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Predictive microbiome signatures for cervical cancer risk

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Abstract

Persistent infection with High-Risk Human Papillomavirus (HRHPV) represents the principal etiological factor in cervical carcinogenesis; however, only a subset of infected women develops high-grade Cervical Intraepithelial Neoplasia (CIN) or invasive cervical cancer, suggesting the involvement of additional host- and microenvironment-related factors. Increasing evidence indicates that the cervicovaginal microbiome plays a significant role in modulating local immunity, epithelial integrity, inflammatory signaling, and HPV persistence.

The present review summarizes current evidence regarding predictive cervicovaginal microbiome signatures associated with HPV persistence, CIN progression, and cervical cancer development. Lactobacillus-dominated microbial communities, particularly those enriched with Lactobacillus cristates, are consistently associated with mucosal homeostasis and viral clearance, whereas dysbiosis anaerobe-rich communities including Gardnerella vaginalis, Autopodium valine, Sabathia spp., and Fusobacterium spp. have been linked to chronic inflammation, immune dysregulation, and progression to high-grade lesions.

Recent advances in metagenomics, multi-omics integration, and machine learning based predictive modeling have enabled identification of microbial signatures with potential applications in cervical cancer risk stratification and precision screening approaches. Nevertheless, current evidence remains limited by methodological heterogeneity, observational study designs, and insufficient functional validation.

Collectively, cervicovaginal microbiome profiling represents a promising non-invasive strategy for cervical cancer risk assessment and may contribute to future precision oncology approaches in HPV-positive women.

Keywords: Cervical cancer; Microbiome; HPV; Biomarkers; CIN; Predictive signatures.

Abbreviations: CIN: Cervical Intraepithelial Neoplasia; HPV: Human Papillomavirus; HRHPV: High-Risk Human Papillomavirus; ML: Machine Learning; SCFAs: Short-Chain Fatty Acids; VMT: Vaginal Microbiota Transplantation

Introduction

Cervical cancer remains a major global public health challenge and is currently the fourth most common malignancy among women worldwide. According to the World Health Organization, approximately 604,000 new cases and 342,000 deaths were reported in 2020, with the highest burden observed in low- and middle-income countries due to limited access to HPV vaccination and screening programs [1].

Persistent infection with high-risk human papillomavirus (HRHPV), particularly HPV16 and HPV18, is recognized as a necessary precursor for the development of Cervical Intraepithelial Neoplasia (CIN) and invasive cervical cancer. However, only a minority of HPV infections progress to malignancy, indicating that additional host- and environment-related cofactors contribute to carcinogenesis.

Recent evidence suggests that the cervicovaginal microbiome plays an important role in shaping the local immune microenvironment and influencing HPV persistence, epithelial integrity, and inflammatory signaling pathways. Lactobacillus-dominated microbial communities, particularly those enriched with Lactobacillus cristates, are generally associated with mucosal homeostasis and HPV clearance. In contrast, dysbiosis microbial communities enriched with anaerobic taxa, including Gardnerella vaginalis, Autopodium valine, Sabathia spp., and Privately spp., have been associated with persistent HPV infection and progression to high-grade lesions [2,4].

Dysbiosis microbial environments may promote chronic inflammation, epithelial barrier disruption, immune dysregulation, and altered cytokine signaling, thereby facilitating HPV persistence and neoplastic progression. Emerging studies also suggest that microbial instability and temporal fluctuations in vaginal microbial composition are associated with delayed viral clearance and increased CIN risk [5,6].

Advances in metagenomics, computational biology, and machine learning approaches have enabled the identification of predictive microbial signatures associated with cervical carcinogenesis. Integration of microbiome profiling with immune and clinical parameters may improve cervical cancer risk stratification and support future precision oncology approaches.

This review summarizes current evidence regarding predictive cervicovaginal microbiome signatures associated with HPV persistence and cervical carcinogenesis, with particular emphasis on microbial composition, immune modulation, and translational applications in cervical cancer risk assessment. The progressive transition from Lactobacillus-dominated communities to dysbiosis anaerobic states across cervical carcinogenesis is summarized in (Figure 1).

Literature search and study selection

A structured literature search was performed using the PubMed, Scopus, and Web of Science databases to identify studies evaluating the association between the cervicovaginal microbiome, HPV persistence, Cervical Intraepithelial Neoplasia (CIN), and cervical cancer.

The search included peer-reviewed articles published between January 2011 and March 2025. The following search terms and Boolean operators were used: “cervical cancer” OR “cervical intraepithelial neoplasia” OR “CIN” AND “microbiome” OR “vaginal microbiota” OR “cervicovaginal microbiome” AND “HPV” OR “human papillomavirus” AND “biomarkers” OR “predictive models” OR “machine learning”.

Eligible studies included human observational studies, longitudinal cohort studies, case-control studies, and translational studies investigating microbial composition, microbial-derived metabolites, immune modulation, or predictive microbiome signatures associated with HPV infection or cervical disease progression.

Studies were excluded if they:

- Involved only animal or in vitro models.
- Lacked microbiome profiling data.
- Did not evaluate HPV status or cervical lesion severity.
- (or) Consisted exclusively of editorials, case reports, or conference abstracts.

Additional relevant studies were identified through manual screening of reference lists from eligible articles.

Given the heterogeneity of sequencing platforms, sampling methodologies, and bioinformatics pipelines across studies, the present review was designed as a narrative synthesis rather than a formal meta-analysis. A total of 87 studies were initially screened, of which 31 studies meeting the inclusion criteria were included in the final narrative synthesis [6].

Current evidence on cervicovaginal microbiome signatures

Cervicovaginal microbiome composition in HPV-positive women

The cervicovaginal microbiome of healthy reproductive age women is typically dominated by Lactobacillus species, particularly L. cristates, L. Jesenia, and L. gasser, which contribute to a low pH and antimicrobial environment protective against HPV [8,9]. However, in women with persistent high-risk HPV infection, a significant reduction in Lactobacillus dominance is often observed, accompanied by increased microbial diversity and overrepresentation of anaerobic taxa such as Gardnerella vaginalis, Autopodium valine, Sabathia spp., and Privately spp. [4,10,11].

Collectively, longitudinal cohort studies suggest that persistent HRHPV infection is consistently associated with depletion of Lactobacillus-dominated microbial communities and enrichment of anaerobic taxa, particularly Gardnerella vaginalis, Autopodium valine, and Sabathia spp. Across geographically distinct populations, women with persistent HPV infection demonstrate increased microbial diversity and reduced mucosal stability compared with women who successfully clear the virus [11,12]. Notably, Lactobacillus inners appears to represent an intermediate or transitional microbial state, frequently coexisting with anaerobic communities and exhibiting reduced protective capacity compared with Lactobacillus cristates [13].

Microbiota signatures associated with CIN and cervical cancer progression

Cervical Intraepithelial Neoplasia (CIN) and invasive cervical cancer are strongly associated with progressive vaginal dysbiosis. Progression from persistent HPV infection to CIN2/3 and invasive cervical cancer is consistently associated with increased anaerobic microbial diversity and enrichment of pro-inflammatory taxa. Multiple sequencing studies and meta-analyses have identified recurrent overrepresentation of Fusobacterium nucleate, Sabathia spp., Pepto streptococcus anaerobium, and Mobil uncus species in high-grade lesions and invasive disease [14,15]. These dysbiosis microbial communities are thought to contribute to chronic inflammation, epithelial barrier disruption, and altered local immune signaling, thereby facilitating neoplastic progression. Additionally, microbial metabolites such as short chain Fatty Acids (SCFAs) and indole derivatives produced by dysbiosis communities may enhance viral persistence and epithelial transformation by altering immune cell recruitment and cytokine signaling pathways [16].

Longitudinal dynamics and microbiota stability as predictors of progression

Temporal instability of the cervicovaginal microbiome appears to represent an additional risk factor for delayed HPV clearance and progression to high-grade lesions. Longitudinal studies consistently demonstrate that transitions from Lactobacillus cristates-dominated communities toward Gardnerella- or Lactobacillus inners-enriched dysbiosis states are associated with increased microbial turnover and persistent HRHPV infection [16,17]. These alterations may be even more pronounced in immunocompromised populations, including women living with HIV, where polymicrobial anaerobic communities are strongly associated with persistent viral infection and elevated cervical cancer risk [18].

Predictive models using microbiome data

Emerging machine learning approaches suggest that integration of microbiome associated biomarkers with immune and clinical parameters may improve cervical cancer risk stratification beyond HPV testing alone. Several sequencing-based studies have demonstrated that anaerobic dysbiosis-associated microbial signatures can distinguish women with persistent HPV infection or high-grade CIN from healthy controls with relatively high predictive accuracy [5,14]. Recent predictive models integrating microbial composition with cytokine profiling have shown promising sensitivity and specificity in selected cohorts, particularly when inflammatory markers such as IL-6 and IFN-γ are incorporated into classification algorithms [1,20]. However, most currently available models remain limited by relatively small cohort sizes, methodological heterogeneity, and lack of external validation.

A synthesis of the data from the included studies is presented in (Table 1), which summarizes key microbial taxa associated with different stages of HPV infection and cervical lesion progression. Across populations, a consistent trend emerges: HPV negative women generally display Lactobacillus cristates-dominated communities that support mucosal immunity, while women with persistent HPV infection or high-grade CIN show enrichment of anaerobic and pro-inflammatory taxa such as Gardnerella vaginalis, Autopodium valine, Sabathia spp., and Fusobacterium nucleate. Invasive cervical cancer is often characterized by highly diverse communities with gut associated species like Bacteroides and Escherichia, suggesting possible systemic microbial influences. The transition from Lactobacillus-dominated microbial communities to anaerobe-enriched dysbiosis states may reflect progressive alterations in local immune regulation and epithelial homeostasis during cervical carcinogenesis. A proposed workflow integrating microbiome profiling with machine learning-based risk stratification is presented in (Figure 2).

Role of vaginal microbiome in immune modulation and HPV persistence

Accumulating evidence indicates that anaerobic cervicovaginal dysbiosis contributes to local immune dysregulation and impaired antiviral responses. Microbial communities enriched with Gardnerella, Sabathia, and Privately have been associated with increased expression of pro-inflammatory cytokines, reduced interferon signaling, and impaired CD8+ T-cell recruitment, thereby favoring persistent HPV infection [18,21]. Furthermore, epithelial barrier disruption and apoptosis induced by dysbiosis taxa may facilitate viral access to basal epithelial cells and promote neoplastic transformation [21]. Key mechanisms linking vaginal dysbiosis to HPV persistence and neoplastic progression are illustrated in (Figure 3).

Microbial metabolites and metabolic reprogramming in cervical carcinogenesis

Emerging evidence suggests that microbial-derived metabolites may play a substantial role in HPV persistence and cervical carcinogenesis by modulating epithelial metabolism, inflammatory signaling, and local immune responses. Similar to observations in gastrointestinal malignancies, dysbiosis cervicovaginal microbial communities may contribute to tumor-promoting metabolic reprogramming through the production of bioactive metabolites, including Short-Chain Fatty Acids (SCFAs), polyamines, secondary bile acids, and tryptophan-derived compounds [14,21].

Under physiological conditions, Lactobacillus-dominated microbial communities contribute to maintenance of epithelial homeostasis through lactic acid production, preservation of low vaginal pH, and regulation of local immune tolerance [7,8]. By contrast, anaerobe-rich dysbiosis communities enriched with Gardnerella vaginalis, privately spp., Fusobacterium spp., and Sabathia spp. may induce chronic inflammatory signaling and alter local metabolic pathways associated with carcinogenesis [10,14,21].

Several microbial metabolites have been implicated in immune modulation and epithelial transformation. SCFAs may exert context-dependent effects on epithelial proliferation, cytokine production, and Histone Deacetylase (HDAC) regulation, thereby influencing inflammatory responses and viral persistence [14,21,32]. Additionally, dysbiosis-associated tryptophan metabolites may alter interferon signaling and T-cell recruitment within the cervical microenvironment, potentially impairing antiviral immunity and facilitating persistent HRHPV infection [15,21].

Recent metabolomics-integrated studies further suggest that microbial dysbiosis may contribute to oxidative stress, epithelial barrier dysfunction, and activation of oncogenic pathways associated with cervical neoplastic progression. Yang et al. demonstrated bidirectional interactions between the vaginal microbiota and metabolome in women with persistent

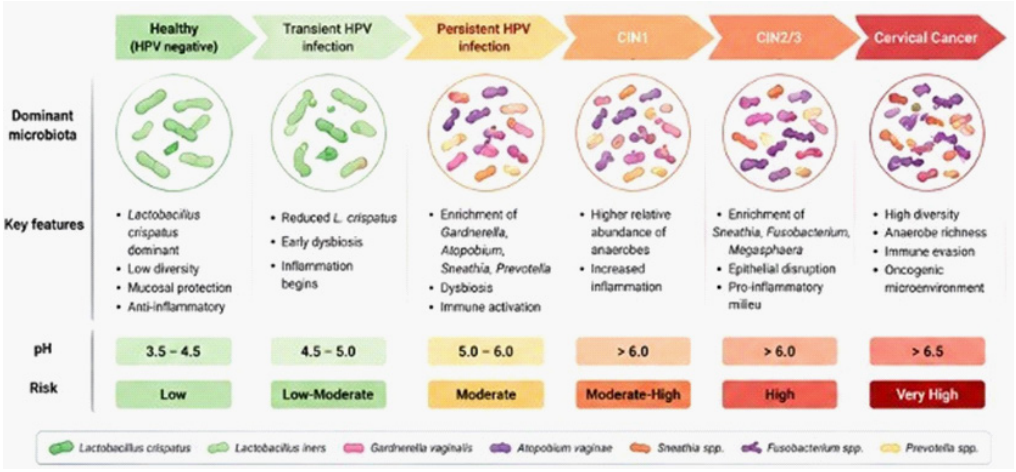


Figure 1: Cervicovaginal microbiome dynamics across cervical carcinogenesis.

Schematic representation of the progressive alterations in cervicovaginal microbiome composition during the transition from healthy cervical epithelium to invasive cervical cancer. Lactobacillus-dominated microbial communities, particularly Lactobacillus crispate, are associated with low vaginal pH, mucosal immune protection, and HPV clearance. In contrast, persistent HPV infection and cervical lesion progression are linked to increased microbial diversity and enrichment of anaerobic taxa, including Gardnerella vaginalis, Autopodium valine, Sabathia spp., Fusobacterium spp., and Privately spp. Progressive dysbiosis is associated with chronic inflammation, epithelial barrier disruption, immune evasion, and increased risk of neoplastic transformation.

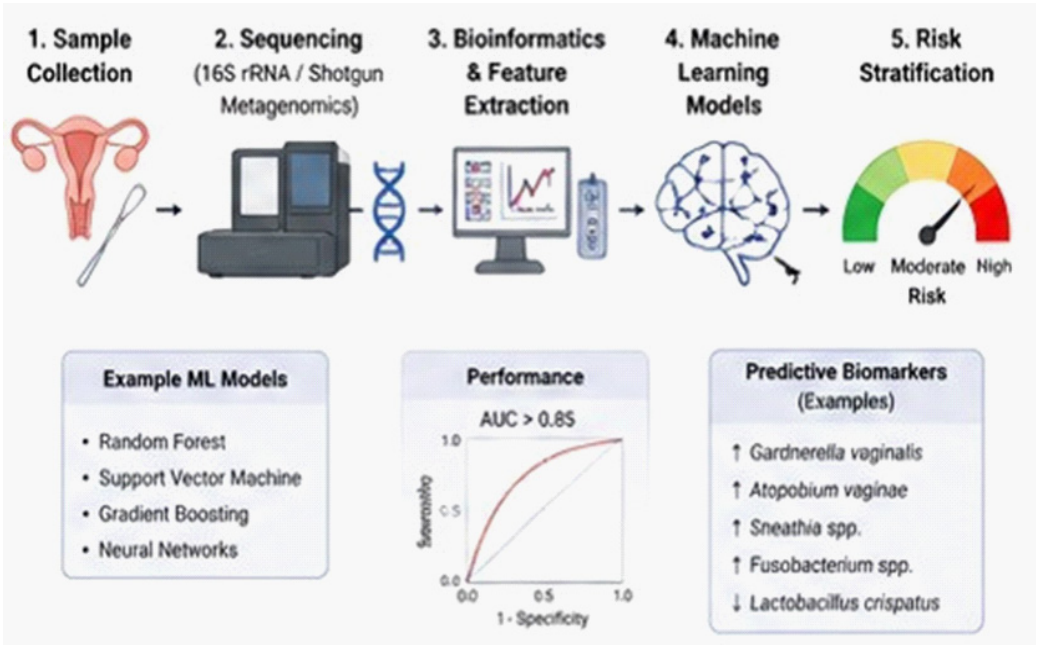


Figure 2: Integration of microbiome profiling and machine learning for cervical cancer risk prediction.

Proposed workflow illustrating the integration of cervicovaginal microbiome profiling with bioinformatics and machine learning approaches for cervical cancer risk stratification. Cervical samples undergo sequencing analysis using 16S rRNA or shotgun metagenomics, followed by computational feature extraction and predictive modeling. Machine learning algorithms, including random forest and support vector machine models, enable identification of microbial signatures associated with HPV persistence and high-grade cervical lesions, supporting personalized screening and precision oncology approaches.

HPV infection and high-grade CIN, highlighting associations between dysbiosis-associated metabolites and inflammatory microenvironment alterations [15]. Likewise, reported that integrated microbiome-metabolome analysis identified significant alterations in lipid metabolism, amino acid pathways, and inflammatory mediators associated with cervical neoplasia progression [21].

These alterations resemble metabolic and inflammatory mechanisms previously described in gastrointestinal and other inflammation-associated malignancies, supporting the concept that microbial-host metabolic interactions represent an important component of cervical carcinogenesis [14,32]. Collectively, integration of microbiome profiling with metabolomics and immune-related biomarkers may improve understanding of microbial-host interactions and contribute to future precision oncology strategies for HPV-associated disease.

Fecal-Vaginal Axis and Systemic Microbiome Influence: Although most studies focus on the local vaginal niche, recent research has highlighted a fecal-vaginal microbial axis, particularly in immunocompromised or postmenopausal populations. In

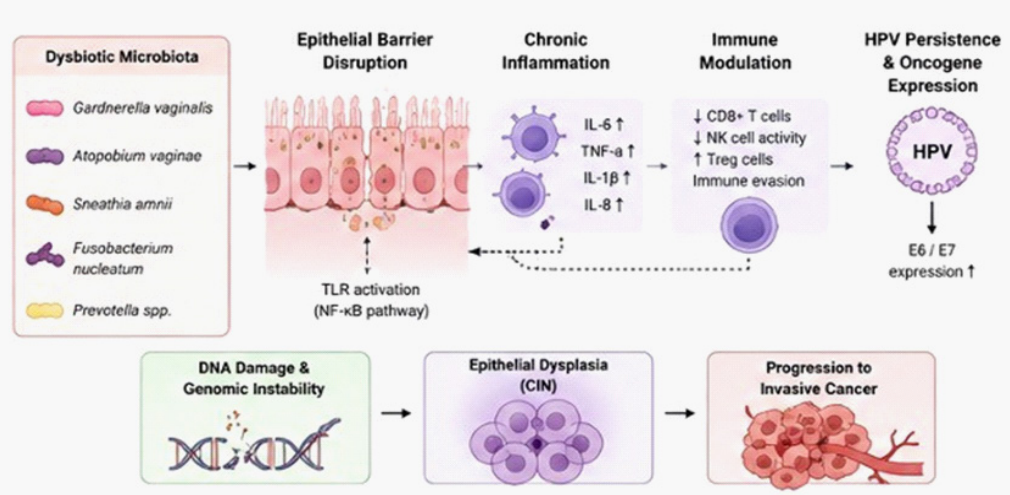


Figure 3: Mechanisms linking vaginal dysbiosis to HPV persistence and cervical carcinogenesis

Illustration of the molecular and immunological mechanisms through which cervicovaginal dysbiosis contributes to persistent HPV infection and cervical carcinogenesis. Dysbiotic microbial communities enriched with anaerobic bacteria promote epithelial barrier disruption, activation of pro-inflammatory pathways, increased cytokine production (IL-1β, IL-6, TNF-α, IL-8), and impaired local immune surveillance. These alterations facilitate HPV persistence, viral oncogene expression, genomic instability, epithelial dysplasia, and progression to invasive cervical cancer.

Table 1: Key microbial taxa associated with HPV status and cervical lesion severity.

Cervical disease stage	Dominant/Enriched taxa	Microbial role	References
HPV-negative (Healthy)	Lactobacillus crispatus, L. jensenii, L. gasseri	Maintains low pH, mucosal immunity, prevents dysbiosis	[8,9]
Transient HPV infection	Lactobacillus iners, L. gasseri (mixed state)	Transitional; less protective; permissive for anaerobes	[5,13]
Persistent HPV infection	Gardnerella vaginalis, Atopobium vaginae, Megasphaera, Sneathia	Induce inflammation, immune suppression, promote persistence	[10-12,15]
CIN 1 (Low-grade)	Lactobacillus iners, Gardnerella vaginalis, Prevotella	Altered immunity, early dysbiosis	[14,15]
CIN 2/3 (High grade)	Fusobacterium nucleatum, Peptostreptococcus, Sneathia amnii, Mobiluncus	Pro-inflammatory, epithelial damage, barrier disruption	[15,17,22]
Invasive cervical cancer	High diversity; enriched Bacteroides, Clostridium, Escherichia	Systemic inflammation, immune evasion, oncogenic potential	[14,22,26]

a multi-omics study involving 400 postmenopausal women, Bacteroides fragilis and Escherichia coli, identified in both fecal and vaginal samples, were more prevalent in women with CIN 2+ lesions [22].

Additionally, microbial metabolites such as secondary bile acids and tryptophan catabolites, produced by gut-associated microbes, may indirectly influence cervical immunity. In a metabolomic-microbiome integration study, demonstrated that high serum levels of Deoxycholic Acid (DCA) were associated with cervical microbial dysbiosis and higher HPV viral load ($r=0.61$, $p<0.001$) [23].

These findings suggest systemic and gut-derived microbial influences may contribute to the risk landscape of cervical carcinogenesis, especially in populations with disrupted epithelial barriers or immune modulation.

Discussion

Accumulating evidence over the last decade has identified the cervicovaginal microbiota as an important modulator of HPV persistence and cervical carcinogenesis. This review synthesizes evidence from sequencing-based and translational studies investigating microbiome-associated biomarkers linked to HPV persistence and cervical carcinogenesis.

Interpretation of microbial shifts and disease risk: A consistent pattern observed across cohorts is the loss of Lactobacillus cristates dominance, which normally maintains acidic pH, produces bacteriocins, and promotes anti-inflammatory immunity [8,9]. Its depletion correlates with HPV persistence and a shift toward polymicrobial, anaerobe-rich communities dominated by Gardnerella vaginalis, Autopodium valine, Sabathia spp., and Fusobacterium nucleate taxa known to induce pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α [5,18,21].

Likewise, a longitudinal cohort in Latin America found that women with Gardnerella dominant microbiota were more likely to have persistent HPV16 infection. However, because these and similar studies were observational, they could not determine whether Gardnerella abundance actively promotes viral persistence or merely reflects secondary HPV-induced mucosal alterations. Without randomized interventional trials, causal inference remains speculative [30].

Dysbiotic microbiota may promote viral integration, impair mucosal immunity, and increase epithelial permeability, facilitating the entry and persistence of HPV in basal epithelial cells [21]. In this inflammatory environment, Sabathia amnio has been shown to cause epithelial apoptosis and neutrophil

infiltration, while G. vaginalis creates biofilms that increase HPV virion survival and avoid immune detection [24].

Furthermore, Lactobacillus inners, although a Lactobacillus species, is increasingly recognized as a "transitional" or "unstable" taxon, often coexisting with anaerobes and associated with progression to CIN2/3 and cancer [13,15]. This suggests that simply measuring Lactobacillus abundance is insufficient; species-level and functional profiling are critical for assessing protective versus pathogenic states.

Diagnostic and clinical implications: These observations support the potential utility of microbiome-based approaches in cervical cancer risk stratification, particularly among HPV-positive women with normal cytology. Recent machine learning models based on microbiome data have achieved promising predictive performance in distinguishing CIN2+ from low-grade or normal samples in selected cohorts [1,6]. Integrating microbial signatures with HPV genotyping and cytokine markers further enhances predictive performance [1,21].

From a public health perspective, microbiome biomarkers could also help triage HPV positive women, reducing unnecessary colposcopies and allowing risk-based surveillance. This is particularly relevant in low- and middle-income countries, where HPV vaccination and cytology-based screening programs remain limited [12].

Moreover, microbial interventions such as probiotics, Vaginal Microbiota Transplants (VMT), or prebiotics are being explored as strategies to restore healthy vaginal flora and support HPV clearance [25]. Early-phase clinical trials of L. cristates probiotics (e.g., LACTIN-V) show promise in reducing dysbiosis and enhancing viral clearance [26].

Emerging areas: Systemic Crosstalk and the Fecal-Vaginal Axis. Emerging studies suggest that systemic microbial-host interactions, including those originating in the gut, may influence cervical cancer risk. Metabolites such as secondary bile acids, indole derivatives, and tryptophan catabolites, produced by gut-resident microbes, can modulate systemic immunity and local cytokine expression in the female reproductive tract [22]. These observations further support the hypothesis that systemic microbial-host interactions may contribute to cervical carcinogenesis through immune and metabolic modulation [22,23].

Moreover, metabolomics-integrated microbiome analysis reveals that microbial composition is closely linked with host serum and mucosal metabolite profiles, which in turn affect HPV persistence and CIN progression [23]. Future work should integrate multi-omics data, including metagenomics, transcriptomics, and metabolomics, to construct a holistic view of microbial-host-tumor interactions.

Recent findings support [27], thematic emphasis that the cervicovaginal microbiota is a dynamic interface between HPV infection and host immunity, dramatically impacting progression risk. As in that study, evidence points to the importance of microbial dysbiosis, chronic inflammation, and barrier disruption as cofactors in cervical carcinogenesis [27]. Longitudinal profiling of women with persistent HPV infection reveals that changes to Gardnerella- and Sabathia-rich communities can occur several months before CIN development, implying that microbiome transitions serve as early indications of malignant transformation.

Collectively, these findings support the concept that microbiota-associated inflammatory pathways may contribute to cervical neoplastic progression [28].

Expanding on the co-evolution concept introduced in the above article, conducted metagenomic profiling across healthy, HPV-infected, CIN, and cervical cancer subjects, identifying nearly 15,000 SNVs in microbial genomes that vary significantly with disease stage (e.g., 9,847 SNVs in HPV-infected vs. 14,892 in cancer) [29]. Their diagnostic model incorporating species-level abundance, SNV frequencies, and metabolic pathway shifts achieved >90% accuracy in distinguishing cervical cancer from CIN or HPV infection. This genomic-level microbial evolution highlights that strain-level variation and functional adaptation offer deeper predictive value than mere presence/absence of a genus.

Despite the growing number of microbiome-associated studies, substantial heterogeneity remains regarding sequencing methodologies, cohort selection, taxonomic resolution, and bioinformatics pipelines. Consequently, direct cross-study comparisons remain challenging and may partially explain inconsistencies in microbial signatures reported across populations. Standardization of sampling protocols and analytical methodologies will therefore be essential before microbiome-based biomarkers can be reliably implemented in clinical practice.

Future clinical translation and precision oncology applications: The integration of microbiome profiling into cervical cancer screening programs may contribute to the development of personalized prevention and surveillance strategies. Microbial signatures associated with persistent HPV infection could potentially help identify HPV-positive women at increased risk for progression despite normal cytology.

In addition, machine learning-driven predictive models integrating microbial, immunological, and clinical data may improve risk stratification and optimize patient selection for colposcopy or intensified follow-up. Such approaches may be particularly valuable in low-resource settings where cytology-based screening remains limited.

Emerging microbiome-targeted interventions, including probiotics, prebiotics, and vaginal microbiota transplantation, are also being investigated as potential adjunctive strategies for restoring microbial homeostasis and supporting HPV clearance. However, large-scale prospective clinical trials are still required before these approaches can be integrated into routine clinical practice.

Limitations and future directions

Despite growing evidence supporting an association between microbial dysbiosis and cervical carcinogenesis, several limitations currently restrict clinical translation. First, substantial heterogeneity exists among studies regarding sampling techniques, sequencing platforms, taxonomic resolution, and bioinformatics pipelines, limiting direct cross-study comparability.

Second, most currently available studies are observational and therefore unable to establish causality between microbiome alterations and cervical cancer progression. Whether dysbiosis directly contributes to carcinogenesis or reflects HPV-induced epithelial and immune alterations remains incompletely understood.

Third, population-specific factors including ethnicity, geographic location, hormonal status, sexual behavior, and antibiotic exposure significantly influence microbial composition and may affect the generalizability of predictive models across populations.

Several studies noted elevated Sabathia amnio abundance in high-grade CIN, but did not perform functional assays to determine whether this organism's virulence factors directly impair epithelial integrity or modulate immune signaling. While some work has associated dysbiosis with changes in cytokine profiles or metabolite production, few studies integrated transcriptomics or metabolomics to confirm mechanistic pathways from microbial composition to cancer progression.

While the review highlights L. inners as a transitional species permissive to anaerobic overgrowth, other research, particularly in pregnancy cohorts has reported L. interdominion microbiomes associated with healthy outcomes and stability. For example, in one African cohort, L. inners presence did not correlate with higher HPV persistence risk, suggesting that its role may depend on community context, strain-level variation, or host immune status [31].

As a result, ethnic, geographic, and hormonal variations influence microbiome composition, and predictive models developed in one population may not generalize globally [12,14,15]. Large-scale multiethnic longitudinal cohorts with repeated sampling and rigorous validation are needed to establish robust microbial risk signatures.

Finally, while species-level taxonomic data are valuable, future studies must emphasize functional macrobiotics, identifying gene expression, metabolite production, and host microbe signaling pathways to truly understand mechanisms underlying HPV persistence and oncogenesis. This review cites metabolomic–microbiome integration showing elevated deoxycholic acid levels in women with dysbiosis and higher HPV viral load, but such studies remain rare. Even fewer combine metagenomics, host transcriptomics, and metabolomics in the same cohort to validate whether observed microbial shifts directly translate into functional metabolic or immune consequences relevant to carcinogenesis [32].

Conclusion

Accumulating evidence supports a significant association between cervicovaginal microbiome composition, persistent HPV infection, and cervical carcinogenesis. Lactobacillus-dominated microbial communities, particularly those enriched with Lactobacillus crispate, appear to exert protective effects by maintaining epithelial homeostasis and promoting viral clearance. In contrast, anaerobe-rich dysbiosis communities have been consistently associated with chronic inflammation, immune dysregulation, and progression to high-grade cervical lesions.

Recent advances in metagenomics and machine learning have enabled the identification of predictive microbial signatures with potential applications in cervical cancer risk stratification and personalized screening strategies. Nevertheless, current evidence remains limited by methodological heterogeneity, observational study designs, and insufficient functional validation.

Future longitudinal and multi-omics studies integrating microbial, immunological, and metabolomic data are required to validate microbiome-based biomarkers and facilitate their translation into clinically applicable tools for cervical cancer prevention and precision oncology.

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All authors read and approved the final manuscript.

Ethics approval and consent to participate: Not applicable.

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