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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

MICROBIOLOGICAL CHARACTERISTICS OF URINARY TRACT INFECTIONS ON THE BACKGROUND OF GENERAL SOMATIC DISEASES

Specialty: 2414.01 – Microbiology

Field of Science: Medicine

Applicant: **Elchin Abulfat Museyibov**

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Dissertation work was performed at The Department of Psychology, Pedagogy, and Social Sciences at Odlar Yurdu University.

Scientific supervisor: Doctor of Medicine, Professor **Mehman Habib Aliyev**

Official opponents: Doctor of Medicine, Professor **Murad Giyas Mammadov**

Doctor of Medicine, Professor **Sadraddin Abdulla Atakishizade**

PhD in Medicine, Associate **Etibar Asabali Karimov**

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Chairman of the Scientific Seminar: Doctor of Medicine, Professor **Akif Irzakhan Gurbanov**

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Tibb elmləri doktoru, professor
Nazim Adil oğlu Pənahov
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GENERAL CHARACTERISTICS OF THE RESEARCH

Relevance of the topic. Urinary tract infections are common infectious diseases leading to high financial costs. Nosocomial urinary tract infections (UTIs) are considered major reservoirs of antibiotic-resistant microorganisms in healthcare facilities. According to epidemiological indicators, UTIs develop more often in women: almost 50% of women experience UTIs at least once in their lifetime. In men, the frequency of infectious diseases of the urinary tract is much lower, 5-8 cases per 10,000 persons. UTIs are the 2nd most common in the elderly and account for about 25% of all infectious diseases[1].

Based on other indicators, UTIs are the most widespread bacterial infections globally, affecting approximately 150 million people annually[2].

Besides, UTIs are more often observed in ambulatory and in-hospital practice (Plekhanov, A.N. Infection of the urinary tract: epidemiology)[3].

The mechanism of infection is bacteria that colonize the urethra or periurethral space and migrate to the bladder, causing an inflammatory reaction.

The bacteria that usually cause this are found in the gastrointestinal tract and are commonly called Enterobacterales.

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1. Белоглазова, И.П. Инфекции мочевыводящих путей: часть 1 / И.П. Белоглазова, А.А. Трошина, Н.Г. Потешкина // – Москва: Лечебное дело, – 2018. №1, – с. 18-25.).
2. (Werneburg, G.T. Catheter–Associated Urinary Tract Infections: Current Challenges and Future Prospects // Research and Reports in Urology, – 2022. 14, – p. 109133).
3. этиология, патогенез, факторы риска, диагностика (обзор литературы) / А.Н. Плеханов, А.Б. Дамбаев // – Иркутск: Acta Biomedica Scientifica, – 2016. №1 (107), – с. 70-74.).

Escherichia coli, Klebsiella pneumonia, and Proteus mirabilis are a few examples. Although it is extremely uncommon, bacteria may also move from the bloodstream to the kidneys or bladder, resulting in a urinary tract infection. Female gender, recent sexual activity, diabetes mellitus, and structural or functional urological abnormalities are risk factors for urinary tract infections[4].

UTIs are more common in women than men, accounting for 81% of all infections reported in women[5].

Urinary tract infections are among the most common diseases in patients with general somatic pathologies[6]

One such somatic disease is diabetes. Currently, diabetes, being one of the more common chronic diseases, has become a major public health problem with life-threatening complications and a negative impact on life expectancy and quality of life[7]. Diabetes increases the risk of infection in several ways, for example, through weakened immune responses in a hyperglycemic environment[8].

4. Al Lawati, H. Urinary Tract Infections: Core Curriculum 2024 / H. Al Lawati, B.M. Blair, J. Larnard // American Journal of Kidney Diseases, – 2024. 83 (1), – p. 90-100.).
5. (Kaur, R. Symptoms, risk factors, diagnosis and treatment of urinary tract infections / R. Kaur, R. Kaur // Postgraduate Medical Journal, – 2021. 97 (1154), p. 803-812).
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7. (Healda A.H., Stedmanc M., Daviesc M. [et al.] Estimating life years lost to diabetes: Outcomes from analysis of National Diabetes Audit and Office of National Statistics data. Cardiovasc / A.H. Healda, M. Stedmanc, M. Daviesc [et al.] // Endocrinology and Metabolism, – 2020. 9, – p. 183-185).
8. Carey I.M. Risk of Infection in Type 1 and Type 2 Diabetes Compared With the General Population: A Matched Cohort Study / I.M. Carey, J.A. Critchley, S. DeWilde [et al.] // Diabetes Care, – 2018. 41 (3), – p. 513-521.).

A study performed in the US revealed that 10% of emergency department visits in patients with diabetes were due to infections, with these patients being at twice the risk of infection compared to the general population[9].

In addition, bacteremia is more common in patients with diabetes. Urinary tract infections have a higher prevalence and mortality rates. Although it is known that these patients are at higher risk of developing various types of infections than others, when considering the complications of diabetes, the risk of infection is often underestimated. Urinary tract infections are more common in people with diabetes, with higher rates of bacteremia, hospitalization, relapse, and death. Even if the bacterial strains isolated from the urine of patients with diabetes during UTIs are similar to the bacterial strains isolated from persons without diabetes, this infection should be considered more dangerous and should be treated within 7-14 days[10].

Besides, UTIs are considered some of the complications of diabetes. In addition, various factors such as socio-demographic characteristics, type of diabetes, fasting blood glucose level, regular monitoring of diabetes, concomitant chronic diseases, HbA1c, body mass index (BMI) and duration of diabetes are also associated with the predisposition to the development of the disease, as well as shows that these patients have a high frequency of development of UTIs[11].

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9. (Korbel, L. Diabetes mellitus and infection: an evaluation of hospital utilization and management costs in the United States / L. Korbel, J.D. Spencer // Journal of Diabetes Complications, – 2015. 29 (2), – p. 192-5).
10. (Confederat, L.G. Particularities of Urinary Tract Infections in Diabetic Patients: A Concise Review / L.G. Confederat, M.I. Condurache, R.E. Alexa [et al.] // Medicina (Kaunas), – 2023. 59 (10), – p. 1-11).
11. Ahmed, A.E. Prevalence and Associated Risk Factors of Urinary Tract Infection among Diabetic Patients: A Cross–Sectional Study / A.E. Ahmed, S. Abdelkarim, M. Zenida [et al.[// Healthcare (Basel), – 2023. 11(6), – p. 1-11).

It takes up to 48-72 hours to conduct such examinations. In most cases, empirical treatment is applied first in patients with urinary tract pathologies. Individuals with different somatic pathologies may show different forms of sensitivity to treatment measures, depending on the type of somatic pathology[12].

It is also necessary to detect the sensitivity of the strains isolated from the biological sample to antibiotics during the treatment of UTIs. According to the authors, in this case, the strains are distinguished by higher resistance[13].

Taking these into account, we determined the frequency of occurrence of UTIs in patients with diabetes, the sensitivity of strains to antibiotics, the frequency of occurrence of UTI complications and relapses after lithotripsy.

Thus, we determined the frequency of occurrence of UTIs in patients with diabetes, the sensitivity of strains to antibiotics, the frequency of occurrence of UTI complications, and relapses after lithotripsy.

The research object: 345 patients applied to Tovuz District Central Hospital during 2015-2019. They had diabetes along with UTIs. The incidence of urinary tract infections was studied in this group. In 180 patients, urinary tract infection complications were recorded, and in 100 persons, no urinary tract infection complications were detected. 90 patients were included in the prospective study. Urinary tract infections were recorded in all of these patients.

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12. (Bischoff, S. Empiric antibiotic therapy in urinary tract infection in patients with risk factors for antibiotic resistance in a German emergency department / S. Bischoff, T. Walter, M. Gerigk [et al.] // BMC Infection Diseases, – 2018. 18 (56), – p. 1-7).
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The purpose of the research: Evaluation of the microbiological nature of urinary tract infections in patients with diabetes.

Tasks of the research:

1. Assessment of the effects of somatic factors such as diabetes mellitus and kidney stone disease on urine microflora during UTIs.
2. Studying the sensitivity of some microorganisms obtained from urine to various antibiotics in diabetic patients suffering from urinary tract infections.
3. Determination of indicators of sensitivity to antibiotics in urine samples obtained from diabetic patients after treatment of urinary tract infections.
4. Studying the sensitivity of lactobacilli and bifidobacteria isolated from the urinary tract of diabetic patients to various antibiotic preparations.
5. Studying the occurrence of urinary tract infections in diabetic patients related to different age groups.
6. Determining the frequency of various microbiological complications of the urinary tract and species of microorganisms before and after lithotripsy of kidney stones in patients suffering from diabetes.
7. Studying the etiological structure of urinary tract infectious complications after lithotripsy surgery in diabetic patients.
8. Comparative analysis of intoxication indicators during the development of various urinary tract infections in diabetic patients who underwent lithotripsy.

Scientific novelty of the research:

- For the first time, in our republic, the effects of somatic factors such as diabetes mellitus and kidney stone disease have been studied on the microflora of urine during UTIs.
- The sensitivity of some microorganisms isolated from the urine of diabetic patients suffering from urinary tract infections to various antibiotics has been determined.

- The sensitivity of different types of microorganisms isolated from the urine samples of diabetic patients to different antibiotic drugs has been studied.
- The sensitivity of lactobacilli and bifidobacteria isolated from the urinary tract of diabetic patients to various antibiotic preparations has been evaluated.
- The occurrence of urinary tract infections in diabetic patients belonging to different age groups has been studied.
- The effect of diabetes on the microflora of urine has been studied before and after lithotripsy.

Practical significance of the study:

1. Conducting a detailed study of the urinary tract microflora in patients suffering from diabetes has created conditions for the emergence of new treatment approaches in experimental nephrology and microbiology.

2. Studying the sensitivity of uropathogens to antibiotics during the complications of UTIs after lithotripsy in diabetic patients has created the basis for more prompt treatment of relevant pathologies.

Research methods: clinical, radiological, microbiological and mathematical-statistical.

The main provisions of the dissertation:

1. One of the reasons for the relatively high occurrence of the traditional UTI agents during diabetes compared to the non-diabetic group is that the pathogenic microflora begins to have a richer character during diabetes.
2. In order to eliminate the development of various infectious-purulent processes of the urinary tract in people suffering from diabetes, it is more appropriate to conduct research in the direction of improving the use of effective selective antibiotic therapy for both preventive and therapeutic purposes.
3. Cases of postoperative infectious complications during lithotripsy are mainly observed in patients with diabetes mellitus who underwent emergency surgery.

4. Determining the antibiotic sensitivity of the microorganism species that cause various complications in the urinary tract before and after lithotripsy in patients suffering from diabetes and kidney stones will provide a basis for optimizing treatment measures.

Approbation of the research.

The results of the research were discussed at the following conferences: Materials of the international scientific-practical conference on "The Heydar Aliyev model of statehood in modern times: realities and facts", the international scientific-practical conference dedicated to the 100th anniversary of the Azerbaijan Democratic Republic and the 95th anniversary of the birth of the National Leader Heydar Aliyev (Baku, May 8, 2018); Current Problems of Medicine (dedicated to the 100th anniversary of the Azerbaijan People's Republic) scientific-practical conference (Baku, 2018); Scientific Dialogue: Medical Issues. XIX International Scientific and Practical Conference (St. Petersburg, May 15, 2019).

The initial defense of the dissertation was held at the extended meeting with the participation of the staff of the Department of Psychology, Pedagogy, and Social Sciences at Odlar Yurdu University (11.05.2019, protocol No. 07) and the dissertation was discussed at the meeting of the Scientific Council of Azerbaijan Medical University holding seminars on the specialty 2414.01- "Microbiology" (17.04.24, Protocol No.3).

Publications. On the topic of the dissertation, 12 scientific articles and theses were published (9 articles, 3 theses), and 1 speech was given. Two theses and two articles were published in the local press, while one thesis and two articles were published abroad.

The volume and structure of the dissertation.

The dissertation covers 159 (222,844 characters) computer typing pages: Introduction (9,949 characters), Literature review (57,043 characters), Materials and Methods (8,788 characters), Chapter III (66,769 characters), Chapter IV (25,217 characters),

Conclusion (52,902 characters), Results (1,686 characters), Practical recommendations (490 characters). There are 15 tables, 13 graphs, and 3 figures in the dissertation. The bibliography consists of 166 sources and 18 of them are the works of national scientists.

MATERIALS AND METHODS

The research was carried out in Tovuz District Central Hospital. It consisted of two stages. In the first stage, a retrospective analysis of medical history was performed. During the retrospective analysis, the medical history of 625 patients was analyzed. Among them, 280 patients had diabetes mellitus and underwent lithotripsy (Shock-wave lithotripsy operation - Karl Storz Calculate II, Holmium) for kidney stones in Tovuz District Central Hospital during 2015-2019 (I retrospective group). In 180 of these patients, urinary tract infection complications were recorded, and no urinary tract infection complications were detected in 100 patients.

Other 345 patients applied to Tovuz District Central Hospital during 2015-2019. They had diabetes along with UTIs (retrospective group II). The incidence of urinary tract infections in this group was studied.

In the second phase, 90 patients were included in the prospective study. Urinary tract infections were recorded in all of these patients.

The mean leukocyte index of the first retrospective intoxication (LII), body temperature and erythrocyte sedimentation rate (ESR) were comparatively studied.

Microbiological examination of urine was performed on all patients, sensitivity of bacteria to antibiotics was determined.

The obtained data were processed by statistical methods taking into account modern requirements. The average values (M), their standard error (SE), the minimum (min) and maximum (max) values of the series, as well as the quality indicators of the occurrence frequency in the groups, were determined.

For the initial evaluation of the difference between the variation series, the Student's t-test parametric method, the mean difference

between indicators selected for pairwise related variants, and the difference between the parts were used. Then, non-parametric criteria - the Wilcoxon- Mann-Whitney U test, and Pearson's $\chi 2$ - criterion were used for frequency analysis. Correlation analysis was conducted in order to determine the strength of the relationship between the studied indicators. The statistical processing of the obtained results was carried out with the Statistica 7.0 computer program.

ANALYSIS OF THE RESULTS OBTAINED ON RETROSPECTIVE GROUPS

The study of the somatic effects UTIs on urine microflora in 20 patients with diabetes and kidney stones showed the presence of E.coli in 13 patients (65.0±10.67%) without kidney stones, with diabetes and urinary tract infections (I group). K.pneumoniae was found in 4 patients in group I (20.0±8.94%). Nevertheless, in another group of 20 people who had neither kidney stones nor diabetes, but had urinary tract infections (group II), E.coli was found to be significantly less - in 7 samples (35.0±10.67%) ($p<0,05$). In group II, K.pneumoniae was also detected in only one out of 20 patients (5.0±4.87%) ($p<0.05$compared to group I).

Enterococcus faecalis type was found in 3 samples (15.0±7.98%) in urine samples taken from patients of group I, with urinary tract infections without kidney stones, suffering from diabetes.

Nevertheless, E. faecalis species was found in only two of the 20 samples obtained from group II, consisting of patients without diabetes and kidney stone disease but with urinary tract infections, which is 10.0±6.71 of the microorganisms isolated from the corresponding group. % ($p>0.05$ compared to group I).

Enterobacter cloacae was found in 7 of the materials taken from group I, or 35.0±10.67% of that group. In group II, the corresponding type of microorganism was detected in 3 samples (15.0±7.98%) ($p<0.05$).

Table 1

Effects of somatic factors such as diabetes mellitus and kidney stone disease on urine microflora during UTIs (for research groups I and II)

Microorganisms	Group I (n=20)		Group II (n=20)	
	Abs.	%	Abs.	%
E.coli	13	65.0±10.67	7	35.0±10.67
K.pneumoniae	4	20.0±8.94	1	5.0±4.87
Enterobacter cloacae	7	35.0±10.67	3	15.0±7.98
Enterococcus faecalis	3	15.0±7.98	2	10.0±6.71
P.aeruginosa	3	15.0±7.98	2	10.0±6.71

While P.aeruginosa in group I was found in 3 samples and accounted for 15.0±7.98% of the isolated microorganisms, in group II this bacterium was detected in relatively few -2 samples and constituted 10.0±6.71% ($p > 0.05$).

As a result of the research, E.coli was detected in 16 of the same number of urine samples obtained from the III group consisting of 25 people with diabetes mellitus and kidney stone disease as well as urinary tract infections, or 64.0±9.6% of the samples for the group. Nevertheless, in group IV of 25 non-diabetic patients with kidney stones and urinary tract infection, the respective microorganism was found in 20 samples and accounted for 80.0±8.0% of the isolated microorganisms ($p<0.05$).

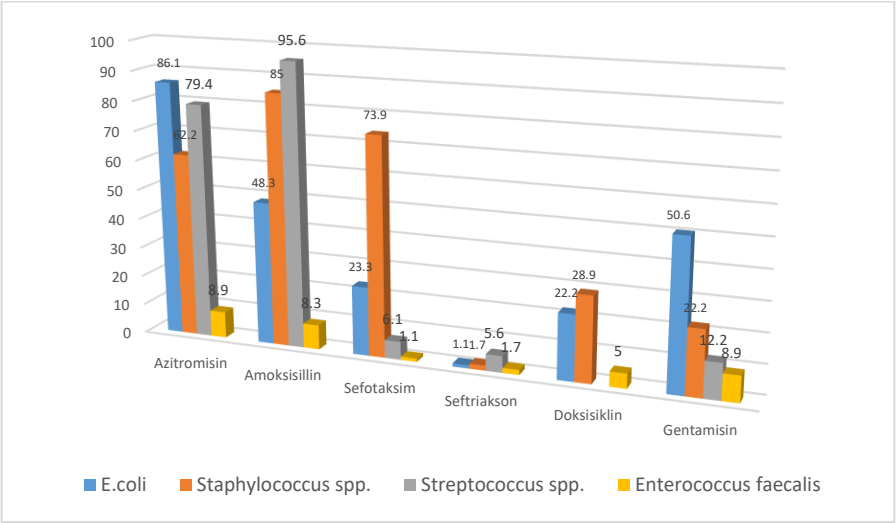
In group III, K.pneumoniae was found in 3 out of 25 urine samples and was 12.0±6.5%. Nevertheless, in group IV, the corresponding species of microorganism was found in 7 out of 25 samples (28.0±8.98%, $p<0.05$). E. cloacae was found in 8 out of 25 samples in group III and constituted 32.0±9.33% of the

microorganisms of the corresponding group. In group IV, the corresponding microorganism was found in 7 out of 25 urine samples (28.0±8.98%), and it was almost indistinguishable from group III ($p>0.05$).

In the first retrospective group, in 180 patients with postoperative complications, the sensitivity of different types of microorganisms isolated from urine samples before lithotripsy was determined. The sensitivities of the same number of staphylococcal samples to various antibiotic drugs obtained from urine samples taken before surgery from 180 patients with diabetes and kidney stones, who were scheduled for lithotripsy surgery, were in the following descending order: Amoxicillin, Azithromycin, Doxycycline, Gentamicin, Cefotaxime, Macropen, Ceftriaxone, and other 3 antibiotic preparations (Ampicillin, Oxacillin and Amikacin).

Representatives of Streptococcus (S. faecalis and S. agalactiae) in 143 (79.4±3.01%) out of 180 patients suffering from diabetes and kidney stone diseases who underwent lithotripsy were sensitive to the Azithromycin drug.

Four (2.2±1.10%) of Enterococcus faecalis colonies showed sensitivity to the Macropen drug. 15 (8.3±2.06%) of the obtained clean isolates of the respective microorganism were sensitive to Amoxicillin. Sensitivity to azithromycin was observed in 16 (8.9±2.12%) E. faecalis isolates. Susceptibility to cefotaxime was detected in only 2 (1.1±0.78%) samples. Susceptibility to ceftriaxone was recorded in 3 samples (1.7±0.95%). Susceptibility to amikacin in E.faecalis strains was recorded in 2 (1.1±0.78%) isolates. Sensitivity to Gentamicin was observed in 16 (8.9±212%) samples.



Graph 1. Indicators of sensitivity of different microorganism species isolated from urine samples to different antibiotic drugs in retrospective group I

Sensitivity to Ampicillin was recorded in 4 of the Streptococcus isolates (2.2±1.10%). The sensitivity indicator of the isolates of the relevant microorganism to oxacillin was detected in 2 samples (1.1±0.78%). Three of the Streptococcus isolates (1.7±0.95%) were sensitive to Amikacin.

Thus, the sensitivities of Streptococcus samples isolated from urine samples taken before the operation from 180 patients suffering from diabetes and kidney stones who had indications for lithotripsy and were scheduled for surgery were observed in the following descending sequence: Amoxicillin, Azithromycin, Gentamicin, Cefotaxime, Ceftriaxone, Ampicillin, Amikacin, and Oxacillin.

In retrospective group I, postoperative complications were studied.

The influence of the operation period on the occurrence of complications of various urinary tract infections in diabetic patients who underwent lithotripsy surgery was studied.

During the first week after emergency lithotripsy, 72 (66.7±4.54%) UTI complications were detected. There were 10 (13.9±4.08%) complications after planned surgery ($p<0.05$).

In 75 (69.4±4.43%) patients who underwent emergency lithotripsy, complications with UTIs were recorded in the 2nd week after lithotripsy. In 72 (58.3±5.81%) patients who underwent planned lithotripsy, complications with UTIs occurred in the 2nd week after surgery ($p<0.05$).

In 90 (83.3±3.59%) patients who underwent emergency surgery, UTI complications were recorded in the third week after the operation. In 48 (66.7±5.56) patients who underwent planned lithotripsy, complications occurred in the 3rd week ($p<0.05$)..

In 96 (88.9±3.02%) patients who underwent emergency lithotripsy, the complication with UTIs occurred in the 4th week. It happened in the 4th week in 53 (73.6±5.19%) people who underwent a planned operation ($p<0.05$).

Thus, the majority of infectious complications after emergency and planned operations occurred in the IV week. The frequency of infectious complications was relatively low in the first week after emergency and planned operations.

The frequency of infectious complications in group I was extremely low in both cases. There were no significant differences in the distribution of complications during the II and III weeks.

The frequency of occurrence of different types of microorganisms in urine samples during various infectious urinary tract complications after lithotripsy of kidney stones in patients suffering from diabetes was studied. E.coli microorganism was detected in 18 (10.0±2.24%) biological samples taken from patients with developed acute pyelonephritis. This microorganism was found in 3 (1.7±0.95%) biological samples obtained from the group of patients with acute cystitis. Proteus species were found in 3 (1.7±0.95%) urine samples in the group of patients with acute cystitis. E.coli species was found in only 2 (1.1±0.78%) of the biological samples taken from the patient with acute pyelonephritis complication.

This microorganism was found in 10 (5.6±1.71%) patients with pyonephrosis. E.coli was present in 1 (0.6±0.55%) patient diagnosed with acute epididymo-orchitis complication. This microorganism was detected in 8 (4.4±1.54%) samples obtained from patients with acute urethritis. E.coli was found in 42 (23.3±3.15%) of the patients included in the study.

Proteus species were found in samples taken from 13 (7.2±1.93%) patients with acute pyelonephritis. Proteus species were recorded in the urine samples of 3 (1.7±0.95%) patients with postoperative complications of acute paranephritis. This microorganism was found in 4 (2.2±1.10%) samples obtained from patients with pyonephrosis complications.

P.aeruginosa microorganism was detected in 14 (7.8±2.00%) samples taken from patients with acute pyelonephritis who had postoperative complications. This species was found in 6 (3.3±1.34%) of post-operative patients with acute cystitis.

S.saprophyticus species was isolated in 2 (1.1±0.78%) samples from patients with acute pyelonephritis. Staphylococcus aureus, another species of staphylococci, was isolated in 1 (0.6±0.55%) sample obtained from patients with this diagnosis. S. saprophyticus species was detected in 5 (2.8±1.22%) biological samples taken from patients with complicated acute cystitis. The representatives of this species were detected in the biological materials of the patients with complications such as pyonephrosis, acute epididymo-orchitis epididymoorchitis, acute orchitis, and urosepsis.

S. aureus species was found in 3 (1.7±0.95%) of the urine samples obtained from patients with a complication such as acute cystitis after lithotripsy. S.aureus was present in only 1 (0.6±0.55%) sample in each of the patient groups with complications such as acute epididymo-orchitis, acute urethritis, and urosepsis. The representatives of this species were not observed in the samples obtained from postoperative patients with complications such as pyonephrosis and suppuration of the wound site.

Representatives of enterococci were found in 4 (2.2±1.10%) of the biological materials taken from each of the groups of patients with

complications such as acute pyelonephritis and acute cystitis. Representatives of this microorganism were found in 2 of the biological materials taken from diabetic patients who underwent lithotripsy and had acute pyelonephritis, or in 1.1±0.78% of the total patients.

In the group of patients with pyonephrosis complication, only 1 (0.6±0.55%) sample contained enterococci species. These species were found in 11 (6.1±1.79%) of all complication cases. In cases of complications such as acute epididymo-orchitis, acute urethritis, wound suppuration, and urosepsis, species of this genus were not found.

Enterococcus faecalis species was found in 6 (3.3±1.34%) samples in the materials taken from the group of patients with acute pyelonephritis complications. This species of Streptococcus was found in 2 (1.1±0.78%) of the patients with acute cystitis. S.faecalis species was found in only 1 (0.6±0.55%) sample in each of the groups of postoperative patients with complications such as acute epididymo-orchitis and acute orchitis. None of the groups with complications such as acute pyelonephritis, pyonephrosis, wound suppuration, and urosepsis were found to have the mentioned species in the biological samples.

Candida albicans fungi were found in 2 (1.1±0.78%) samples obtained from the group of patients with acute cystitis. In the group of patients with complications of wound suppuration, the appropriate indicator of the corresponding microorganism was evaluated as in cases of acute cystitis. In each of the groups where postoperative complications such as acute pyelonephritis and pyonephrosis were observed, only 1 (0.6±0.55%) sample contained the mentioned microorganism. Postoperative complications such as acute pyelonephritis, acute epididymo-orchitis, acute urethritis, and urosepsis were not found in any of the samples.

Postoperative complications such as pyonephrosis, acute urethritis, and urosepsis, other microorganism species not mentioned in the study, were recorded in only 1 (0.6±0.55%) sample per group in the materials of the examined patients. None of the patients with

complications such as acute pyelonephritis, acute cystitis, acute pyelonephritis, acute epididymo-orchitis, and purulent inflammation of the wound site were found to have unconventional pathogens.

The occurrence of various microorganism species in urine samples obtained from non-diabetic patients who underwent lithotripsy and developed various urinary tract infections after the operation was studied. Representatives of E.coli were found in 9 or 9.0±2.86% of all biological samples taken from patients without diabetes who underwent lithotripsy and developed acute pyelonephritis. This microorganism was found in the biological samples of 4 (4.0±1.96%) of 18 patients who developed acute cystitis. E.coli was detected in urine samples obtained from 4 (4.0±1.96%) of 21 patients with acute pyelonephritis.

In 2 (2.0±1.40%) of 21 patients with developed pyonephrosis who underwent lithotripsy but did not have diabetes, E.coli, the main pathogen of UTIs, was isolated. E.coli was detected in 1 (1.0±0.99%) patient with developed acute epididymo-orchitis. E.coli was detected in only 3 (3.0±1.71%) of the biological materials taken from 15 non-diabetic patients who underwent lithotripsy and developed acute urethritis.

E.coli species were not found in any of the urine samples taken from 2 patients with surgical site suppuration and 2 other patients who developed urosepsis. Thus, E.coli species was found in 23 (23.0±4.21%) of the biological materials taken from 100 patients with developed UTIs who underwent lithotripsy but did not have diabetes.

Two proteus representatives were isolated from 2 (2.0±1.40%) biological samples of the patients with acute pyelonephritis. This microorganism was found in 18 (2.0±1.40%) biological materials that developed acute cystitis. Proteus was isolated from only 1 (1.0±0.99%) of the biological materials of 16 patients with pyonephrosis. Proteus was observed in one (1.0±0.99%) of the 15 patients with developed acute urethritis who underwent lithotripsy but did not have diabetes.

P.aeruginosa species were isolated from 25 (5.0±2.18%) urine samples taken from non-diabetic patients who underwent lithotripsy

and developed acute pyelonephritis. This microorganism was found in 3 (3.0±1.71%) materials obtained from 18 patients with developed acute cystitis who underwent lithotripsy. P.aeruginosa species was isolated from 5 (5.0±2.18%) samples obtained from patients with developed acute pyelonephritis. This species was obtained in 3 (3.0±1.71%) samples from 16 patients with pyonephrosis. However, P. aeruginosa was not detected in biopsy material obtained from only 1 patient who developed acute epididymo-orchitis. In only 2 (2.0±1.40%) samples from 15 patients with acute urethritis, the relevant microorganism was found.

Thus, P. aeruginosa species was found in 19 (19.0±3.92) urine samples obtained from 100 patients who underwent lithotripsy and subsequently developed UTIs.

Enterococcus faecalis was not found in any of the biological materials taken from 36 patients with complications such as acute epididymo-orchitis, pyonephrosis, acute urethritis, wound suppuration, and urosepsis.

Candida albicans fungi were found in only 1 (1.0±0.99%) of the biological samples taken from 25 patients with acute pyelonephritis who underwent lithotripsy. The corresponding species of the microorganism was not found in patients with acute cystitis. Candida was isolated in 3 (3.0±1.71%) of the materials taken from 16 surgical patients with developed pyonephrosis. No representatives of Candida albicans were isolated from biological materials obtained from 5 patients with complications such as acute epididymo-orchitis, wound suppuration, and urosepsis. Nevertheless, in the urine samples taken from a total of 36 patients with acute pyelonephritis and acute urethritis, representatives of the respective fungi were found in only 1 sample (1.0±0.99%) in each group.

The association of at least 4 of the above-mentioned microorganisms was not recorded in any of the biological materials obtained from 25 patients with acute pyelonephritis complications. The same situation was observed in urine samples obtained from patients with acute cystitis. Nevertheless, in 2 (2.0±1.40%) of the biological

materials of 21 patients with developed acute pyelonephritis, UTIs with the mentioned etiology were observed.

In 1 (1.0±0.99%) out of 16 biological samples taken from patients with developed pyonephrosis after lithotripsy, the association of at least 4 species of microorganisms was observed. None of the biological materials taken from 5 patients with complications such as acute epididymo-orchitis, wound suppuration, and urosepsis showed any of the mentioned associative processes. The corresponding association was recorded in 2 (2.0±1.40%) of materials obtained from 15 patients who underwent lithotripsy operation and developed acute urethritis.

In 2 out of 25 patients with acute pyelonephritis complication (2.0±1.40%), other microorganism species that were not mentioned in the study were found

Other species of microorganisms were recorded in only 1 (1.0±0.99%) of the biological materials taken from 18 patients with acute cystitis who underwent lithotripsy. The association of the mentioned microorganisms was not recorded in the biological materials of the patients with acute epididymo-orchitis. Microorganism associations were found in 2 (2.0±1.40%) urine samples taken from 21 patients with acute pyelonephritis.

As a result of our study on the etiological structure of infectious complications of the urinary tract after lithotripsy in diabetic patients, the E.coli microorganism was found in biological samples of 45 (25.0±3.23%) out of 180 patients who underwent lithotripsy and subsequently developed UTIs.

19 (10.6±2.29%) cases of complications with UTIs dominated by Proteus representatives were observed.

P.aeruginosa was dominant in biological material samples taken from 32 (17.8±2.85%) out of 180 diabetic patients who underwent lithotripsy surgery. Klebsiella was recorded in 10 (5.6±1.71%) samples.

In 14 (7.8±2.00%) samples taken from the patients included in the study, the UTI complications were caused by Staphylococcus epidermidis species, while in 15 (8.3±2.06%) samples,

Staphylococcus saprophyticus species caused UTIs. In 4 (2.2±1.10%) samples, Staphylococcus aureus species play the role as the main etiological factor for UTIs in the patients.

There were 9 (5.0±1.62%) cases of Enterococcus representatives playing the role of the main etiological factor in diabetic patients who underwent lithotripsy. In diabetic patients who underwent lithotripsy surgery, 11 (6.1±1.79%) cases of Enterococcus faecalis species playing the role of the main etiological factor of the infectious process were found. Candida albicans was found to be the main etiological factor in 7 (3.9±1.44%) materials.

The associations of at least 4 of the microorganisms was detected in 6 (3.3±1.34%) urine samples.

In 8 (4.4±1.54%) patients, the main etiological factors of UTIs were other microorganisms not included in our study.

As a result of the comparative study of intoxication indicators during the development of various urinary tract infections in diabetic patients who underwent lithotripsy surgery, the average LII indicator for the group during the UTIs was 4.57±0.049 c.u. in the group of 180 patients who developed UTIs after lithotripsy. However, after the elimination of UTIs with treatment measures, this indicator decreased up to 4 times to 1.78±0.060 c.u. ($p<0.001$). While the average temperature index for the group was 37.9±0.039°C during the UTIs, after the elimination of UTIs with treatment measures, this indicator decreased to 36.8±0.032°C ($p<0.001$).

While the average ESR index was found to be 21.2±0.082 mm/s for the group during the UTI complications, it significantly decreased to 10.6±0.098 mm/s after the elimination of UTI complications ($p<0.001$).

In the 2nd stage of the study, intoxication indicators of 180 patients subjected to lithotripsy and subsequently developed UTIs, and 100 patients who underwent lithotripsy and had diabetes but did not develop UTIs were compared.

The research revealed that 180 patients who underwent lithotripsy surgery and later developed UTIs had an ILI index of 4.57±0.049 c.u. on average for the group. However, in the group of 100 patients with diabetes who underwent lithotripsy but did not develop UTIs, this indicator was on average 1.66±0.031 c.u. ($p<0.001$).

In the group of patients involved in the study who underwent lithotripsy and developed UTIs, the average body temperature of the group was 37.9±0.039°C, but the average body temperature of 10 diabetic patients who underwent lithotripsy and did not develop symptoms of UTIs was 36.7±0.017°C ($p<0.001$).

In 180 patients who underwent lithotripsy and subsequently developed UTIs, the ESR indicator was 21.2±0.082 mm/s, while in 100 people who did not develop UTIs after the operation, the corresponding indicator was significantly lower, 9.4±0.042 mm/s.

Our research conducted on the sensitivity of some microorganisms isolated from the urine of diabetic patients suffering from urinary tract infections to various antibiotics revealed that Staphylococci, E.coli type, P.aeruginosa, Klebsiella, and Proteus were resistant to the Ampiox drug. Nevertheless, Streptococci showed weak resistance to the Ampiox drug.

The reaction of microorganisms against Ampicillin was recorded to be similar to the case with the Ampiox drug. Only Streptococci showed low sensitivity to the drug.

E. coli species, P. aeruginosa, Kleibsella, and Proteidae showed resistance to oxacillin. The sensitivity of staphylococci to the drug was high. Streptococci showed moderate sensitivity.

During the studies conducted to determine the sensitivities of various microorganisms isolated from urine samples to Lincomycin, the sensitivities of staphylococci to the corresponding drug were found to be high. The same situation was observed with Streptococci. E.coli species, P.aeruginosa, Kleibsella, and Proteus showed resistance to Lincomycin (Table 2).

Table 2.

Indicators of susceptibility of some microorganisms obtained from the urine of diabetic patients suffering from urinary tract infections to different antibiotics

Antibiotics	Microorganims					
	Staphylo coccus	Strepto coccus	E.coli	P.aerugi-nosa	Klebsiel la	Prote us
Ampiox	t	l/s	t	t	t	t
Ampicillin	t	l/s	t	t	t	t
Oxacillin	h/s	m/s	t	t	t	t
Lincomycin	h/s	h/s	t	t	t	t
Gentamicin	h/s	h/s	h/s	h/s	m/s	h/s
Streptomycin	h/s	h/s	t	t	t	t
Azithromycin	t	t	l/s	t	t	m/s
Erythromycin	h/s	m/s	t	t	l/s	t
Kanamycin	l/s	l/s	m/s	t	t	t
Chloramphenicol	m/s	l/s	h/s	t	m/s	m/s
Sulfamethaxazole-trimethoprim	m/s	h/s	m/s	t	t	m/s
Ciprofloxacin	m/s	m/s	m/s	l/s	m/s	l/s
Polymixin	l/s	l/s	h/s	t	m/s	l/s
Norfloxacin	h/s	h/s	t	t	t	t
Amikacin	t	t	t	h/s	t	t
Neomycin	t	t	t	t	t	l/s
Cephalothin	t	t	t	t	m/s	m/s
Cephalexin	m/s	h/s	h/s	l/s	m/s	h/s
Cefotaxime	m/s	m/s	h/s	l/s	m/s	h/s

Note: h/s-high sensitivity to antibiotics, m/s- moderate sensitivity to antibiotics, "z/h", l/s-low sensitivity to antibiotics, "t"-tolerant to antibiotics

Gentamicin was the most successful drug in terms of the sensitivity of microorganisms in the research conducted in this direction. Thus, the sensitivity of Staphylococci, Streptococci, E.coli,

P.aeruginosa, and Proteus to this preparation was high. Only Klebsiella showed moderate sensitivity to this drug.

While the sensitivity of isolated staphylococci and streptococci to Streptomycin is high in the nutrient environment, E.coli, P.aeruginosa, and Proteidae showed resistance to this drug.

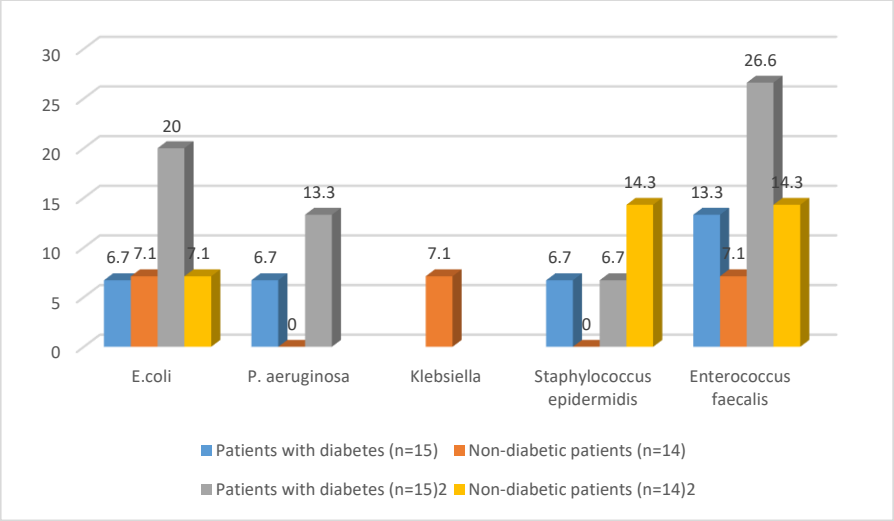
The results of the study showed that the P. aerruginosa microorganism was the most resistant to antibiotics such as Ampiox, Ampicillin, Oxacillin, Lincomycin, Gentamicin, Streptomycin, Azithromycin, Erythromycin, Kanamycin, Chloramphenicol, Sulfamethoxazole-trimethoprim, Ciprofloxacin, Polymyxin, Norfloxacin, Amikacin, Neomycin, Cephalothin, Cephalexin, and Cefotaxime. Gentamicin, Cephalexin, and Cefotaxime were the broadest spectrum antibiotics that could affect all of the mentioned microorganisms to some extent.

Antibiotic susceptibility indicators were again determined in urine samples obtained from diabetic patients after treatment of urinary tract infections. For this purpose, the sensitivities of the microorganisms obtained from the urine samples taken after 1 week from the diabetic patients, whose UTI complications were eliminated, to various antibiotic preparations were determined. Staphylococcus species showed resistance to the Telithromycin preparation. This trend was also recorded for genera and species of P.aeruginosa, Klebsiella, and Streptococcus. They also showed resistance to the corresponding drug. Nevertheless, the E.coli species showed weak sensitivity to the mentioned preparation. Proteus species showed moderate sensitivity to the respective microorganism (Graph 1).

Of the same number of urine samples obtained from 27 diabetic patients recruited for this phase of the study, 22 were sensitive to Rifampicin, which means 81.5% of patient samples. The same result was observed during the study of sensitivities of the relevant microorganism colonies to Erythromycin. A similar trend continued when determining the sensitivity of bifidobacteria to drugs such as Lincomycin and Vancomycin. Nevertheless, during the study of the sensitivity of bifidobacteria isolates from urine cultures of diabetic patients, all samples showed sensitivity to the Cefazolin drug. The

same result was observed during the determination of sensitivity indicators of bifidobacteria against antibacterial drugs such as Cefalotin, Fusidin, Cefaclor, and Cefuroxime.

As a result of our research on the effects of diabetes on the microflora of urine before and after the lithotripsy operation, E.coli species was found in 1 sample (6.7±6.44%) in the urine samples taken from 15 diabetic patients before the lithotripsy operation. E.coli species was found in 1 (7.1±6.88%) urine sample. In 14 non-diabetic patients, E.coli was found in 1 sample (7.1±6.88%). Proteus representatives were found in 1 (7.1±6.88%) sample. In patients of this group, after the lithotripsy operation, this microorganism was found in 2 (14.3±9.35%) samples of stagnant urine.



Graph 2. Urine microflora parameters for diabetes before and after lithotripsy surgery

P.aeruginosa species was found in only 1 (6.7±6.44%) of urine samples taken from patients with diabetes and kidney stones. One (7.1±6.88%) representative of Klebsiella was found in the biological material. Staphylococcus epidermidis was in 1 (6.7±6.44%) sample. S. epidermidis species was detected in 2 samples (14.3±9.35%) of

non-diabetic patients. Staphylococcus saprophyticus was observed in one (6.7±6.44%) sample. Staphylococcus saprophyticus was also found in 1 (7.1±6.88%) sample of non-diabetic patients.

No enterococci were found in the biological samples taken before surgery from 14 patients without diabetes and suffering from kidney stones, as a result of which lithotripsy was planned. Enterococcus faecalis species was found in 2 of 15 patients with diabetes and kidney stone disease who underwent lithotripsy. The occurrence of the corresponding microorganism in the group was in 2 (13.3±8.78%) of the urine samples taken from the patients immediately after lithotripsy. Candida albicans was not found in biological samples.

Association of at least 4 of the microorganisms studied was found in 2 (13.3±8.78%) of the materials taken before the surgical operation from the group of 15 patients with both diabetes and kidney stones. The same result was obtained in "stagnant" urine samples taken from the patients after lithotripsy.

Thus, it was found that in the case of diabetes, there are relatively more pathogens of URIs compared to the non-diabetic group. This is due to the fact that the pathogenic microflora becomes more active and rich in diabetes. In order to stop the development of various infectious-purulent processes of the urinary tract after lithotripsy for kidney stones in patients with diabetes, it is necessary to determine the sensitivity to antibiotics for effective selective antibiotic therapy. Infectious complications after lithotripsy for kidney stones are mainly observed in patients with diabetes mellitus who underwent emergency surgery.

CONCLUSIONS

1. E.coli, K.pneumoniae, E.cloacae, E.faecalis bacteria were significantly more common in urine samples obtained from patients without kidney stones and with diabetes and urinary tract infections compared to samples of the patients having only urinary tract infections.

2. E.coli and K.pneumoniae bacteria were significantly more common in urine samples obtained from patients with kidney stone disease, diabetes and urinary tract infections compared to the samples of the patients without kidney stone disease and diabetes, who had only urinary tract infections.

3. Bacteria obtained from patients with kidney stone disease, diabetes, and urinary tract infections are mainly sensitive to Amoxicillin, Azithromycin, Gentamicin, Doxycycline, Cefotaxime and Ceftriaxone.

4. The resistance of the bacteria obtained before and after the lithotripsy operation to antibiotics such as Oxacillin, Sulfamethoxazole-trimethoprim, and Ciprofloxacin was determined in patients with diabetes and kidney stone disease.

5. E.coli, Proteus spp., P.aeruginosa, Klebsiella spp., S.aureus and S.epidermidis prevail in the etiological structure of urinary tract infectious complications after lithotripsy surgery in diabetic patients.

6. After the lithotripsy operation for kidney stones and anti-UTI treatment measures, there was a decrease in all parameters of intoxication indicators - body temperature, erythrocyte sedimentation rate, and leukocyte index of intoxication.

PRACTICAL RECOMMENDATIONS

1. When urinary tract infections develop in diabetic patients, microbiological analyses should be performed as soon as possible and treatment should be organized against the main pathogens.

2. In connection with the treatment tactics of UTIs developed in diabetic patients, sensitivity to various microorganisms isolated from biological samples of the patients should be determined before wide-spectrum antibiotics are applied, and the main treatment should be carried out according to these results.

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LIST OF ABBREVIATIONS

ESR-erythrocyte sedimentation rate
LII – leukocyte index of intoxication
UTIs– urinary tract infections
DM – diabetes mellitus

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