DOI 10.66073/ReFocus-Conf/3010122

CERVICOVAGINAL DYSBIOSIS AS A COFACTOR OF PERSISTENT HUMAN PAPILLOMAVIRUS INFECTION AND PROGRESSION OF CERVICAL NEOPLASIA

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Abstract: Studies published in 2011–2025 on the role of cervicovaginal dysbiosis in the persistence of high-risk human papillomavirus (HPV) and the progression of cervical intraepithelial neoplasia (CIN) were analysed. The *Lactobacillus*-depleted community state CST IV, dominated by anaerobic bacteria, increases the odds of HPV detection, and its share rises from 10% in normal cytology to 40% in invasive cancer. Assessment of the microbiocenosis in HPV-positive women may improve risk stratification.

Keywords: human papillomavirus, cervicovaginal microbiota, dysbiosis, *Lactobacillus*, bacterial vaginosis, CIN.

Annotatsiya: Tezisda servikovaginal disbiozning yuqori onkogen xavfli inson papillomavirusi (HPV) persistensiyasi va bachadon bo‘yni intraepitelial neoplaziyasi (CIN) rivojlanishidagi o‘rni bo‘yicha 2011–2025-yillarda chop etilgan tadqiqotlar tahlil qilindi. Laktobatsillalar kamaygan va anaerob flora ustun bo‘lgan CST IV holati HPV aniqlanish ehtimolini oshirishi, uning ulushi normal sitologiyadan invaziv saratonga qadar 10% dan 40% gacha ortishi ko‘rsatildi. HPV-musbat ayollarda mikrobiotsenozni baholash xavfni tabaqalashtirishni yaxshilashi mumkin.

Kalit so‘zlar: inson papillomavirusi, qin mikrobiotasi, disbioz, *Lactobacillus*, bakterial vaginoz, CIN.

Аннотация: В тезисе проанализированы исследования 2011–2025 гг. о роли нарушения цервиковагинального микробиоценоза в персистенции вируса папилломы человека (ВПЧ) высокого онкогенного риска и прогрессировании цервикальной интраэпителиальной неоплазии (CIN). Показано, что состояние CST IV с дефицитом лактобактерий и преобладанием анаэробной флоры повышает вероятность выявления ВПЧ, а его доля возрастает с 10% при нормальной цитологии до 40% при инвазивном раке. Оценка микробиоценоза у ВПЧ-позитивных женщин может улучшить стратификацию риска.

Ключевые слова: вирус папилломы человека, вагинальная микробиота, дисбиоз, *Lactobacillus*, бактериальный вагиноз, CIN.

Introduction

Cervical cancer remains one of the leading causes of cancer death in women: according to GLOBOCAN 2022, about 661,000 new cases and 348,000 deaths were registered worldwide [1]. Almost all cases are initiated by persistent high-risk HPV infection, although most infections are cleared within one to two years and only a small proportion progresses through CIN to cancer [2]. In healthy women of reproductive age the cervicovaginal ecosystem is normally dominated by lactobacilli [3], and its disturbance is regarded as one of the cofactors that turn a transient infection into a persistent one. The aim was to summarise evidence on the contribution of cervicovaginal

FOR CITATION
Abdullayeva M.I. Cervicovaginal dysbiosis as a cofactor of persistent human papillomavirus infection and progression of cervical neoplasia // Proceedings of the Republican Scientific and Practical Conference “Status and Development Prospects of Fundamental and Applied Microbiology: The Viewpoint of Young Scientists”. – Tashkent, 2026. – P. 434–436.
DOI: https://doi.org/10.66073/ReFocus-Conf/3010122

dysbiosis to HPV persistence and CIN progression and to substantiate microbiocenosis assessment in HPV-positive women.

Materials and methods

Cross-sectional, case-control and cohort studies and meta-analyses published in 2011–2025 and indexed in PubMed, Scopus and Web of Science were analysed. The search combined “HPV” with “vaginal microbiota”, “bacterial vaginosis”, “community state type” and “cervical intraepithelial neoplasia”. Studies were included if the microbiota was characterised by 16S rRNA gene sequencing or by Nugent/Amsel criteria and HPV status was determined by molecular methods (PCR, hybrid capture). Case reports, studies in pregnant women and animal studies were excluded; proportions and odds ratios with 95% CI were compared descriptively.

Results

Lactobacillus-dominated community state types (CST I, II, III, V) are distinguished from the polymicrobial state CST IV with predominance of *Gardnerella vaginalis*, *Fannyhessea vaginae*, *Prevotella*, *Sneathia* and *Megasphaera*; CST IV was found in 27.0% of 396 asymptomatic women [3]. A meta-analysis of 12 studies (6,372 women) showed that bacterial vaginosis increases the odds of cervical HPV detection (OR 1.43; 95% CI 1.11–1.84) [4]. The anaerobic state CST IV-B is associated with the slowest viral clearance [5], and *Lactobacillus*-depleted and *L. iners*-dominated communities carry higher odds of HPV infection and dysplasia than *L. crispatus* dominance [6]. The share of CST IV increases from 10% in normal cytology to 21% in LSIL, 27% in HSIL and 40% in invasive cancer [7]. In women with untreated CIN2, regression within 12 months was observed in 70.0% of those with a *Lactobacillus*-dominant microbiota and in only 42.1% of those with depletion of lactobacilli [8].

Discussion

Several mechanisms link dysbiosis with HPV-associated carcinogenesis. The fall in lactic acid production and the rise of vaginal pH above 4.5 weaken the virucidal and anti-inflammatory action of lactic acid [9]; sialidases and mucinases of *Gardnerella* and *Prevotella* degrade cervical mucus and damage the epithelium; anaerobic bacteria maintain chronic inflammation with production of IL-1β, IL-8 and TNF-α, which leads to oxidative stress and DNA damage [10]. HPV oncoproteins E6 and E7, in turn, suppress local immunity, so the relationship is bidirectional. For Uzbekistan, where HPV vaccination of girls began in 2019 and the adult female population remains unvaccinated, Gram-stain microscopy of vaginal smears already performed in clinical diagnostic laboratories allows microbiocenosis assessment without significant additional costs.

Conclusion

Depletion of lactobacilli and predominance of anaerobic flora in the cervicovaginal microbiocenosis act as a cofactor that favours HPV persistence and CIN progression. The share of the dysbiotic community state increases four-fold from normal cytology to invasive cancer, and *Lactobacillus* dominance is associated with more frequent regression of CIN2. Evaluating the microbiocenosis (pH, Nugent score, quantitative PCR of lactobacilli) alongside HPV genotyping may improve risk stratification in screening programmes.

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