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Clinical, laboratory, and microbiological characteristics of culture-positive cases of the inflammatory process exacerbation in the urinary tract in patients with urolithiasis following laser lithotripsy

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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Aim. To establish the clinical, laboratory and microbiological characteristics of culture-positive cases of urinary tract inflammatory process exacerbation in patients with urolithiasis following laser lithotripsy.

Materials and methods. The study included 36 patients with urolithiasis who presented with laboratory signs of urinary tract inflammation exacerbation on the second day following laser lithotripsy. Before lithotripsy, the patients showed no pathological changes in their general urine analysis. The patients ranged in age from 19 to 77 years. The study was conducted at Vitacenter, Ltd. between 2023 and 2026. Patients with kidney stone disease (KSD) underwent bacteriological analysis of their urine; when a pathogen was detected, antibiotic sensitivity or resistance was determined. Based on whether bacteriological confirmation of the etiology of the inflammatory process exacerbation in the urinary tract was obtained on the second day after surgery, patients were divided into groups: Group I – 7 patients with pathogen detection; Group II – 29 patients with no etiological confirmation. The data were statistically analyzed using Statistica 13 for Windows.

Results. Among patients with KSD showing laboratory signs of an exacerbation of the inflammatory process in the urinary tract, a positive bacteriological urine culture was detected in 19.4 % of cases on the second day following laser lithotripsy. Among culture-positive cases, Gram-negative microflora predominated, accounting for 85.7 %. The most frequently isolated organisms were *Escherichia coli* (42.9 %) and *Pseudomonas* spp. (28.6 %), which demonstrated heterogeneous antibiotic susceptibility profiles, including individual isolates with broad-spectrum resistance. In patients with KSD who showed laboratory evidence of an exacerbation of the inflammatory process in the urinary tract on the second day following lithotripsy and a positive bacteriological test result, leukocyturia was three times higher than in patients in whom no pathogen was detected ($p = 0.0013$). Leukocyturia ≥242 cells/μL has diagnostic and prognostic significance for assessing the likelihood of a subsequent positive bacteriological urine analysis result: AUC = 0.899 (95 % CI 0.778–0.980), with a sensitivity of 100.0 % and a specificity of 75.9 %.

Conclusions. In patients with KSD presenting with laboratory evidence of urinary tract inflammatory process exacerbation, a positive bacteriological urine culture was detected in 19.4 % on the second day following laser lithotripsy. The isolated microorganisms showed heterogeneous antibiotic susceptibility profiles, including individual isolates with broad-spectrum resistance. A leukocyturia level of ≥242 cells/μL has diagnostic and prognostic significance for assessing the likelihood of a subsequent positive result in bacteriological urine analysis, with a sensitivity of 100.0 % and a specificity of 75.9 %.

Ключові слова: сечокам'яна хвороба, літотрипсія, запальний процес, діагностика, мікробіологічний профіль, антибіотикограма.

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Клініко-лабораторні та мікробіологічні особливості культурально-позитивних випадків загострення запального процесу у сечовивідних шляхах пацієнтів із сечокам'яною хворобою після лазерної літотрипсії

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Мета роботи – встановити клініко-лабораторні та мікробіологічні особливості культурально-позитивних випадків загострення запального процесу у сечовивідних шляхах пацієнтів із сечокам'яною хворобою (СКХ) після лазерної літотрипсії.

Матеріали і методи. До дослідження залучено 36 хворих на СКХ, які мали лабораторні ознаки загострення запального процесу у сечовивідних шляхах на другу добу після лазерної літотрипсії. До проведення літотрипсії у хворих не було патологічних змін у загальному аналізі сечі. Вік хворих становив від 19 до 77 років. Дослідження проведено на базі ТОВ «Вітацентр» (м. Запоріжжя) у 2023–2026 роках. Хворим на СКХ було проведено бактеріологічне дослідження сечі; у разі виявлення збудника було визначено чутливість / резистентність до антибіотиків. Залежно від наявності бактеріологічного підтвердження етіології загострення запального процесу у сечовивідних шляхах на другу добу після оперативного втручання пацієнтів поділили на групи: I група – 7 хворих, у котрих збудник було виділено; II група – 29 хворих, у яких не отримано етіологічного підтвердження. Статистично дані опрацювали в програмі Statistica 13 for Windows.

Результати. Серед пацієнтів із СКХ та лабораторними ознаками загострення запального процесу у сечовивідних шляхах на другу добу після лазерної літотрипсії позитивний бактеріологічний посів сечі отримано в 19,4 % випадків. Серед культурально-позитивних випадків визначено переважання грамнегативної мікрофлори – 85,7 %. Найчастіше виділяли *Escherichia coli* (42,9 %) та *Pseudomonas* spp. (28,6 %), які характеризувалися неоднорідними профілями антибіотикочутливості, включаючи окремі ізоляти з широкою резистентністю. У пацієнтів із СКХ, лабораторними ознаками загострення запального процесу в сечовивідних шляхах на другу добу після літотрипсії та позитивним результатом бактеріологічного дослідження рівень

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лейкоцитурії втричі вищий, ніж у хворих, у котрих збудник не було виділено (p = 0,0013). Рівень лейкоцитурії ≥242 клітин/мкл має діагностично-прогностичне значення для оцінки ймовірності отримання надалі позитивного результату бактеріологічного дослідження сечі: AUC = 0,899 (95 % ДІ 0,778–0,980) із чутливістю 100,0 % та специфічністю 75,9 %.

Висновки. У пацієнтів із СКХ та лабораторними ознаками загострення запального процесу у сечовивідних шляхах на другу добу після лазерної літотрипсії позитивний бактеріологічний посів сечі отримано в 19,4 % випадків. Виділені мікроорганізми характеризувалися неоднорідними профілями антибіотикочутливості, включаючи окремі ізоляти з широкою резистентністю. Рівень лейкоцитурії ≥242 клітин/мкл має діагностично-прогностичне значення для оцінки ймовірності отримання надалі позитивного результату бактеріологічного дослідження сечі з чутливістю 100,0 % і специфічністю 75,9 %.

Urolithiasis remains one of the most common disorders of the urinary system and is characterized by a recurrent course. According to the Global Burden of Disease analysis, urolithiasis remains a global problem. The clinical significance of kidney stone disease (KSD) is associated not only with pain and obstruction of the urinary tract, but also with the risk of infectious and inflammatory complications, impaired renal function and the need for surgical treatment [1,2].

Although the development of urolithiasis is multifactorial, and current understanding of its pathogenesis extends beyond a purely physicochemical model of crystal formation, the inflammatory response, urothelial damage, and the interaction of crystals with microorganisms in the urinary tract play a significant role. Numerous urological microbiome studies provide evidence that the bacterial flora contributes to the formation and recurrence of stones [3,4,5].

In the surgical treatment of kidney and ureteral stones, endoscopic techniques using contact laser lithotripsy play a key role. Laser energy effectively fragments stones of varying composition and density; however, it does not act solely on the stone. Direct damage to the urothelium can occur when the laser fibre contacts the ureteral wall, with the depth of the lesion depending on the energy settings and exposure duration [6]. A separate mechanism of iatrogenic damage during laser lithotripsy is the local thermal effect. The temperature of the irrigation fluid in the pelvi-calyceal system depends on laser power, the surgical procedure duration, the irrigation rate, and other technical factors. Recent clinical experiments confirm that with insufficient irrigation or prolonged laser activation, the temperature can reach levels that are potentially hazardous to the urothelium [7,8,9,10].

Alongside mechanical and thermal damage, the microbiological composition of the calculi themselves may play a significant role. Culture studies confirm the presence of microorganisms both within the calculus and on its surface as part of biofilms. The microbiota composition in the stone and urine may differ, indicating local microbial niches within the stone and the renal pelvis and calyx system [4,5,11,12].

An important feature of the interaction between bacteria and calculi is the ability of microorganisms to form biofilms. Within the biofilm, bacterial cells attach to the stone surface and are embedded in the extracellular matrix, promoting their persistence, intercellular interaction and reduced susceptibility to antibacterial agents. In a recent study of human stones, pathogenic bacteria were detected in almost 40 % of stones; the authors demonstrated how targeted destruction of stone-associated biofilms can reduce infectious complications during stone surgery [13,14,15].

During laser fragmentation, the integrity of the calculus and the associated bacterial biofilms is compromised. As a result, bacteria, biofilm matrix and bacterial components may be released into the irrigation fluid and the urinary tract lumen. The clinical significance of this mechanism is confirmed by the fact that a stone culture may be positive even when a midstream urine sample is sterile, and a positive stone culture is associated with a higher incidence of severe infectious complications following laser lithotripsy [16,17].

The bacterial spectrum in patients with KSD is variable. Recent studies suggest that the most frequently identified organisms in urine and stone cultures are members of the order *Enterobacterales*, primarily *Escherichia coli* and *Klebsiella pneumoniae*, as well as *Proteus* spp., *Pseudomonas* spp., *Enterococcus* spp., *Staphylococcus* spp. and other microorganisms. The prevalence of individual pathogens varies significantly by patient population, culture sample site, presence of drains, prior use of antibacterial agents, and the local antibiotic resistance pattern [12,17,18,19,20].

The clinical importance of bacteriological monitoring is also determined by the risk of postoperative infectious complications. A positive pre-operative urine culture, comorbidities, duration of the procedure, prior stenting, and calculi characteristics have repeatedly been identified as risk factors for post-operative infection or sepsis following ureteroscopy and endoscopic lithotripsy. A systematic review of nearly 940,000 ureteroscopies [21] showed that infectious complications remain a major problem after such procedures [22,23,24].

Postoperative inflammatory changes following laser lithotripsy may develop due to a combination of mechanical and thermal urothelial damage with bacterial factors. At the same time, the variability of the microbial spectrum, a possible mismatch between the urine and stone microflora, and the spread of resistant strains make it impossible to reliably predict the nature of the bacterial process without a culture test [17,18,19,20,25]. Consequently, the above justifies the need to evaluate bacteriological results in conjunction with early laboratory signs of an exacerbation of the inflammatory process in the urinary tract following laser lithotripsy.

Aim

To establish the clinical, laboratory and microbiological characteristics of culture-positive cases of exacerbation of the urinary tract inflammatory process in patients with urolithiasis following laser lithotripsy.

Materials and methods

The study included 36 patients (26 men and 10 women; age range, 19–77 years) with urolithiasis who presented with laboratory signs of the urinary tract inflammatory process exacerbation on the second day following laser lithotripsy. Urinalysis was performed for all patients before lithotripsy; the results were analyzed on the second day following lithotripsy using the Laura XI Erba automated urine

Table 1. Spectrum of microorganisms, frequency of their detection in bacteriological urine tests of patients with KSD with laboratory signs of urinary tract inflammatory process exacerbation on the second day after laser lithotripsy, and characteristics of the antibiotic susceptibility profile

Microorganism	Detection rate, abs. (%)	Sensitivity profile
Escherichia coli	3 (42.9)	Two isolates showed broad susceptibility to β-lactams, carbapenems, aminoglycosides and ciprofloxacin; one isolate was resistant to amoxicillin/clavulanate, piperacillin/tazobactam, cephalosporins and fluoroquinolones, whilst retaining susceptibility to carbapenems, gentamicin, colistin and tigecycline
Klebsiella pneumoniae	1 (14.3)	Widespread resistance to β-lactams, carbapenems, amikacin and fluoroquinolones; sensitivity to gentamicin was retained
Pseudomonas putida	1 (14.3)	Susceptibility to piperacillin/tazobactam, ceftazidime, cefepime, imipenem, amikacin, gentamicin, tobramycin and colistin; intermediate susceptibility to meropenem; resistance to ciprofloxacin
Pseudomonas aeruginosa	1 (14.3)	Resistance to most of the drugs tested; susceptibility to colistin remains
Enterococcus faecalis	1 (14.3)	Susceptibility to amoxicillin, ampicillin, amoxicillin / clavulanate, ampicillin / sulbactam, imipenem, daptomycin, tigecycline and nitrofurantoin; resistance to several cephalosporins, linezolid, teicoplanin, vancomycin and trimethoprim/sulfamethoxazole

analyzer (Germany) in the University Clinic Laboratory of Zaporizhzhia State Medical and Pharmaceutical University. Before lithotripsy, the patients showed no pathological changes in urinalysis.

The study was conducted at Vitacenter, Ltd. between 2023 and 2026. The diagnosis of urolithiasis was established based on medical history and clinical data, imaging studies (ultrasound and computed tomography of the urinary tract), and laboratory tests, in accordance with the guidelines of the European Association of Urology (2025) and the national guidelines of the Ministry of Health of Ukraine: Guideline 00238 "Kidney Stone Disease" dated 6 September 2017, and Guideline 00232 "Urinary Tract Infections" dated 22 May 2017.

Laser lithotripsy was performed using a MultiPulse HoPlus holmium laser (Asclepion Laser Technologies GmbH, Germany) in fragmentation mode with the following parameters: pulse energy 1.2 J, frequency 20 Hz.

All patients underwent bacteriological urinalysis; when a pathogen was detected, antibiotic sensitivity/resistance was determined.

Depending on whether bacteriological confirmation of the etiology of the urinary tract inflammatory process exacerbation was present on the second day after surgery, the patients were divided into groups: Group I comprised 7 patients with the presence of the pathogen; Group II included 29 patients without etiological confirmation.

The data were statistically analyzed using Statistica 13 for Windows (StatSoft Inc., No. JPZ804I382130ARCN10-J). Results were presented as absolute and relative numbers (n, %), as well as the median (Me) and interquartile range [Q_{25}; Q_{75}]. The statistical significance of differences between categorical variables was assessed using the chi-squared (χ^2) test, and between quantitative values using the Mann–Whitney test. To establish the diagnostic and prognostic significance of leukocyturia in assessing the probability of a subsequent positive result in bacteriological urine analysis, an ROC analysis was performed to determine the cut-off point. The difference was considered statistically significant at $p < 0.05$.

Results

The results of the study showed that, in the presence of laboratory signs of urinary tract inflammatory process exacerbation on the second day after lithotripsy, according to bacteriological examination data, the pathogen was detected in only one in five patients – 19.4 % (7 out of 36) of patients (Group I). In the 7 culture-positive cases, five species of microorganisms were isolated. *Escherichia coli* was the most frequently detected, in 3 (42.9 %) patients. *Pseudomonas* spp. were represented by two isolates: *Pseudomonas putida* (1 – 14.3 %) and *Pseudomonas aeruginosa* (1 – 14.3 %). *Klebsiella pneumoniae* and *Enterococcus faecalis* were isolated in one case each (14.3 % each). Gram-negative microorganisms accounted for 6 out of 7 (85.7 %) of all culture-positive cases, while *Enterobacterales* accounted for 4 out of 7 (57.1 %) *(Table 1)*.

Analysis of the antibiotic susceptibility profiles revealed a heterogeneous pattern of susceptibility among the isolated uropathogens. Of the three *Escherichia coli* isolates, two retained broad susceptibility to β-lactam antibiotics, carbapenems, aminoglycosides and ciprofloxacin, while one isolate was resistant to amoxicillin/clavulanate, piperacillin/tazobactam, cephalosporins and fluoroquinolones, retaining susceptibility to carbapenems, gentamicin, colistin and tigecycline *(Table 1)*.

The *Klebsiella pneumoniae* isolate showed a broad resistance profile, including most β-lactams, carbapenems, amikacin and fluoroquinolones, while retaining susceptibility to gentamicin. *Pseudomonas aeruginosa* was resistant to most of the antibacterial agents tested, while retaining susceptibility to colistin. *Pseudomonas putida* was susceptible to piperacillin/tazobactam, ceftazidime, cefepime, imipenem, aminoglycosides and colistin; intermediate susceptibility was observed to meropenem, while resistance was observed to ciprofloxacin. *Enterococcus faecalis* remained susceptible to amoxicillin, ampicillin, amoxicillin/clavulanate, ampicillin/sulbactam, imipenem, daptomycin, tigecycline, and nitrofurantoin *(Table 1)*.

In 80.6 % (29 out of 36) of patients (Group II), despite laboratory signs of an inflammatory process, no bacterial growth was detected in urine cultures.

To elucidate the clinical and laboratory characteristics of culture-positive urinary tract inflammatory process exacerbations in patients with KSD on the second day following lithotripsy, we compared changes in the urinalysis of patients in Groups I and II. Statistically significant differences were recorded only in the severity of leukocyturia. In Group I patients, in whom the pathogen was detected by bacteriological examination, the level of leukocyturia was 432 [357.5; 2,734] cells/μL compared with 139 [82; 195] cells/μL in Group II patients ($p = 0.0013$). Although the median erythrocyte count was higher in Group I than in Group II (3,940.0 [1,198.5; 6,919.0] vs. 859.0 [710.0; 1,157.0] cells/μL), this difference did not reach statistical significance ($p = 0.0523$). Other parameters, particularly epithelial cells, crystals, and even the presence of bacteria

as determined by the instrumental method of general urine analysis, did not differ significantly between the patient groups under study (p > 0.05) *(Table 2)*.

Given the threefold higher level of leukocyturia in patients with KSD in Group I compared with those in Group II, we performed a ROC analysis to determine a cut-off point of diagnostic and prognostic significance for assessing the likelihood of a subsequent positive result in a bacteriological urine test. It was found that leukocyturia of ≥242 cells/μL indicates a high probability of a positive bacteriological test result (AUC = 0.899; 95 % CI 0.778–0.980), with the proposed model having a sensitivity of 100 % and a specificity of 75.9 % *(Fig. 1)*.

A comparison of demographic characteristics, comorbidities, and parameters of the course of KSD before lithotripsy in patients, depending on the presence of bacteriological confirmation of an exacerbation of the inflammatory process in the urinary tract on the second day after lithotripsy, demonstrated no statistically significant differences between patients in Groups I and II (p > 0.05) *(Table 3)*.

Discussion

Our results revealed a significant discrepancy between the frequency of early laboratory signs of inflammatory process exacerbation following laser lithotripsy and the frequency of culture-confirmed bacterial infection. Among 36 patients with urinary tract inflammatory changes, only 19.4 % showed a positive bacteriological result. Thus, in most patients, laboratory signs of an inflammatory reaction on the second day after the procedure were not accompanied by the detection of microbial growth in urine culture.

The culture-positive frequency we observed generally aligns with data from selected recent studies in patients with urolithiasis, although differences in study design limit direct comparison. For example, L. Wang et al., among 759 patients who underwent flexible ureteroscopic lithotripsy, found a positive pre-operative urine culture in 164 (21.6 %) cases. When examining 173 patients with upper urinary tract stones, Y. Cao and H. Cao found a positive urine culture in 46 (26.6 %) of the patients. In our study, a positive culture on the second day after the procedure was detected in 19.4 % of patients with laboratory signs of inflammation, i. e., the frequency was slightly lower. This may be attributed to the post-operative timing of specimen collection, to perioperative antibiotic prophylaxis, and to the specific patient selection criteria [17,19].

According to the literature, our result may have several pathogenetic explanations [6,7,8,9,10,26,27]. Laser lithotripsy presumes mechanical trauma to the urothelium caused by endoscopic instruments and calculus fragments, local thermal effects of laser energy, intensive irrigation, and fluctuations in intravesical pressure. Together, these factors can trigger a local inflammatory response even in the absence of viable microbial growth in post-operative urine cultures. The release of bacterial components from colonized calculi and biofilms during stone fragmentation may also be significant. Furthermore, the impact of perioperative antibiotic prophylaxis, which can reduce the frequency of positive culture results, should be considered [28,29].

Table 2. Comparison of changes in urine in patients with KSD presenting with laboratory signs of the urinary tract inflammatory process exacerbation on the second day after laser lithotripsy depending on the presence of bacteriological confirmation, Me [Q_{25}; Q_{75}]

Parameter, units of measurement	Patients with KSD, n = 36	Group I, n = 7	Group II, n = 29
White blood cells, No./μL	154.5 [93.0; 427.0]	432.0 [357.5; 2,734.0]	139.0 [82.0; 195.0]*
Epithelial cells, No./μL	26.0 [0.0; 45.0]	31.0 [13.0; 74.5]	26.0 [0.0; 36.0]
Squamous epithelium, No./μL	2.5 [0.0; 10.0]	0.0 [0.0; 7.5]	5.0 [0.0; 10.0]
Non-squamous epithelium, No./μL	18.0 [0.0; 36.0]	31.0 [7.5; 59.0]	15.0 [0.0; 31.0]
Red blood cells, No./μL	962.0 [710.0; 3071.0]	3,940.0 [1,198.5; 6,919.0]	859.0 [710.0; 1157.0]
Bacteria, No./μL	216.0 [77.0; 278.0]	242.0 [51.5; 321.5]	195.0 [87.0; 278.0]
Cocci, No./μL	128.5 [51.0; 206.0]	144.0 [39.0; 200.5]	113.0 [51.0; 206.0]
Rod-shaped, No./μL	64.5 [20.0; 98.0]	72.0 [12.5; 134.0]	62.0 [20.0; 88.0]
Yeast, No./μL	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]
Crystals, No./μL	95.5 [31; 319]	57.0 [5.0; 95.5]	159.0 [36.0; 319.0]

*: the difference is statistically significant compared with Group I (p = 0.0013).

Table 3. Comparison of demographic characteristics, comorbid conditions and parameters of the course of KSD before lithotripsy in patients, depending on the presence of bacteriological confirmation of the urinary tract inflammatory process exacerbation on the second day after lithotripsy

Parameter, units of measurement	Group I, n = 7	Group II, n = 29
Demographic indicators		
Age, years	56.0 [47.5; 56.5]	48.0 [43.0; 61.0]
Male, abs. (%)	6 (85.7)	20 (69.0)
Female, abs. (%)	1 (14.3)	9 (31.0)
Comorbid conditions		
Diabetes mellitus, abs. (%)	3 (42.9)	5 (17.2)
Chronic pyelonephritis, abs. (%)	5 (71.4)	17 (58.6)
Course of KSD before lithotripsy		
History of stone passage, abs. (%)	0 (0)	6 (20.7)
Presence of a stent before lithotripsy, abs. (%)	0 (0)	12 (41.4)
Location of stones in the kidney, abs. (%)	5 (71.4)	17 (58.6)
Stone size ≥20 mm, Me [Q25; Q75] mm	11.0 [9.0; 25.0]	10.0 [8.0; 14.0]
Duration of lithotripsy ≥60 minutes, Me [Q25; Q75] min	60.0 [37.5; 60.0]	60.0 [40.0; 60.0]

There is no statistically significant difference when comparing patient groups (p > 0.05).

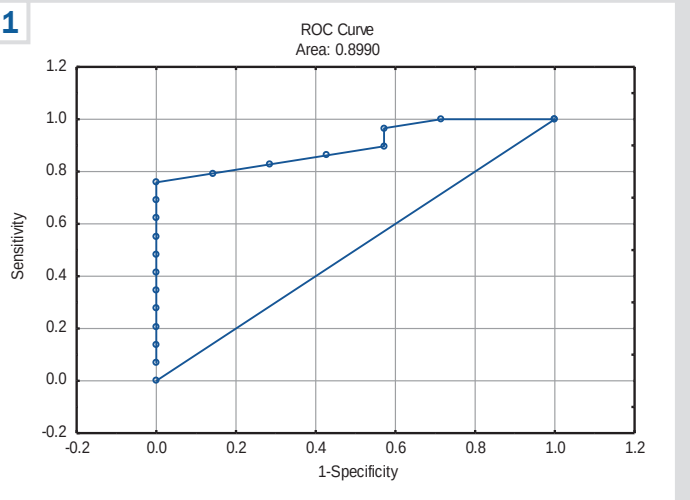

Fig. 1. Diagnostic and prognostic significance of leukocyturia in patients with KSD on the second day after lithotripsy in assessing the probability of a positive result in bacteriological urine analysis.

The hydrodynamic component of the post-operative inflammatory response also has pathogenetic significance. During ureteroscopy, irrigation fluid pressure elevates intrarenal pressure, leading to pyelorenal, pyelovenous and pyelolymphatic reflux. Recent reviews indicate that an increase in intrarenal pressure beyond physiological limits is associated with an increased risk of infectious complications, fluid extravasation, and tissue damage; however, a universally safe threshold for clinical practice has not yet been definitively established. In our study, intrarenal pressure was not measured; therefore, it is not possible to quantify the contribution of this mechanism, although it may partly explain marked laboratory signs of inflammation in the absence of a positive urine culture [26,27].

The effect of antimicrobial therapy on culture results warrants separate consideration. In a prospective multicenter study by G. John et al., 86 out of 87 (99 %) urine cultures were positive before the administration of the first dose of antibiotic, whereas in the first urine sample taken after administration of the antibiotic, a positive result was observed in only 26 out of 75 (35 %) cases; in subsequent consecutive samples, the frequency of positive cultures decreased to 30 % and 7 %. The median time to loss of culture positivity was only a few hours. Given that all patients in our study received perioperative antibiotic prophylaxis, some of the culture-negative results could potentially be attributed to a reduction in the sensitivity of the culture following antibiotic exposure, rather than to the complete absence of a bacterial component [28].

For interpreting culture-negative cases, the discrepancy between the microbiological status of the urine and that of the calculus itself is particularly important. In a multicentre study by H. W. Schuil et al., stone cultures were positive in 43 % of procedures. In contrast, in only 66 % of cases, complete concordance between pre-operative urine analysis and stone culture was observed. Furthermore, a positive stone culture was associated with a post-operative systemic inflammatory response (OR 3.12; 95 % CI 1.01–9.65), whereas a positive pre-operative urinalysis did not demonstrate such an association. Although this study concerned percutaneous nephrolithotripsy, its results confirm that microorganisms can be present within the stone structure even when a standard urine culture does not have them [30].

At the same time, we found that leukocyturia clearly depended on the bacteriological examination results. In patients with a positive urine culture, the median leukocyte count was more than three times higher than in culture-negative patients. This difference was statistically significant (p = 0.0013). Thus, it is not the mere presence of leukocyturia, but its severity, that may have additional diagnostic value regarding the likelihood of a culture-confirmed bacterial infection.

Our data on the severity of leukocyturia are also consistent with the findings of L. Wang et al., who demonstrated that a urine leukocyte count of ≥200 cells/μL was an independent risk factor for urogenital sepsis following flexible ureteroscopic lithotripsy (OR 3.84; 95 % CI 1.39–10.64; p = 0.0097). In our study, the median leukocyturia in culture-positive patients was 432 [357.5; 2734.0] cells/μL compared with 139 [82; 195] cells/μL in culture-negative patients; ROC analysis identified a cut-off of ≥242 cells/μL. The proximity of these quantitative thresholds further confirms that it is the degree of leukocyturia, rather than merely its presence, that may be clinically informative; at the same time, the different endpoints of the studies – a positive culture in our study and urogenital sepsis in the study by L. Wang et al. – do not allow these thresholds to be regarded as interchangeable [19].

ROC analysis confirmed high diagnostic significance of quantitative leukocyturia. The area under the ROC curve was 0.899, and the cut-off level of ≥242 cells/μL in the study sample was characterized by a sensitivity of 100.0 % and a specificity of 75.9 %. The negative predictive value with the specified cut-off was 100.0 %; i. e., among the examined patients, there were no culture-positive cases with a white blood cell count below this threshold. Alongside, due to the small number of positive cultures, the cut-off point cannot be regarded as a definitive clinical criterion and requires confirmation in an independent sample.

In our study, the quantitative bacterial load, as determined by an automated urine analyzer, did not differ significantly between the culture-positive and culture-negative groups, whereas leukocyturia showed clear discriminatory power. Similar limitations of automated bacteriuria detection have been described by P. Iezzi et al.: in 5,490 urine samples, a bacterial count threshold of 180 cells/μL yielded a sensitivity of 88.1 %, a specificity of 82.1 % and a negative predictive value of 95.2 %; however, the authors concluded that automated analysis cannot reliably replace culture testing to rule out infection. Thus, the absence of intergroup differences in instrument-detected bacteriuria in our study does not contradict the established diagnostic role of quantitative leukocyturia and emphasizes the need for bacteriological verification [31].

The microbiological profile of culture-positive cases was dominated by Gram-negative flora, accounting for 85.7 %. *E. coli* was the most frequently isolated organism, detected in 42.9 % of positive cultures. *Pseudomonas* spp. accounted for 28.6 %. *P. aeruginosa* and *K. pneumoniae*, with broad resistance profiles, demonstrate the clinical utility of bacteriological verification in patients with pronounced post-operative inflammatory changes, particularly in the absence of an adequate response to empirical antibacterial therapy.

The spectrum of microorganisms we isolated was generally consistent with current data on urolithiasis-associated infections. However, the literature claims that, among positive urine cultures, *E. coli* accounted for 53.06 %, *K. pneumoniae* for 10.2 %, and *P. aeruginosa* for 4.08 % [17]. In L. Wang et al.'s study, *E. coli* accounted for 34.4 %, *E. faecalis* for 6.1 %, and *K. pneumoniae* and *P. aeruginosa* for 1.8 % each. In our sample, *E. coli* also accounted for the largest proportion (42.9 %), while *E. faecalis* and *K. pneumoniae* each accounted for 14.3 %. The most notable difference was the higher proportion of *Pseudomonas* spp. – 28.6 %; however, with only seven positive cultures, a single isolate accounts for 14.3 %, so this figure cannot be regarded as indicative of the local epidemiological structure without further data collection [17,19].

The predominance of Gram-negative flora in our study (85.7 %) also aligns with current observations. According to the latest published studies, Gram-negative microorganisms were detected in 66 % of cultures from patients with urolithiasis-associated urosepsis, with *E. coli* being the most common pathogen, accounting for 50 %. In this study, *E. coli* was highly susceptible to ertapenem, imipenem, meropenem and

amikacin (92 % each). In our observations, two of three *E. coli* isolates also showed a broad susceptibility profile, while one isolate was characterized by resistance to several β-lactams and fluoroquinolones; individual isolates of *K. pneumoniae* and *P. aeruginosa* demonstrated broad resistance profiles. Given the small number of isolates, these data do not substantiate a quantitative assessment of local resistance. Nevertheless, they confirm the clinical utility of culture-based testing to determine antibiotic susceptibility [25].

However, we did not find a statistically significant correlation between leukocyturia severity and the specific species of the isolated microorganism. This may indicate that the intensity of the inflammatory response following lithotripsy is determined not only by the taxonomic classification of the pathogen, but also by the bacterial load, the properties of the calculus, the presence of a microbial biofilm, the degree of urothelial damage and the individual reactivity of the host [13,30]. However, the small size of the culture-positive group does not allow for definitive conclusions regarding interspecies differences.

From a pathogenetic point of view, the absence of a statistically significant association between a specific pathogen species and the degree of leukocyturia may be expected in our sample. Recent studies demonstrate that the clinical effect of microorganisms in KSD depends not only on species but also on their ability to form biofilms, their localization within the calculus structure, and their possible release during fragmentation. In bacteriological studies of calculi, some authors detected pathogenic bacteria in almost 40 % of the calculi examined and demonstrated their presence within protected biofilms. At the same time, other researchers reported a broad spectrum of microorganisms in stone cultures and only a partial correlation with urinalysis results. This suggests that the severity of the post-operative leukocyte reaction may reflect total bacterial, and tissue burden rather than being specific to a particular type of microorganism [13,30].

In our analysis of clinical factors, we found no statistically significant intergroup differences in gender, diabetes mellitus, chronic pyelonephritis, pre-operative stenting, the location and size of the calculus, or the duration of lithotripsy. A systematic review by A. Pischetola et al., which included 19 studies and 939,860 ureteroscopies, identified female sex, a positive pre-operative urine culture, the presence of comorbidities, a pre-operative JJ stent and increased duration of the procedure as factors associated with post-operative infectious complications. The discrepancy with our findings may be explained by the fact that we analyzed a narrowly selected cohort of patients with established laboratory evidence of an inflammatory process, while the culture-positive subgroup comprised only seven patients, substantially limiting the statistical power to assess categorical factors [21].

More recent data confirm the heterogeneity of factors specifically associated with a positive culture following endoscopic treatment. For instance, H. Wang and W. Gao, in their analysis of 864 patients with suspected infection after flexible ureteroscopic lithotripsy, identified an independent association between a positive culture and older age, female sex, positive urine nitrites and glucose, catheterization, hydronephrosis, and ureteral stricture. However, calculus diameter and the presence of a post-operative stent did not differ between culture-positive and culture-negative patients. These results suggest that the likelihood of culture-confirmed infection following lithotripsy is determined by a combination of patient-related factors, urinary tract condition, and microbiological characteristics. The significance of any individual predictor may depend substantially on the composition of the study population [32].

This study's limitations include its single-center nature and the small number of culture-positive cases. Furthermore, no parallel culture study of calculus fragments was conducted, and the antimicrobial agent panels varied by microorganism type. The cut-off point for leukocyturia, determined by ROC analysis, was obtained and evaluated in a single sample, which necessitates further validation.

Conclusions

1. Among patients with kidney stone disease presenting with laboratory signs of urinary tract inflammatory process exacerbation on the second day after laser lithotripsy, a positive bacteriological urine culture was detected in 19.4 % of cases. Among culture-positive cases, Gram-negative microflora predominated, accounting for 85.7 %. *Escherichia coli* was the most frequently isolated organism, accounting for 42.9 %, while the proportion of *Pseudomonas* spp. was 28.6 %. The isolated microorganisms were characterized by heterogeneous antibiotic susceptibility profiles, including individual isolates with broad-spectrum resistance.

2. In patients with kidney stone disease presenting with laboratory evidence of urinary tract inflammatory process exacerbation on the second day after lithotripsy and a positive bacteriological test result, the level of leukocyturia was three times higher than in patients in whom no pathogen was detected ($p = 0.0013$). Leukocyturia ≥242 cells/μL has diagnostic and prognostic significance for assessing the likelihood of a subsequent positive result in bacteriological urine analysis: AUC = 0.899 (95 % CI 0.778–0.980), with a sensitivity of 100.0 % and a specificity of 75.9 %.

Prospects for further research. Further studies should be aimed at confirming the diagnostic value of leukocyturia ≥242 cells/μL in predicting positive urine culture results after laser lithotripsy in a broader patient population. It is also important to investigate the possible causes of inflammatory changes in patients with negative urine culture results, particularly the role of microorganisms present in urinary stones. Further studies, including the evaluation of additional inflammatory markers, may help improve the early diagnosis of postoperative infectious complications in patients with urolithiasis.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and Helsinki declaration and its later amendments. Informed consent was obtained from all participants included in the study. The Bioethics Committee of Zaporizhzhia State Medical and Pharmaceutical University reviewed the materials presented in the article and confirmed their compliance with all moral and ethical standards stipulated by the current regulatory and legal documents (Protocol No. 14 dated 17.09.2026).

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