

## **ANTIBIOTIC RESISTANCE AND PATHOGEN SHIFTS IN VAGINAL MICROBIOTA: A RETROSPECTIVE STUDY ON IMPLICATIONS FOR SUTURE SOAKING IN SURGICAL SITE INFECTION PREVENTION**

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### **ABSTRACT**

Surgical site infections (SSIs) remain a critical challenge in gynecological surgeries, including those for genital prolapse. The vaginal microbiota, comprising diverse bacterial and fungal species, plays a pivotal role in SSIs by introducing pathogens into surgical sites. Understanding local bacterial flora and antibiotic resistance patterns is essential for developing targeted strategies, such as soaking sutures in antibiotics preoperatively. This study analyzes hospital data from 2019 to 2023 to identify prevalent vaginal pathogens and their antibiotic sensitivity, informing evidence-based suture-soaking protocols.

**Key words:** pelvic organ prolapse, surgical site infections (SSIs), vaginal microbiota, antibiotic sensitivity.

### **INTRODUCTION**

The prevalence of genital prolapse (pelvic floor and pelvic organ prolapse syndrome in isolation or in combination) in women ranges from 11.4 to 41%, with a tendency to increase with age and a subsequent risk of surgery for this disease in 2.7-11% of cases [12, 4]. Anterior colporrhaphy and posterior colpoperineoplasty are among the most common types of surgery in the field of gynecology. However, like any other surgery, these interventions cannot be excluded from the possibility of developing complications. This in turn leads to an increase in the number of infectious complications developing in surgical patients. SSI account for 14-38% of all nosocomial infections [4] or accompany 3-4% of operations in general surgery and are the most frequent cause of postoperative mortality (up to 77%) [8]. To date, there are over 40 definitions of SSI, but only 4 of them are characterised

as standardised, created by multidisciplinary 12 groups: CDC-1998 - Central and Prevention; SESG - Surgical Infection Study Group; NPS - National Prevalence Survey; PHLS - Public Health Laboratory Service. According to the definition of the Centre for Disease Control and Prevention (CDC) for the National Programme of epidemiological control of nosocomial infections (NNIS - National Nosocomial Infection Surveillance) SSIs are defined as nosocomial infections occurring within 30 days of any type of surgical intervention or within one year of implant use [6, 7, 10]. Currently, microbiologists have established that the implanted material is very quickly colonized by pathogenic microflora due to the fact that all bacteria and multicellular fungi during reproduction form communities protected from the environment by additional shells - extracellular membranes, so-called biofilms [1]. The result of community and biofilm formation is the survival of bacteria and fungi in the presence of antibiotics in amounts 10-100 times greater than the minimum suppressive concentration [5]. Systemic administration of antibiotics is ineffective. Taking into account this situation, it is advisable to apply antimicrobial compounds from the surface of the suture material [1, 11]. The problem of correction of vaginal dysbiosis is widely enough covered in the literature, nowadays various treatment regimens are used for this purpose, but often used antibacterial drugs and probiotics are not effective enough, which leads to a high rate of disease recurrence, development of complications and side effects. The data on etiotropic correction of vaginal dysbiosis before elective surgeries are practically absent and of controversial nature. [3, 9].

Therefore, preoperative preparation (monitoring of vaginal biocenosis, its etiotropic correction, prognosis and prevention of purulent-septic complications, especially before and after surgery) is an urgent issue.

### **MATERIAL AND METHODS OF RESEARCH**

This retrospective study analyzed vaginal swab cultures from 10,925 women aged 25–70 years undergoing gynecological examination at Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health between 2019 and 2023. Swabs were collected from the cervical canal and cultured to identify bacterial species, and antibiotic sensitivity testing was performed using standard methods. Data were stratified by year to assess temporal trends in pathogen prevalence and antibiotic resistance. Antimicrobial resistance poses a significant global threat to the treatment of bacterial infections, especially in low- and middle-income regions such as Uzbekistan. This study aims to analyze antimicrobial resistance patterns in cervical swab samples collected from female patients at the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health between 2019 and 2023. To obtain a representative data

set, we used a continuous sampling method that included all available laboratory records of patients with complete data for the study period. This retrospective method was employed to minimize systematic selection error and obtain a complete picture of antimicrobial resistance patterns in the study group. To create a representative dataset, we used a continuous sampling method that included all available laboratory records of patients with complete data for the study period. This methodology was chosen to minimize systematic selection error and ensure comprehensive coverage of antimicrobial resistance trends.

The data collection instrument included variables such as patient age, year of analysis, pathogen isolated, and the nature of resistance exhibited by the isolated organism. Resistance patterns were categorized according to established criteria to ensure uniformity in data interpretation.

The sample from the cervical canal was taken with a disposable swab and placed in a transport system with Amies medium. The specimen was then sown on Petri dishes with blood agar, chocolate agar, yolk-salt agar and Sabouraud's agar. After incubation at 35-37 °C for 18-24 hours, the Petri dishes were examined for morphology, size, color, consistency and number of colonies. Gram staining was performed to identify the predominant organisms and to separate the colonies into Gram-positive and Gram-negative groups.

Then, appropriate biochemical tests were performed to identify suspected bacteria and antibiotic sensitivity tests were performed. Finally, using the growth characteristics on each Petri dish and/or the results of the biochemical tests (catalase, deoxyribonuclease (DNase test), triple sugar agar (TSI), Simmons citrate, urease test, indole, amino acid decarboxylation tests and carbohydrate fermentation tests), possible identification and sensitivity results were determined and documented.

#### Antibiotic sensitivity test (AST)

Antimicrobial sensitivity was determined using the diffusion method in Mueller-Hinton agar. Briefly, bacterial turbidity was measured by comparing pure colonies emulsified in normal saline and McFarland's 0.5 solution. The isolated bacteria were seeded into Muller-Hinton agar dishes with appropriate antimicrobial-impregnated discs and cultured overnight at 35-37 °C. Antibiotic inhibition zones were measured from the center to different edges of the antibiotic inhibition zones using a ruler. AST discs from HIMEDIA were used

Bacteria were sensitive to ampicillin (Amp) (10 µg), gentamicin (GEN) (10 µg), erythromycin (ERY) (15 µg), amikacin (AMK) (30 µg), ceftazidime (CAZ) (30 µg), penicillin (PEN) (10 IU), tetracycline (TET) (30 µg g), nalidixic acid (NAL) (30 µg g), ciprofloxacin (CIP) (5 µg g), chloramphenicol (CHL) (30 µg g),

(30 µg g), ceftriaxone (CRO) (30 µg g), nitrofurantoin (F) (300 µg), clindamycin (CD) (2 µg), oxacillin (ox) (1 µg), (5 µg) and vancomycin (Van) (30 µg).

Interpretation of the results of bacterial sensitivity to AMPs was performed according to the international system EUCAST.

## RESULTS AND DISCUSSION

### 2019 Data

The vaginal microbiota in 2019 was characterized by a diverse array of pathogens, with *Candida* sp. (15.2%) emerging as the most prevalent organism, followed by *Escherichia coli* (12.6%), *Gardnerella vaginalis* (11%), *Enterococcus* spp. (8%), and *Staphylococcus epidermidis* (7.9%). Less common isolates included *Staphylococcus aureus* (2.02%), *Streptococcus* spp. (4.9%), and *Klebsiella pneumoniae* (1.4%).

Antibiotic sensitivity testing revealed notable patterns:

- *Escherichia coli* demonstrated high susceptibility to gentamicin (94.3%) and levofloxacin (69.1%), but moderate sensitivity to ceftriaxone (40.1%) and amoxicillin-clavulanate (24.1%).

- *Enterococcus* spp. showed robust sensitivity to penicillin (93.3%) and amoxicillin-clavulanate (88%), yet poor responses to vancomycin (22.2%) and levofloxacin (24%).

- *Staphylococcus epidermidis* exhibited near-universal sensitivity to gentamicin (94.1%) and levofloxacin (94.2%), while *Staphylococcus aureus* remained highly susceptible to levofloxacin (93%), ceftriaxone (81%), and gentamicin (96%).

### 2020 Data

The vaginal microbiota in 2020 revealed distinct shifts in pathogen prevalence, though antibiotic sensitivity data were unavailable for this year, except for *E.coli*. *Candida* spp. (24.2%) emerged as the most common isolate, followed by other prevalent pathogens including *Escherichia coli* (9.8%), *Staphylococcus haemolyticus* (8.5%), and *Enterococcus* spp. (7.4%). In contrast, less common pathogens were identified, with *Staphylococcus epidermidis* (3.5%) and *Staphylococcus aureus* (1.1%) occurring at notably lower frequencies.

### 2021 Data

The vaginal microbiota in 2021 revealed distinct shifts in pathogen prevalence, though antibiotic sensitivity data were unavailable for this year, except for *E.coli*. *Escherichia coli* (19.4%) emerged as the most common isolate, followed by *Candida* spp. (19.2%), *Staphylococcus haemolyticus* (16.8%), *Enterococcus* spp. (14.5%), and *Staphylococcus aureus* (4.8%) and *Staphylococcus epidermidis* (5.7%) as less common pathogens.

### 2022 Data

By 2022, the microbiota composition shifted, with *Candida* spp. (20.3%), *Gardnerella vaginalis* (20.7%) and *Escherichia coli* (19%) remaining dominant. *Enterococcus* spp. (14%) and *Streptococcus* spp. (7.9%) emerged as secondary pathogens, while *Staphylococcus aureus* (3.5%) persisted as a less common isolate. Notably, *Gardnerella vaginalis*- a key driver of bacterial vaginosis (BV) in other cohorts was absent from the top pathogens, suggesting either regional variability or transient suppression.

Antibiotic sensitivity patterns revealed both strengths and limitations:

- *Escherichia coli* retained high sensitivity to amoxicillin-clavulanate (92%) but showed declining efficacy against gentamicin (57%) and ceftriaxone (32%).
- *Enterococcus* spp. exhibited paradoxical responses: ampicillin (100%) and vancomycin (100%) were highly effective, yet levofloxacin (37%) and doxycycline (15.4%) were less reliable.
- *Staphylococcus aureus* maintained strong susceptibility to levofloxacin (95%) and ceftriaxone (80%), aligning with its role as a target for broad-spectrum antibiotics.

#### 2023 Data

In 2023, *Candida* spp. (23.8%) and *Gardnerella vaginalis* (22.3%) solidified its dominance, while *Escherichia coli* (14.9%) and *Staphylococcus haemolyticus* (13%) emerged as secondary pathogens. *Enterococcus* spp. (12.9%) reappeared, reflecting dynamic shifts in microbial ecology. Less common isolates included *Staphylococcus aureus* (2.8%) and *Staphylococcus epidermidis* (4.4%).

Antibiotic responses highlighted both vulnerabilities and opportunities:

- *Escherichia coli* sensitivity to gentamicin plummeted to 45.4%, contrasting with levofloxacin (70.1%) and ceftriaxone (51%), which retained moderate efficacy.
- *Staphylococcus haemolyticus* demonstrated exceptional susceptibility to levofloxacin (94.2%) and amoxiclav (78.8%), positioning these antibiotics as ideal candidates for targeting this pathogen.
- *Staphylococcus aureus* maintained robust responses to levofloxacin (93.7%) and ceftriaxone (73%), though gentamicin sensitivity dipped to 70.8%.

The findings of this five-year study provide critical insights into the evolving vaginal microbiota and antibiotic resistance patterns, offering actionable strategies for reducing SSIs in gynecological surgeries. Below, we contextualize these results within existing literature and highlight clinical implications:

#### 1. Temporal Shifts in Pathogen Prevalence

*Candida* spp. emerged as the most persistent pathogen across all years (21–23.8%), aligning with studies showing its resilience in vaginal dysbiosis. This dominance underscores the necessity of antifungal adjuncts (e.g., fluconazole) in

suture-soaking protocols, as *Candida* biofilms are notoriously resistant to conventional antibiotics.

*Escherichia coli* prevalence fluctuated (17.5% in 2019 → 14.9% in 2023), while *Staphylococcus haemolyticus* (13% in 2023) and *Enterococcus* spp. (12.9% in 2023) gained prominence. These shifts mirror broader trends in vaginal microbiota, where hormonal fluctuations, antibiotic use, and age influence microbial composition. For example, post-menopausal women often exhibit reduced *Lactobacillus* dominance, favoring pathogens like *Gardnerella* and *Prevotella*. However, our data highlight a unique regional or demographic profile, with *Staphylococcus* species and *Enterococcus* spp. as key players.

## 2. Antibiotic Resistance Dynamics

Gentamicin, once highly effective against *E. coli* (94.3% sensitivity in 2019), showed alarming resistance by 2023 (45.4%). This decline parallels global trends of antibiotic misuse accelerating resistance, emphasizing the need for periodic reassessment of suture-soaking agents. Conversely, levofloxacin and ceftriaxone retained moderate-to-high efficacy against *E. coli* (70.1% and 51%, respectively) and *Staphylococcus aureus* (93.7% and 73%), positioning them as viable candidates.

*Enterococcus* spp. posed a paradox: ampicillin and vancomycin achieved near-universal sensitivity (100% in 2022), yet levofloxacin (37%) and doxycycline (15.4%) were less reliable. This aligns with studies showing vancomycin-resistant *Enterococcus* (VRE) as a growing concern in healthcare settings, though your data suggest vancomycin remains effective locally.

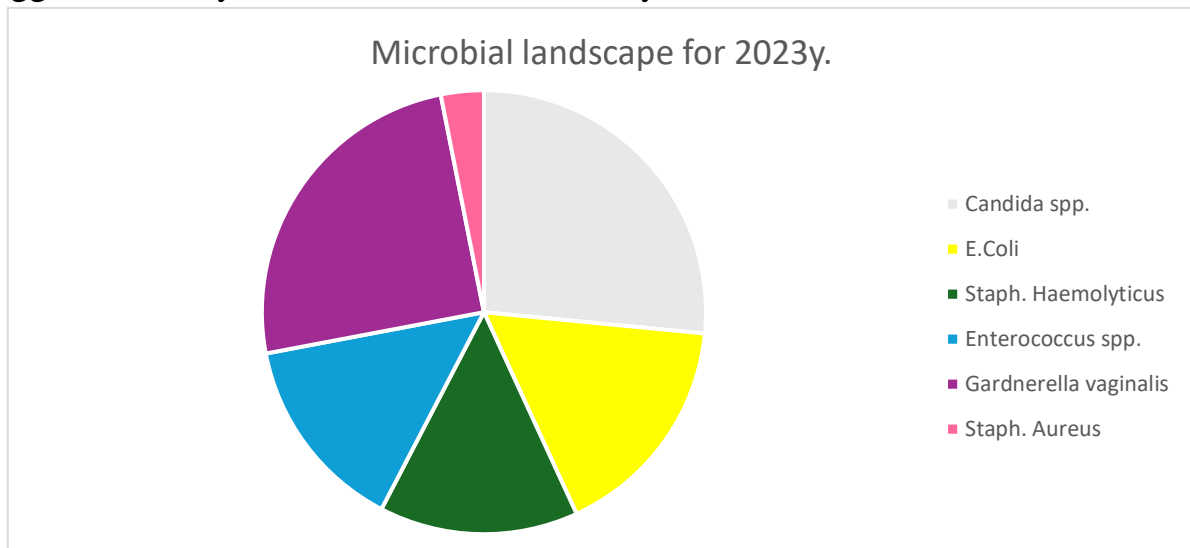


Fig. 1 illustrates the distribution of vaginal microbiome pathogens in 2023. The pie chart shows *Candida* spp., *Escherichia coli*, and *Gardnerella vaginalis* as the most prevalent pathogens. Less common pathogens include *Staphylococcus aureus*, *Staphylococcus haemolyticus*, and *Enterococcus* spp. This distribution highlights the diversity of potential pathogens in the vaginal microbiome, with both fungal and bacterial species represented among the most common isolates.



## CONCLUSION

This five-year analysis identifies *Candida* spp., *E. coli*, and *Staphylococcus* spp. as persistent targets for suture soaking. Levofloxacin and ceftriaxone are prioritized due to their broad-spectrum efficacy, while gentamicin may require caution given declining *E. coli* sensitivity. Future studies should validate these findings in vitro and explore antifungal-antibiotic combinations to address *Candida* spp.

### Clinical Implications for Suture Soaking

**Levofloxacin:** Broad-spectrum activity against *E. coli*, *Staphylococcus aureus*, and *Staphylococcus haemolyticus* (94.2% sensitivity) makes it a prime candidate. However, its efficacy against *Candida* is limited, necessitating antifungal combinations.

- **Gentamicin:** While effective against *Staphylococcus epidermidis* (94.1% sensitivity in 2019), its declining utility against *E. coli* warrants caution.

- **Ceftriaxone:** Moderate sensitivity across pathogens (51–73%) and stability over time support its inclusion in protocols.

### Limitations and Future Directions

This study's reliance on retrospective data limits causal inferences about antibiotic resistance drivers. Prospective studies should explore in vitro efficacy of antibiotic-soaked sutures and antifungal-antibiotic synergies to address *Candida*. Additionally, regional microbiota variability underscores the need for localized guidelines rather than one-size-fits-all approaches.

### E.Coli and antibiotic resistance

Year	Gentamicin	Levofloxacin	Ceftriaxone	Amoxicillin-Clavulanate
2019	94,3%	69,1%	40,1%	24,1%
2020	89,1%	67,9%	35,3%	26,6%
2021	78,6%	64,2%	33,3%	35%
2022	57%	67%	32%	92,5%
2023	45,4%	58,6%	51%	43,8%

*Fig. 2.1 depicts the antibiotic resistance trends of Escherichia coli from 2019 to 2023 against four antibiotics: Gentamicin, Levofloxacin, Ceftriaxone, and Amoxicillin-Clavulanate. The graph shows varying resistance patterns over the five-year period, with Ceftriaxone consistently demonstrating high resistance rates. Levofloxacin and Amoxicillin-Clavulanate exhibited fluctuating resistance levels, while Gentamicin generally showed lower resistance compared to the other antibiotics. These trends highlight the ongoing challenge of antibiotic resistance in E. coli and emphasize the importance of continued monitoring and appropriate antibiotic use.*

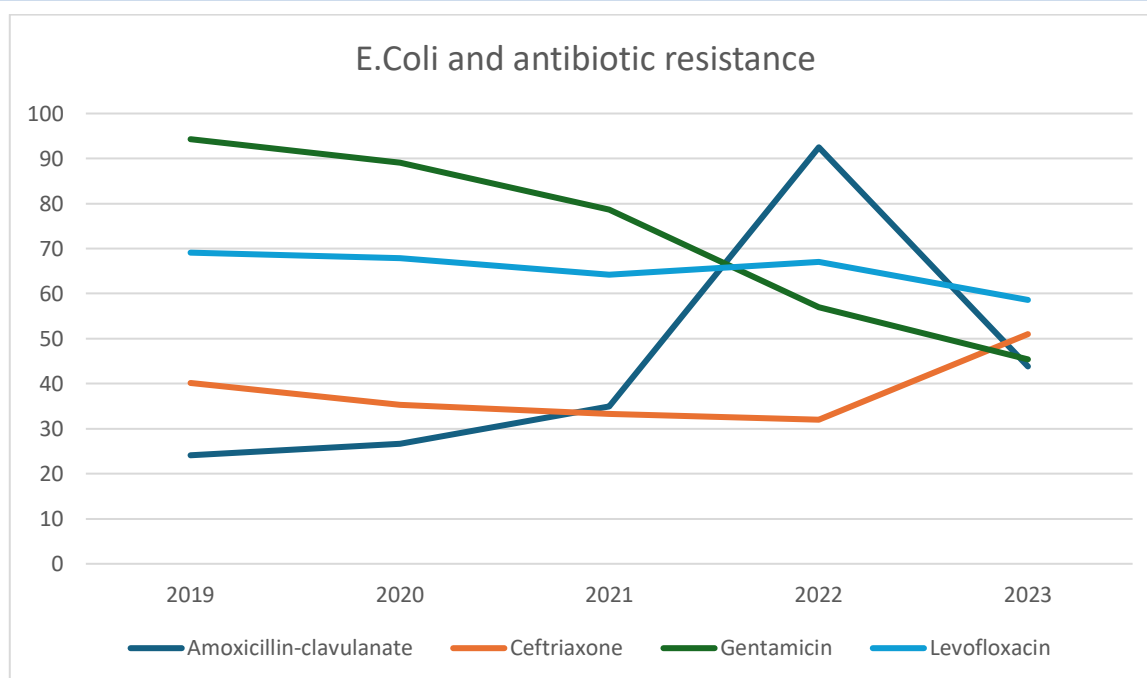


Fig. 3.2 depicts the antibiotic resistance trends of *Escherichia coli* in the vaginal microbiome from 2019 to 2023. The graph shows resistance patterns for four antibiotics: Ceftriaxone, Amoxicillin-Clavulanate, Gentamicin, and Levofloxacin.

Year	Candida. spp	E.coli	Staph. haemolyticus	Enterococcus SPP	Gardnerella vaginalis	Staph. aureus	Staph. epidermidis
2019	15,2%	12,6%	6,2%	8%	11%	2,02%	7,9%
2020	24,2%	9,8%	8,5%	7,4%	12,1%	1,1%	3,5%
2021	19,2%	19,4%	16,8%	14,5%	18,9%	4,8%	5,7%
2022	20,3%	19%	12,6%	14%	20,7%	3,5%	5,5%
2023	23,8%	14,9%	13%	12,9%	22,3%	2,8%	4,4%

Fig. 3 illustrates the prevalence trends of various pathogens in the vaginal microbiome from 2019 to 2023. The graph highlights the following key pathogens: *Candida* species; *Gardnerella vaginalis*; *Escherichia coli*; *Staphylococcus* species, including *S. haemolyticus*, *S. aureus*, and *S. epidermidis*; *Enterococcus* species.

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