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THE VULVAR MICROBIOME IN LICHEN SCLEROSUS: DYSBIOSIS, BARRIER DYSFUNCTION AND THERAPEUTIC IMPLICATIONS

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ABSTRACT

Vulvar lichen sclerosus is a chronic inflammatory and fibrosing dermatosis of the anogenital region, associated with pruritus, pain, dyspareunia, architectural distortion, and an increased risk of vulvar squamous cell carcinoma in a subset of patients. Although its pathogenesis has traditionally been interpreted through autoimmune, hormonal, genetic, and inflammatory mechanisms, emerging evidence suggests that local and systemic microbial dysbiosis may contribute to disease development or persistence. Current studies do not support the presence of a single causative pathogen. Instead, vulvar lichen sclerosus appears to be associated with heterogeneous alterations in the vulvar, vaginal, urinary, and gut microbiota, including changes in Lactobacillus-dominated communities, anaerobic taxa, urinary microbial profiles, and short-chain fatty acid-producing bacteria. These microbial disturbances may interact with epithelial barrier impairment, altered antimicrobial peptide expression, local hormonal changes, urine exposure, and chronic immune activation. Mechanistic data further suggest that microbiota-derived metabolites, particularly butyrate and other short-chain fatty acids, may influence epithelial integrity, inflammatory signaling, and metabolic-epigenetic regulation through pathways involving SIRT1. This review summarizes current evidence on the microbiome in vulvar lichen sclerosus, integrates findings from female and male genital disease models, and discusses potential therapeutic implications. Microbiome-directed strategies, including postbiotics, metabolite-based interventions, and barrier-restorative approaches, remain investigational but may represent promising adjuncts to established anti-inflammatory therapy.

KEYWORDS

Vulvar Lichen Sclerosus; Microbiome; Dysbiosis; Vulvar Microbiota; Vaginal Microbiota; Gut-Skin Axis; Lactobacillus; SIRT1; Postbiotics

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1. Introduction

Lichen sclerosus (LS) is a chronic inflammatory dermatosis that predominantly affects anogenital skin. In women, vulvar lichen sclerosus (VLS) may present with pruritus, burning, pain, dyspareunia, fissuring, white atrophic plaques, and progressive scarring with architectural changes, including narrowing of the introitus, labial fusion, or clitoral burying. The disease may substantially impair sexual function, quality of life, and psychological well-being. Long-standing disease is also associated with an increased risk of vulvar squamous cell carcinoma, although the absolute risk remains limited and depends on disease duration, control of inflammation, and surveillance. (Filippini et al., 2021; Nygaard et al., 2023)

The pathogenesis of VLS remains incompletely understood. Autoimmunity, genetic susceptibility, hormonal factors, oxidative stress, chronic mechanical irritation, local trauma, infection, and epithelial barrier dysfunction have all been proposed as contributing factors. The autoimmune hypothesis is supported by the coexistence of autoimmune diseases and detectable autoantibodies in some patients. However, association does not necessarily imply causation. A competing or complementary hypothesis proposes that primary local epithelial injury may precede systemic immune activation. According to this "outside-in" framework, chronic exposure to urine, friction, occlusion, irritants, or microbiome-derived inflammatory stimuli could damage the epithelial barrier and basement membrane zone, expose previously hidden antigens, and promote epitope spreading and secondary autoimmunity. (Gupta, 2025)

The microbiome has emerged as a plausible mediator between epithelial barrier integrity and immune activation. In other inflammatory and autoimmune skin diseases, dysbiosis may influence immune homeostasis, antimicrobial peptide expression, epithelial metabolism, and inflammatory cytokine networks. However, whether dysbiosis represents a primary driver, a disease modifier, or a consequence of tissue inflammation is often uncertain. (Baglama & Trčko, 2022) This uncertainty is particularly relevant in VLS because the vulvar region represents a complex ecological interface between keratinized skin, mucosa, urine, vaginal secretions, fecal contamination, hormones, hygiene practices, sexual activity, topical therapies, and age-related changes.

The purpose of this review is to synthesize the available evidence on the vulvar microbiome in VLS, with particular emphasis on dysbiosis, epithelial barrier dysfunction, gut–urogenital interactions, male genital LS as a mechanistic analogue, and therapeutic implications. The central argument of this review is that VLS should not be viewed as a disease caused by a single microorganism. Rather, current evidence supports a more nuanced model in which microbial community shifts interact with epithelial damage, local metabolites, antimicrobial peptides, immune activation, and fibrosis.

2. Methods

This article is a targeted narrative review based on a predefined corpus of publications concerning VLS, genital LS, the vulvar microbiome, urinary and vaginal microbiota, gut microbiota, epithelial barrier dysfunction, antimicrobial peptides, male genital LS, LS-associated urethral stricture disease, penile microbiome studies, and emerging therapeutic approaches. Direct studies of the vulvar, vaginal, urinary, and gut microbiota in women with VLS were prioritized. Studies in pediatric VLS were included because they may help separate disease-associated microbial changes from postmenopausal hormonal effects. Studies in male genital LS and LS-associated urethral stricture disease were included as mechanistic analogues, particularly in relation to urine exposure, occlusion, and genital microbial communities.

The review also incorporates selected mechanistic and therapeutic studies addressing antimicrobial peptides, short-chain fatty acids, postbiotics, epithelial barrier integrity, hormone landscapes, CO2 laser therapy, and carcinogenesis-related epithelial barrier changes. Because the included studies differed substantially in population, sample size, anatomical sampling site, diagnostic criteria, sequencing method, bioinformatic pipeline, and clinical endpoints, no meta-analysis was performed. Findings are therefore presented qualitatively and interpreted with attention to methodological heterogeneity.

3. The Vulvar Microbiome as a Distinct Ecological Niche

The vulva is not simply an extension of either the vagina or adjacent keratinized skin. It is a transitional anatomical site exposed to secretions from multiple compartments. Healthy vulvar microbial communities may contain taxa typically associated with skin, such as Staphylococcus, Cutibacterium, and Corynebacterium, as well as taxa more often associated with the vagina, including Lactobacillus, Gardnerella, and Prevotella. This mixed ecological signature is important when interpreting VLS microbiome studies because the expected microbial background varies according to sampling site, age, menopausal status, estrogen exposure, hygiene, sexual activity, and proximity to vaginal or perianal niches. (Mieremet et al., 2025; Pagan et al., 2023)

Shotgun metagenomic profiling of vulvar samples from healthy women has suggested that the vulvar microbiome may be organized into different ecological patterns, including skin-like, vaginal-like, and mixed communities. Aging appears to be associated with changes in Lactobacillus species, including reduced relative abundance of Lactobacillus iners, Lactobacillus crispatus, and Lactobacillus gasseri. These age-related effects are clinically relevant because VLS is common in postmenopausal women, and an observed reduction in Lactobacillus in VLS may partly reflect disease biology, hypoestrogenism, or both. (Mieremet et al., 2025)

These considerations explain why the search for a universal "VLS microbiome" has been difficult. Some studies have identified reduced Lactobacillus and increased anaerobes or opportunistic taxa, whereas others found differences only in low-abundance bacteria or beta-diversity metrics. Therefore, VLS-associated dysbiosis is better conceptualized as a context-dependent disturbance of a vulnerable ecological niche than as a uniform microbial state.

4. Adult Vulvar Lichen Sclerosus and Local Microbial Dysbiosis

4.1. Evidence from vulvar skin microbiota studies

One of the most direct investigations of vulvar skin microbiota in VLS compared postmenopausal women with biopsy-confirmed VLS and asymptomatic controls using 16S rRNA sequencing. This study reported no significant difference in alpha diversity, but beta diversity differed between groups. At the phylum level, VLS samples showed a lower proportion of Firmicutes and a higher proportion of Proteobacteria. At the genus level, Lactobacillus was predominant in controls but markedly reduced in VLS, whereas Prevotella was among the most prevalent genera in VLS. Several other genera, including Finegoldia, Ralstonia, Peptoniphilus, Anaerococcus, Campylobacter, Providencia, Klebsiella, Ezakiella, and Escherichia-Shigella, were increased in VLS, while Atopobium and Gardnerella were decreased. (Liu et al., 2022)

A more recent study focused on genital LS and the vulvar microbiome found significant differences in beta diversity between women with LS and healthy controls. In that cohort, LS was associated with reduced relative abundance of Lactobacillus, Finegoldia, Lawsonella, Staphylococcus, Cutibacterium, and unidentified Actinomycetaceae, while Porphyromonas and Ezakiella were increased. This pattern partly overlaps with earlier findings, particularly with respect to reduced Lactobacillus and increased anaerobic or mucosa-associated taxa, but it also differs in the direction of some organisms such as Finegoldia, emphasizing that taxonomic results are not fully consistent across cohorts. (Jerkovic Gulin et al., 2025)

A shotgun metagenomic study comparing LS, high-grade squamous intraepithelial lesions, and healthy vulvar sites found that LS samples had increased Papillomaviridae and decreased Prevotella and Bacteroidales compared with controls. The same study reported that healthy vulvar samples contained a mixture of Prevotella, Lactobacillus, Gardnerella, Staphylococcus, Cutibacterium, and Corynebacterium. Importantly, this study also assessed epithelial barrier parameters, including transepidermal water loss and pH, thereby connecting microbial ecology with local barrier status. (Office, 2024; Pagan et al., 2023)

Taken together, adult vulvar microbiome studies suggest that VLS is associated with altered community structure rather than a single reproducible pathogen. The most consistent signal is not a specific organism but the presence of ecological disturbance, often involving reduced Lactobacillus or altered anaerobic taxa, with beta-diversity differences appearing more consistently than alpha-diversity changes.

4.2. Vaginal and urinary microbiota in women with genital LS

Because the vulva is anatomically adjacent to the vagina and urethra, several studies have evaluated whether VLS is associated with microbiota changes beyond lesional skin. In a case-control study of women with genital LS, investigators collected midstream urine, upper vaginal swabs, lower vaginal swabs, and fecal samples. They observed no LS-specific clustering by hierarchical clustering or weighted beta-diversity metrics. However, unweighted UniFrac analyses demonstrated significant differences in the urinary and lower vaginal microbiota, suggesting that less abundant taxa rather than dominant organisms may distinguish LS from

controls. Linear discriminant analysis effect size identified a higher relative abundance of Streptococcus in urinary and lower vaginal samples from women with LS, while Euryarchaeota was increased in fecal samples. (Nygaard et al., 2023)

The distinction between upper and lower vaginal samples is particularly important. The same study reported no significant differences in alpha diversity in upper or lower vaginal swabs. However, the lower vaginal microbiota, but not the upper vaginal microbiota, clustered differently in LS when assessed with unweighted UniFrac. LEfSe analysis demonstrated increased Pseudomonadales, Pseudomonadaceae, Streptococcaceae, Pseudomonas, Streptococcus, and Ezakiella in the lower vagina of women with LS. This supports the hypothesis that the microbial changes most relevant to VLS may be located near the vulvar-vestibular interface rather than deeper in the vaginal canal. (Nygaard et al., 2023)

The same study also found that the gut microbiota of women with LS differed from controls in Bray-Curtis beta diversity, with increased Eubacterium-coprostanoligenes, Euryarchaeota, and Methanobacteriales, while Bacteroidaceae, Bacteroides, and Megasphaera were more abundant in controls. These findings do not establish causality, but they suggest that LS may be associated with multi-compartment microbial variation, including the gut, urinary tract, and lower vaginal niche. (Nygaard et al., 2023)

4.3. Pediatric vulvar LS

Pediatric VLS provides a useful model because the disease occurs before puberty and before the hormonal environment typical of postmenopausal VLS. A pilot case-control study of girls with VLS found no significant differences in alpha diversity between VLS, labial adhesion controls, and healthy controls. However, beta diversity differed between groups, and VLS was associated with increased Parvimonas and Fastidiosipila. These findings again support the concept that VLS-related dysbiosis may be reflected more strongly in community composition than in simple richness metrics. (Sun et al., 2025)

The pediatric data are important for two reasons. First, they suggest that dysbiosis is not merely a consequence of postmenopausal hypoestrogenism. Second, they raise the possibility that local irritation, urine exposure, hygiene, and barrier immaturity may be relevant across age groups. However, the small sample size and cross-sectional design prevent conclusions about whether dysbiosis precedes or follows VLS onset. (Gupta, 2025; Sun et al., 2025)

5. Antimicrobial Peptides and the Barrier–Microbiome Interface

The epithelial barrier is not a passive physical structure. It participates in host defense through tight junctions, lipid organization, pH regulation, antimicrobial peptides, cytokine release, and immune cell recruitment. In VLS, chronic inflammation and epithelial remodeling may alter this defense system, while microbial dysbiosis may further amplify epithelial stress.

Human beta defensins are antimicrobial peptides with immunomodulatory effects and potential relevance to the vaginal and vulvar microenvironment. In postmenopausal women with LS, one study reported lower human beta defensin 1 levels and higher human beta defensin 2 and 3 levels compared with controls. The same study described a vaginal microbiome dominated by potentially harmful bacteria, including Lactobacillus iners, Streptococcus anginosus, and Gardnerella vaginalis. The authors suggested that microbiome correction could be explored as an adjunctive strategy to restore beneficial flora without increasing beta defensin 2 and 3 expression. (Brunner et al., 2021)

These findings support a bidirectional interpretation. On one hand, microbial dysbiosis may induce antimicrobial peptide expression and inflammatory signaling. On the other hand, an inflamed epithelial surface with altered defensin expression may select for different microbial communities. The increase in beta defensin 2 and 3 may therefore represent either a response to dysbiosis, a marker of inflammation, or a contributor to altered host-microbe equilibrium. (Brunner et al., 2021)

The relevance of epithelial junctions is also supported indirectly by studies of vulvar carcinogenesis. Claudins are tight-junction proteins involved in epithelial barrier function and cancer biology. Although claudin-focused studies in vulvar cancer do not directly prove a role for claudin disruption in VLS-associated dysbiosis, they reinforce the broader concept that epithelial barrier integrity is central to vulvar disease biology and may influence inflammatory and neoplastic progression. (Georg Klamminger et al., 2025)

6. Hormonal Landscape, Menopause, and Microbial Composition

Menopause is one of the strongest contextual variables in VLS microbiome research. Estrogen depletion affects vulvar and vaginal epithelial thickness, glycogen availability, pH, Lactobacillus dominance, and susceptibility to irritation. Therefore, microbiome differences in postmenopausal VLS must be interpreted in the context of local hormonal changes.

A study assessing cutaneous hormone landscapes and microbiomes in VLS found that postmenopausal women with VLS had altered cutaneous hormone profiles compared with controls. The study reported lower groin estrone and altered progesterone and adrenal steroid-related markers. Following treatment with a daily class I topical steroid, several hormone abnormalities improved, although testosterone remained suppressed. The study also documented bacterial and fungal microbiome alterations, suggesting that inflammation, local hormones, and microbial ecology may be interdependent rather than isolated phenomena. (Pyle et al., 2024)

The implication is not that hormonal abnormalities alone cause VLS, but that the vulvar microenvironment is shaped by endocrine, inflammatory, and microbial inputs simultaneously. This is clinically relevant because reduced Lactobacillus in VLS may reflect disease-specific dysbiosis, postmenopausal physiology, topical treatment exposure, or a combination of these factors. (Mieremet et al., 2025; Pyle et al., 2024)

7. Gut-Vulvar and Gut-Reproductive Tract Axis in VLS

The gut microbiome may influence distant epithelial surfaces through metabolites, immune modulation, systemic inflammatory tone, and endocrine-metabolic pathways. In inflammatory skin diseases, the gut-skin axis has been proposed as a mechanism linking intestinal dysbiosis with cutaneous inflammation. In VLS, this concept remains early but biologically plausible. (Baglama & Trčko, 2022)

The case-control study of urinary, vaginal, and gut microbiota in women with genital LS found gut-level differences, including increased Euryarchaeota and Methanobacteriales in LS. The authors noted that Euryarchaeota has been associated with other immune-mediated diseases, although the inflammatory significance of this finding in LS remains uncertain. (Nygaard et al., 2023)

A multi-site study of perimenopausal and postmenopausal women with VLS also evaluated skin, gut, and vaginal microbiomes, supporting the idea that VLS may involve more than a purely local vulvar disturbance. However, the sample size was small, and such findings require confirmation in larger, stratified cohorts. (Ma et al., 2024)

The most mechanistically developed evidence comes from a multi-omics study of VLS in which fecal and reproductive tract samples from patients and healthy controls were analyzed longitudinally. VLS was associated with reduced microbial diversity, increased Prevotella and Gardnerella, decreased Bifidobacterium and Lactobacillus, increased inflammatory genes such as IL-6 and TNF-α, reduced metabolic regulators including FOXO3 and SIRT1, and reduced short-chain fatty acid levels. Patient-derived microbiota impaired epithelial and fibroblast homeostasis in vitro by reducing proliferation, increasing apoptosis, and amplifying inflammatory signaling. In vivo, short-chain fatty acid supplementation restored SIRT1 expression, reduced inflammatory cytokines, and improved metabolic balance in a VLS model. (Chen et al., 2026)

This study provides a plausible mechanistic bridge between dysbiosis, epithelial barrier dysfunction, metabolic impairment, and inflammation. Nevertheless, because it includes experimental models and a relatively small human cohort, it should be interpreted as hypothesis-generating rather than definitive evidence that short-chain fatty acid depletion causes VLS in humans. (Chen et al., 2026)

8. Male Genital Lichen Sclerosus as a Mechanistic Analogue

Male genital LS offers an important comparative model because urine exposure and occlusion are more explicitly recognized in its pathogenesis. In men, LS often affects the foreskin, glans, and urethral meatus, and it may lead to phimosis, meatal stenosis, or urethral stricture disease. The urine/occlusion hypothesis proposes that chronic contact between susceptible genital epithelium and urine trapped under the foreskin or within occluded anatomical spaces may initiate or perpetuate inflammation. (Tanasov & Tiplica, 2026)

A study of male LS-associated urethral stricture disease found that balanopreputial swab communities in LS-associated strictures were more similar to urine communities than those in non-LS strictures, supporting a relationship between LS, urine exposure, and local genital microbiota. Although alpha diversity did not significantly differ, beta diversity of swab samples differed, and Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes were prominent phyla. These findings suggest that urine exposure may influence the genital microbial microenvironment in male LS. (Wang et al., 2024)

Another study comparing urinary microbiomes in LS-induced and non-LS-induced urethral stricture disease reported significant alterations in diversity and differential abundance in LS-associated disease. Preoperative urine samples differed in alpha diversity between LS and non-LS groups, whereas postoperative differences were not significant. Weighted UniFrac distances were significantly associated with disease and operative status. These data suggest that the urinary microbiome may be linked to LS-associated urethral disease phenotype and could influence recurrence or severity, although causality remains unresolved. (Jamil et al., 2023)

A multi-omics analysis of male genital LS-induced urethral strictures further supported host-microbe interactions. This study reported altered tissue microbiota and transcriptomic evidence of immune activation, inflammatory response, innate immunity, and response to pathogens. These findings are consistent with a model in which genital dysbiosis and local immune activation coexist in LS-associated tissue remodeling. (Yu et al., 2025)

The relevance of male LS to VLS should not be overstated because male and female genital anatomy, hormonal exposure, microbiota, and disease phenotype differ. However, male LS studies strengthen the plausibility of a local exposure model in genital LS more broadly. They also challenge a purely systemic autoimmune interpretation by showing that anatomical occlusion, urine exposure, and local microbial ecology may be central in at least some forms of genital LS. (Gupta, 2025; Tanasov & Tiplica, 2026)

9. Microbiome, Chronic Inflammation, and Carcinogenesis

The relationship between VLS, dysbiosis, and vulvar carcinogenesis remains incompletely defined. VLS is associated with HPV-independent vulvar squamous cell carcinoma through chronic inflammation and epithelial remodeling. In penile carcinoma, a similar conceptual distinction exists between HPV-related carcinogenesis and HPV-independent pathways associated with chronic inflammation, poor hygiene, phimosis, smoking, compromised immunity, and LS-related disease. (García-Perdomo et al., 2024)

A scoping review of penile cancer and the microbiome concluded that knowledge of the penile microbiome and its role in oncogenesis remains minimal. It identified multiple factors capable of disturbing the penile microbiome, including sexual behavior, circumcision status, LS, poor genital hygiene, compromised immune status, smoking, and HPV infection. These factors overlap with known genital cancer risk frameworks, but direct evidence that microbiome alteration causes penile or vulvar cancer remains insufficient. (García-Perdomo et al., 2024)

The study of the vulvar microbiome in LS and high-grade intraepithelial lesions is particularly relevant because it included both inflammatory and premalignant vulvar disease. In that study, LS and HSIL showed distinct microbial and barrier-associated features, with LS associated with increased Papillomaviridae and decreased Prevotella/Bacteroidales, while HSIL showed increased Alphapapillomavirus and higher transepidermal water loss. These findings suggest that microbial and barrier alterations may differ across inflammatory and premalignant vulvar states. (Pagan et al., 2023)

At present, it would be premature to propose microbial biomarkers for vulvar cancer risk stratification in VLS. However, future studies should investigate whether chronic dysbiosis, impaired epithelial barrier function, persistent antimicrobial peptide activation, and HPV-independent inflammatory pathways jointly influence malignant transformation risk.

10. Therapeutic Implications

10.1. Microbiome-informed treatment should remain adjunctive

Ultra-potent topical corticosteroids remain the foundation of VLS treatment in current clinical practice. The microbiome literature does not support replacing anti-inflammatory treatment with probiotics, postbiotics, antibiotics, laser therapy, or dietary interventions. Instead, the current evidence suggests that microbiome-directed strategies may eventually become adjunctive approaches for selected patients, particularly those with recurrent symptoms, persistent dysbiosis, or impaired barrier recovery despite adequate anti-inflammatory therapy. (Pyle et al., 2024)

The study of cutaneous hormones and microbiomes in VLS reported partial normalization of several local hormone abnormalities after topical class I steroid treatment, supporting the idea that controlling inflammation may itself reshape the local microenvironment. Therefore, observed microbiome abnormalities should not automatically be interpreted as requiring antimicrobial correction; they may improve when inflammation and epithelial integrity are restored. (Pyle et al., 2024)

10.2. Postbiotics and Lactobacillus-derived interventions

A randomized, double-blind controlled trial evaluated postbiotics derived from Lactobacillus crispatus NCU-31 as an adjunct to glucocorticoid therapy in VLS. In the exploratory phase, VLS was associated with increased microbial richness and diversity, reduced Lactobacillus, and elevated Prevotella, Gardnerella, Dialister, and Streptococcus. In the randomized phase, all patients received clobetasol, while the intervention group additionally received Lactobacillus crispatus NCU-31 cell-free supernatant. The postbiotic adjunct improved clinical indices including Investigator Global Assessment, Dermatology Life Quality Index, and Vulvar Quality of Life Index, and partially normalized the local microbiota. (Liao et al., 2026)

This trial is important because it moves beyond descriptive microbiome profiling toward intervention. However, replication in independent populations is necessary before postbiotic therapy can be integrated into standard VLS management. Key unanswered questions include optimal formulation, dose, duration, maintenance schedule, effect on relapse, safety in long-term use, and whether benefit depends on baseline microbiome composition. (Liao et al., 2026)

10.3. Short-chain fatty acids and the SIRT1 axis

The multi-omics butyrate study suggests that microbiota-derived short-chain fatty acids may preserve epithelial integrity through SIRT1-mediated metabolic-epigenetic regulation. VLS was associated with reduced SCFA levels, decreased SIRT1 and FOXO3, increased inflammatory cytokines, and impaired epithelial/fibroblast homeostasis. In experimental models, SCFA supplementation restored SIRT1 expression and reduced inflammatory signaling. (Chen et al., 2026)

This line of evidence suggests several potential therapeutic directions: restoration of SCFA-producing microbes, topical or systemic SCFA supplementation, dietary modulation of microbial metabolites, or pharmacologic activation of SIRT1-related pathways. However, these strategies remain investigational. Human clinical trials are needed to determine whether SCFA modulation improves symptoms, histology, relapse rate, or cancer-risk biomarkers in VLS. (Chen et al., 2026)

10.4. CO2 laser therapy and epithelial remodeling

Fractional microablative CO2 laser therapy has been studied as a rescue option for symptomatic VLS resistant to long-term ultra-potent topical corticosteroids. In one prospective longitudinal study, 40 women with histologically confirmed VLS underwent two laser cycles 30-40 days apart. Significant improvements were reported in vulvar itching, dryness, superficial dyspareunia, and sensitivity during intercourse, with no systemic or local adverse effects during the study period. However, the study was nonrandomized, lacked a sham control, included a limited sample size, and had relatively short follow-up. (Pagano et al., 2020)

Another prospective study of fractional CO2 laser therapy in histologically confirmed VLS reported significant improvement in pain, burning, itching, dyspareunia, introitus discomfort, and dryness after three treatment sessions, with many patients reporting high satisfaction. These findings suggest that laser therapy may improve symptoms and epithelial remodeling in selected patients, but they do not establish microbiome normalization or long-term disease modification. (Filippini et al., 2021)

From a microbiome perspective, CO2 laser therapy should be considered indirectly relevant. By modifying epithelial thickness, keratinization, local wound repair, and possibly pH or moisture, laser therapy could theoretically alter microbial communities. However, direct studies evaluating microbiome changes before and after CO2 laser treatment in VLS are needed before any microbiome-based claims can be made. (Filippini et al., 2021; Pagano et al., 2020)

10.5. Antibiotics and antifungals

The current evidence does not support empirical antibiotic or antifungal therapy for VLS-associated dysbiosis in the absence of documented infection. Several organisms reported in VLS studies may represent commensals, opportunistic colonizers, or markers of altered tissue ecology rather than pathogens. Moreover, broad antimicrobial treatment could worsen dysbiosis, reduce beneficial Lactobacillus or Bifidobacterium, and impair microbial metabolite production. Therefore, antimicrobial therapy should be reserved for clinically and microbiologically confirmed infections, not for VLS itself. (Brunner et al., 2021; Chen et al., 2026; Nygaard et al., 2023)

11. Limitations of Current Evidence

The current literature has several important limitations. First, most studies are small and cross-sectional, limiting statistical power and preventing causal inference. Second, studies differ in diagnostic criteria, with some requiring biopsy confirmation and others relying on clinical diagnosis. Third, anatomical sampling is heterogeneous: some studies sample lesional vulvar skin, others lower vagina, upper vagina, urine, feces, preputial swabs, urethral swabs, or mixed samples. These sites cannot be assumed to represent the same microbial niche.

Fourth, sequencing methods vary substantially. Studies using different 16S rRNA hypervariable regions may produce different taxonomic resolution and bias. Shotgun metagenomics provides greater resolution but has been used in fewer cohorts. Fifth, important confounders are often incompletely controlled, including age, menopause, hormone therapy, sexual activity, hygiene, menstruation, urinary incontinence, topical corticosteroid exposure, antibiotics, antifungals, emollients, disease severity, symptom duration, and coexisting infections.

Sixth, the interpretation of Lactobacillus is complex. Some studies report reduced Lactobacillus in VLS, but Lactobacillus species differ in function. Lactobacillus crispatus is often considered protective in the vaginal niche, whereas Lactobacillus iners may appear in transitional or dysbiotic states. Therefore, genus-level results may obscure species-level biological differences. (Brunner et al., 2021; Liao et al., 2026)

Finally, dysbiosis may be either a cause or consequence of VLS. Inflammatory tissue damage, altered pH, scratching, steroid use, urine exposure, and architectural changes may all modify the microbiome. Longitudinal studies beginning before disease onset are unlikely in practice, but early-disease cohorts, treatment-response studies, and relapse-prediction designs may help clarify directionality.

12. Future Directions

Future research should move beyond descriptive taxonomic studies and integrate microbial, epithelial, immunologic, metabolic, and clinical endpoints. Several priorities are particularly important.

First, future studies should use standardized anatomical sampling protocols. Lesional vulvar skin, non-lesional vulvar skin, vestibule, lower vagina, upper vagina, urine, and feces should be clearly distinguished. Second, studies should stratify by age, menopausal status, hormone exposure, topical corticosteroid use, disease severity, sexual activity, hygiene practices, and urinary symptoms. Third, shotgun metagenomics, metatranscriptomics, metabolomics, and proteomics should be used where feasible to identify microbial function rather than taxonomy alone.

Fourth, barrier measurements should be incorporated into microbiome studies. Transepidermal water loss, pH, claudin expression, antimicrobial peptides, cytokines, and histological markers of epithelial integrity could help determine whether dysbiosis tracks with barrier dysfunction. (Brunner et al., 2021; Georg Klamminger et al., 2025; Pagan et al., 2023)

Fifth, interventional studies are needed. Postbiotic therapy, SCFA-based interventions, targeted restoration of Lactobacillus crispatus, barrier-repair strategies, and microbiome-informed maintenance regimens should be evaluated as adjuncts to standard anti-inflammatory therapy, not as replacements. Clinical outcomes should include symptoms, validated quality-of-life scales, objective lesion scoring, relapse frequency, histology where appropriate, and microbiome/metabolite endpoints. (Chen et al., 2026; Liao et al., 2026)

Sixth, research should investigate whether microbiome or barrier markers predict malignant progression in VLS. This will require large prospective cohorts and careful separation of HPV-related and HPV-independent pathways. (García-Perdomo et al., 2024; Pagan et al., 2023)

13. Conclusions

The vulvar microbiome in VLS is altered, but not in a uniform or pathogen-specific manner. Across studies, VLS is associated with changes in community structure, low-abundance taxa, Lactobacillus representation, anaerobic organisms, urinary and vaginal microbial patterns, gut microbiota, antimicrobial peptides, and microbial metabolites. These findings support a model in which dysbiosis interacts with epithelial barrier dysfunction, urine exposure, local hormones, innate immune activation, and fibrosis.

The most clinically useful interpretation is not that VLS is an infectious disease, but that the microbiome may participate in the maintenance and amplification of inflammation. Microbiome-directed therapies, including postbiotics and SCFA-based approaches, are promising but remain investigational. For now, they should be studied as adjuncts to established anti-inflammatory treatment. The next generation of VLS research should integrate microbiome profiling with barrier assessment, metabolomics, immune markers, and longitudinal clinical outcomes to determine whether microbial signatures can guide personalized therapy.

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