

Original Research

Study on the Correlation between Cervical Intraepithelial Lesions and Human Papillomavirus Infection and Vaginal Microecology

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Abstract

Background: The aim of this study was to explore the correlation between high-risk human papillomavirus (HR-HPV) infection and changes in vaginal microecology, as well as the severity of cervical intraepithelial lesions (CIN). **Methods:** A retrospective analysis was conducted on 221 inpatients (aged 23–80 years) who underwent simultaneous testing of vaginal secretions for microecological parameters, HR-HPV genotyping, and cervical tissue biopsy at the Department of Gynecology, Second Affiliated Hospital of Xinjiang Medical University, Urumqi, from October 2021 to January 2023. The study subjects were analyzed to determine the association between HR-HPV infection and alterations in vaginal microecology, as well as CIN. **Results:** Among the 221 cases, 69 were positive for HR-HPV, resulting in a positivity rate of 31.22% (69/221). Out of the 139 cases with normal vaginal microecology, 26 were positive for HR-HPV, yielding a positivity rate of 18.71% (26/139). Among the 82 cases with abnormal vaginal microecology, 43 were positive for HR-HPV, resulting in a positivity rate of 52.44% (43/82). Out of the 162 cases with normal cervix, 26 were positive for HR-HPV, resulting in a positivity rate of 16.00% (26/162). Among the 59 cases with abnormal cervix, 43 were positive for HR-HPV, resulting in a positivity rate of 72.88% (43/59). In the cases of abnormal cervix, 10 presented cervical inflammation, with a HR-HPV positivity rate of 70.00% (7/10); 20 cases had cervical intraepithelial lesions (CIN) I, with a HR-HPV positivity rate of 70.00% (14/20); 20 cases had CIN II, with a HR-HPV positivity rate of 75.00% (15/20); and 9 cases had CIN III, with a HR-HPV positivity rate of 77.80% (7/9). Moreover, among the 162 cases with normal cervix, 36 had abnormal vaginal microecology, resulting in an abnormality rate of 22.22% (36/162). Among the 59 cases with abnormal cervix, 46 had abnormal vaginal microecology, resulting in an abnormality rate of 77.97% (46/59). In the cases of abnormal cervix, 10 had cervical inflammation, with an abnormal vaginal microecology rate of 70.00% (7/10); 20 cases had CIN I, with an abnormal vaginal microecology rate of 70.00% (14/20); 20 cases had CIN II, with an abnormal vaginal microecology rate of 80.00% (16/20); and 9 cases had CIN III, with an abnormal vaginal microecology rate of 100.00% (9/9). The differences in HR-HPV positivity rates between the group with normal vaginal microecology and the group with abnormal vaginal microecology were statistically significant ($p < 0.05$). Similarly, the differences in HR-HPV positivity rates for different degrees of CIN were statistically significant ($p < 0.05$), as well as the differences in abnormal vaginal microecology rates for different degrees of CIN ($p < 0.05$). **Conclusions:** HR-HPV infection was found to be significantly associated with alterations in vaginal microecology and CIN.

Keywords: human papillomavirus; cervical intraepithelial lesion; vaginal microecology; correlation

1. Introduction

Cervical cancer is the most prevalent infection-associated neoplasm among women. Infection with high-risk human papillomavirus (HR-HPV) has been implicated in the development of cervical intraepithelial neoplasia and cervical cancer, and there may be synergistic effects in their progression [1,2]. Similar to other mucosal sites in the body, the female genital tract harbors a distinct microbial community, primarily dominated by *Lactobacillus* genus, which plays a vital role in maintaining health and homeostasis. Growing evidence suggests that dysbiosis of the reproductive tract, along with specific bacteria and cytokines, may contribute to HPV infection and the advancement of cervical intraepithelial lesions (CIN). Therefore, this study aims to examine the relationship between CIN, HPV infec-

tion, and changes in vaginal microecology, offering novel insights for the prevention and treatment of these conditions.

2. Data and Methods

2.1 Study Subjects

A total of 221 inpatients, aged 23–80 years, were selected as study subjects from October 2021 to January 2023 at the Department of Gynecology, Second Affiliated Hospital of Xinjiang Medical University. These patients underwent simultaneous microecological testing of vaginal secretions, genotyping of HPV, and cervical tissue biopsy. The study received approval from the Ethics Committee of the Second Affiliated Hospital of Xinjiang Medical University, and all participants provided informed consent. Inclu-



Table 1. Comparison of HR-HPV Positivity Rate between the Abnormal Vaginal Microecology Group and the Normal Group.

		HR-HPV positive rate (%)	Total	χ^2	p
Vaginal microecology	Positive	43 (52.44)	82	27.332	0.000
	Negative	26 (18.71)	139		

HR-HPV, high-risk human papillomavirus.

Table 2. Differences in HR-HPV Positive Expression Rates Across Various Cervical Lesions.

Cervical lesions	Number	HR-HPV positive rate (%)		χ^2	p
		Positive	Negative		
Normal	162	26 (16.00)	136 (84.00)	17.681	0.000
Cervical inflammation	10	7 (70.00)	3 (30.00)		
CIN I	20	14 (70.00)	6 (30.00)	30.218	0.000
CIN II	20	15 (75.00)	5 (25.00)	35.448	0.000
CIN III	9	7 (77.80)	2 (22.20)	20.861	0.000
Total	221	69 (31.20)	152 (68.80)	65.309	0.000

CIN, cervical intraepithelial lesions; HR-HPV, high-risk human papillomavirus.

sion criteria consisted of a history of sexual intercourse, informed consent, and cooperation, while exclusion criteria included irregular vaginal or menstrual bleeding, pregnancy or lactation, presence of other tumors, severe gynecological or endocrine diseases, and inability to cooperate.

2.2 Methods

2.2.1 Vaginal Micro-Ecological Test

Specimen collection: The patient assumed a cystoscopy position, and the lateral wall of the vagina and the cervical area were fully exposed. A sterile cotton swab was used to collect an appropriate amount of secretion from the upper 1/3 of the lateral wall, which was then placed in a test tube.

Detection method: The vaginitis joint detection kit and Bpr-2014A vaginitis automatic detection workstation (Master Biotechnology Co., Ltd, Suzhou, Jiangsu, China), was employed according to manufacturer's instructions.

Test content and significance: The microscopic detection after Gram staining assessed the density, diversity, dominant flora, and presence of special pathogens such as spores, budding spores, fungal hyphae, and trichomonas. An aerobic vaginitis (AV) score greater than 3 diagnosed the presence of AV. Additionally, the normal range of vaginal pH was considered to be between 3.8 and 4.5. An abnormal vaginal microecology was diagnosed if there were abnormalities in any of the flora densities, diversity, dominant flora, pH, or *Lactobacillus* function.

2.2.2 HPV Genotyping Test

Specimen collection: The cervix was exposed, excess secretions were wiped away using a sterile cotton swab, and a special cervical brush was inserted into the cervical canal. By rotating it clockwise five times, exfoliated ep-

ithelial cells at the squamocolumnar junction of the cervix were collected and placed in a specimen bottle containing HPV preservation solution.

Detection method: The HR-HPV typing nucleic acid assay kit (Beijing Bohui Innovation Biotechnology Group Co., Beijing, China), was used to detect specific DNA nucleic acid fragments of 18 HR-HPV subtypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, 83).

2.2.3 Statistical Processing

Statistical analysis was performed using SPSS 19.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics, Chi-square (χ^2) test, calculation of odds ratios (OR) and their 95% confidence intervals (CI) were conducted. Statistical significance was considered at $p < 0.05$.

3. Results

3.1 Comparison of HR-HPV Positivity Rate between the Abnormal Vaginal Microecology Group and the Normal Group

A significant difference was observed in the HR-HPV positivity rate between the groups with abnormal and normal vaginal microecology. The positive rate in the abnormal microecology group was significantly higher than that in the normal group ($p < 0.05$), as shown in Table 1.

3.2 Differences in HR-HPV Positive Expression Rates among Different Cervical Lesions

Significant differences were observed in the HR-HPV positivity rates across different cervical lesions. These rates demonstrated an increase in conjunction with the severity of the different analyzed cervical lesions ($p < 0.05$). These statistical findings are presented in Table 2.

Table 3. Variations in Positive Expression Rates of Vaginal Microecology Across Different Cervical Lesions.

Cervical lesions	Number	Vaginal microecology		χ^2	<i>p</i>
		Positive (%)	Negative (%)		
Normal	162	36 (22.22)	126 (77.78)		
Cervical inflammation	10	7 (70.00)	3 (30.00)	20.395	0.000
CIN I	20	14 (70.00)	6 (30.00)	29.120	0.000
CIN II	20	16 (80.00)	4 (20.00)	26.600	0.000
CIN III	9	9 (100.00)	0 (0)	11.467	0.000
Total	221	82 (37.10)	139 (62.90)	60.311	0.000

CIN, cervical intraepithelial lesions; HR-HPV, high-risk human papillomavirus.

3.3 Variations in Positive Vaginal Microecology Expression Rates among Different Cervical Lesions

Significant disparities in vaginal microecology were observed among distinct cervical lesions. Notably, as the severity of cervical lesions increased, the positive rate of vaginal microecology also showed a corresponding escalation. These findings are statistically significant ($p < 0.05$) and are presented in Table 3, for reference.

4. Discussion

HPV, a double-stranded closed-loop DNA virus, exhibits the ability to self-replicate and encode within vaginal epithelial cells during their differentiation process. By manipulating cell growth patterns, the virus can effectively evade the immune system. Over time, persistent infection in the host can lead to the development of various cervical tissue lesions [3]. Among the 100+ identified HPV types, approximately 40 can infect the genital tract [4]. These types are classified as high- or low-risk based on their propensity to induce intraepithelial lesions in the cervix [5,6]. In our study, out of the 69 cases of HPV infection, the most common types were HPV16, HPV52, and HPV58, which are also prevalent in China. Persistent infection with HPV16, HPV52, and HPV58, showed a strong association with viral load and grade II and III CIN [7–9]. Notably, HPV58 infection is particularly prevalent among 90% of patients with CIN, or cervical squamous cell carcinoma in our country. It is important to note that while HR-HPV infection is widespread, only a small proportion (5–10%) of these infections are considered genuinely risky, indicating persistence [10–12]. However, there is some ambiguity in defining the duration of persistence required to represent a “risk”. Approximately 75% of HR-HPV infections leading to cervical squamous cell carcinoma occur before the age of 30, with cancer development peaking after 10 years. This suggests that, on average, 10–20 years of persistent infection is necessary for the development of cervical squamous cell carcinoma [13,14]. The extended timeframe allows for preventive measures and interventions, including HPV testing, cytological screening, and local treatment of identified precancerous lesions.

HR-HPV serves as a significant risk factor for the development of pre-cancerous and cancerous conditions in the cervix. Due to its high sensitivity for cervical disease, it is commonly employed as an early detection tool for cervical lesions. The lower genital tract of women encompasses a crucial microecological environment, where various microflora coexist in a state of relative balance within the vagina of healthy individuals [15]. Among these, *Lactobacillus* species play a predominant role and contribute to the maintenance of vaginal microecological equilibrium by producing lactic acid, hydrogen peroxide, and other enzymes under optimal temperature and pH conditions [16,17]. Findings from this study indicate that an imbalance in vaginal microecology tends to facilitate the expression of HPV, thereby leading to cervical tissue lesions. Disruption of the vaginal mucosa and abnormal elevation of pH weaken the local vaginal microecology, impairing its ability to inhibit pathogenic microorganisms. Concurrently, lactobacilli, which play a critical role in maintaining homeostasis, are suppressed within the vaginal flora, resulting in an increased prevalence of *Candida* and *Trichomonas*. Consequently, the rate of HPV virus infection significantly rises, and individuals infected with HR-HPV are at a substantially higher risk of developing various cervical lesions, which pose significant health risks [18].

CIN do not typically present with distinctive clinical symptoms, and high-grade lesions are more commonly observed in patients over the age of 46 [1,19]. HPV is implicated in approximately 5% of global cancer cases, including cervical, vaginal, oropharyngeal, and other malignancies. Among these, cervical cancer exhibits the highest incidence, accounting for around 260,000 annual deaths [20]. Worldwide, cervical cancer remains the most prevalent form of cancer within the female reproductive system, posing a severe threat to women’s lives and overall health.

Despite the availability of the HPV vaccine, the burden of cervical cancer is projected to remain high in the next 30–50 years due to low immunization rates in low- and middle-income countries, and inadequate cervical cancer screening worldwide [21]. Recent evidence suggests that the composition of vaginal flora in cervical disease may influence the persistence of HPV infection and disease pro-

gression. A deeper understanding of the impact of vaginal flora composition could contribute to the development of more advanced markers for detecting microflora and provide valuable insights and targets for the development of novel preventive and therapeutic interventions.

5. Conclusions

In conclusion, this study highlights the increased risk of developing CIN associated with both HR-HPV infection and vaginal microecological abnormalities. Vaginal microecological imbalances may potentially synergize with HR-HPV infection in the development of cervical lesions. Therefore, it is recommended to conduct concurrent vaginal microecological testing in HR-HPV-positive patients to assess the presence of vaginal microecological abnormalities. However, further investigation is warranted to elucidate the synergistic mechanism involving vaginal microecology, HR-HPV infection, and CIN. Additionally, it is crucial to determine whether the treatment of vaginal microecological abnormalities can influence the conversion of HR-HPV infection.

Availability of Data and Materials

In accordance with the journal's guidelines, we will provide our data for the reproducibility of this study if our institution approved the request.

Author Contributions

QHZ: Conception, data curation, formal analysis, investigation, methodology, writing - original draft, Writing - review & editing. YSL: Participate in the completion of writing - original draft, interpretation of data. CSX: Conception, funding acquisition, resources. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study received approval from the Ethics Committee of the Second Affiliated Hospital of Xinjiang Medical University (approval number: 2022H024), and all participants provided informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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