Clin. Lab. 2026;72:XXX-XXX

ORIGINAL ARTICLE

Retrospective Analysis of HPV Infection Status and Genotyping in East China: 2023 - 2024

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ABSTRACT

Background: **Aim is to investigate the prevalence and genotypic distribution of human papillomavirus (HPV) infections among males and females in East China, providing epidemiological evidence for cervical cancer prevention.**

Methods: **HPV genotyping data were collected from HPV-positive individuals diagnosed through outpatient, inpatient, and physical examinations at the First Affiliated Hospital, Zhejiang University School of Medicine between January 2023 and December 2024. Genotype distribution was analyzed by age, gender, and ThinPrep Cytologic Test (TCT) results. HPV genotyping was performed based on the principles of multiplex polymerase chain reaction (PCR) and capillary electrophoresis.**

Results: **A total of 15,315 HPV-positive cases were identified. Single-genotype infections accounted for 65.81% of cases, dual-genotype infections for 21.53%, and multiple-genotype infections for 12.66%. The five most prevalent high-risk HPV genotypes were HPV52 (24.19%), HPV58 (13.47%), HPV16 (9.72%), HPV51 (9.68%), and HPV39 (8.54%). The leading low-risk genotypes were HPV42, HPV81, and HPV43. The highest infection rate occurred in the 30 - 39 age group (30.89%), and the lowest in individuals under 20 (0.9%), with significant differences across age groups (χ^2 = 9,891.28, p < 0.001). Males were primarily infected with HPV6, 52, and 11, while females most commonly harbored HPV52, 58, 51, 16, and 81. Genotypes HPV58, HPV52, and HPV16 were more frequently associated with TCT abnormalities. Specifically, HPV39 was linked to atypical squamous cells (ASC), HPV16 to low-grade lesions (LSIL), and HPV53 to high-grade lesions (HSIL). HPV52 showed the highest frequency across all abnormal cytological categories.**

Conclusions: **HPV infections are highly prevalent in East China, mainly involving single genotypes. Infection patterns vary by age and gender, and certain genotypes are closely linked to cervical cytological abnormalities.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250942)

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Manuscript accepted October 27, 2025

KEYWORDS

human papillomavirus, genotype distribution, infection prevalence, ThinPrep cytologic test, East China

INTRODUCTION

Human papillomavirus (HPV) is a common sexually transmitted virus that primarily infects epithelial tissues [1]. HPV is classified into two types: high-risk and low-risk. High-risk types can lead to malignant tumors, such as cervical cancer [2], whereas low-risk types are associated with benign lesions, such as genital warts [3]. Existing studies have demonstrated that the prevalence and

predominant genotypes of HPV infection vary across countries and regions [4]. In this study, we retrospectively analyzed HPV genotyping data from 15,315 individuals collected between 2023 and 2024 at the First Affiliated Hospital, Zhejiang University School of Medicine. HPV genotyping was performed in conjunction with cervical liquid-based cytology (ThinPrep Cytologic Test, TCT) to assess infections in the female genital tract, aiming to better understand the epidemiology of HPV infection in East China and to inform regional strategies for cervical cancer prevention and control.

SUBJECTS AND METHODS

Study population

Clinical samples from 15,315 individuals who tested positive for HPV genotyping at the First Affiliated Hospital, Zhejiang University School of Medicine, between January 2023 and December 2024 were included in this study. The study population consisted of 2,118 males and 13,197 females.

Methods

Grouping

The study population was categorized based on the number of HPV genotypes detected into three groups: a single-genotype infection group (infected with only one HPV genotype), a dual-genotype infection group (infected with two genotypes simultaneously), and a multiple-genotype infection group (infected with three or more genotypes simultaneously). Based on the risk level of the HPV genotypes, individuals were classified into two groups: a high-risk HPV (HR-HPV) group and a low-risk HPV (LR-HPV) group. In addition, participants were stratified into seven age groups: < 20 years, 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, 60 - 70 years, and > 70 years.

Sample collection and processing

Cervical exfoliated cell samples from female patients were collected by clinicians using a cervical brush and placed into specialized test tubes containing cell preservation solution. Male samples were obtained by clinicians using swabs to collect specimens from the anus, glans penis, or urethral secretions, or by collecting wart tissues when present. All samples were either immediately submitted for testing or stored at 4°C and processed for HPV genotyping within 3 days using standardized laboratory protocols.

HPV genotyping

HPV genotyping was performed based on the principles of multiplex polymerase chain reaction (PCR) and capillary electrophoresis. HPV DNA was extracted using the A-96 series automated nucleic acid extractor (Ningbo Hailshi Genetics Co., China). PCR amplification was carried out with the A300 Langji Gene Amplifier (Hangzhou Langji Scientific Instrument Co., China). Genotyping was completed using the 3500xL Dx Genetic Analyzer (Applied Biosystems, USA), which detects 25 HPV genotypes (16, 18, 26, 31, 33, 35, 39, 42, 43, 44, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 6, 81, 82, 83, and 11).

ThinPrep cytologic test

The TCT cytopathology results for seven high-risk HPV genotypes with high infection rates in women were analyzed. The TCT findings were classified as no intraepithelial lesion or malignancy (NILM) and epithelial cell abnormalities, which were further subdivided into the following subgroups: atypical squamous cells (ASC), low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL).

Statistical analysis

Statistical analysis was performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, and comparisons between groups were conducted using the chi-squared (χ^2) test. A p-value of < 0.05 was considered statistically significant.

RESULTS

HPV infection status

Of the 15,315 HPV-positive samples, 13,197 were from females and 2,118 from males. Among these, 10,079 cases (65.81%) involved single-type HPV infection, 3,297 cases (21.53%) had dual-type infections, and 1,939 cases (12.66%) showed multiple-type (≥ 3 types) infections, as detailed in Table 1.

HPV infection status

The top five genotypes with the highest infection rates for high-risk human papillomavirus (HPV) are type 52 (24.19%), type 58 (13.47%), type 16 (9.72%), type 51 (9.68%), and type 39 (8.54%). The top three genotypes with the highest infection rates for low-risk HPV are type 42 (9.04%), type 81 (8.98%), and type 43 (6.02%), as shown in Table 2.

HPV infection in different age groups

The overall HPV infection rates (including single, double and multiple infections) in each age group < 20 years, 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, 60 - 70 years and > 70 years were 0.94%, 26.63%, 30.89%, 17.77%, 17.72%, 8.87%, and 1.36%. The 30 - 39 years having the highest overall infection rate, followed by 20 - 29 years, while the < 20-year age group had the lowest. A statistically significant difference was observed in the distribution of infection rates across age groups ($\chi^2 = 9891.28$, $p < 0.001$). Pairwise comparisons showed statistically significant differences ($p < 0.05$) between all age groups except for the 40 - 49 and 50 - 59 age groups (Figure 1).

Table 1. HPV infection.

Type of infection	Number of people (n)	Proportion (%)
Single infection	10,079	65.81
Double infection	3,297	21.53
Multiple infections	1,939	12.66
Total	15,315	100

Table 2. Detection of HPV genotypes.

HPV genotype	Male (n)	Female (n)	Total (n)	Percentage (%)
HR-HPV				
HPV52	367	3,338	3,705	24.19
HPV58	240	1,823	2,063	13.47
HPV16	232	1,256	1,488	9.72
HPV51	215	1,267	1,482	9.68
HPV39	196	1,112	1,308	8.54
HPV53	118	1,152	1,270	8.29
HPV56	163	1,082	1,245	8.13
HPV66	141	834	975	6.37
HPV68	108	824	932	6.09
HPV59	118	709	827	5.4
HPV18	105	534	639	4.17
HPV33	69	531	600	3.92
HPV31	51	505	556	3.63
HPV35	52	300	352	2.3
HPV82	45	229	274	1.79
HPV45	41	212	253	1.65
HPV73	34	158	192	1.25
HPV26	12	37	49	0.32
LR-HPV				
HPV42	199	1,186	1,385	9.04
HPV81	171	1,205	1,376	8.98
HPV43	192	730	922	6.02
HPV6	452	450	902	5.89
HPV11	317	338	655	4.28
HPV44	46	282	328	2.14
HPV83	14	73	87	0.57

Relationship between HPV infection and TCT results

The top seven high-risk human papillomavirus (HPV) genotypes by infection rate among women were types 52, 58, 51, 16, 53, 39 and 56. Of the 11,030 total cases, 5,365 cases (48.64%) underwent ThinPrep cytologic test (TCT). The negative for intraepithelial lesion or malignancy (NILM) category accounted for over 89% of cases for each genotype. Cervical cell abnormalities associated with types 58, 52, and 16 accounted for 11% of TCT cases. Specifically, in type 39, atypical squamous cells (ASC) accounted for 64% of total abnor-

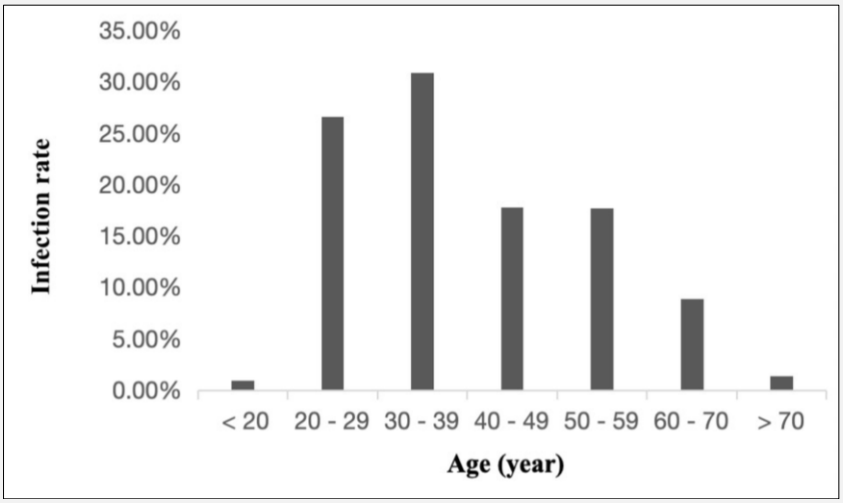

Figure 1. Age-specific HPV infection rates.

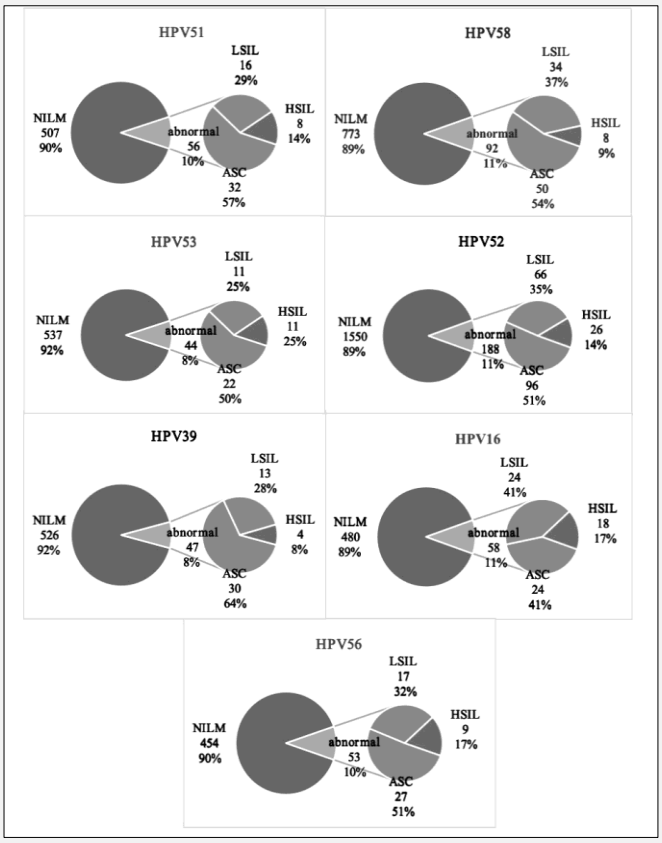

Figure 2. Number and proportion of TCT samples per genetic type.

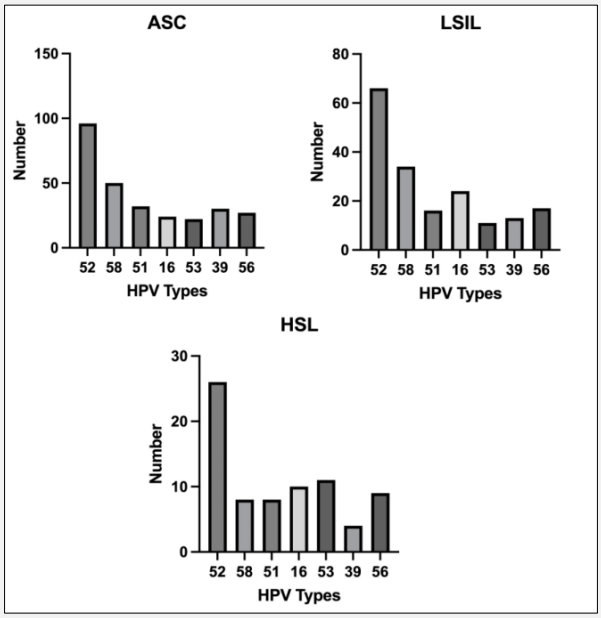

Figure 3. Statistical grouping of cervical cell abnormalities based on HPV genetic types.

malities; in type 16, low-grade squamous intraepithelial lesions (LSIL) comprised 41% of total abnormalities; and in type 53, high-grade squamous intraepithelial lesions (HSIL) comprised 25% of total abnormalities (Figure 2). In the ASC group, type 52 had the highest prevalence, followed by types 58 and 51. In the LSIL group, type 52 was the most prevalent, followed by types 58 and 16. In the HSIL group, type 52 was the most prevalent, followed by types 53 and 16 (Figure 3).

DISCUSSION

Cervical cancer is the fourth most common malignant tumor among women worldwide, with China accounting for approximately 18.6% of the global incidence [5]. Persistent infection with high-risk human papillomavirus (HR-HPV) is the primary etiological factor for the development of cervical cancer and cervical intraepithelial neoplasia (CIN) [6]. Therefore, HPV screening is essential to reduce the incidence of cervical cancer and other related diseases. To date, more than 200 HPV genotypes have been identified. However, the prevalence of HPV infection and the distribution of genotypes vary not only between countries but also across different regions within a single country [7]. Regional analysis of HPV infection patterns is thus crucial for understanding local epidemiological characteristics and for informing targeted prevention and control strategies.

In this retrospective study, 15,315 HPV-positive patients were analyzed. The majority of infections involved a single HPV genotype, with HR-HPV being significantly more prevalent than low-risk HPV (LR-HPV). Among women in East China, the five most common HR-HPV genotypes were HPV 52, 58, 51, 16, and 53, in descending order. This differs from prior reports in Asian female populations, where HPV 16, 52, 58, 18, and 33 are the most prevalent [8], indicating regional variation in genotype distribution.

We also found significant gender differences in HPV genotype distribution. Among male patients, the most common types were HPV 6, 52, and 11, whereas among females, HPV 52, 58, and 51 were the most frequently detected. Males are often diagnosed with HPV infection following the onset of symptoms [9], underscoring the necessity of vaccinating men. Notably, many men infected with HR-HPV are asymptomatic carriers, capable of transmitting the virus to female partners . Given that HPV 52 is not included in the quadrivalent vaccine, our findings suggest that the nonavalent vaccine - covering HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 - may be more suitable for male populations in this region.

Age-specific differences in infection rates were also observed. The 30 - 39 age group had the highest overall HPV prevalence, followed by the 20 - 29, 40 - 49, and 50 - 59 groups. This supports previous findings that HPV is primarily transmitted through sexual contact [10]. Several studies have reported lower infection rates

in individuals under 20 or over 60 years of age compared to those aged 20 - 59 [11]. The variation among age groups reinforces age as a significant risk factor for HPV infection [5,9,12], highlighting the importance of age-specific screening strategies. The highest HPV infection rate in the 30 - 39 age group suggests that this population should be a primary focus for monitoring. Additionally, HPV infection in women has been associated with factors such as education level, smoking status, sexual frequency, number of sexual partners, condom use, post-coital hygiene practices, cervical erosion, and immunosuppression [13,14], These patterns provide a reference for regional HPV screening programs and underscore the importance of women adopting protective measures and receiving HPV vaccination. Studies have shown that HPV types 52 and 58 are the most prevalent subtypes in atypical squamous cells (ASC) and low-grade squamous intraepithelial lesions (LSIL) among Asian populations, whereas HPV types 16 and 18 are the most common in high-grade squamous intraepithelial lesions (HSIL) and cervical carcinoma [15-17]. In this study, we found that cervical cell abnormalities associated with HPV types 58, 52, and 16 accounted for 11% of cases examined via ThinPrep cytologic test (TCT). Specifically, in the ASC group, the top three genotypes were 52, 58, and 51, in the LSIL group, the top three genotypes were 52, 58, and 16, and in the HSIL group, the top three genotypes were 52, 53, and 16. HPV type 52 was the most frequent across all abnormality subgroups. Due to differences in the prevalence of each genotype, the proportion of abnormalities was calculated for each genotype. In HPV type 39, ASC accounted for 64% of the total abnormalities, in type 16, LSIL comprised 41% of the total abnormalities, and in type 53, HSIL represented 25% of the total abnormalities. These findings in the ASC group are consistent with previous studies. However, in the LSIL and HSIL groups, the higher prevalence of types 52 and 53, likely due to limited sample base, deviates from previous research. Notably, HSIL associated with type 53 accounted for one-quarter of the total abnormalities, which is a pre-cancerous lesion of the cervix. HSIL is a key stage of cervical pre-cancer and is closely related to the development of cervical cancer [18]. This suggests that TCT screening for HPV type 53 should be prioritized in this region. The high proportion of cervical cell abnormalities associated with types 52, 58, and 16 may provide clinicians with valuable reference data for assessing the carcinogenic risk of HPV genotypes. In addition, the small sample size of women diagnosed with HSIL via TCT in this study is a major limitation of cytologic analysis.

In summary, HPV infection in East China is primarily characterized by single infections. Among the high-risk types, types 52, 58, and 16 are most prevalent. These types exhibit distinct infection patterns across age groups, with the highest prevalence observed in individuals aged 30 - 39 years. Additionally, there are significant gender-specific differences in the infection of major subtypes. Furthermore, types 52, 58, 16, and 53 have higher percentages of abnormal findings on TCT screening, indicating that these genotypes should receive greater attention in cervical cancer screening efforts within East China. These findings highlight the importance of actively promoting HPV screening, vaccination, and prevention strategies in this region.

Data Availability Statement:
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Source of Funds:
No funding was received for this study.

Ethics Approval and Consent to Participate:
This study was approved by the Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (approval number: 2025B-0949) and was conducted in accordance with the Declaration of Helsinki. The Ethics Committee waived the requirement for informed consent.

Declaration of Generative AI Use:
The authors declare that generative artificial intelligence (e.g., ChatGPT) was used only to assist in language polishing and grammar checking during manuscript preparation. The authors reviewed and edited all parts of the text and take full responsibility for the content and integrity of the manuscript.

Declaration of Interest:
All authors declare no conflicts of interest.

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