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SPECTRUM OF PATHOGENS AND THEIR ANTIMICROBIAL RESISTANCE IN CYSTITIS, PYELONEPHRITIS, AND PROSTATITIS

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Introduction. Infectious and inflammatory diseases of the genitourinary tract account for approximately 42% of all outpatient urology cases, and disorders such as cystitis, pyelonephritis, and prostatitis are often characterized by a chronic, recurrent course. One of the key contributors to recurrent urinary tract infections is inappropriate therapy that does not take into account the local microbial spectrum and pathogen resistance profiles.

Aim. To determine the spectrum of uropathogens and their antimicrobial resistance patterns in patients with cystitis, pyelonephritis, and prostatitis.

Materials and methods. We analyzed the results of microbiological urine cultures from outpatient urology patients processed by the Invitro Laboratory between 2022 and 2024. In total, 4031 bacterial isolates were included: 2903 (72.0%) from patients with cystitis, 1017 (25.2%) from patients with pyelonephritis, and 111 (2.8%) from patients with chronic prostatitis.

Results. The structure of the microbial landscape differed by diagnosis. E. coli was the predominant pathogen in all groups, with a detection rate of 73.8–75.3% in cystitis and pyelonephritis, while in chronic prostatitis the rate was markedly lower at 53.1%. Klebsiella pneumoniae and Enterococcus faecalis were more frequently isolated in prostatitis (19.0% and 15.3%, respectively) compared with urinary infections, where their combined frequency ranged from 6.9% to 11.9%. Other pathogens (Proteus mirabilis, Streptococcus agalactiae, Enterobacter cloacae, Pseudomonas aeruginosa) accounted for 6.4% of isolates in cystitis, 7.6% in pyelonephritis, and 12.6% in prostatitis.

Antimicrobial resistance was assessed for E.coli isolates. Resistance to amoxicillin/clavulanate was 24.9% in cystitis, 31.0% in pyelonephritis, and 38.9% in prostatitis. Levofloxacin resistance was observed in approximately one third of isolates from cystitis and in about half of isolates from pyelonephritis, whereas all E.coli isolates from prostatitis cases were susceptible. Resistance to trimethoprim-sulfamethoxazole in prostatitis was approximately twice as high as in cystitis and pyelonephritis.

Conclusion. Urinary tract infections are predominantly caused by E.coli, while chronic prostatitis is associated with a more diverse spectrum of pathogens, with E.coli detected in only 53.1% of cases. Antimicrobial resistance profiles differ substantially between urinary infections and prostatitis, underscoring the importance of tailoring empirical therapy to local pathogen distribution and resistance patterns.

K e y w o r d s: *bacteriuria, urinary tract infections, cystitis, pyelonephritis, prostatitis, antimicrobial resistance*

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Introduction. Urinary tract infections (UTIs) are the most common bacterial infections and affect at least one million people worldwide each year [1–4]. Among nosocomial infections, UTIs rank second only to upper respiratory tract infections, which account for 24% in developing countries [5]. UTIs have been shown to adversely affect mental health and quality of life [6].

Unfortunately, UTIs are associated with a high recurrence rate [1]. Women are at higher risk of developing UTIs than men; within six months, recurrence occurs in one in five women [7–8]. Chronic UTI increases the likelihood of gestational pyelonephritis [9]. Postmenopausal women are more prone to recurrent UTIs because lower estrogen levels lead to unfavorable changes in the urogenital epithelium and the urogenital microbiome [10].

UTIs are caused by a wide range of pathogens, including Gram-negative and Gram-positive bacteria, as well as fungi. Uropathogenic E. coli (UPEC) is the principal etiological agent of UTIs, accounting for about 75% of uncomplicated UTI cases; however, less common pathogens such as Klebsiella pneumoniae (K. pneumoniae), Staphylococcus saprophyticus (S. saprophyticus), Enterococcus faecalis (E. faecalis), group B Streptococcus (GBS), Proteus mirabilis (P. mirabilis), Pseudomonas aeruginosa (P. aeruginosa), Staphylococcus aureus (S. aureus), and other microorganisms cause opportunistic UTIs [1].

UPEC is responsible for complicated UTIs in at least half of cases [2]. The insufficient efficacy of initial antibacterial therapy for UTIs and the subsequent development of conditions favoring recurrence are largely

explained by pathogen evolution, particularly the development of antimicrobial resistance.

Aim. To determine the spectrum of uropathogens and their antimicrobial resistance in cystitis, pyelonephritis, and prostatitis.

Materials and methods. The results of microbiological urine studies from urology outpatients performed by the Invitro laboratory network (https://www.invitro.ru/) over a three-year period (2022–2024) were analyzed. A total of 4031 bacterial isolates were evaluated: 2903 (72.0%) strains were obtained from patients with acute cystitis or chronic cystitis during exacerbation, 1017 strains (25.2%) from patients with acute pyelonephritis or chronic pyelonephritis during exacerbation, and 111 strains (2.8%) from patients with chronic bacterial prostatitis.

The study included patients residing in the Siberian Federal District (Altai Republic, Altai Krai, Irkutsk Region, Kemerovo Region, Krasnoyarsk Krai, Novosibirsk Region, Omsk Region, Tomsk Region, Republic of Tyva, Republic of Khakassia) during the period from January 1, 2022 to December 31, 2024. All urine samples were taken at the outpatient basis. Midstream urine samples were collected at any time of day, 2–3 hours after the previous voiding; in patients with prostatitis, urine was collected after prostatic massage. To avoid contamination, genital hygiene procedures were observed. Samples were collected in sterile plastic Uri-swab transport containers (COPAN Diagnostics Inc.) and delivered to local offices and laboratories of the commercial Invitro network within two hours after voiding at ambient temperature. When prompt delivery of urine samples to the laboratory was not possible, they were refrigerated at +5° C for no longer than 24 hours. Samples with a bacterial load $\geqslant 10^4$ CFU/mL underwent pathogen identification followed by antimicrobial susceptibility testing. Preanalytical processing of clinical samples was performed using the automated WASP processor (COPAN, Italy). E-swab tubes were processed using the WASP system (standard culture and preparation of microscopy slides with Gram staining). Standard culture was performed using the four-quadrant streak method with the WASP system on CLED agar (bioMerieux, France) or Columbia agar with 5% sheep blood (Becton Dickinson, USA). Microorganism identification was carried out by a semi-automated method using the VITEK2 system (bioMerieux, France) and MALDI Biotyper Microflex (Bruker Daltonik GmbH, Germany). Antimicrobial susceptibility was determined by an automated method using the VITEK2 analyzer (bioMerieux, France) in accordance with the manufacturer's recommendations. For quality control, internal and external quality assurance procedures were performed at least twice a year. External quality control was carried out using the procedures of the Center for External Quality Control of Clinical Laboratory Investigations (FSVOK, Russian Federation, www.fsvok.ru). As part of internal quality control, at least once a month, reference strains were used for pathogen identification and antimicrobial susceptibility testing.

The raw laboratory data were exported from the laboratory information system in CSV format and processed using proprietary software for subsequent analysis. The transformed data were stored as two-dimensional tables and analyzed by creating appropriate queries written in the Python programming language. Relevant patents were obtained for the original algorithm for data transformation and analysis, the software, and the databases containing the processed information.

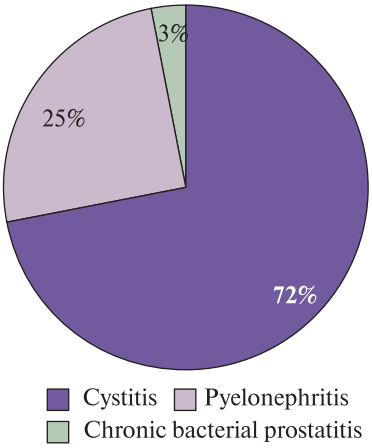

Fig. 1. Disease structure of patients included in the study

Results. The distribution of nosologies is presented in *Figure 1.* The structure of the microbial landscape differed depending on the diagnosis. E. coli was the predominant pathogen in all groups; however, while in cystitis and pyelonephritis it was detected in 73.8 and 75.3%, respectively, in patients with chronic prostatitis the detection rate of E. coli was 53.1%. The growth of Klebsiella pneumoniae and Enterococcus faecalis was more frequently observed in prostatitis, at 19.0 and 15.3%, respectively, whereas in urinary tract infections the frequency of identification of these pathogens ranged from 6.9 to 11.9%. The "other" group included Proteus mirabilis, Streptococcus agalactiae, Enterobacter cloacae, and Pseudomonas aeruginosa. Their proportion in the microbial landscape ranged from 0.7 to 6.3%; overall, "other microorganisms" were identified in 6.4% of cases of cystitis, 7.6% of pyelonephritis, and 12.6% of chronic prostatitis. The spectrum of uropathogens by nosology is presented in *Figure 2.*

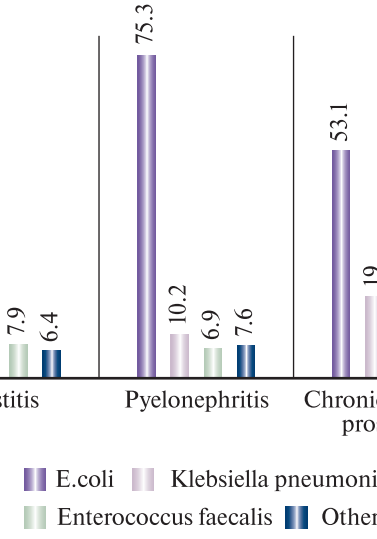

Fig. 2. Microbial spectrum structure (%)

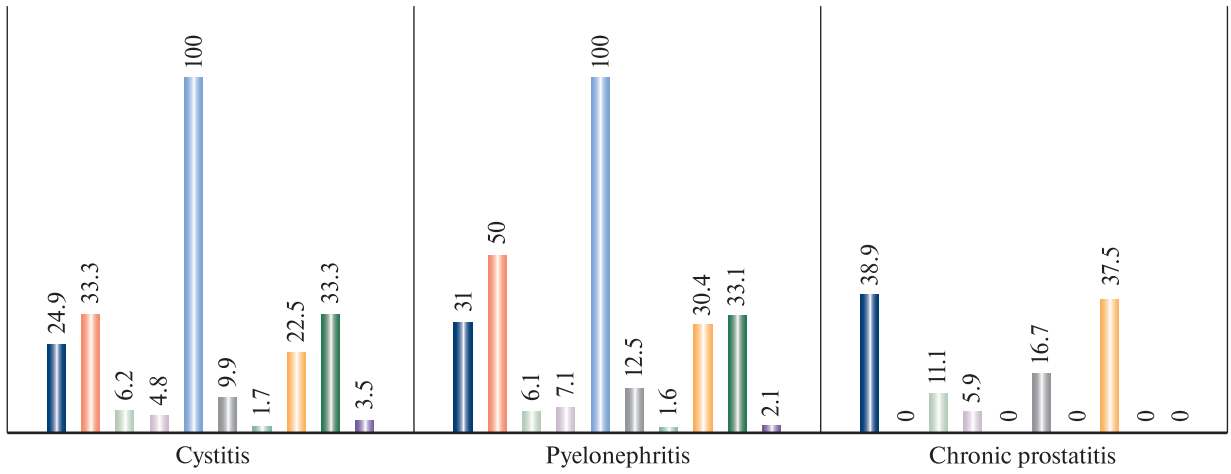

Fig. 3. Proportion of resistant uropathogens by UTI locus (%)

Resistance of the pathogenic microflora was assessed for E. coli. The proportion of E. coli strains resistant to amoxicillin/clavulanate was 24.9% in cystitis, 31.0% in pyelonephritis, and 38.9% in prostatitis. Every third E. coli strain isolated from a patient with cystitis was resistant to levofloxacin, as was every second strain in pyelonephritis; however, in prostatitis all E. coli strains were susceptible to this antibiotic. In prostatitis, E. coli resistance to co-trimoxazole was twice as high as that observed in cystitis and pyelonephritis. These results are illustrated in *Figure 3*.

Discussion. Antibiotics and antimicrobial chemotherapeutic agents have been used to treat UTIs since the introduction of sulfonamides in the 1940s, and this class of drugs remains the most commonly recommended therapeutic option for UTIs [1]. Efforts should be made to minimize the development of resistance by adhering to recommended treatment courses and dosages [11]. According to recent studies, older adults are at increased risk of UTIs caused by multidrug-resistant pathogens [12]. The use of empirical antibiotics should be limited to cases in which symptoms are pronounced and/or there is concern about a more serious infection [13]. When selecting an antibiotic, local resistance patterns of uropathogens should be taken into account [14].

There is no convincing evidence supporting the use of antibiotic prophylaxis for recurrent UTIs; on the contrary, increasing evidence supports non-antibiotic preventive regimens for recurrent UTIs [15]. The 2025 European Association of Urology guidelines state that alternative methods of prevention and treatment have reduced antibiotic use for UTIs by 63% [16]. Since excessive antibiotic use is the main driver of the emergence of multidrug-resistant bacteria, and because about 25% of all antibiotic prescriptions are issued for UTIs, antibiotic prophylaxis should be used only after all non-antibiotic treatment options have been exhausted [17]. Recent studies have demonstrated the potential of bacteriophage therapy for the treatment of urinary tract infections caused by multidrug-resistant bacteria such as E. coli and K. pneumoniae [18]. However, although the preliminary data obtained with this therapy are highly promising, substantial preclinical and clinical work is still required before bacteriophages can become an alternative to antibiotics in the future. The results of our study showed that knowledge of antimicrobial susceptibility of uropathogens in a specific region may also be insufficient; fluctuations in microbial resistance depending on the site of inflammation should also be taken into account. Antimicrobial resistance of uropathogens is continuously monitored worldwide, including in different patient categories [19–26]. In the Russian Federation, the large-scale DARMIS study is conducted regularly [27–29]; however, previous investigators examined the characteristics of uropathogens depending on the region, whereas we determined the spectrum and resistance of pathogens depending on the site of inflammation.

Conclusion. Thus, urinary tract infection is caused predominantly by E. coli, whereas in prostatitis the spectrum of pathogens is more diverse and the proportion of E. coli is 53.1%. Antimicrobial resistance of pathogens differs substantially between urinary tract infections and prostatitis, but regardless of the diagnosis, it is highest to amoxicillin/clavulanate and lowest to nitrofurans and fosfomycin.

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