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Comorbid vaginal conditions in chronic cystitis

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ABSTRACT

BACKGROUND: Bacterial vaginosis is a significant risk factor for recurrent cystitis in women.
AIM: The study aimed to determine comorbid diseases as risk factors for recurrence of chronic cystitis.
METHODS: The study included 50 female patients. Group 1 included 25 women with chronic recurrent cystitis, whereas Group 2 consisted of 25 women with lower urinary tract symptoms and gynecological pathology. Vaginal microbiota was assessed by polymerase chain reaction (PCR). A clinical examination was conducted at the initial visit, on day 15, and on day 30 of treatment. A comparative analysis was performed using Student's t-test (or, if applicable, Mann–Whitney U test). The data processing was executed using the Excel 2003 software package.
RESULTS: Bacteriuria was detected in 84% of patients in group 1, with *Escherichia coli* identified in 40% of patients. In group 2, bacteriuria was present in 64% of women. The PCR results in group 2 showed a predominance of pathogenic vaginal flora. By day 15, clinical improvement was achieved in 72% of patients in group 1. By day 30, treatment was completed by all 25 (100%) patients in this group. In contrast, by day 15, only 52% of women in group 2 reported positive trends, and by day 30, 36% continued treatment due to persistent symptoms.
CONCLUSION: Bacterial vaginosis with a predominance of opportunistic flora is a risk factor for recurrent lower urinary tract infections.

Keywords: vaginal dysbiosis; chronic recurrent cystitis; bladder microbiota; vaginal flora.

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Коморбидные заболевания влагалища при хроническом цистите

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АННОТАЦИЯ

Актуальность. Бактериальный вагиноз является значимым фактором риска рецидивирующего цистита у женщин.
Цель. Определить коморбидные заболевания как факторы риска рецидивов хронического цистита.
Материал и методы. В исследовании приняли участие 50 пациенток. В 1-й группе — 25 женщин с хроническим рецидивирующим циститом, во 2-й группе — 25 женщин с симптомами нижних мочевых путей и сопутствующей гинекологической патологией. Для диагностики микробиоты влагалища использовали тест полимеразной цепной реакции. Клинический осмотр проводили при обращении, на 15-й и 30-й день лечения. Сравнительный анализ осуществляли с применением непараметрического критерия Стьюдента. Обработку данных выполнили с помощью Excel 2003.
Результаты. Установлено, что у 84% пациенток 1-й группы выявлена бактериурия (*Escherichia coli* — у 40% и др.). Во 2-й группе бактериурия имела место у 64% женщин. Результаты теста у пациенток 2-й группы показали преобладание патогенной флоры влагалища. Через 15 дней у 72% пациенток 1-й группы был достигнут клинический эффект, через 30 дней лечение завершили 25 (100%) пациенток этой группы. Через 15 дней лишь 52% женщин 2-й группы отметили положительную динамику, а через 30 дней 36% женщин продолжили лечение в связи с сохранением жалоб.
Заключение. Бактериальный вагиноз с преобладанием условно-патогенной флоры является фактором риска возникновения рецидивирующей инфекции нижних мочевых путей.

Ключевые слова: дисбиоз влагалища; хронический рецидивирующий цистит; микробиота мочевого пузыря; флора влагалища.

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BACKGROUND

Chronic cystitis is the most common prevalent recurrent condition in women, often leading to anxiety about one's health, reduced productivity, and impaired ability to work [1, 2], as well as a diminished quality of life [3–5].

The high incidence of cystitis in women is attributed to the anatomical and positional characteristics of the urogenital tract, which facilitate the migration of microbiota into the urethral lumen [2, 3]. The vagina serves as a potential reservoir for infection, increasing susceptibility to urinary tract infections (UTIs) [4–6].

Risk factors for uncomplicated cystitis include frequent changes in sexual partners, lower urinary tract dysfunction, postmenopause, a history of UTIs, uropathogen virulence factors, and immune system disorders. Patients with chronic recurrent cystitis often require repeated antibiotic treatment, which can disrupt the intestinal and vaginal microbiota, leading to bacterial vaginosis and symptoms such as discomfort and genital itching. In some cases, this results in a cycle of uncontrolled antibiotic use [6–9].

According to clinical guidelines from the Russian Society of Obstetricians and Gynaecologists, approved by the Ministry of Health of the Russian Federation, bacterial vaginosis is a polymicrobial infectious syndrome characterized by vaginal microbiota dysbiosis. It is marked by a significant reduction or complete absence of lactobacilli and an overgrowth of obligate and facultative anaerobic opportunistic microorganisms (Standard of medical care for bacterial vaginosis, Order of the Ministry of Health of Russia No. 385n, dated July 26, 2023).

The exact causes of bacterial vaginosis remain unclear. However, it is known that *Gardnerella vaginalis*, an invasive pathogen, replaces the normal vaginal flora and forms a biofilm that serves as a protective matrix for other pathogenic bacteria, making antimicrobial penetration more difficult [8–12].

Vaginal dysbiosis (bacterial vaginosis) increases susceptibility to lower UTIs and elevates the risk of cystitis by 2.9 times [13–20]. Some researchers advocate for expanding the range of identified pathogens to include vaginal microbiota, as these microorganisms may damage the bladder epithelium and act as uropathogens [21–23].

The study aimed to identify comorbid conditions that contribute to chronic cystitis recurrence.

METHODS

A retrospective analysis was conducted on inpatient and outpatient records to assess treatment outcomes in 50 female patients with chronic recurrent cystitis. These patients received treatment at the clinic of Kazan State Medical University, the Urology Department of the Medical Diagnostic Center "Family Health" in Kazan, and the Gorki Polyclinic of the Central City Clinical Hospital No. 18 named after K. Sh. Ziyatdinov in Kazan between 2019 and 2023. Each patient was hospitalized once for treatment in the Urology Department of Kazan State Medical University during the observation period.

Patients underwent evaluation based on the standard diagnostic protocol for chronic cystitis, which included clinical urinalysis and blood tests, bacteriological urine culture with antibiotic susceptibility testing, ultrasound (US) of the kidneys and bladder to assess bladder wall thickness and residual urine volume, completion of urination diaries before and after treatment, and a gynecological consultation. Cystoscopy was not performed due to signs of an active inflammatory process, and following treatment, once clinical urine tests had normalized, there were no indications for the procedure.

Inclusion criteria:

- Women diagnosed with chronic cystitis
- Women presenting with lower urinary tract symptoms and concomitant gynecological pathology

Exclusion criteria:

- Pregnancy
- Benign or malignant tumors of the urinary tract
- Overactive bladder
- Sexually transmitted infections
- History of pelvic or urinary organ surgery

Patients underwent examination and consultation at the initial visit, as well as on days 15 and 30 during outpatient follow-ups.

Reported symptoms included painful and frequent urination, a sensation of incomplete bladder emptying, and suprapubic pain.

Patients were divided into two groups (50 women) matched for age, symptoms, and disease duration:

- Group 1 (25 women) with chronic recurrent cystitis but no gynecological pathology
- Group 2 (25 women) with lower urinary tract symptoms and concomitant gynecological pathology

Patients in group 2 initially sought care from a gynecologist due to lower urinary tract symptoms and gynecological complaints and were subsequently referred to a urologist for further evaluation and treatment. All women in group 2 had confirmed gynecological pathology.

The standard gynecological examination included the following:

- Physical examination
- Cytological and microscopic evaluation
- Vaginal cleanliness assessment
- US of the uterus and adnexa
- Polymerase chain reaction smear test (Femoflor Screen) to detect pathogenic vaginal flora in group 2 patients

Group 1 consisted of 25 women aged 20–40 years (mean age, 33.2 ± 1.6 years) diagnosed with chronic cystitis without gynecological complaints.

An analysis of medical history showed that in 18 (72%) patients of group 1, chronic cystitis developed during their working years, with a disease duration ranging from 1 to 10 years and a recurrence frequency of 3–5 episodes per year. The longest recurrence-free period recorded was 3 years.

Table 1. Comparative characteristics of clinical data in group 1 patients with chronic cystitis without gynecological pathology and in group 2 patients with chronic cystitis suffering from gynecological pathology before treatment at the first visit

Parameter	Patients with chronic cystitis without gynecological pathology (n = 25)	Patients with chronic cystitis and gynecological pathology (n = 25)	Statistical significance
Leukocyturia, n (%)	25 (100)	25 (100)	—
Bacteriuria, n (%)	21 (84)	16 (64)	$p = 0.1963$
Frequent urination, n (%)	25 (100)	25 (100)	$p = 1$
Painful urination, n (%)	22 (88)	25 (100)	$p = 0.2347$
Sensation of residual urine, n (%)	14 (56)	18 (72)	$p = 0.3772$
Urination frequency up to 16 times per day, n (%)	24 (80)	14 (28)	$p = 0.002$
Nocturnal polyuria, n (%)	16 (64)	10 (40)	$p = 0.1564$
Bladder volume (ml)	141.8 ± 14	106.0 ± 57	$p = 0.061$
Bladder wall thickness (mm)	5.2 ± 0.2	5.5 ± 0.3	$p = 0.836$
Residual urine volume (ml)	34.8 ± 8	35.4 ± 15	$p = 0.035$
Profuse vaginal discharge, n (%)	—	25 (100)	—
Genital itching, n (%)	—	24	—
Genital pain, n (%)	—	21	—

All patients in group 1 underwent gynecological evaluation, which confirmed the absence of infectious-inflammatory diseases of the female reproductive system.

Group 2 included 25 patients with chronic cystitis accompanied by gynecological pathology, with a mean age of 31.9 ± 1.1 years.

In 20 (80%) patients of group 2, chronic cystitis developed during their working years, with a disease duration of 3–10 years and a recurrence frequency of 2–6 episodes per year. The longest recurrence-free period was 1 year.

To assess the dysuria severity, patients completed urination diaries before and after treatment.

Urine analysis in both groups showed findings consistent with an infectious-inflammatory process in the bladder, including leukocyturia, bacteriuria, and microhematuria.

Clinical and biochemical blood tests revealed no pathological abnormalities (Table 1).

As shown in Table 1, the primary symptoms reported by patients in both groups included frequent urination, urgency, and painful urination. However, in group 2, which had chronic cystitis combined with infectious-inflammatory diseases of the female reproductive system, additional symptoms such as varying degrees of urethral itching and burning, along with vaginal discharge, were observed. These symptoms were not present in group 1.

The clinical manifestations of the disease, confirmed by US bladder examination in patients with gynecological pathology, were comparable to the findings in group 1 and indicated signs of an inflammatory process (Table 1).

Patients in group 2 underwent gynecological treatment due to confirmed vaginal pathology. The study found that in 18 patients (72%), the gynecologist diagnosed vaginitis combined with colpitis; in one patient (4%), adnexitis and genital herpes; in another patient, vaginitis combined with endometritis; and in five patients (20%), bacterial vaginosis. All patients received anti-inflammatory treatment for their gynecological condition.

During the gynecological examination, the Femoflor Screen test was used to assess vaginal microbiota imbalance in patients with chronic recurrent cystitis and concomitant gynecological pathology (Fig. 1).

The Femoflor Screen test (Fig. 1) detected an elevated titer of opportunistic vaginal flora in group 2 patients. Specifically, eight patients (32%) had a combination of *Gardnerella vaginalis* and *Ureaplasma parvum*, five patients (20%) had *Gardnerella vaginalis* levels exceeding 10^4, four patients (16%) had a combination of *Candida* and *Ureaplasma*, and eight patients (32%) had mixed infections involving *Gardnerella* with human papillomavirus, *Enterobacter*, *Ureaplasma parvum*, or *Candida*. These findings indicate a higher risk of recurrent lower urinary tract symptoms in patients with gynecological disorders. Medical history data confirmed that patients with concomitant gynecological pathology experienced recurrence at least three times per year.

Bacteriological urine analysis was performed for all 50 patients.

The bacterial spectrum of the urine microbiota in group 1 before treatment is shown in Fig. 2.

Bacteriological urine analysis detected bacteriuria in 16 patients (64%) in group 2 (Fig. 3).

A comparative analysis of urine bacteriological findings between the two groups revealed differences in the microbiota spectrum.

Treatment effectiveness was assessed based on the following criteria: normalization of laboratory and bacteriological

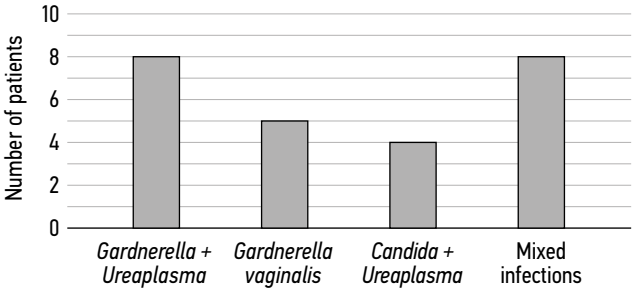

Fig. 1. Spectrum of vaginal flora in patients of the second group before treatment.

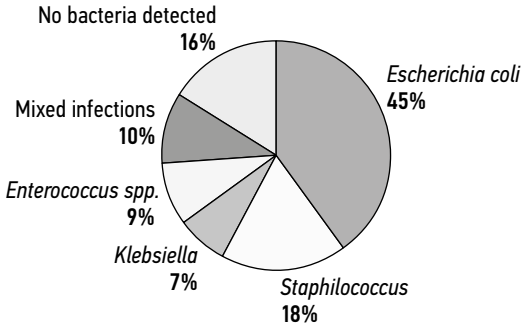

Fig. 2. The spectrum of urine microflora in chronic cystitis in patients with recurrent cystitis without gynecological pathology.

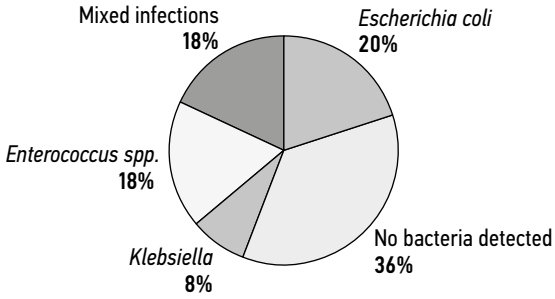

Fig. 3. Spectrum of uropathogens in patients of the second group before treatment.

urine tests, normalization of urination frequency, and improvement in bladder US parameters over time.

A comparative analysis of quantitative data reflecting the clinical-laboratory and functional state of the urinary system, as well as clinical vaginal smears, was conducted using descriptive statistics and the nonparametric Student's t-test. Data processing and graphical presentation were performed using Excel 2003.

RESULTS

Patient treatment followed clinical guidelines for managing chronic cystitis. Antimicrobial therapy was prescribed based on microbiota sensitivity: cefixime (400 mg once daily for 6 days), furazidin (50 mg, two tablets three times daily for 10 days), or nifuratel (400 mg once daily for 10 days). Additionally, patients received D-mannose-based supplements and phytotherapy in accordance with clinical recommendations.

Treatment outcomes were assessed on days 15 and 30 using the established diagnostic algorithm.

Urine culture results showed that in group 1, *Escherichia coli* was the predominant pathogen (40%). In patients with both urological and gynecological pathologies, mixed infections (24%), *Enterococcus* spp. (16%), and *Escherichia coli* (16%) were more common. Therefore, treatment selection was tailored to the antibacterial sensitivity of the identified microbiota.

Most patients in group 1 completed treatment with normalized clinical urine test parameters and symptom resolution: 18 patients (72%) by day 15 and the remaining 7 patients (28%) by day 30. By day 30, all 25 patients (100%) achieved a positive treatment outcome.

By day 15, 18 patients (72%) in group 1 reported overall improvement and a positive trend in urological symptoms, including reduced urination frequency (72%), urgency (72%), and a decreased sensation of incomplete bladder emptying (80%). Urination frequency ranged from six to nine times per day after 15 days and from five to seven times per day after 30 days, as recorded in the urination diaries.

By day 15, only 13 patients (52%) in group 2 experienced significant symptom relief, requiring continued treatment. At this time, 12 out of 25 patients in this group had a urination frequency of 9–14 times per day, and by day 30, 9 patients (36%) still reported dysuria. These nine patients also continued to experience gynecological symptoms, including vaginal discharge and urethral discomfort. As a result, they received concurrent treatment from both urologists and gynecologists.

US findings indicated that by day 15, all 25 patients (100%) in group 1 showed a significant increase in mean bladder volume to 142 ± 3.0 mL, while seven patients (30%) had a residual urine volume of 30–40 mL. Bladder wall thickness had significantly decreased in 23 patients (92%), averaging 4.2 ± 0.2 mm in a filled bladder. By day 30, urination frequency had reduced to five to seven times per day. Clinical recovery was achieved in the remaining 7 patients (28%) by the end of the observation period, and by day 30, all 25 patients (100%) in group 1 had fully recovered.

In group 2, by day 15, the mean bladder volume was 128.4 ± 2.2 mL, with 17 patients (50%) having a residual urine volume of 40–50 mL. The mean bladder wall thickness was 4.5 ± 0.2 mm. Follow-up data confirmed the treatment's effectiveness; however, complete normalization of these parameters was not achieved, necessitating continued therapy with further monitoring on day 30.

The treatment of gynecological pathology included the use of antifungal agents (fluconazole, itraconazole, sertaconazole, ketoconazole, and clotrimazole) and vaginal suppositories containing various active ingredients, such as metronidazole 100 mg + miconazole 100 mg; neomycin 65,000 IU + nystatin 100,000 IU + prednisolone 3 mg + ternidazole 200 mg; metronidazole 500 mg + miconazole 100 mg; lactic acid

Table 2. Dynamics of bladder ultrasound parameters after 30 days of therapy in patients of both groups

US parameters	Patients with chronic cystitis without gynecological pathology	Patients with chronic cystitis and gynecological pathology	Statistical significance
Bladder volume, mL	221.7 ± 22.6	205.0 ± 55	$p = 0.28$
Bladder wall thickness, mm	4.0 ± 0.3	4.4 ± 0.3	$p = 0.95$
Residual urine volume, mL	12.5 ± 8.5	31.5 ± 6.7	$p = 1.75$

Abbreviation: US, ultrasound

100 mg; clindamycin 100 mg; chlorhexidine; lactic acid 225 mg; lyophilized culture of *Lactobacillus casei rhamnosus Doderleini*; human recombinant interferon alpha-2b (at least 50,000 IU) + metronidazole 250 mg + fluconazole 150 mg; and ornidazole 500 mg + neomycin sulfate 65,000 IU + prednisolone sodium phosphate 3 mg + econazole nitrate 100 mg. Ornidazole was used for bacterial vaginosis, acyclovir for herpes infections, and Isoprinosine® as an antiviral agent. Antibacterial therapy included doxycycline 100 mg twice daily for 10 days.

After 30 days, laboratory urine tests showed no pathological changes in either group, and bacteriuria was absent. A notably increase in bladder volume and a decrease in residual urine volume were observed, contributing to the resolution of lower urinary tract symptoms in patients without gynecological pathology (Table 2). However, 9 (36%) women in group 2 continued to experience gynecological symptoms, which accounted for the persistence of dysuria and urethral discomfort.

As shown in Table 2, parameters such as bladder volume and bladder wall thickness in both groups following combination therapy confirmed the treatment's effectiveness ($p = 0.28$). However, the significant difference in residual urine volume between the two groups indicates the persistence of lower urinary tract symptoms in women with gynecological pathology ($p = 1.75$). This finding highlights the need for extended therapy in patients with coexisting gynecological conditions and may serve as a criterion for assessing the effectiveness of combination treatment.

Therefore, despite the appropriately selected treatment in patients with concurrent urological and gynecological pathology, prolonged therapy beyond 1 month is recommended to achieve a full therapeutic effect. Persistent gynecological symptoms may contribute to recurrent episodes of chronic cystitis.

CONCLUSION

Bacterial vaginosis, characterized by an overgrowth of opportunistic flora, is a risk factor for recurrent bladder infections and serves as a key predictor of the disease.

Lower urinary tract symptoms in patients with bacterial vaginosis tend to persist for a prolonged period, even with appropriate pharmacotherapy.

ADDITIONAL INFORMATION

Authors' contribution. V.I.M. — methodology, validation, investigation, writing — original draft; M.E.S. — conceptualization, formal analysis, writing — review and editing, supervision. Thereby, all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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Competing interests. The authors declare that they have no competing interests.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией). Наибольший вклад распределён следующим образом: В.И.М. — методология, валидация, исследование, создание черновика; М.Э.С. — концептуализация, анализ, редактирование рукописи, общее руководство.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования и подготовке публикации.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с проведенным исследованием и публикацией настоящей статьи.

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