

## Microbiological Aspects of Antibiotic Resistance in Patients with Urolithiasis and Combined Injuries.

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### ABSTRACT

The aim of the study was to study the microbiological features and the level of antibiotic resistance in patients with urolithiasis on the background of combined traumatic injuries.

**Materials and methods.** A clinical and microbiological study of 126 patients with urolithiasis was conducted, of which 78 patients had combined injuries. Clinical, laboratory, instrumental and microbiological studies were performed. The identification of microorganisms was carried out by bacteriological and molecular genetic methods with determination of sensitivity to antibacterial drugs and assessment of the ability to biofilm formation.

**Results.** Severe infectious and inflammatory complications of the urinary tract prevailed in patients with combined injuries. The structure of pathogens was dominated by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa*. A high level of antibiotic resistance to third-generation cephalosporins and fluoroquinolones was revealed. A significant prevalence of extended-spectrum beta-lactamases and carbapenem-resistant strains has been established. More than 68% of clinical isolates had a pronounced ability to biofilm formation. Patients in the main group were significantly more likely to develop urosepsis, septic shock, and other severe complications.

**Conclusion.** The combination of urolithiasis and severe trauma is accompanied by a high prevalence of polyresistant hospital microflora and a severe course of infectious complications. The results obtained confirm the need for continuous microbiological monitoring, rational antibacterial therapy and the introduction of antimicrobial control programs..

**Keywords:** urolithiasis, antibiotic resistance, urinary tract infections, combined trauma, polyresistant microorganisms, biofilms, urosepsis.

### INTRODUCTION

Urolithiasis (urolithiasis) is one of the most common urological diseases characterized by the formation of calculi in the kidneys and urinary tract, a tendency to recurrent course and a high incidence of infectious and inflammatory complications. In recent decades, the problem of ICD has acquired not only clinical, but also pronounced socio-economic significance due to a steady increase in morbidity, an increase in the number of patients of working age, frequent hospitalizations and the need for expensive surgical interventions. According to various epidemiological studies, the prevalence of urolithiasis in the world ranges from 5 to 15%, while in a number of industrialized countries there is a tendency for a further increase in the incidence. This pathology occupies one of the leading places among diseases of the urinary system and is characterized by significant variability in clinical manifestations, a high frequency of relapses and a close relationship with infectious complications. [1]

The problem of ICD becomes particularly relevant in patients with combined injuries. Combined trauma is a severe pathological condition accompanied by damage to several anatomical regions and body systems, the development of a pronounced stress response, multiple organ disorders and immunological disorders. This category of patients has a significantly increased risk of infectious complications due to prolonged hospital stay, the need for invasive diagnostic and

therapeutic procedures, urinary tract catheterization, artificial lung ventilation, massive antibacterial therapy and impaired immune reactivity of the body. The presence of urolithiasis in patients with combined trauma worsens the course of the underlying disease, promotes the development of urinary tract obstruction, impaired urodynamics, the formation of foci of chronic infection and creates favorable conditions for colonization of the urinary tract by polyresistant microflora.

In modern clinical practice, one of the most serious problems is the antibiotic resistance of microorganisms that cause urinary tract infections in patients with ICD. Given the widespread and often unjustified use of antibacterial drugs, there is a rapid spread of resistant bacterial strains with multiple mechanisms of resistance. This trend poses a serious threat to the healthcare system, as it leads to a decrease in the effectiveness of standard antibiotic therapy regimens, an increase in the duration of treatment, an increase in the incidence of complications and mortality. The situation is particularly unfavorable in patients of intensive care units and trauma hospitals, where resistant hospital strains of microorganisms are formed.

Infectious and inflammatory complications of urolithiasis occupy an important place in the structure of urological pathology. Violation of the outflow of urine, traumatization of the mucous membrane of the urinary tract with concretions, ischemic tissue changes and the presence of biofilms create optimal conditions for the adhesion and persistence of microorganisms. The most common causative agents of urinary tract infections in ICD are gram-negative bacteria of the Enterobacteriaceae family, primarily *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterobacter* spp., as well as non-fermenting gram-negative microorganisms, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Gram-positive microorganisms such as *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus* and coagulase-negative staphylococci also play a significant role. [2]

The microbial spectrum of infections in patients with ICD is highly variable and depends on many factors, including the patient's age, the presence of concomitant diseases, the duration of the disease, the features of previous antibacterial therapy, the nature of urological interventions and the conditions of inpatient treatment. In patients with combined injuries, the microbiological profile becomes even more complicated due to prolonged stay in intensive care units, widespread use of reserve antibiotics, and a high probability of nosocomial infection. In these conditions, the importance of hospital microflora, characterized by multidrug resistance and the ability to form biofilms, increases. One of the key factors in the pathogenesis of infectious complications in urolithiasis is the ability of microorganisms to form biofilms on the surface of calculi, urinary catheters and the mucous membrane of the urinary tract. A biofilm is a complex organized structure consisting of microbial cells surrounded by an extracellular polymer matrix. The formation of biofilms significantly increases the resistance of microorganisms to the action of antibacterial drugs and immune defense factors of the body. Microorganisms contained in biofilms can exhibit antibiotic resistance exceeding the sensitivity of planktonic forms by tens and hundreds of times. This causes a chronic recurrent course of the infectious process and significantly complicates effective therapy. Of particular importance in the development of urolithiasis are urease-producing microorganisms, primarily *Proteus mirabilis*, *Klebsiella* spp., *Pseudomonas* spp. and some types of staphylococcus. The production of urease leads to the breakdown of urea to form ammonia, an increase in the pH of urine and the formation of struvite nodules. Infectious stones are not only a consequence of microbial colonization, but also an independent reservoir of infection that supports chronic inflammation and bacterial persistence. In patients with combined injuries, metabolic disorders, physical inactivity, prolonged immobilization, and changes in water and electrolyte balance additionally contribute to stone formation and the chronization of the infectious process. [3]

Antibiotic resistance of microorganisms in urinary tract infections is formed under the influence of various mechanisms, including the production of extended-spectrum beta-lactamases (BLRS), carbapenemases, changes in cell wall permeability, active efflux of antibiotics, and mutations of drug targets. In recent years, the spread of carbapenem-resistant strains of Enterobacterales, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), as well as the multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* has been of particular concern. The presence of such microorganisms significantly limits the possibilities of etiotropic therapy and requires the use of reserve drugs with high toxicity and cost. Patients with combined injuries are at high risk of developing nosocomial infections and colonization by resistant microflora. The severity of the condition, the need for surgical interventions, massive infusion therapy, the use of invasive devices, and immunosuppression create conditions for the activation of opportunistic microflora and the formation of stable microbial associations. In this category of patients, urinary tract infections are often severe, accompanied by bacteremia, sepsis, and multiple organ failure. In the presence of urolithiasis, the risk of such complications increases significantly due to urinary tract obstruction and impaired urinary passage. An important feature of modern antibiotic resistance is the ability of microorganisms to horizontally transfer resistance genes. Plasmids, transposons, and integrons ensure the rapid spread of resistance genes among various bacterial species, which contributes to the formation of polyresistant microbial communities. In hospital settings, especially intensive care units, there is an active circulation of resistant strains capable of causing outbreaks of nosocomial infections. The presence of chronic foci of infection in ICD contributes to the long-term persistence of such microorganisms and increases the likelihood of their further spread. [4]

Despite a significant number of studies on antibiotic resistance in urinary tract infections, the problem of microbiological features in patients with urolithiasis and combined injuries remains insufficiently studied. The available data are often fragmentary and do not reflect the full picture of the interaction between the pathogens of infection, the mechanisms of resistance and the clinical features of this category of patients. The lack of unified approaches to microbiological monitoring

and rational antibacterial therapy makes it difficult to develop effective methods for the prevention and treatment of infectious complications. [5]

Modern approaches to the diagnosis of urinary tract infections include the use of both traditional bacteriological methods and molecular genetic technologies that identify microorganisms and determine antibiotic resistance genes. The use of polymerase chain reaction, next-generation sequencing, and mass spectrometry significantly expands the possibilities of clinical microbiology and allows for a more accurate assessment of the structure of the microbial landscape. However, in real clinical practice, these methods are used to a limited extent, especially in urological and trauma hospitals. [6]

The irrational use of antibacterial drugs plays an important role in the development of antibiotic resistance. The empirical administration of broad-spectrum antibiotics without taking into account local data on the sensitivity of microorganisms contributes to the selection of resistant strains. An additional factor is the insufficient duration of microbiological monitoring and the lack of control over the effectiveness of antibacterial therapy. In patients with ICD and combined injuries, this problem becomes particularly important due to the severity of the condition and the need to start treatment immediately. [7] It should be noted that infectious complications in patients with urolithiasis can develop both before surgery and in the postoperative period. Endoscopic treatments, including contact ureterolithotripsy, percutaneous nephrolithotomy, and stent placement, are associated with the risk of bacterial translocation and generalization of infection. The presence of resistant microflora increases the likelihood of postoperative complications, including urosepsis and septic shock. Therefore, the study of microbiological features and mechanisms of antibiotic resistance is important for improving the safety of urological interventions. [8]

A particular problem is the formation of associations of microorganisms with synergistic mechanisms of pathogenicity and resistance. Polymicrobial infections are often detected in patients with long-term stones, chronic pyelonephritis, and repeated hospitalizations. The interaction of different bacterial species in biofilms enhances their virulence and increases antibiotic resistance. In conditions of combined trauma, such microbial associations can become a source of generalized infection and septic complications. [9]

The study of regional characteristics of antibiotic resistance is an important area of modern clinical microbiology. The structure of pathogens and the level of their sensitivity to antibacterial drugs can vary significantly depending on the geographical region, the profile of the hospital and the characteristics of the applied antibacterial therapy. Local microbiological monitoring makes it possible to optimize empirical therapy regimens and reduce the risk of ineffective treatment. For patients with urolithiasis and combined injuries, such studies are of particular practical importance.

In recent years, much attention has been paid to the concept of antimicrobial stewardship, aimed at the rational use of antibiotics and preventing the further spread of resistance. The implementation of antibacterial therapy control programs includes optimizing drug selection, dosage, duration of treatment, and microbiological support. In urological and traumatology departments, the introduction of such programs helps to reduce the frequency of infectious complications and reduce the prevalence of polyresistant microflora. [10]

Thus, the problem of antibiotic resistance in patients with urolithiasis and combined injuries is extremely relevant and multifactorial. The high prevalence of infectious and inflammatory complications, the growing number of resistant strains of microorganisms, the difficulty in choosing effective antibacterial therapy and the risk of severe septic conditions determine the need for further study of the microbiological aspects of this pathology. The study of the structure of pathogens, mechanisms of resistance and factors contributing to the formation of a stable microflora will allow us to develop more effective approaches to the diagnosis, prevention and treatment of infectious complications in this category of patients. [11]

## METHODS

The study was performed to study the microbiological features and mechanisms of antibiotic resistance in patients with urolithiasis complicated by urinary tract infections, against the background of combined traumatic injuries. The work was carried out on the basis of the urological and traumatology departments of the multidisciplinary hospital in the period from 2021 to 2025.

### Research design

An open clinical and laboratory study was conducted, which included retrospective and prospective stages. The study was comparative in nature and included the analysis of clinical, microbiological and laboratory data of patients with urolithiasis and combined injuries.

All the examined people were divided into two groups:

- \* the main group consists of patients with urolithiasis and combined trauma complicated by infectious and inflammatory diseases of the urinary tract;
- \* the comparison group consisted of patients with urolithiasis without combined injury.

Characteristics of the examined patients

The study included 126 patients undergoing inpatient treatment. Of these, 78 patients made up the main group and 48 patients — the comparison group.

The age of the patients ranged from 18 to 74 years. The average age of the examined persons was  $46.8 \pm 12.4$  years. Men predominated among the patients, which is due to the higher prevalence of combined injuries and urolithiasis among men of working age.

Patients in the main group were most often diagnosed with:

- \* fractures of the pelvic bones;
- \* combined chest injuries;
- \* traumatic brain injuries;
- \* abdominal injuries;
- \* multiple fractures of long tubular bones.

The severity of traumatic injuries was assessed on the Injury Severity Score (ISS) scale. The average ISS index in patients of the main group was  $24.6 \pm 6.8$  points.

Criteria for inclusion in the study

The inclusion criteria were:

- \* the presence of confirmed urolithiasis;
- \* over the age of 18;
- \* signs of urinary tract infection;
- \* the presence of a combined injury;
- \* inpatient treatment in a specialized department;
- \* informed consent to participate in the study.

Exclusion criteria

Patients were excluded from the study:

- \* with end-stage chronic renal failure;
- \* with oncological diseases of the urinary system;
- \* with severe congenital immunodeficiency;
- \* with HIV infection in the stage of severe immunodeficiency;
- \* with the absence of microbiological examination results;
- \* those who refused to participate in the study.

Clinical research methods

All patients underwent a comprehensive clinical examination, which included:

- \* collection of complaints and medical history;
- \* physical examination;
- \* assessment of urological status;
- \* assessment of the severity of the general condition;
- \* analysis of the duration of the disease;
- \* analysis of previous antibacterial therapy;
- \* assessment of the availability of urological interventions.

Special attention was paid to the presence of risk factors for the development of antibiotic resistance:

- \* prolonged catheterization of the bladder;
- \* nephrostomy;
- \* repeated hospitalizations;

- \* Previous antibiotic use;
- \* stay in the intensive care unit;
- \* the presence of chronic foci of infection.

#### Laboratory research methods

The laboratory examination included:

- \* general blood test;
- \* general urinalysis;
- \* biochemical blood analysis;
- \* determination of creatinine levels;
- \* determination of urea level;
- \* determination of glomerular filtration rate;
- \* determination of the level of C-reactive protein;
- \* the study of procalcitonin.

The total blood count was evaluated:

- \* White blood cell count;
- \* neutrophil index;
- \* Erythrocyte sedimentation rate;
- \* Hemoglobin levels.

The general urinalysis took into account:

- \* leukocyturia;
- \* bacteriuria;
- \* proteinuria;
- \* microhematuria;
- \* urine pH level.

#### Instrumental research methods

To confirm urolithiasis and assess the condition of the urinary tract, the following methods were used:

- \* ultrasound examination of the kidneys;
- \* overview urography;
- \* multispiral computed tomography;
- \* excretory urography;
- \* Computed tomography of the urinary system organs.

Evaluated:

- \* localization of concretions;
- \* the size of the stones;
- \* the presence of hydronephrosis;
- \* the degree of urodynamic disorder;
- \* signs of inflammatory changes.

The following methods were used to diagnose combined injuries::

- \* Radiography;
- \* Computed tomography;
- \* Magnetic resonance imaging;

\* Ultrasound examination of abdominal organs.

Microbiological research methods

The material for microbiological research was:

- \* average portion of morning urine;
- \* urine from the catheter;
- \* urine from a nephrostomy;
- \* blood in case of suspected sepsis;
- \* Wound discharge.

The material was collected before the start of antibacterial therapy or 48-72 hours after the withdrawal of antibiotics.

Urine culture was performed by the quantitative method on the following nutrient media:

- \* blood agar;
- \* Agar McConkey;
- \* chromogenic media.

Incubation was carried out at 37 °C for 24-48 hours.

Identification of microorganisms was carried out using:

- \* Morphological methods;
- \* Biochemical tests;
- \* VITEK 2 Compact automatic microbiological analyzer;
- \* MALDI-TOF mass spectrometry.

The growth of microorganisms  $\geq 10^5$  CFU/ml was considered to be diagnostically significant.

Determination of antibiotic sensitivity

The sensitivity of the isolated microorganisms to antibacterial drugs was determined by the disco-diffusion method on Muller–Hinton agar in accordance with the recommendations of EUCAST.

Sensitivity to the following groups of drugs was studied:

- \* penicillins;
- \* Inhibitor-protected beta-lactams;
- \* cephalosporins of the III–IV generations;
- \* carbapenems;
- \* aminoglycosides;
- \* Fluoroquinolones;
- \* nitrofurans;
- \* Glycopeptides;
- \* polymyxins.

To identify the mechanisms of stability, we carried out:

- \* Extended-spectrum beta-lactamase production test;
- \* Carbapenemase test;
- \* MRSA detection;
- \* detection of vancomycin-resistant enterococci.

Biofilm formation research

The ability of clinical isolates to form biofilms was evaluated using microtiter plates.

The microorganisms were cultured in wells of polystyrene tablets for 24 hours, followed by staining with crystalline purple. After removing the unbound dye, the optical density was measured by spectrophotometric method.

According to the intensity of biofilm formation, the strains were divided into:

- \* weak;
- \* moderate;
- \* Pronounced biofilm-forming agents.

Molecular genetic methods

The polymerase chain reaction method was used to identify antibiotic resistance genes in a number of clinical isolates.

The following genes were identified:

- \* blaTEM;
- \* blaSHV;
- \* blaCTX-M;
- \* blaNDM;
- \* mecA;
- \* vanA;
- \* vanB.

Amplification was performed using standard test systems according to the manufacturer's protocols.

Evaluation of treatment effectiveness

The effectiveness of the therapy was assessed according to the following criteria:

- \* elimination of clinical manifestations of infection;
- \* normalization of body temperature;
- \* reducing the level of inflammatory markers;
- \* eradication of the pathogen;
- \* reducing the duration of hospitalization;
- \* no recurrence of infection.

Additionally analyzed:

- \* the incidence of urosepsis;
- \* length of stay in the intensive care unit;
- \* the need for repeated interventions;
- \* Lethality.

Statistical processing of results

Statistical data processing was performed using the Statistica 13.0 and SPSS 26.0 programs.

Quantitative indicators are presented as an arithmetic mean and a standard deviation ( $M \pm SD$ ). To assess the reliability of the differences, we used:

- \* Student's t-test;
- \* The Mann–Whitney criterion;
- \*  $\chi^2$  Pearson;
- \* Fischer's exact criterion.

The differences were considered statistically significant at  $p < 0.05$

## RESULTS

The study analyzed clinical, microbiological and laboratory parameters in 126 patients with urolithiasis. The main group consisted of 78 patients with urolithiasis on the background of combined traumatic injuries, the comparison group consisted of 48 patients with urolithiasis without combined injury.

The analysis of the age-sex structure showed the predominance of men in both groups. In the main group, men made up

67.9%, women — 32.1%, while in the comparison group, men made up 60.4%, women — 39.6%. The average age of patients in the main group was  $45.9 \pm 11.8$  years, the comparison group —  $48.2 \pm 13.1$  years.

The most frequent localization of concretions were:

- \* kidney stones — in 58.7 % of patients;
- \* ureteral stones — in 29.4 %;
- \* Multiple concretions occurred in 11.9% of the examined patients.

In the main group of patients, signs of urodynamic disorders and urinary tract obstruction were significantly more common. Hydronephrosis of varying severity was diagnosed in 61.5% of patients in the main group and in 35.4% of patients in the comparison group ( $p < 0.05$ ).

The most common cases among patients with combined trauma were:

- \* fractures of the pelvic bones — 41.0 %;
- \* combined traumatic brain injury - 37.2 %;
- \* chest injuries — 33.3 %;
- \* abdominal injuries — 26.9 %;
- \* multiple fractures of long tubular bones — 48.7%.

The average severity of the injury on the ISS scale was  $24.6 \pm 6.8$  points, which corresponded to a severe combined injury.

When analyzing the risk factors for the development of infectious complications, it was found that patients in the main group were significantly more likely to:

- \* prolonged catheterization of the bladder — 74.4 %;
- \* stay in the intensive care unit for more than 5 days — 62.8 %;
- \* previous antibacterial therapy — 83.3 %;
- \* repeated invasive urological interventions — 39.7 %;
- \* nephrostomy — 28.2% of cases.

The clinical picture of urinary tract infections was characterized by pronounced inflammatory manifestations. Patients in the main group were significantly more likely to have:

- \* febrile body temperature;
- \* severe pain syndrome;
- \* macrohematuria;
- \* signs of a systemic inflammatory reaction;
- \* episodes of hypotension.

Leukocytosis was detected in 82.1% of patients in the main group and in 58.3% of patients in the comparison group ( $p < 0.05$ ). The average level of C-reactive protein in the main group was  $96.4 \pm 24.8$  mg/l, which significantly exceeded the values of the comparison group —  $48.7 \pm 18.3$  mg/l ( $p < 0.01$ ).

According to the results of a microbiological study, positive growth of microorganisms was detected in 89.7% of patients in the main group and in 72.9% of patients in the comparison group.

The following microorganisms were most frequently isolated:

- \* Escherichia coli — 34,6 %;
- \* Klebsiella pneumoniae — 21,8 %;
- \* Proteus mirabilis — 14,1 %;
- \* Pseudomonas aeruginosa — 11,5 %;
- \* Enterococcus faecalis — 9,0 %;
- \* Acinetobacter baumannii — 5,1 %;
- \* Staphylococcus aureus — 3,9 %.

In patients with combined trauma, there was an increase in the proportion of hospital strains of Pseudomonas aeruginosa and

*Acinetobacter baumannii* compared with the comparison group.

Polymicrobial associations were detected in 29.5% of patients in the main group and only in 10.4% of patients in the comparison group ( $p < 0.05$ ). Combinations were most often identified:

- \* *Klebsiella pneumoniae* + *Enterococcus faecalis*;
- \* *Pseudomonas aeruginosa* + *Acinetobacter baumannii*;
- \* *Escherichia coli* + *Proteus mirabilis*.

The study of antibiotic sensitivity demonstrated a high level of resistance of clinical isolates to widely used antibacterial drugs.

Among gram-negative microorganisms, high resistance to:

- \* ampicillin — 82.6 %;
- \* ceftriaxone — 61.3 %;
- \* ciprofloxacin — 58.7%;
- \* levofloxacin — 54.8%.

The highest sensitivity remained to:

- \* carbapenems;
- \* colistin;
- \* amikacin.

Extended-spectrum beta-lactamase production was detected in 46.1% of Enterobacterales strains. The most commonly BLRS-producing strains were identified among *Klebsiella pneumoniae* and *Escherichia coli*.

Carbapenem-resistant strains have been identified in:

- \* 18,2 % *Pseudomonas aeruginosa*;
- \* 27,3 % *Acinetobacter baumannii*;
- \* 9,5 % *Klebsiella pneumoniae*.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected in 40.0% of the isolated staphylococcal strains.

Vancomycin-resistant enterococci were found in 11.1% of *Enterococcus faecium* strains.

The following antibiotic resistance genes were most often identified in molecular genetic research:

- \* blaCTX-M — in 38.5 % of isolates;
- \* blaTEM — at 30.8 %;
- \* blaSHV — at 26.9 %;
- \* blaNDM — y 7.7 %;
- \* mecA — in 40.0 % of staphylococcal strains;
- \* vanA — in 11.1% of enterococci.

A study of the ability of microorganisms to biofilm formation showed that 68.4% of the isolated strains had a pronounced ability to form biofilms.

The most pronounced biofilm formation was observed in:

- \* *Pseudomonas aeruginosa*;
- \* *Klebsiella pneumoniae*;
- \* *Acinetobacter baumannii*;
- \* *Enterococcus faecalis*.

A statistically significant relationship has been established between the ability to biofilm formation and the level of antibiotic resistance ( $r=0.72$ ;  $p < 0.01$ ).

Patients in the main group were significantly more likely to develop severe infectious complications:

- \* acute obstructive pyelonephritis — 43.6 %;

\* urosepsis — 19.2 %;

\* Septic shock — 7.7%.

In the comparison group, urosepsis was diagnosed in only 4.2% of patients ( $p < 0.05$ ).

The average duration of hospitalization in patients of the main group was  $21.4 \pm 6.2$  days, which significantly exceeded the same indicator in the comparison group —  $12.7 \pm 4.3$  days ( $p < 0.01$ ).

The need for repeated surgical interventions was noted in 23.1% of patients with combined trauma, mainly due to the progression of the infectious and inflammatory process and impaired drainage of the urinary tract.

The mortality rate in the main group was 8.9%, while no deaths were recorded in the comparison group.

Thus, the results of the study indicate a high prevalence of antibiotic-resistant microorganisms in patients with urolithiasis on the background of combined injuries. In this category of patients, hospital-acquired polyresistant strains with a pronounced ability to biofilm formation and associated with severe infectious and inflammatory complications prevailed. The data obtained confirm the need for constant microbiological monitoring, rational antibacterial therapy and the development of individualized approaches to the treatment of patients in this group.

## DISCUSSION

The results of the study indicate the high clinical and microbiological significance of the problem of antibiotic resistance in patients with urolithiasis on the background of combined traumatic injuries. The analysis showed that the presence of a combined injury significantly worsens the course of infectious and inflammatory complications of the urinary tract, promotes colonization of the urotractum by hospital polyresistant microflora and is associated with an increased risk of severe septic conditions.

One of the key results of the study was the predominance of gram-negative microflora in the structure of pathogens of urinary tract infections. *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* were the most frequently isolated, which corresponds to the data of most modern studies on infectious complications of urolithiasis. However, in patients with concomitant trauma, there was a significant increase in the proportion of nosocomial microorganisms, primarily *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, characterized by a high level of multidrug resistance.

The revealed predominance of hospital strains in patients of the main group is probably due to prolonged stay in intensive care units, the need for invasive interventions, urinary tract catheterization, and the widespread use of broad-spectrum antibacterial drugs. These factors create favorable conditions for the breeding of stable microflora and the formation of stable microbial associations. The results obtained are consistent with the current understanding that patients with severe concomitant trauma are at high risk of developing nosocomial infections and colonization by multidrug-resistant microorganisms.

Special attention should be paid to the high frequency of polymicrobial associations detected in patients of the main group. The presence of combined microbial communities can significantly complicate the course of the infectious process, increase the virulence of microorganisms and reduce the effectiveness of antibacterial therapy. The formation of microbial associations is especially typical for chronic urinary tract infections and patients with prolonged urotractal obstruction. In urolithiasis, the presence of calculi creates an additional substrate for the adhesion of microorganisms and the formation of biofilms, which contributes to the long-term persistence of pathogens.

The results of the study demonstrated a high level of antibiotic resistance among the selected clinical strains. The most pronounced resistance was observed to ampicillin, third-generation cephalosporins, and fluoroquinolones. This trend reflects the global problem of reducing the effectiveness of traditionally used drugs for the treatment of urinary tract infections. Of particular concern is the high prevalence of extended-spectrum  $\beta$ -lactamases among Enterobacterales, primarily in *Klebsiella pneumoniae* and *Escherichia coli*.

The presence of BLRS-producing strains significantly limits the possibilities of empirical antibacterial therapy and requires the use of reserve drugs. It should be noted that the revealed frequency of BLRS-producers in this study was higher in patients with concomitant trauma, which is probably due to the more intensive use of antibiotics in intensive care units. The data obtained confirm the need for constant local monitoring of antibiotic resistance and revision of existing empirical therapy regimens in this category of patients.

Of particular importance is the identification of carbapenem-resistant strains of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*. The spread of carbapenemase-producing microorganisms poses a serious threat to modern clinical practice, as it significantly limits therapeutic possibilities and is associated with high mortality. The detection of bla<sub>NDM</sub> genes in some clinical isolates indicates the circulation of highly resistant strains and confirms the need to strengthen infection control in the hospital.

## CONCLUSIONS

1. Patients with urolithiasis with combined traumatic injuries have a high incidence of infectious and inflammatory complications of the urinary tract, characterized by a severe clinical course and a high risk of developing urosepsis.
2. Gram-negative microorganisms prevailed in the structure of pathogens of urinary tract infections, among which *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* were most often detected. Hospital-acquired polyresistant strains were significantly more common in patients with combined injuries.
3. Patients in the main group were characterized by a high prevalence of antibiotic resistance to widely used antibacterial drugs, including third-generation cephalosporins and fluoroquinolones. A significant part of the clinical isolates had the ability to produce extended-spectrum beta-lactamases and carbapenemases.
4. A high frequency of biofilm formation in clinical strains of microorganisms was revealed, which was associated with an increase in the level of antibiotic resistance, chronization of the infectious process and a decrease in the effectiveness of antibacterial therapy.
5. The presence of combined trauma, prolonged urinary tract catheterization, intensive care unit stay, and repeated invasive interventions are significant risk factors for colonization of the urinary tract by a multi-resistant hospital microflora.
6. Patients with urolithiasis and combined injuries were characterized by a higher incidence of severe complications, increased duration of hospitalization, the need for repeated surgical interventions, and a higher mortality rate compared with patients without combined injury.
7. The results obtained confirm the need for regular microbiological monitoring, early diagnosis of antibiotic resistance and individualized selection of antibacterial therapy in patients with urolithiasis on the background of combined traumatic injuries.
8. To increase the effectiveness of treatment and prevention of the spread of antibiotic-resistant strains, it is advisable to introduce antimicrobial stewardship programs, the rational use of antibacterial drugs and a comprehensive interdisciplinary approach to the management of this category of patients

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