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The Vaginal Microbiome and Recurrent Vulvovaginal Candidiasis: A Narrative Review

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Abstract

Recurrent vulvovaginal candidiasis affects approximately 140 million women annually, yet its pathogenesis remains incompletely understood. This narrative review synthesizes current evidence on the role of the vaginal microbiome in recurrent vulvovaginal candidiasis, emphasizing emerging paradigms that extend beyond candida centric models. Many metagenomic studies reveal that recurrent vulvovaginal candidiasis is associated with distinct vaginal microbiota signatures, notably characterized Lactobacillus iners dominance and increased abundance of an aerobics. Biofilm formation by Candida albicans isolates from recurrent vulvovaginal candidiasis patients demonstrates significantly higher biomass production, potentially contributing to treatment failure and relapse. The interkingdom interplay between bacterial communities and fungal pathogens, alongside host immune responses, appears central to disease persistence. Beyond standard antifungal therapy, novel therapeutic approaches including microbiome modulating strategies and selective inhibitors such as Oteseconazole show promise in extending recurrence free intervals. This integrated perspective on host, microbiome, and pathogen interactions may inform the development of personalized preventive and therapeutic strategies for this debilitating condition.

Keywords: *recurrent infection, fungal infection, candida, dysbiosis, lactobacillus*

Introduction

For countless women worldwide, the itching, burning, and discharge of a yeast infection is not merely an occasional nuisance but a recurring and debilitating fact. Vulvovaginal candidiasis stands as one of the most prevalent fungal infections affecting women's health, with epidemiological estimates suggesting that approximately 70 – 75 % of all women will experience at least one episode during their reproductive years [1]. While many endure this transient discomfort and move on, a significant portion estimated at 5 – 10% of those affected find themselves trapped in a vicious cycle of recurrence infections, with four or more symptomatic episodes per a year, a condition defined as recurrent vulvovaginal candidiasis [2].

The global burden is staggering, with recent projections indicating that approximately 140 million women suffer from recurrent vulvovaginal candidiasis each year, a figure that highlights the urgent need for more effective management strategies [3].

For many years ago, our clinical approach to vulvovaginal candidiasis and recurrent vulvovaginal candidiasis has been overwhelmingly pathogen focused. The overgrowth of candida species, most commonly candida albicans, invades the vaginal mucosa, and antifungal therapy is deployed to eradicate

it. This approach works for acute episodes, but it maybe fails in preventing the return of symptoms [4]. Surprisingly, even after adhering to standard antifungal regimens, typically involving weekly or monthly maintenance suppressive therapy for up to six months; approximately half of women experience a relapse when treatment ceases. This disappointing statistic results encourage us to ask an important question: why some women remain vulnerable despite repeated antifungal exposure?

The answer, as a growing body of research suggests, the cause not only with the pathogen itself but within the complex ecological battlefield of the vaginal microenvironment [5]. The vaginal microbiome, traditionally known for its protective role, largely mediated by lactobacillus species that produce lactic acid and bacteriocins to inhibit pathologic microorganism, is increasingly recognized as a central determinant of susceptibility to recurrent vulvovaginal candidiasis [6].

In women with recurrent infection, this finally turned ecosystem usually shows signs of dysbiosis, characterized by reduced lactobacilli dominance and a shift toward more diverse, less stable bacterial communities. However, the condition is not of simple depletion of good bacteria [7]. A lot of research reveals a dynamic and paradoxical relationship where the immune response meant to protect the host inadvertently contribute to the symptoms and recurrence of disease [8] [9].

This review aims to navigate the evolving paradigm shift from viewing recurrent vulvovaginal candidiasis as a simple monoinfection to understanding it as a multifactorial syndrome shaped by intricate host, pathogen and microbiome interactions.

We will synthesize current knowledge on how the vaginal microbial ecosystem, both bacterial and fungal influences the transition from asymptomatic colonization to symptomatic disease. As well as, we thoroughly examine the emerging evidence regarding host immune dysfunction, and how this interacts with microbial ecology to perpetuate the cycle of recurrence. Finally, we will explore how this integrated perspective is paving the way for novel therapeutic and preventive strategies that move beyond conventional antifungals toward microbiome restoration and personalized medicine.

Materials and Methods

This narrative review synthesized the 27 sources included in the manuscript to examine the relationship between the vaginal microbiome and recurrent vulvovaginal candidiasis (RVVC). The literature was organized thematically around Candida virulence and dimorphic transition, host immune responses, antifungal resistance and treatment failure, the protective and dysbiotic roles of vaginal bacterial communities, the vaginal mycobiome and community state types, and established or emerging therapeutic strategies. Because the article is a narrative review rather than a systematic review, the evidence was integrated qualitatively to identify recurring biological mechanisms, clinically relevant patterns, therapeutic implications, and remaining knowledge gaps; no quantitative meta-analysis or pooled effect estimate was performed.

Result and discussion

Results

The reviewed evidence converged on a multifactorial model of RVVC in which fungal pathogenicity, host inflammatory responses, antifungal exposure, and vaginal microbial ecology interact to influence persistence and recurrence. The principal findings were grouped into six themes: Candida virulence and biofilm-associated persistence; immune-mediated symptomatic inflammation; antifungal resistance and non-albicans Candida; the protective functions of Lactobacillus-dominated communities; dysbiosis and altered community composition; and bacterial-fungal interactions within the vaginal mycobiome. These themes are presented below using the evidence and terminology of the cited literature.

Virulence factors and dimorphic transition

The pathogenesis of recurrent vulvovaginal candidiasis extends significantly beyond simple fungal

overgrowth. candida albicans, the predominant etiologic agent, possesses a major virulence determinant that facilitate tissue invasion, immune evasion and persistence [6]. The head of these is the capacity for dimorphic transition, the reversible morphological shift from yeast to filamentous forms. This transition is crucial because hyphae and pseudohyphae are more adept at tissue penetration and biofilm formation, representing a key distinction between commensal colonization and pathogenic infection [1]. Additional virulence factors include the secretion of aspartyl proteinases and phospholipases, which degrade the host tissue and mucosal barrier, as well as the ability to form biofilms that enhance antifungal tolerance and immune resistance [10]. [11].

The immunological paradox

A growing body of evidence suggests that the symptoms of recurrent vulvovaginal candidiasis are not solely driven by fungal burden but are significantly amplified by host immunopathology. Unlike other mucosal infections where immunodeficiency predisposes to disease, recurrent vulvovaginal candidiasis frequently occurs in immunocompetent women [2]. The inflammatory response to candida involves the activation of pattern recognition receptors on epithelial cells, which triggers the release of pro inflammatory cytokines and the recruitment of neutrophils. While theses mechanisms are intended to control infection, they paradoxically contribute to tissue damage and symptomatic inflammation [12].

Genetic predispositions affecting immune signaling, such as polymorphisms in IL-4 gene, have been associated with increased susceptibility to recurrent vulvovaginal candidiasis, strengthening the concept that host factors are important determinants of disease recurrence [2]. This paradigm positions recurrent vulvovaginal candidiasis as a disorder of host-microbe interaction where neutrophil associated dysfunction and dysregulated inflammation drive clinical manifestations, independent of pathogen load [2].

Antifungal resistance and treatment failure

The emergence of antifungal resistance compounds the challenge of recurrent vulvovaginal candidiasis management. Prolonged and repeated exposure to azole antifungals, particularly Fluconazole, exerts selective pressure that favors resistant strains. Resistance mechanisms include overexpression of efflux pumps, target enzyme mutations, and biofilm associated tolerance [13].

The growing prevalence of non albicans candida species such as C. glabrata, C. krusei, and C. tropicalis is clinically significant because these species exhibit reduced susceptibility or intrinsic resistance to standard azole therapies, contributing to higher recurrence rate. This epidemiological shift underscores the need for diagnostic strategies capable of distinguishing between C. albicans and non albicans candidal infections to guide appropriate therapeutic choices [14].

The protective role of lactobacillus dominated communities

In a state of health, the vaginal ecosystem is typically characterized by a microbial community dominated by a Lactobacillus species particularly L. crispatus, L. gasseri, L.jensenii, and L. iners. These beneficial organisms serve as a primary biological defense against pathogen colonization through multiple mechanisms. They produce lactic acid, which maintains an acidic vaginal pH typically between 3.5 to 4.5, directly inhibiting the growth of Candida and other pathogens. As well as, hydrogen peroxide production and the secretion of bacteriocins and biosurfactants further suppress fungal proliferation and biofilm formation [15].

Experimental data demonstrate that Lactobacillus crispatus can significantly reduce Candida abundance, with one clinical trial showing a 236 folds reduction in Candida species following administration of a multi strain L. crispatus symbiotic [16].

Dysbiosis: the permissive microenvironment

Disruption of this Lactobacillus which they are dominated equilibrium is termed vaginal dysbiosis, creates a microenvironment permissive to Candida overgrowth and recurrence. In women with vulvovaginal candidiasis and recurrent vulvovaginal candidiasis, the vaginal microbiome frequently exhibits a reduced proportion of lactobacilli, accompanied by overgrowth of pathogenic Candida and other microorganisms [14].

Studies have reported a relative overrepresentation of L. iners and underrepresentation of hydrogen peroxide producing species such as L. crispatus in patients with vulvovaginal candidiasis, suggesting that not all Lactobacillus species confer equivalent protective benefits. The loss of lactobacilli can be triggered by antibiotic use, hormonal fluctuations, and elevated estrogen levels [17].

The mycobiome and community state types

The fungal component of the vaginal ecosystem interacts dynamically with the bacterial microbiome. Advanced molecular techniques have revealed the Candida species are present in a substantial proportion of asymptomatic women, challenging the notion that fungal presence alone is diagnostic of infection [18].

The concept of community state types, defined by bacterial community composition, has been extended to incorporate mycobiome data, enabling a more nuanced understanding of how microbial communities influence disease susceptibility [19]. Community state type I, dominated by L. crispatus is generally associated with optimal health and resilience against infection, while community state type III, dominated by L. iners and community state type IV, diverse anaerobes are linked to dysbiosis and increased susceptibility to recurrent vulvovaginal candidiasis [16].

Discussion

Taken together, the findings support a shift from a strictly Candida-centric explanation of RVVC toward an integrated host-microbiome-pathogen framework. This interpretation helps explain why fungal eradication during suppressive therapy may not translate into durable remission: recurrence can reflect persistent ecological instability, strain- and species-specific microbial interactions, biofilm-associated tolerance, and an inflammatory host response that is not fully captured by fungal burden alone. The therapeutic literature therefore becomes especially relevant when considered in relation to microbiome restoration, susceptibility-guided antifungal selection, and individualized prevention of recurrence.

Current antifungal regimens

Management of recurrent vulvovaginal candidiasis typically involves a two phase approach: acute induction therapy followed by long term suppressive maintenance.

Standard guidelines recommend initial antifungal therapy often Fluconazole 150 mg every 72 hours for three doses, followed by weekly maintenance therapy for up to six months [20]. While this approach is effective during the treatment period, relapse rates are high, approximately half of women experience recurrence within six months of discontinuing maintenance therapy. This high relapse rate, coupled with concerns regarding azol resistance, has driven interest in alternative and adjunctive strategies [21].

Microbiome modulation: probiotic and symbiotics

Restoration of a healthy, Lactobacillus-dominated vaginal ecosystem represents a rational strategy for preventing recurrence. Probiotics containing vaginal derived lactobacilli have shown promise as adjuncts to antifungal therapy. A randomized trial in Indian women with recurrent vaginitis demonstrated that adjunctive probiotic therapy reduced symptoms in 76% of subjects compared to 48% in the control group at 8 weeks, with a significant reduction in recurrence (86% vs. 62%) over 24 weeks [22]. The multi-strain L. crispatus symbiotic achieved a 90% conversion to an optimal community state type I microbiome and significantly reduced Candida abundance [15]. These findings support the concept that live biotherapeutic products can help reestablish protective vaginal communities and reduce the risk of recurrence. However, it is increasingly recognized that lactobacilli species indigenous to vaginal tract may exert more potent anti Candida effects than non indigenous strains, highlighting the importance of careful strain selection in probiotic design [23].

Emerging antifungal and novel approaches

The limitations of current azole based therapies have encouraged developments of novel antifungal agents. Ibrexafungerp, a glucan synthase inhibitor with activity against azole resistant Candida species, represents a promising addition to the armamentarium [24].

Osteseconazole, a tetrazole antifungal, has demonstrated efficacy in preventing recurrence in recurrent

vulvovaginal candidiasis patients [25]. Additionally, immune modulating approaches targeting fungal virulence pathways, for example, candidalysin inhibition and experimental vaccine strategies are under investigation [26] [27].

The integration of personalized medicine approaches, guided by microbiome profiling and antifungal susceptibility testing, offers the potential to tailor therapy based on individual microbial and immunological characteristics [6].

From a clinical perspective, the reviewed studies suggest that durable management of RVVC may require both control of active Candida infection and attention to the ecological context in which recurrence occurs. Conventional azole maintenance remains important, but its limitations after discontinuation reinforce the need for strategies that address resistant or non-albicans species, restore protective vaginal communities, and target fungal virulence or maladaptive host responses. At the same time, differences in study design, patient populations, microbiome methods, probiotic strains, and treatment protocols limit direct comparison across the literature. Future work should therefore prioritize longitudinal, clinically standardized studies capable of linking microbiome states with symptoms, recurrence, antifungal susceptibility, and treatment response.

Conclusion

Recurrent vulvovaginal candidiasis represents a multifactorial clinical challenge rooted in the complex interplay between fungal virulence, host immune response, and vaginal microbial ecology. The traditional focus on antifungal therapy alone is increasingly recognized as insufficient for achieving durable remission. A paradigm shifts toward a microbiota-centric approach, integrating antifungal therapy with microbiome restoration and host immune modulation, hold promise for breaking the cycle of recurrence.

Several critical gaps remain. First, clinically validated thresholds distinguishing commensal colonization from pathogenic infection, particularly for non-albicans Candida species and using molecular diagnostics, are needed. Second, the functional heterogeneity among Lactobacillus species and strains requires elucidation to guide rational probiotic selection and development. Third, longitudinal studies examining the temporal dynamics of the vaginal microbiome and microbiome before, during, and after recurrence are essential to identify predictive biomarkers and early intervention opportunities. Finally, personalized therapeutic algorithms integrating microbial, immunological, and clinical data represent the border of recurrent vulvovaginal candidiasis management, aiming to move beyond empiric approaches toward precision medicine that optimizes outcomes for this debilitating condition.

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