Hormonal Contraceptive Use and Risk of Recurrent Vaginitis: Towards Understanding Microbial and Clinical Interactions

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Abstract

Recurrent vaginitis remains a significant clinical challenge, with inconsistent definitions and multifactorial etiologies. Emerging evidence suggests a potential link between hormonal contraceptive use and increased recurrence rates, particularly in the context of *Mycoplasma* and *Ureaplasma* infections. This paper reviews existing literature, presents new hypotheses on the mechanisms of hormonal influence on the vaginal microbiome, and outlines directions for clinical management and future research.

Keywords: mycoplasma, ureaplasma, multifactorial etiologies, vaginal microbiome

Introduction

Vaginitis is one of the most common gynecologic complaints among women of reproductive age and remains a significant burden on both individual well-being and healthcare systems worldwide [1, 2]. It is estimated that nearly 75% of women will experience at least one episode of vaginitis during their lifetime, and a considerable proportion will have recurrent episodes that impair quality of life, sexual health, and reproductive outcomes [3]. Ambulatory visits for vaginitis constitute a substantial portion of gynecology consultations each year, with symptoms such as vaginal discharge, pruritus, pain, and odor leading women to seek clinical evaluation. In addition to its clinical burden, vaginitis also carries psychological and economic consequences due to repeated office visits, laboratory testing, and prolonged treatments [4, 5].

The Centers for Disease Control and Prevention (CDC) currently defines recurrent vulvovaginal infections as four or more symptomatic episodes within a single year [6]. While this definition has been widely adopted, it may not adequately capture the true spectrum of recurrence seen in outpatient practice. Many women self-treat with over-the-counter antifungal or antibacterial preparations and may only present for medical care once symptoms persist or worsen. Consequently, the clinical definition of recurrence may underestimate the number of women affected and may fail to identify those at high risk of ongoing microbial imbalance [7].

Within the etiologic landscape of recurrent vaginitis, common pathogens such as *Candida albicans* and bacterial vaginosis-associated organisms have been well studied, yet the role of atypical bacteria such as *Mycoplasma* and *Ureaplasma* remains under-recognized. These organisms are frequently considered commensals of the urogenital tract, but growing evidence indicates that they may contribute to persistent or recurrent vaginitis symptoms, particularly when standard therapies are ineffective. Their association with cervicitis, pelvic inflammatory disease, and infertility further underscores the importance of re-examining their role in recurrent infections [8].

Preliminary data from recent retrospective studies suggest that the recurrence of vaginitis is disproportionately higher in women using hormonal contraceptives compared with those using barrier or non-hormonal methods. Although hormonal contraceptives are widely used for family planning and menstrual regulation, they may alter the vaginal microenvironment by influencing local immune responses, epithelial barrier function, and lactobacillus colonization. These changes could facilitate the persistence or re-emergence of pathogens such as *Mycoplasma* and *Ureaplasma*, potentially explaining the higher rates of recurrence observed.

The present study aims to critically assess the association between contraceptive choice and recurrent vaginitis, with a particular emphasis on hormonal methods. By integrating epidemiological data, microbiological insights, and clinical outcomes, this paper seeks to highlight the potential contribution of contraceptive-related changes to the vaginal microbiome and to identify strategies for improved diagnostic and preventive approaches. Ultimately, this work intends to inform clinical guidelines and counseling practices for women at risk of recurrent vaginitis.

Background and Literature Review

Vaginal Microbiome and Vaginitis

The healthy vaginal ecosystem is typically dominated by *Lactobacillus* species that acidify the milieu through lactic acid production, sustain a low pH (generally 3.5–4.5), and produce antimicrobial compounds (e.g., hydrogen peroxide, bacteriocins) that inhibit pathogen overgrowth [9]. This lactobacillus-dominant state supports epithelial integrity, limits adherence of opportunistic organisms, and modulates local immune responses, including neutrophil function and pattern-recognition

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signaling along the mucosa [10].

Disruptions to this equilibrium ("dysbiosis") can precipitate symptomatic vaginitis via several well-characterized pathways. In bacterial vaginosis (BV), depletion of *Lactobacillus* and enrichment of anaerobes (e.g., *Gardnerella*, *Atopobium*, *Prevotella*) lead to elevated pH, amine production, biofilm formation, and inflammation-associated symptoms [11]. In vulvovaginal candidiasis, overgrowth of *Candida*, most commonly *C. albicans* but also non-*albicans* species, is facilitated by local factors (antibiotic exposure, glycemic status, hormonal milieu) and by host-pathogen interactions that enable hyphal transition and epithelial invasion. Less emphasized in routine practice, atypical bacteria such as *Mycoplasma* and *Ureaplasma* (mollicutes) may contribute to persistent or recurrent symptomatology, co-occur with BV or candidiasis, and have been associated with cervicitis, pelvic inflammatory disease, and adverse reproductive outcomes [12]. These organisms lack a cell wall, can colonize the urogenital tract asymptomatically, and may evade standard diagnostic and treatment pathways, complicating management in recurrent cases.

Contraceptive Methods and Vaginal Ecology

Contraceptive choice can influence vaginal ecology through hormonal, mechanical, and immunologic mechanisms. Combined oral contraceptives (OCPs) and progestin-only methods (including levonorgestrel intrauterine devices, etonogestrel implants, and transdermal/vaginal delivery systems) modulate systemic and local sex steroids, with downstream effects on glycogen deposition, epithelial turnover, cervical mucus viscosity, and immune effector profiles (e.g., secretory IgA, antimicrobial peptides). These shifts may alter *Lactobacillus* dominance, epithelial barrier function, and susceptibility to dysbiosis or pathogen persistence [13].

Intrauterine devices (IUDs) represent a heterogeneous category with potentially distinct effects. Levonorgestrel-releasing IUDs introduce continuous local progestin exposure, which can thicken cervical mucus and may variably impact the microbiome; copper IUDs, while hormone-free, create a localized inflammatory environment that can modify mucosal immunity. Barrier methods (e.g., condoms) reduce exposure to semen-associated alkalinization and exogenous microflora, potentially supporting maintenance of low vaginal pH and *Lactobacillus* dominance. Observational data suggest that, in some populations, users of hormonal contraception report different rates of recurrent vaginitis relative to barrier or non-hormonal users, but directionality and magnitude of effect depend on method, population characteristics, and coexisting microbial states [14, 15].

Mechanistically, estrogen tends to favor glycogen-rich epithelium and lactobacillus predominance, whereas certain progestins may shift mucosal immunity or epithelial dynamics in ways that predispose to dysbiosis in susceptible individuals. Additionally, method-specific behaviors (e.g., condom use consistency, douching, antibiotic exposure, sexual practices) act as confounders that require careful control in study design.

Prior Studies

Evidence on the relationship between levonorgestrel IUDs and infection risk is mixed. Several studies report minimal or no clinically meaningful perturbation of the vaginal microbiota following LNG-IUD initiation, while others note method-specific patterns or transient changes without consistent links to symptomatic vaginitis [16, 17, 18]. Differences in sampling frame, sequencing depth, and clinical endpoints (microbiome composition versus symptomatic recurrence) likely contribute to heterogeneity.

Critically, the literature addressing mollicute-associated recurrent vaginitis remains sparse. Most reports either exclude *Mycoplasma/Ureaplasma* from testing algorithms or treat these organisms as colonizers unless overt cervicitis is present. Retrospective ambulatory data indicate that a substantial subset of women with recurrent symptoms may harbor *Mycoplasma/Ureaplasma*, often alongside BV or candidiasis, and that many receive repeated empiric therapies with incomplete eradication or rapid recurrence [19]. Robust prospective studies that (i) adopt a standardized definition of recurrence suitable for outpatient practice (e.g., $\geq$2 symptomatic episodes/year), (ii) systematically test for mollicutes alongside BV and *Candida*, and (iii) stratify by contraceptive method are needed. Such designs should incorporate multivariable modeling to control for behavioral, demographic, and clinical confounders; integrate molecular diagnostics (NAATs, metagenomics) to improve sensitivity; and evaluate patient-centered outcomes (symptom burden, time-to-recurrence, quality of life). Addressing these gaps will clarify whether particular hormonal methods confer differential risk for mollicute-positive recurrence and will inform targeted counseling and management algorithms.

Methodological Proposal

To address the research question of whether contraceptive choice is associated with recurrent vaginitis, we propose a study design that combines both retrospective and prospective elements. Retrospective review of electronic medical records can provide initial estimates of prevalence and associations, while a prospective cohort will allow for standardized data collection, microbiological confirmation, and temporal analysis of recurrence patterns.

Participants should be stratified by contraceptive method into four primary categories: (1) hormonal contraceptives, including oral contraceptive pills, hormonal intrauterine devices (IUDs), implants, patches, and vaginal rings; (2) non-hormonal IUDs (e.g., copper IUD); (3) barrier methods, such as condoms; and (4) women not currently using any contraception. Stratification in this manner will allow for clear comparisons across groups while minimizing misclassification bias.

Recurrent vaginitis should be defined using a standardized and clinically relevant threshold of at least two symptomatic episodes per year, or one episode annually for two consecutive years. This definition is more suitable for the ambulatory set-

Table 1: Recurrence Rates of Vaginitis by Contraceptive Method (Estimated Data)

Contraceptive Method	Total Patients (N)	Recurrent Cases (N)	Recurrence Rate (%)
Barrier (Condoms)	105	88	83.8
Hormonal (OCPs, IUD, implant, patch)	228	166	72.8
Non-hormonal (Copper IUD, withdrawal)	35	31	88.6
None	185	121	65.4

ting than the current CDC guideline of four episodes per year, as it captures a broader spectrum of women who experience clinically meaningful recurrences and seek care.

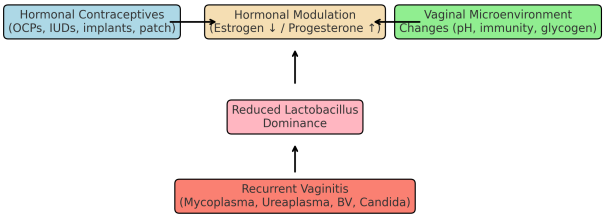

Figure 1: Proposed Mechanism: Hormonal contraceptives may alter vaginal immunity, epithelial integrity, and lactobacillus dominance, leading to increased susceptibility to recurrent vaginitis.

All suspected episodes of vaginitis should undergo laboratory confirmation of causative pathogens. Diagnostic testing should include nucleic acid amplification tests (NAATs) or culture methods for *Mycoplasma* and *Ureaplasma*, as well as routine assessment for bacterial vaginosis and vulvovaginal candidiasis. Incorporating comprehensive microbiological testing will ensure that recurrent cases are not attributed solely to more commonly recognized organisms, and will allow exploration of co-infections.

Table 2: Baseline Demographics of Study Participants (Estimated Values)

Characteristic	Recurrent Vaginitis (N=270)	Non-recurrent (N=144)
Mean Age (years)	27.0 ± 5.0	27.0 ± 5.5
Ethnicity: White (%)	56.7	54.9
Ethnicity: Black/African American (%)	16.7	18.1
Ethnicity: Hispanic (%)	12.6	11.8
Smokers (%)	20.0	22.2
Single relationship status (%)	83.7	79.2

For statistical analysis, baseline demographic and behavioral data (age, ethnicity, smoking status, relationship status, parity, antibiotic use, and sexual practices) should be collected to serve as covariates. Logistic regression models can be employed to estimate the odds of recurrent vaginitis in relation to contraceptive type, adjusting for confounding variables. Secondary analyses may use survival models (time-to-event) to examine duration until recurrence, and stratified subgroup analyses can assess whether specific contraceptive subtypes (e.g., levonorgestrel IUD versus oral contraceptives) carry distinct risk profiles.

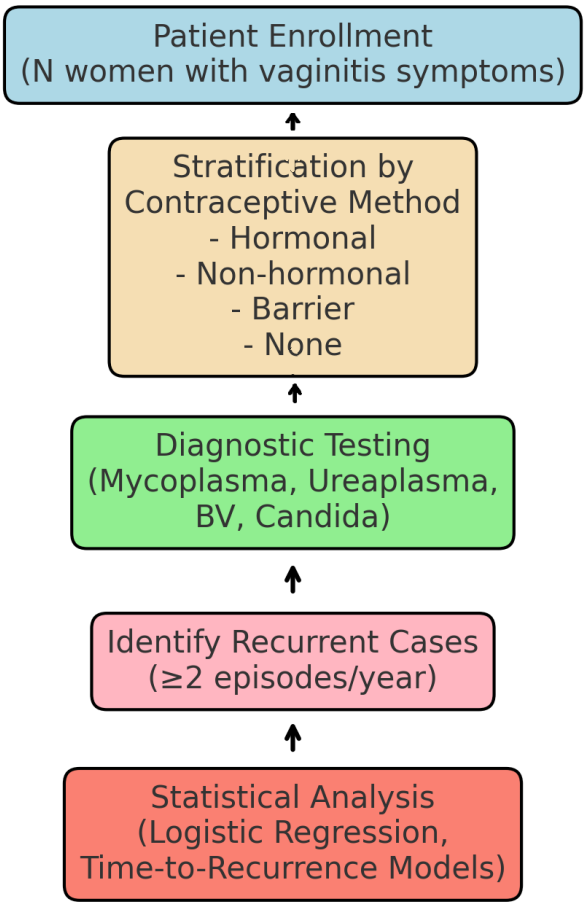

Figure 2: Proposed Study Design Flowchart: Stratification by contraceptive method, screening for recurrent vaginitis, and pathogen identification.

This methodological framework will enable a robust evaluation of the interplay between contraceptive method, vaginal microbiome disruption, and recurrent vaginitis, and will provide clinically actionable evidence to guide patient counseling and management.

Discussion

Biological Plausibility

Hormonal modulation of the vaginal microenvironment provides a biologically plausible link between contraceptive

method and susceptibility to recurrent vaginitis [20]. Estrogen and progesterone shape epithelial turnover, cervical mucus rheology, and local immune tone through effects on pattern-recognition signaling, antimicrobial peptide expression, and secretory immunoglobulins. Estrogen generally promotes a glycogen-rich squamous epithelium; glycogen is metabolized by *Lactobacillus* species to lactic acid, sustaining the low pH that suppresses pathogen overgrowth. By contrast, certain progestin-dominant states may shift epithelial dynamics and mucosal immunity in ways that reduce *Lactobacillus* dominance or blunt host responses to dysbiosis [21].

Beyond endocrine signaling, substrate availability and surface integrity are central. Altered glycogen stores can reduce lactic acid production, increase pH, and create permissive conditions for anaerobes implicated in bacterial vaginosis, for *Candida* expansion under select host conditions, and for persistence of mollicutes such as *Mycoplasma* and *Ureaplasma* [22, 23]. Synthetic progestins may also influence tight-junction organization and desquamation rates, subtly weakening epithelial barrier function and facilitating adherence or biofilm formation by pathogenic consortia. These mechanisms are not mutually exclusive and likely operate in concert with behavioral and clinical cofactors (antibiotics, semen exposure, douching, comorbidities), helping to explain heterogeneous results across populations and contraceptive subtypes [24, 25].

Clinical Implications

The intersection of contraceptive choice and recurrent vaginitis carries immediate implications for counseling and care pathways. For women with frequent symptomatic recurrences, contraceptive counseling should incorporate discussion of potential microbiome effects and individualized risk–benefit tradeoffs, including consideration of non-hormonal alternatives when clinically acceptable. When symptoms persist or recur despite standard therapy for bacterial vaginosis or vulvovaginal candidiasis, clinicians should consider targeted testing for mollicutes alongside routine diagnostics, particularly in ambulatory settings where recurrence thresholds of two or more episodes per year capture a larger at-risk popu

Conclusion

The evidence reviewed highlights a noteworthy association between hormonal contraceptive use and the risk of recurrent vaginitis, particularly in cases where atypical pathogens such as *Mycoplasma* and *Ureaplasma* are present. While causality cannot yet be definitively established, the convergence of epidemiologic data, biologic plausibility, and preliminary clinical observations suggests that hormonal modulation of the vaginal environment may predispose certain women to recurrent symptomatic episodes.

Greater recognition of this association is essential for improving patient care. Incorporating contraceptive history into the diagnostic workup of women with recurrent vaginitis can refine clinical decision-making, and targeted testing for mollicute pathogens may provide valuable insights when conventional diagnoses fail to explain persistent symptoms. From a preventive standpoint, personalized contraceptive counseling, judicious consideration of non-hormonal alternatives, and adjunctive measures to preserve or restore *Lactobacillus*-dominant microbiota represent practical strategies to reduce recurrence.

Future research should prioritize prospective, multicenter studies that integrate standardized recurrence definitions, molecular diagnostics, and careful adjustment for behavioral confounders. Such work will clarify the magnitude of risk associated with different contraceptive methods, inform clinical guidelines, and ultimately support women in making informed choices that balance contraceptive needs with reproductive health outcomes.

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