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# Human Papillomavirus Genotyping and Viral Load as a Predictor of Cervical Lesions: A Prospective Study

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**Keywords:** cervical lesions | HPV genotyping | human papillomavirus | multiple infections | viral load

## ABSTRACT

This prospective study aims to examine the impact of changes in viral load on the occurrence of cervical lesions and to evaluate viral load as a biomarker for predicting cervical lesions and triaging HPV-positive patients. From September 2022 to August 2023, 1150 women aged 25–60 were enrolled at the Changzhou Maternal and Child Health Hospital. All participants tested positive for HPV and negative for both cytology and pathology. A follow-up was conducted 6 months later to reassess HPV status and perform colposcopy. BMRT was employed to detect various HPV types and their viral loads. The ROC curve was utilized to determine the viral load cut-off values for different HPV types to predict cervical lesions. From baseline to follow-up, women whose HPV infection cleared were significantly younger than those with persistent HPV infection ($p < 0.001$). At baseline, the viral loads of the virus clearance, maintenance, and progression groups demonstrated an increasing trend ($p < 0.001$). Among women diagnosed with CIN during follow-up, the viral load increased significantly from baseline to follow-up ($p = 0.001$). The combination of HPV genotyping and viral load in the initial screening of cervical cancer enhances the prediction and identification of cervical lesions.

## 1 | Introduction

Cervical cancer is the fourth most common cancer in terms of both incidence and mortality in women, with an estimated 660 000 new cases and 350 000 deaths worldwide in 2022 [1]. The burden of cervical disease should be further reduced, with the ultimate goal of eradicating cervical cancer [2]. Due to the discovery that high-risk human papillomavirus (hrHPV) is a required cause of cervical cancer [3], HPV-based cervical cancer screening and vaccinations have been developed. The genotyping findings for the following 14 HR-HPV strains were reported by the International Agency for Research on Cancer (IARC): 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. The most prevalent HR-HPV among them is HPV-16, which is followed by HPV-31 and HPV-18 [4]. More than 50% of lesions that are grade 3 or higher in cervical intraepithelial neoplasia (CIN) are associated with HPV16 infection [5]. As a virus of the same genus as HPV16, studies [6] have shown that women infected with Alpha-9 (HPV16, 31, 33, 35, 52, 58) are more likely to develop CIN2+ lesions. Since the start of the global HPV vaccination campaign, the prevalence of HPV16/18 infections has steadily decreased, but the incidence of infections with other high-risk genotypes, like HPV52 and HPV58, has slightly increased [7, 8]. High-grade cervical lesions are

more likely to have the HR-HPV genotypes 31, 33, 52, and 58 than 18 [9, 10].

The use of HPV genotyping for risk assessment was recommended by the ASCCP guidelines in 2019 [11]. The HPV screening alone or the HPV and cytology co-test is suggested as a "risk-based" treatment strategy [11]. The use of Pap smears or liquid-based cytology in the triage of women who have HPV increases specificity, but it has drawbacks: the method's performance is operator-dependent, and it is difficult to repeat and standardize [12]. Additionally, self-collected samples cannot be used for cervical cytology, despite the fact that they are increasingly being used in screening programs to increase the participation of women. The use of more standardized and repeatable molecular approaches, such as genotype-specific HR-HPV viral load [13] and comprehensive high-risk HPV (HR-HPV) genotyping, could enhance the risk stratification in cervical cancer screening programs. The expression of HPV viral load in the "Chinese Cervical Cancer Screening Guidelines" in 2023 [14], the "Consensus of the European Society of Gynecological Oncology and the European Colposcopy Federation" in 2020 [15], and the "French Cervical Cancer Screening Guidelines" in 2022 [16] are relatively consistent. The influence of HPV types and viral load on the emergence of low-grade and high-grade cervical lesions has been examined in several studies [17–20], but a large sample of prospective research data still needs to be accumulated.

This study uses the combined screening of HPV genotyping and viral load to explore the relationship between the viral load of persistent infection of different HPV types and the progress of cervical lesions, meanwhile, evaluating the importance of HPV typing and viral load in the first screening of cervical cancer.

## 2 | Methods

### 2.1 | Patients

From September 2022 to August 2023, women who visited the cervical disease diagnosis and treatment center at Changzhou Maternal and Child Health Hospital for their first cervical cancer screening were included in the study. Participants were considered eligible if they were 25–60 years old, cytology-negative, free of cervical lesions, and had a positive HPV quantitative typing test (BMRT-HPV). Patients were excluded if they had undergone prior treatment for cervical lesions (e.g., cold knife conization (CKC), loop electrosurgical excision procedure (LEEP), cryotherapy), had a hysterectomy, or planned to become pregnant in the near future (Figure 1). All projects were performed in compliance with relevant laws and institutional guidelines and in accordance with the ethical standards of the Declaration of Helsinki, and all patients provided their written informed consent to participate in this study.

### 2.2 | Follow-Up

Follow-up was conducted by the research team 6 months later. All patients in the cohort ($N = 1150$) were notified to attend follow-up visits. This resulted in 1012 follow-ups being successfully completed. During the follow-up, the subjects underwent HPV quantitative typing tests. If the virus was cleared, colposcopy was deemed unnecessary. However, if the HPV quantitative typing test was positive, colposcopy was required. If colposcopy results indicated CIN2+ lesions, appropriate treatment was administered.

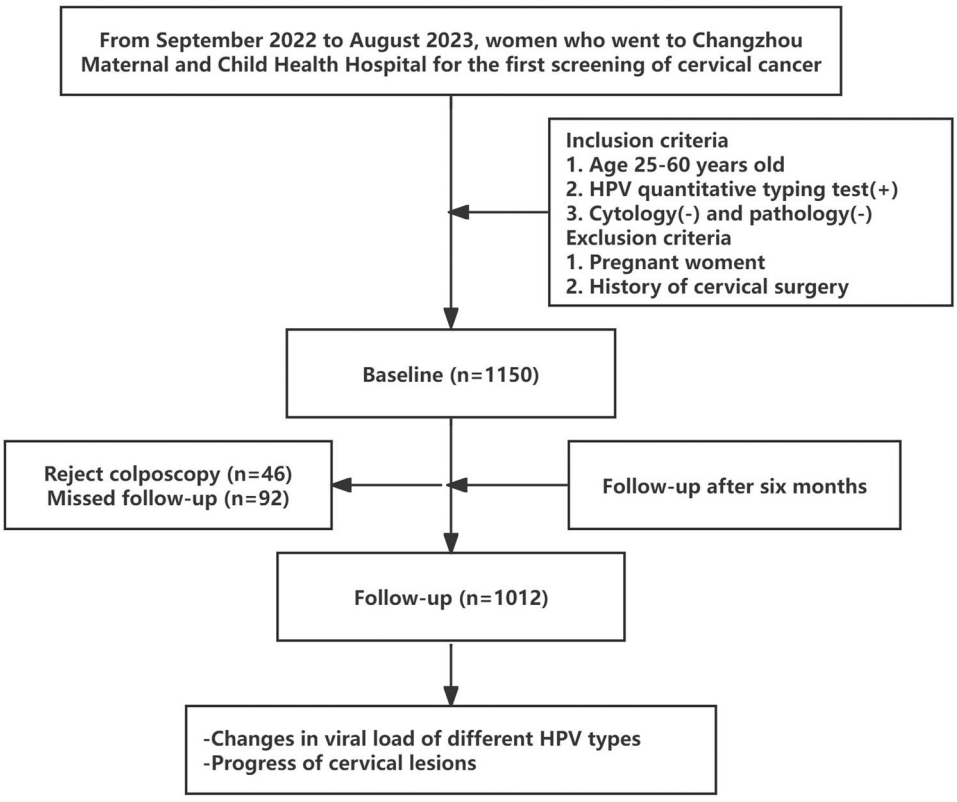


**FIGURE 1** | Study flowchart.

### 2.3 | Liquid-Based Cytology

Two experienced cytopathologists blindly assessed cytological samples. In the event that the diagnosis was different, the cervical samples were reviewed once more to reach a consensus. The Bethesda system was used to evaluate the results. Atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), squamous cervical cancer (SCC), atypical glandular cells (AGC), and adenocarcinoma (ADC) in situ were the classifications given to the samples.

### 2.4 | BMRT HPV PCR Assay

The fluorescence-based multiplex HPV DNA genotyping kit (Bioperfectus Ltd, Jiangsu, P.R. China) was used for the BMRT, a PCR-based high-risk HPV assay. For the 21 most common HPV types, including 14 HR-HPV genotypes (HPV16,18,31,33,35,39, 45,51,52,56,58,59,66, and 68) and 7 MR and LR-HPV genotypes (HPV26,53,82,73,6,11, and 81). HPV nucleic acids were genotyped and quantitatively analyzed using Perfectus, v1.0 (Bioperfectus Ltd.).

### 2.5 | Colposcopy and Biopsy

Colposcopy and punch biopsy were recommended for women who were HPV positive and/or had an abnormal cytological outcome. Specimens were routinely prepared for paraffin embedding after being preserved in 10% formalin. Then, using the conventional technique, 4-μm-thick histological slices were cut and stained with H&E.

### 2.6 | Statistical Analysis

*t*-tests or non-parametric statistics were used to examine the counting data, while $\chi^2$ tests were used to assess the measuring data. The type-specific HPV viral loads were determined using log10-transformed absolute viral copy counts per 10 000 human cells, and the mean and standard deviation (SD) are presented. The best cut-off value for predicting cervical lesions based on type-specific HR-HPV viral loads was using a receiver operating characteristic (ROC) curve. SPSS 23.0 software was utilized for all data analysis in this study, with a two-sided significance level of 0.05.

## 3 | Results

### 3.1 | Study Population

The baseline cohort included a total of 1150 patients, with 816 (71.0%) single-infected and 334 (29.0%) multiple-infected. The participants had a median age of 40 years (range, 33–48), with those whose HPV infection had cleared being younger than those whose HPV infection had persisted ($p < 0.001$). The HPV quantitative typing results showed that 1030 (89.6%) women had high-risk HPV infection, 236 (20.5%) had medium- and low-risk HPV infection, 597 (51.9%) were infected with α-9 HPV, 249 (21.7%) had HPV16 infection, and 264 (23.0%) had HPV52 infection. Only 95 (8.3%) women were infected with HPV18. At baseline, the average viral load for different HPV types was $4.30 \pm 1.58$ (HPV16), $3.63 \pm 1.40$ (HPV18), $4.15 \pm 1.19$ (HPV52), $4.25 \pm 1.40$ (α-9 HPV), $4.26 \pm 1.48$ (high-risk HPV), and $4.19 \pm 1.66$ (medium- and low-risk HPV). In the follow-up, 509 (50.3%) had a single infection, and 210 (20.7%) had multiple infections; 293 (29.0%) women had cleared the virus. The distribution of different HPV types was as follows: 12.9% (HPV16), 17.2% (HPV52), 4.8% (HPV18), 62.9% (high-risk HPV), 41.6% (α-9 HPV), and 14.2% (medium- and low-risk HPV). No statistical difference was observed from baseline ($p = 0.18$). In the follow-up, the average viral load for different HPV types was slightly higher than at baseline, with statistical differences observed only in high-risk HPV ($p = 0.024$). In the follow-up, 46 patients refused colposcopy, 471 had inflammation, 237 had LSIL, and 14 had HSIL (Table 1).

### 3.2 | Comparison of HPV Viral Loads Based on Follow-Up Outcomes

Compared with the baseline, 293 individuals experienced HPV virus clearance, 469 individuals exhibited persistent HPV infection without cervical lesions, and 250 individuals had persistent HPV infection with low- or high-grade lesions. These patients were categorized into the virus clearance group, maintenance group, and progression group. The baseline viral load among the three groups exhibited an increasing trend across different HPV genotypes. Significant statistical differences ($p < 0.001$) were observed among the virus clearance, maintenance, and progression groups for 21 HPV types, medium- and low-risk HPV, high-risk HPV, HPV16, and α-9 HPV. However, for HPV52, no significant difference in viral load was detected between the virus clearance and maintenance groups. In contrast, the viral load in the progression group was significantly higher than that in both the virus clearance and maintenance groups ($p < 0.001$) (Figure 2).

During the follow-up, the viral load in CIN patients was significantly higher than that in lesion-free patients. Specific results by HPV type included HPV16 ($p < 0.001$), HPV52 ($p < 0.001$), α-9 HPV ($p < 0.001$), high-risk HPV ($p < 0.001$), and medium- and low-risk HPV ($p < 0.001$) (Table 2).

### 3.3 | Changes in Viral Load From Baseline to the Follow-Up

The study employed a one-to-one self-pairing method to compare changes in viral load between baseline and follow-up. Among women diagnosed with CIN during follow-up, a significant increase in viral load was observed from baseline to follow-up. The specific HPV types showing this increase were 21 HPV types ($p = 0.001$), α-9 HPV ($p = 0.043$), HR-HPV ($p = 0.011$), and M/LR-HPV ($p = 0.032$). For patients who remained lesion-free during follow-up, the viral load decreased from baseline to follow-up. A statistically significant reduction in viral load was observed for high-risk HPV and α-9 HPV

**TABLE 1** | Clinical characteristics of patients.

| Items | Baseline ($n = 1150$) $n$ (%) | Follow-up ($n = 1012$) $n$ (%) | $p$-value[a] |
|---|---|---|---|
| Age (year) | | | — |
| HPV-persistent | 40 (33–48) | 41 (34–49) | < 0.001 |
| HPV-clearance | — | 38 (32–46) | |
| HPV infection | | | 0.94 |
| Single infection | 816 (71.0%) | 509 (50.3%) | |
| Multiple infections | 334 (29.0%) | 210 (20.7%) | |
| HPV-clearance | — | 293 (29.0%) | — |
| HPV genotyping[b] | | | 0.18 |
| HPV16 | 249 (21.7%) | 131 (12.9%) | |
| HPV18 | 95 (8.3%) | 49 (4.8%) | |
| HPV52 | 264 (23.0%) | 174 (17.2%) | |
| Alpha9 | 597 (51.9%) | 421 (41.6%) | |
| HR-HPV | 1030 (89.6%) | 637 (62.9%) | |
| M/LR-HPV | 236 (20.5%) | 144 (14.2%) | |
| HPV viral load[c] | | | |
| HPV16 | 4.30 ± 1.58 | 4.47 ± 1.53 | 0.43 |
| HPV18 | 3.63 ± 1.40 | 3.83 ± 1.33 | 0.55 |
| HPV52 | 4.15 ± 1.19 | 4.43 ± 1.38 | 0.083 |
| Alpha9 | 4.25 ± 1.40 | 4.46 ± 1.42 | 0.065 |
| HR-HPV | 4.26 ± 1.48 | 4.47 ± 1.47 | 0.024 |
| M/LR-HPV | 4.19 ± 1.66 | 4.46 ± 1.68 | 0.30 |
| Colposcopy | | | — |
| lesion-free | 1150 (100%) | 471(46.5%) | |
| LSIL | — | 237(23.4%) | |
| HSIL | — | 14(1.4%) | |

Abbreviations: HPV, human papillomavirus; HR-HPV, high-risk HPV; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; M/LR-HPV, medium-risk and low-risk HPV.
[a]$p < 0.05$ is statistically significant.
[b]The prevalence of HPV genotype was calculated type estimate (Any). Any was calculated in all HPV infection populations, and multiple HPV infections were calculated more than once.
[c]The logarithm of HPV gene copy number/10 000 cells.

($p = 0.047$, $p = 0.028$). However, the reduction in viral load for 21 HPV types did not reach statistical significance ($p = 0.13$) (Table 3). This indicates that the progression from lesion-free status to cervical lesions is accompanied by an increase in HPV viral load, consistent with previous research findings [21, 22]. Conversely, when HPV infection persists without cervical lesions, the viral load decreases, which may be influenced by the body's immune response.

### 3.4 | The Performance and Cut-Off Values of Viral Loads in Predicting CIN

Baseline and follow-up HPV viral loads were used to predict and diagnose the progression of cervical lesions (Figure 3). According to the ROC curve analysis, the optimal cut-off values for the viral loads of 21 HPV types at baseline and follow-up were 5.01 (Se = 55.38%, Sp = 73.32%) and 4.90 (Se = 68.80%, Sp = 69.08%), respectively. For high-risk HPV viral loads, the optimal cut-off values at baseline and follow-up were 4.56 (Se = 71.25%, Sp = 62.78%) and 5.04 (Se = 62.78%, Sp = 75.98%), respectively. The optimal cut-off values for α-9 HPV's viral loads were 4.16 (Se = 80.40%, Sp = 58.90%) and 4.87 (Se = 66.67%, Sp = 75.13%) at baseline and follow-up, respectively. The appropriate cut-off values for M/LR-HPV viral loads were 4.46 (Se = 72.41%, Sp = 75.71%) and 5.33 (Se = 73.08%, Sp = 83.93%) at baseline and follow-up, respectively. Similarly, the optimal cut-off values for HPV 16 viral loads were 4.81 (Se = 67.74%, Sp = 69.31%) and 3.91 (Se = 78.38%, Sp = 56.25%), while for HPV 52 viral loads, they were 4.18 (Se = 82.35%, Sp = 63.39%) and 4.87 (Se = 72.97%, Sp = 80.00%) (Table 4).

As the results indicate, except for HPV16, the baseline cut-off values demonstrated high sensitivity, whereas the follow-up cut-off values exhibited high specificity. This suggests that baseline cut-off values can be used for preliminary prediction of cervical lesions, while follow-up cut-off values are better suited for diagnostic prediction and referral for colposcopy due to their high specificity.

## 4 | Discussion

At present, the relationship between HPV viral load and cervical lesions is still controversial. Most scholars [23, 24] believe that there is a direct link between HPV viral load and the degree of cervical lesion. Martinelli et al. [25] confirmed that HPV16 viral load was associated with CIN 3 only, while Berggrund et al. [26] demonstrated that high-risk HPV viral load was associated with CIN 2+ lesions. A correlation between HPV viral load and the progression of cervical precancerous lesions was identified in this study. The baseline viral load, whether in 21 HPV types, high-risk HPV, medium- and low-risk HPV, α-9 HPV, or HPV16 and HPV52, was significantly associated with the outcomes of cervical lesions during follow-up. Additionally, the study revealed that the viral load during follow-up was correlated with pathological outcomes, with CIN patients exhibiting significantly higher viral loads at both baseline and follow-up compared to patients without lesions. Persistent high viral load infections were more likely to result in cervical lesions, whereas persistent infections with low viral loads were less likely to do so. These findings indicate that, in addition to persistent infection, a high viral load is a key factor contributing to the development of cervical lesions [27].

Among women diagnosed with LSIL or HSIL during follow-up, a significant increase in viral load was observed from baseline to follow-up, whereas patients who remained lesion-free experienced a decrease in viral load during the same period. A 15-year cohort study conducted by Zhao et al. at Peking Union Medical

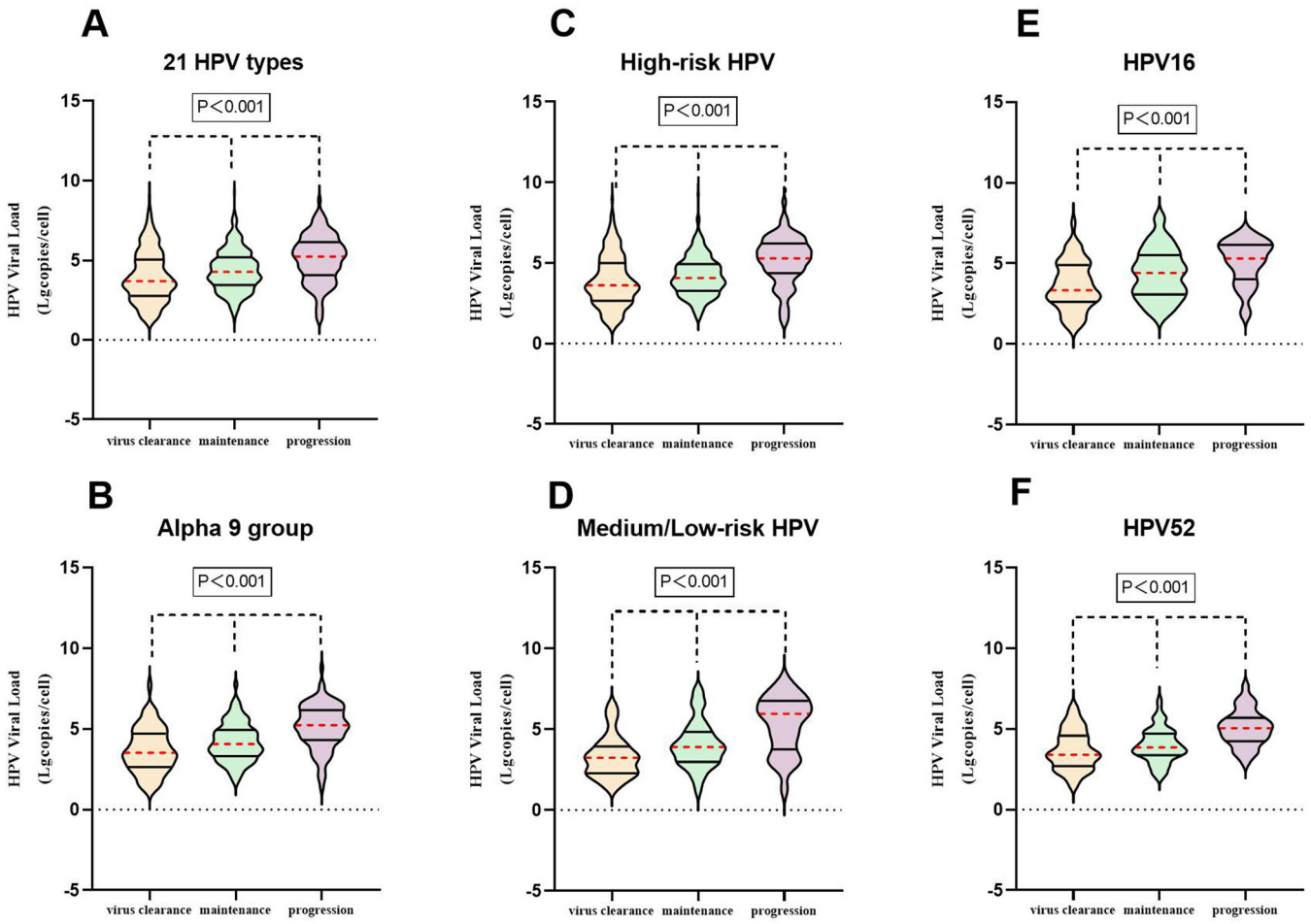


**FIGURE 2** | Differences in baseline viral load of different outcomes during the follow-up. (A) 21 HPV types; (B) Alpha 9 group; (C) High-risk HPV; (D) Medium/Low-risk HPV; (E) HPV16; (F) HPV52.

**TABLE 2** | Correlation between viral load and cervical lesions in follow-up.

| HPV types | Mean (SD) of log10-transformed HPV viral load | | *p*-value[a] |
|---|---|---|---|
| | Lesion-free | CIN | |
| 21 HPV types[b] | 4.21 ± 1.36 | 5.41 ± 1.47 | < 0.001 |
| Alpha9[c] | 4.01 ± 1.25 | 5.26 ± 1.33 | < 0.001 |
| HR-HPV[c] | 4.11 ± 1.33 | 5.31 ± 1.43 | < 0.001 |
| M/LR-HPV[c] | 3.96 ± 1.37 | 5.76 ± 1.63 | < 0.001 |
| HPV16 | 4.03 ± 1.47 | 5.03 ± 1.42 | 0.002 |
| HPV52 | 3.98 ± 1.15 | 5.38 ± 1.36 | < 0.001 |

Abbreviations: CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HR-HPV, high-risk HPV; M/LR-HPV, medium-risk and low-risk HPV.
[a]$p < 0.05$ is statistically significant.
[b]Including all single infections and multiple infections.
[c]Including patients with multiple infections, whose infection types are all corresponding to the infected group.

College [23] demonstrated that among women with CIN1 or normal pathology at baseline, the cumulative incidence and risk of developing CIN2+ increased with higher initial HPV viral loads, particularly in women with medium to high initial viral loads.

The ROC curves for 21 types of HPV, high-risk HPV, medium- and low-risk HPV, α-9 HPV, HPV16, and HPV52 viral loads were plotted in this study to predict the progression of cervical lesions (LSIL and HSIL) and determine the optimal cut-off values for different HPV types to guide clinical treatment. A cross-sectional study conducted by Shi et al. in Xinjiang [28] demonstrated that when the viral load cut-off values for HPV16, HPV52, and HPV58 were set at 4.38, 3.69, and 4.11, respectively, the sensitivity for predicting CIN2+ was 79.49%, 82.61%, and 73.33%, while the specificity was 58.22%, 54.96%, and 62.50%, respectively. Compared with the results of Shi et al., the sensitivity and specificity of the cut-off values identified in this study are higher. Additionally, the baseline cut-off value demonstrated higher sensitivity, while the follow-up cut-off value exhibited greater specificity. The combination of baseline and follow-up data allows for improved identification of patients with cervical lesions, enabling more accurate colposcopic referral.

This study also found that women with persistent infection are older than women in the population of HPV. In other words, young women who are HPV positive are more likely to eliminate the HPV virus, which may be related to the body's immunity [29]. Equally, a single infection is more likely to turn negative than multiple infections, which is consistent with the view that multiple infections may promote persistent infection in previous studies [30]. These findings provided credence to

**TABLE 3** | Changes in viral load from baseline to follow-up.

| HPV types | Baseline | Follow-up | Differ[a] | *p*-value[b] |
|---|---|---|---|---|
| 21 HPV types | | | | |
| Lesion-free | 4.31 ± 1.27 | 4.21 ± 1.37 | −0.10 ± 1.44 | 0.13 |
| CIN | 5.12 ± 1.47 | 5.45 ± 1.46 | 0.33 ± 1.42 | 0.001 |
| Alpha9[c] | | | | |
| Lesion-free | 4.25 ± 1.18 | 4.02 ± 1.26 | −0.23 ± 1.10 | 0.028 |
| CIN | 5.03 ± 1.34 | 5.30 ± 1.35 | 0.28 ± 1.40 | 0.043 |
| HR-HPV[c] | | | | |
| Lesion-free | 4.28 ± 1.24 | 4.11 ± 1.32 | −0.17 ± 1.43 | 0.047 |
| CIN | 4.94 ± 1.55 | 5.25 ± 1.47 | 0.31 ± 1.39 | 0.011 |
| M/LR-HPV[c] | | | | |
| Lesion-free | 3.81 ± 1.38 | 3.87 ± 1.43 | 0.059 ± 1.53 | 0.79 |
| CIN | 4.96 ± 1.66 | 5.72 ± 1.77 | 0.91 ± 1.90 | 0.032 |

Abbreviations: CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HR-HPV, high-risk HPV; M/LR-HPV, medium-risk and low-risk HPV.
[a]The difference between the baseline and follow-up viral load.
[b]$p < 0.05$ is statistically significant.
[c]Including patients with multiple infections, whose infection types are all corresponding to the infected group.

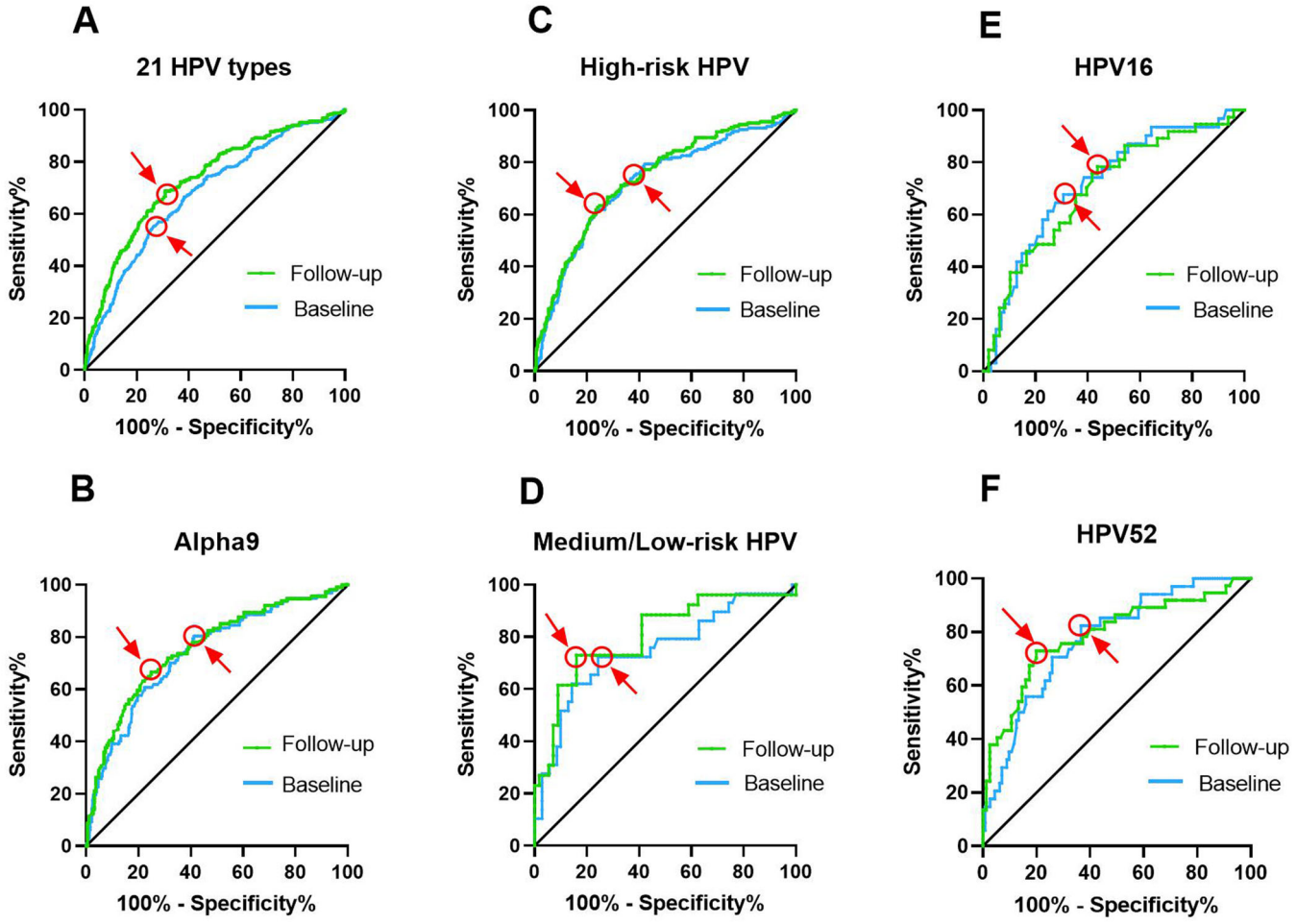


**FIGURE 3** | The performance and cut-off values of viral loads in predicting CIN. (A) 21 HPV types; (B) Alpha 9 group; (C) High-risk HPV; (D) Medium/Low-risk HPV; (E) HPV16; (F) HPV52.

**TABLE 4** | Screening efficiency of different types of viral load.

| HPV types | AUC[a] | Sensitivity | Specificity | Cut-off | Youden's index[b] |
|---|---|---|---|---|---|
| 21 HPV types | | | | | |
| Baseline | 0.68 | 55.38% | 73.32% | 5.01 | 0.29 |
| Follow-up | 0.73 | 68.80% | 69.08% | 4.90 | 0.38 |
| Alpha9 | | | | | |
| Baseline | 0.74 | 80.4% | 58.9% | 4.16 | 0.39 |
| Follow-up | 0.76 | 66.67% | 75.13% | 4.87 | 0.42 |
| HR-HPV | | | | | |
| Baseline | 0.72 | 71.25% | 66.61% | 4.56 | 0.38 |
| Follow-up | 0.74 | 62.78% | 75.98% | 5.04 | 0.39 |
| M/LR-HPV | | | | | |
| Baseline | 0.75 | 72.41% | 75.71% | 4.46 | 0.48 |
| Follow-up | 0.81 | 73.08% | 83.93% | 5.33 | 0.57 |
| HPV16 | | | | | |
| Baseline | 0.72 | 67.74% | 69.31% | 4.81 | 0.37 |
| Follow-up | 0.70 | 78.38% | 56.25% | 3.91 | 0.35 |
| HPV52 | | | | | |
| Baseline | 0.77 | 82.35% | 63.39% | 4.18 | 0.46 |
| Follow-up | 0.79 | 72.97% | 80.00% | 4.87 | 0.53 |

Abbreviations: AUC, area under curve; HPV, human papillomavirus; HR-HPV, high-risk HPV; M/LR-HPV, medium-risk and low-risk HPV.
[a]The area surrounded by the coordinate axis under the ROC curve, and the value range of AUC is between 0.5 and 1.0. The closer the AUC is to 1.0, the higher the authenticity of the detection method; when it is equal to 0.5, the authenticity is the lowest and has no application value.
[b]The Youden's index is the sum of sensitivity and specificity minus 1. It indicates the total ability of the screening method to find real patients and non-patients. The larger the index, the better the effect of the screening experiment and the greater the authenticity.

the idea that multiple infections might increase the risk of progression through persistent infection [31, 32].

The expanded HPV typing test is integrated into the first screening for cervical cancer [33]. The advantage is that women who participate in cervical cancer screening can be stratified, and high-risk HPV women can immediately undergo colposcopy, which greatly improves the sensitivity of screening, but the disadvantage is that the specificity of screening will be reduced, resulting in unnecessary colposcopy referral [34, 35]. However, this study shows that applying HPV viral load to the first screening of cervical cancer will improve specificity. We can refer to the viral load cut-off value of each genotype according to genotyping for further colposcopy.

The baseline of this study includes people infected with HPV without cervical lesions, which can help us more clearly understand the natural history of cervical lesions and analyze the changes of various factors in the process of lesions. There are some limitations of this study. First, it is uncertain how long the infections have been present in the women participating in this study. Second, the follow-up was scheduled to commence 6 months after enrollment in the study. However, due to personal circumstances of the participants, delays in follow-up, or missed visits may occur.

## 5 | Conclusion

It can be concluded that high viral load persistent infection is related to cervical lesions. HPV genotype and viral load may be able to predict cervical lesions progress. The application of HPV viral load to the first screening of cervical cancer can better predict and identify cervical lesions.

### Author Contributions

**Yilu Zhou:** writing – review and editing, writing – original draft, project administration, methodology, investigation, formal analysis, and data curation. **Jiaxin Liu:** writing – review and editing, visualization, formal analysis, and data curation. **Shuai Chen:** project administration, methodology, investigation, and formal analysis. **Wenjun Pan:** project administration, investigation, and formal analysis. **Yiqing Lai:** project administration, investigation, and formal analysis. **Mohan Xiao:** project administration, methodology, and data curation. **Zhonghua Shi:** Project administration, Methodology, Supervision. **Xianzhen Xin:** project administration, formal analysis, and data curation. **Lina Zhang:** writing – review and editing, visualization, supervision, funding acquisition, formal analysis, data curation, and conceptualization.

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### Ethics Statement

All projects were performed in compliance with relevant laws and institutional guidelines and in accordance with the ethical standards of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Changzhou Maternal and Child Health Care Hospital, Changzhou Medical Center, Nanjing Medical University (approval ID 2021 [62]). All patients provided their written informed consent to participate in this study. This clinical trial has been prospectively registered in Chinese Clinical Trial Registry (ChiCTR), registration number is ChiCTR2000040964.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data sets used and/or analysed during the current study available from the corresponding author on reasonable request.

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