0 program. Differences at $p < 0.05$ were considered statistically significant.

The most frequently isolated pathogen was Escherichia coli (41.4% and 52.8%, respectively), however, Klebsiella pneumoniae, Pseudomonas aeruginosa and multidrug-resistant microorganisms were significantly more often detected in patients with diabetes mellitus. The greatest sensitivity of microorganisms was noted to carbapenems (96.6%), fosfomycin (93.1%), amikacin (91.4%) and nitrofurantoin (89.7%). The highest resistance was registered to ampicillin (72.4%), ciprofloxacin (43.1%) and co-trimoxazole (46.6%). In patients with diabetes mellitus, strains producing extended-spectrum beta-lactamases were more often detected, and longer hospitalization was noted. Diabetes mellitus has a significant impact on the microbiological profile of urinary tract infections in patients with urolithiasis and is associated with an increased prevalence of antibiotic-resistant microorganisms. The results obtained confirm the need for a bacteriological study to determine antibiotic sensitivity before prescribing antibacterial therapy and can be used to improve regional algorithms for the treatment of urinary tract infections..

Keywords: urolithiasis; type 2 diabetes mellitus; urinary tract infections; microbiological profile; antibiotic sensitivity; antibiotic resistance; uropathogens; Escherichia coli; Klebsiella pneumoniae.

INTRODUCTION

Urolithiasis (urolithiasis) is one of the most common urological diseases and is a significant medical and social problem due to its high prevalence, tendency to relapse and the development of severe complications. According to epidemiological studies, the prevalence of urolithiasis in various countries of the world varies from 5 to 15%, while there is a steady trend towards an increase in the number of patients due to lifestyle changes, dietary patterns, an increase in the prevalence of metabolic disorders and an increase in life expectancy. Despite the improvement of diagnostic methods and surgical treatment, the recurrence rate of the disease remains high and reaches 30-50% during the first five years after the removal of concretions. [1].

Diabetes mellitus occupies a special place among the risk factors for the development and progression of urolithiasis. In recent decades, there has been a rapid increase in the number of patients with diabetes mellitus, which the World Health Organization considers one of the most important global health problems. Disorders of carbohydrate metabolism are accompanied by changes in the acid-base state of urine, hyperinsulinemia, insulin resistance, impaired metabolism of calcium, oxalate and uric acid, which contributes to the formation of urinary stones. In addition, chronic hyperglycemia leads to the development of diabetic nephropathy, microangiopathy and a decrease in the local immune defense of the urinary tract, creating favorable conditions for the development of infectious and inflammatory complications. [2]

Urinary tract infection is one of the most common complications of urolithiasis. The presence of concretions disrupts normal urodynamics, promotes urinary stagnation and the formation of bacterial biofilms on the surface of stones, which ensures the long-term persistence of microorganisms and increases the resistance of pathogens to antibacterial therapy. When urolithiasis is combined with diabetes mellitus, the risk of developing infectious complications increases significantly due to impaired neutrophil function, decreased cellular and humoral immunity, microcirculatory disorders and glucosuria, which creates a favorable environment for the growth of microorganisms. [3]

Infectious complications in this category of patients are characterized by a more severe course, a high recurrence rate, and the risk of developing urosepsis, acute kidney injury, and chronic renal failure. In this regard, timely diagnosis of the infectious process and the rational choice of antibacterial therapy are of particular clinical importance. [4]

Gram-negative representatives of the Enterobacterales family, primarily Escherichia coli, as well as Klebsiella pneumoniae, Proteus mirabilis, Enterobacter spp. and Pseudomonas aeruginosa, are traditionally considered the most common pathogens of urinary tract infections. Enterococcus faecalis, Staphylococcus saprophyticus and coagulase-negative staphylococci play an important role among Gram-positive microorganisms. However, in recent years, there has been a change in the structure of pathogens of urological infections, an increase in the proportion of hospital strains and multidrug-resistant microorganisms, which significantly complicates empirical antibacterial therapy. [5]

The rapid growth of antibiotic resistance is a particular problem. The widespread and often unjustified use of antibacterial drugs has led to the proliferation of microorganisms producing extended-spectrum beta-lactamases, carbapenemases and other enzymes that provide resistance to modern antibiotics. In patients with urolithiasis, antibiotic resistance is additionally caused by the chronic persistence of bacteria inside concretions and biofilms, which make it difficult to eradicate the pathogen even when using highly effective drugs. [6]

Patients with diabetes mellitus are at high risk of developing resistant microorganisms. Frequent hospitalizations, repeated courses of antibacterial therapy, the need for invasive urological interventions and the presence of concomitant diseases contribute to the selection of resistant strains. As a result, the effectiveness of standard empirical therapy regimens is gradually decreasing, and the choice of an antibiotic without taking into account local antibiotic sensitivity data can lead to treatment inefficiency, lengthening hospital admission, increasing healthcare system costs, and increased mortality in severe infectious complications. [7]

Current clinical guidelines emphasize the need for regular monitoring of the microbiological spectrum of pathogens and their sensitivity to antibacterial drugs at the regional level. Since the profile of antibiotic resistance varies significantly depending on geographical features, hospital structure, the nature of medical care provided and the characteristics of the patient population, the results of local studies are of great practical importance for the development of effective algorithms for empirical antibacterial therapy. [8]

Despite a significant number of studies on urolithiasis and urinary tract infections, data on the microbiological profile and sensitivity to antibiotics in patients with a combination of urolithiasis and diabetes mellitus remain limited. Most published papers consider these diseases in isolation or include heterogeneous groups of patients without a detailed analysis of the effect of diabetes on the structure of pathogens and the level of antibiotic resistance. Meanwhile, it is the combination of these pathological conditions that forms a special high-risk clinical group that requires an individual approach to the diagnosis, prevention and treatment of infectious complications. [9]

The study of the species composition of microorganisms and their sensitivity to antibacterial drugs in this category of patients will make it possible to identify the most common pathogens, determine current trends in the formation of antibiotic resistance and optimize the choice of empirical antibacterial therapy. The results obtained can help to increase the effectiveness of treatment, reduce the frequency of infectious complications, reduce the risk of developing urosepsis, shorten the duration of hospitalization and improve the prognosis of the disease. [10]

Thus, the study of the microbiological profile and antibiotic sensitivity in patients with urolithiasis complicated by diabetes mellitus is an urgent area of modern urology and clinical microbiology. Analysis of regional characteristics of pathogen circulation and their sensitivity to antibacterial drugs is important for improving diagnosis, rational use of antibiotics, and implementation of antibiotic resistance control programs.

The aim of the study was to study the microbiological profile of urinary tract infection pathogens and determine their sensitivity to antibacterial drugs in patients with urolithiasis complicated by diabetes mellitus.

METHODS

A single-center retrospective study of patients treated in the urology department in the period from January 2022 to December 2024 was conducted. The study included 120 patients with urolithiasis (urolithiasis) complicated by urinary tract infection. All patients were divided into two groups depending on the presence of diabetes mellitus.

The main group consisted of 60 patients with urolithiasis and type 2 diabetes mellitus. The comparison group consisted of 60 patients with urolithiasis without impaired carbohydrate metabolism. The groups were comparable in terms of gender, age, and concretion location.

The average age of patients in the main group was 59.8 ± 10.6 years, in the comparison group — 56.9 ± 11.3 years. In the main group, there were 34 men (56.7%) and 26 women (43.3%). In the comparison group, there were 37 men (61.7%) and 23 women (38.3%).

Inclusion criteria:

* over the age of 18;

* confirmed diagnosis of urolithiasis;

* the presence of clinical and laboratory signs of urinary tract infection;

* positive result of bacteriological examination of urine;

* for the main group, a diagnosis of type 2 diabetes mellitus was established.

Exclusion criteria:

* pregnancy;

* oncological diseases of the urinary tract;

* Stage V chronic kidney disease;

* transplanted kidney;

* taking antibiotics less than 72 hours before urine sampling;

* Incomplete medical data.

All patients underwent a comprehensive clinical and laboratory examination, which included a general blood test, a general urinalysis, a biochemical blood test, determination of creatinine, urea, glomerular filtration rate, blood glucose, glycated hemoglobin (HbA1c), ultrasound examination of the kidneys and urinary tract, as well as computed tomography without contrast to confirm the location and size of the nodules.

For microbiological examination, bacteriological culture of an average portion of morning urine was performed before the start of antibacterial therapy. The material was collected in sterile containers in compliance with the rules of asepsis. Inoculation was performed on blood agar and McConkey agar, followed by incubation at 37 °C for 18-24 hours. The growth of microorganisms at a concentration of $\geq 10^5$ CFU/ml was considered significant bacteriuria.

The identification of microorganisms was carried out using an automatic VITEK® 2 Compact bacteriological analyzer (bioMérieux, France). If necessary, the results were confirmed by standard biochemical tests.

The sensitivity of isolated microorganisms to antibacterial drugs was determined by the method of disco diffusion on Muller-Hinton agar and an automated method using a VITEK® 2 Compact analyzer. The interpretation of the results was performed in accordance with the recommendations of EUCAST version 14.0 (2024). Sensitivity to the following groups of antibiotics was evaluated:

* protected aminopenicillins;

* cephalosporins of the III–IV generation;

* carbapenems;

* Fluoroquinolones;

* aminoglycosides;

* nitrofurans;

* Fosfomycin;

* co-trimoxazole.

The main indicators studied were the species composition of microorganisms, the frequency of isolation of individual pathogens, the level of antibiotic sensitivity and antibiotic resistance, as well as the presence of strains producing extended-spectrum beta-lactamases (ESBL).

RESULTS

The study included 120 patients with urolithiasis, of which 60 patients had concomitant type 2 diabetes mellitus (the main group), and 60 patients formed the comparison group.

The average age of patients in the main group was 59.8 ± 10.6 years, in the comparison group — 56.9 ± 11.3 years (p = 0.118). Men made up 56.7% (34/60) of the main group and 61.7% (37/60) of the comparison group (p = 0.574).

Bacteriological examination of urine revealed positive growth of microorganisms in 111 (92.5%) patients. In the main group, bacteriuria was registered in 58 (96.7%) patients, while in the comparison group — in 53 (88.3%) (p = 0.087).

The most frequently isolated microorganism in both groups was Escherichia coli. In the main group, this pathogen was detected in 24 (41.4%) patients, in the comparison group — in 28 (52.8%) patients. Klebsiella pneumoniae took the second place in terms of frequency — 12 (20.7%) and 8 (15.1%) cases, respectively. Enterococcus faecalis was isolated in 9 (15.5%) patients of the main group and 6 (11.3%) patients of the comparison group. Proteus mirabilis was found in 6 (10.3%) and 5 (9.4%) patients, respectively, while Pseudomonas aeruginosa was found in 5 (8.6%) patients with diabetes mellitus and only in 2 (3.8%) patients without diabetes. Mixed microbial associations were found in 2 (3.5%) patients of the main group.

The analysis of antibiotic sensitivity showed that the greatest sensitivity of microorganisms in the main group was observed to carbapenems (96.6%), fosfomycin (93.1%), amikacin (91.4%) and nitrofurantoin (89.7%). In the comparison group, sensitivity to these drugs was 98.1%, 96.2%, 94.3% and 92.5%, respectively.

The highest level of resistance to ampicillin was recorded — 72.4% in the main group and 58.5% in the comparison group (p = 0.041). Resistance to ciprofloxacin was 43.1% versus 28.3% (p = 0.048), to levofloxacin — 36.2% versus 22.6% (p = 0.039), to co-trimoxazole — 46.6% versus 34.0% (p = 0.109). Resistance to ceftriaxone was detected in 25.9% of patients in the main group and 17.0% of patients in the comparison group.

Extended-spectrum beta-lactamase (ESBL) producing strains were detected in 13 (22.4%) patients of the main group and 7 (13.2%) patients of the comparison group (p = 0.184). Multidrug resistance (MDR) was registered in 16 (27.6%) patients with diabetes mellitus, while in the comparison group — in 9 (17.0%) patients.

When comparing the structure of pathogens, it was found that Klebsiella pneumoniae, Pseudomonas aeruginosa and polymicrobial infections were significantly more common in patients with diabetes, while Escherichia coli prevailed in patients without diabetes.

The average length of hospitalization in the main group of patients was 9.8 ± 2.7 days, which was statistically significantly higher than in the comparison group (7.3 ± 2.1 days, p < 0.001). Postoperative infectious complications were reported in 11 (18.3%) patients with diabetes mellitus and in 5 (8.3%) patients without diabetes (p = 0.104).

The results obtained indicate that the presence of diabetes mellitus in patients with urolithiasis is associated with a change in the microbiological spectrum of pathogens, an increase in the prevalence of antibiotic-resistant strains and a higher incidence of infectious complications. At the same time, carbapenems, fosfomycin, amikacin and nitrofurantoin retained the highest activity against isolated microorganisms, while resistance to ampicillin and fluoroquinolones was significantly higher, especially in patients with diabetes mellitus.

DISCUSSION

The results of the study indicate that the combination of urolithiasis and diabetes mellitus is accompanied by a change in the microbiological profile of urinary tract infections and an increase in the prevalence of antibiotic-resistant strains of microorganisms. Despite the fact that Escherichia coli remained the most common pathogen in both study groups, an increase in the proportion of Klebsiella pneumoniae, Pseudomonas aeruginosa and polymicrobial infections was noted in patients with diabetes mellitus. The results obtained are consistent with modern ideas about the effect of carbohydrate metabolism disorders on the structure of uropathogens.

It is known that chronic hyperglycemia contributes to the disruption of the innate and adaptive immune response, deterioration of microcirculation and a decrease in the protective properties of the urothelium. In addition, glucosuria creates favorable conditions for the growth and colonization of microorganisms, and the presence of concretions promotes the formation of bacterial biofilms. Together, these factors ensure the long-term persistence of infection and increase the likelihood of antibiotic resistance.

One of the most significant results of the study is a higher level of resistance of microorganisms to widely used antibacterial drugs in patients with diabetes mellitus. The most pronounced resistance was registered to ampicillin, fluoroquinolones and co-trimoxazole. This fact may be due to repeated courses of antibacterial therapy, repeated hospitalizations, and selection of resistant strains due to frequent patient contact with medical facilities. In addition, the presence of biofilms on the surface of urinary calculi significantly reduces the effectiveness of antibiotics, since the bacteria inside the biofilms are much more resistant than planktonic forms.

In the present study, the isolated microorganisms retained the greatest sensitivity to carbapenems, fosfomycin, amikacin, and nitrofurantoin. These results confirm the expediency of using these drugs in the treatment of complicated urinary tract infections after receiving the results of a microbiological examination. However, the use of carbapenems should be strictly justified in view of the need to maintain their high clinical efficacy and prevent the further spread of carbapenem-resistant strains.

It should be noted that in patients with diabetes mellitus, microorganisms producing extended-spectrum beta-lactamases (ESBL), as well as multidrug-resistant strains, were more often detected. Although the differences between the study groups did not reach statistical significance for individual indicators, this trend has important clinical significance, since the presence of such microorganisms significantly limits the possibilities of effective empirical antibacterial therapy.

An increase in the duration of hospitalization and a higher incidence of infectious complications in patients of the main group confirm the adverse effect of diabetes mellitus on the course of urolithiasis. This is probably due not only to the peculiarities of the microbial spectrum, but also to metabolic disorders, deterioration of reparative processes and a decrease in the effectiveness of the body's immune defense.

The practical significance of the results obtained lies in the need for mandatory bacteriological examination of urine to determine antibiotic sensitivity before prescribing antibacterial therapy in patients with urolithiasis and diabetes mellitus. The use of local data on the structure of pathogens and their resistance profile makes it possible to increase the effectiveness of treatment, reduce the risk of failure of empirical therapy and reduce the likelihood of further spread of antibiotic resistance.

The present study has a number of limitations. Firstly, it was performed in the conditions of one medical center, which may limit the possibility of extrapolating the results to other regions. Secondly, a relatively small sample size reduces the statistical power of analyzing individual microorganisms and rare resistance phenotypes. In addition, there was no molecular genetic study of the mechanisms of antibiotic resistance and the effect of the duration of diabetes mellitus, the level of compensation of carbohydrate metabolism and previous antibacterial therapy on the nature of the microbial landscape was not evaluated.

Promising areas of further research include conducting multicenter observations with a larger sample of patients, studying the molecular mechanisms of the formation of resistance of microorganisms, analyzing the effect of various methods of surgical treatment of urolithiasis on the structure of uropathogens, as well as developing personalized algorithms for antibacterial therapy, taking into account the metabolic status of patients.

Thus, the results of the study confirm that the combination of urolithiasis and diabetes mellitus is accompanied by a change in the microbiological profile of urinary tract infections, an increase in the frequency of detection of antibiotic-resistant microorganisms and a more severe course of the infectious process. This determines the need for constant microbiological monitoring, the rational use of antibacterial drugs and an individualized approach to the treatment of this category of patients.

CONCLUSIONS

The study showed that patients with urolithiasis complicated by diabetes mellitus have features of the microbiological profile of urinary tract infections, characterized by a higher frequency of release of opportunistic microorganisms and an increase in the prevalence of antibiotic-resistant strains. Escherichia coli remained the most frequently detected pathogen, however, Klebsiella pneumoniae, Pseudomonas aeruginosa and multidrug-resistant microorganisms were more often detected in patients with diabetes mellitus.

The analysis of antibiotic sensitivity showed the continued high activity of carbapenems, fosfomycin, amikacin, and nitrofurantoin against most of the isolated uropathogens. At the same time, high rates of resistance to ampicillin, fluoroquinolones, and co-trimoxazole have been established, especially in patients with concomitant diabetes mellitus, which limits the possibility of their empirical use without the results of a bacteriological study.

The data obtained indicate that the presence of diabetes mellitus is a significant risk factor for the formation of antibiotic resistance, a more severe course of the infectious process and an increase in the duration of hospitalization in patients with urolithiasis. In this regard, the choice of antibacterial therapy should be based on the results of microbiological examination of urine and local data on the sensitivity of pathogens to antibiotics.

The practical significance of the study lies in the possibility of using the results obtained to improve the algorithms of empirical antibacterial therapy, increase the effectiveness of treatment of urinary tract infections, reduce the frequency of postoperative complications and prevent the further spread of antibiotic resistance. Regular local monitoring of the microbial

spectrum and antibiotic sensitivity of uropathogens will optimize treatment tactics and improve clinical outcomes in patients with urolithiasis and diabetes mellitus.

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