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Investigation and analysis of female HPV infection and genotype distribution in Xuhui District, Shanghai

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Abstract

Objective In China, Cervical cancer is one of the common malignant tumors in females, and high-risk human papillomavirus (HR-HPV) infection is one of its main causative factors. However, human papillomavirus (HPV) infection rates may vary significantly among patients of different ages and HPV subtypes. This study aims to provide insights into developing cervical cancer screening strategies and selecting HPV vaccine antigen targets in the area.

Methods A retrospective analysis was conducted on the HPV testing results of 47,423 women from January 2017 to April 2023 at the Clinical Laboratory of the Eighth People's Hospital in Shanghai. HPV DNA genotyping was performed using real-time quantitative polymerase chain reaction (PCR) in the molecular laboratory. Statistical analysis was carried out using GraphPad Prism 8.0.1 software. Binomial distribution analysis was used to calculate the 95% confidence intervals (95% CI), and the chi-square test was employed to compare categorical variables among different age groups, with a p-value of less than 0.05 indicating statistical significance.

Results Among the 47,423 cervical HPV DNA test results, the overall infection rate was 18.9%, with single infections accounting for 13.93%, dual infections for 3.47%, and multiple infections for 1.5%. The age-specific prevalence of HPV infection exhibited a "U"-shaped curve, with the highest infection rates observed in the age groups under 30 and between 50 and 59 years. The five most common HR-HPV subtypes in Xuhui District were types 16, 39, 51, 52, 56, and 58 (accounting for 10.3%, 7%, 8%, 20.3%, 6%, and 12%, respectively), with type 52 showing the highest infection rate. The prevalence of moderate/severe HPV infection rates in the HPV 59, HPV 33, and HPV 35 gene subtypes increased over time, highlighting the importance of monitoring these subtypes.

Conclusion This study identified the primary HR-HPV genotypes prevalent among females in Xuhui District, Shanghai, and explored correlations between age, genotype, and HPV infection rates. While the findings provide a basis for recommending HPV screening for younger and older age groups, further studies integrating clinical outcomes such as cytological and pathological results are necessary to substantiate these conclusions and refine

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screening strategies. Due to variations in HPV trends globally and regional differences in genotypes, epidemiological analysis of HPV can accurately and visually reflect the distribution of specific HPV genotypes in a particular area, thereby aiding in the development of regional cervical cancer screening strategies and the selection of HPV vaccine antigen targets.

Keywords Human papillomavirus, Age, Genetic typing, Female, Infection rate

Introduction

Cervical cancer is the fourth most common cancer in females globally and the fourth leading cause of cancer-related deaths among females. In China, it ranks as the tenth leading cause of cancer-related deaths [1]. Data from 2020 indicated 110,000 new cases and 59,000 deaths, showing a noticeable upward trend, with one out of every 20,000 individuals succumbing to cervical cancer [2]. According to the latest global cancer burden data released by the International Agency for Research on Cancer of the World Health Organization in 2020, there were approximately 110,000 new cases of cervical cancer and 60,000 deaths in China in 2020. Epidemiological data show that 99.7% of cervical cancer patients are found to have persistent infections of high-risk human papillomavirus (HR-HPV), confirming a clear causal relationship between human papillomavirus (HPV) infection and cervical cancer, making HPV infection a primary causative factor of cervical cancer [3]. By global data from the World Health Organization, HPV-16 and HPV-18 are the most common HR-HPV types causing cervical cancer [4]. However, there are significant differences in the prevalence and distribution of HPV infections and subtypes among different geographic regions and ethnicities. The likelihood of HPV-induced tumors is typically low, as most HPV infections are transient and self-limiting, spontaneously cleared by the host's immune system without clinical intervention. Persistent HPV infections are important risk factors for cervical cancer and precancerous lesions [5]. However, it may take several decades for persistent HR-HPV subtypes to progress to cervical cancer [6]. In the majority of sexually active populations, HR-HPV infections are common, and a minority of infections may lead to high-grade precancerous lesions and subsequently develop into cervical cancer. Therefore, early and regular screening for HPV infections is crucial for cervical cancer prevention [7]. Despite several cervical cancer screening programs in the general population in China, many areas, particularly rural regions, do not have access to regular screening. As a result, the burden of Cervical screening remains heavy in China, and due to the lack of comprehensive national cancer registration, the incidence of cervical cancer is significantly underestimated [8].

HPV infection is considered a primary cause of cervical cancer [9], with approximately 40 subtypes of the over 200 identified HPV types known to infect the genital area [10]. Among these, 13 to 15 h-HPV types are considered to be oncogenic. Globally, HPV types 16 and 18 account for over 70% of cervical cancer cases [11], while the other six types (HPV 31, 33, 35, 45, 52, and 58) make up 20%. However, the pathogenicity of specific HPV types for Cervical diseases varies across different regions and environments, possibly due to geographical differences in the type-specific prevalence of HPV among different populations [12]. For instance, the prevalence of HPV 16 and 18 in cervical cancer patients and healthy females in East Asia is relatively lower compared to global rates.

In addition, studies have found that the prevalence of high-risk HPV (HR-HPV) increases with age and shows a significant upward trend with the severity of cervical lesions. HPV16 and HPV52 are the most common types in this region [13]. The incidence of multiple infections rises during early adulthood and then declines with increasing age, with significant differences in the distribution of the 15 common HPV genotypes between multiple and single infections [14]. Although various HPV vaccines are currently undergoing clinical trials, the development of future vaccines will need to incorporate more antigen types to enhance efficacy and coverage [15]. Therefore, conducting detailed studies on HPV infection in developed areas like Shanghai can provide valuable references for nationwide vaccination strategies and screening programs. This study aims to analyze HPV infections among 47,423 women to identify high-risk subtypes and infection patterns, providing scientific evidence for optimizing regional screening and vaccination strategies.

Materials and methods

Study population

This study collected cervical HPV-DNA data from 47,423 women who visited the Shanghai Eighth People's Hospital from November 2017 to April 2023. These women underwent HPV-DNA testing at the hospital's laboratory. Participants were divided into five age groups based on differences in HPV infection rates observed in epidemiological studies, with the selected age ranges corresponding to reproductive and postmenopausal stages: Group 1 (G1) < 30 years, Group 2 (G2) 30–39 years, Group 3 (G3) 40–49 years, Group 4 (G4) 50–59 years, and Group 5 (G5) ≥ 60 years [14]. The reasons for hospital visits varied, including routine gynecological examinations, vaginal infections, and gynecological tumors, among others. All females participating in this study had to meet the

following criteria: (1) a history of sexual activity and (2) no sexual intercourse or vaginal medication use in the past 72 h. Exclusion criteria included females diagnosed with Cervical cancer, pregnant women, individuals lacking key information such as age, those who had undergone cervical excision procedures or had autoimmune diseases, and patients who had received cervical physical and hormonal treatments within the previous 10 months. The specific procedure is outlined in Figure S1. This study has been approved by the Ethics Committee of the Shanghai Eighth People's Hospital (Approval No. 2023-061-21).

Specimen collection

The cervical sample collection procedure involves using a sterile cervical brush. The brush is gently inserted into the cervical canal until reaching the posterior fornix of the cervix to ensure full contact of the brush head with the inner walls of the cervical canal and the external os of the cervix. The cervical brush is then rotated 360 degrees clockwise at the cervical canal and external os to gently brush the cells, ensuring an adequate collection of cervical epithelial cells. This process is repeated twice to improve the completeness of cell collection. After collection, the samples are immediately transferred to 2 milliliters of cell preservation solution to preserve the integrity of the samples and the stability of cellular DNA. All samples are stored at 2–8 °C for no more than 7 days to minimize cell degradation and DNA damage, ensuring the accuracy of subsequent HPV-DNA detection and analysis.

HPV genotyping detection

DNA extraction and typing qualitative detection were performed using the HPV Genotyping Nucleic Acid Detection Kit (Fluorescence PCR method) from Shanghai Zhijiang Biotechnology Co., Ltd. This test kit is designed to detect 15 h-HPV genotypes (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 66, 82) in cervical exfoliated cells. The basic principle involves using specific primers and fluorescent probes for different HPV genotypes, applying polymerase chain reaction (PCR) combined with Taqman technology to qualitatively detect specific nucleic acid segments. The basic steps are: first, HPV DNA is isolated and extracted. After enzymatic digestion of cervical cells, HPV is adsorbed to magnetic glass beads, and the released DNA is washed and purified using the QIAGEN QIAcube automated nucleic acid extraction system. After DNA extraction, 4 μL are taken as the PCR reaction template for PCR amplification. The amplification reagent is prepared by mixing 0.4 μL of DNA polymerase and 36 μL of PCR mixture. The DNA template of each individual is amplified using the SLAN-9600 S thermal cycler, with PCR cycling conditions of 94 °C for 2 min, 93 °C for 10 s, and 62 °C for 30 s, for a total of 40 cycles. If the channel Ct value is ≤ 38 and the amplification curve shows a typical S shape, the gene result corresponding to that curve is considered positive. Internal quality control measures, including the detection of the single-copy conserved gene MNBH as a reference gene, are implemented during testing to ensure accurate quantification of HPV content in the sample and to prevent false negative results. The MNBH gene serves as the internal control, ensuring the integrity and accuracy of the DNA amplification and genetic typing process. All experiments undergo quality control, including DNA amplification and genetic typing, with positive and negative controls set in the PCR detection.

The reference gene chosen is the single-copy conserved gene MNBH in human cells. If the reference gene detection is negative and the HPV detection is also negative, resampling for testing is required. The MNBH gene contains only one copy per cell, meaning 1 MNBH gene ≈ 1 cell. The amount of cervical epithelial cell counting needed for the sample is determined to be 10,000 cells, equivalent to 10,000 copies of the MNBH gene (determined by plasmid calibration with a detection Ct value of 28), to normalize the Ct values of HPV genotypes and ensure consistent interpretation of sample detection results at the same cell counting level. Based on the viral load of HPV, the infection levels are classified as mild, moderate, and severe. The classification criteria are as follows: Mild infection: 10^2-10^4 copies/10^4 cells, Moderate infection: 10^5-10^7 copies/10^4 cells, and Severe infection (> 10^7 copies/10^4 cells) [16, 17]. All experimental procedures are conducted according to the instructions in the kit.

Statistical analysis

All statistical analyses in this study were performed using GraphPad Prism 8.0.1 software. The analyses involved independent evaluations of HPV infection rates, genotype distribution, and single, dual, and multiple HPV infections (defined as infection with one, two, or multiple HPV genotypes). Comparisons of HPV infection rates for single and multiple HPV genotypes in different groups were conducted using binomial distribution analysis to calculate the 95% confidence intervals (95% CI). Two-tailed p-values less than 0.05 were considered statistically significant. The analysis calculated the HPV infection rates and their respective 95% CI between different groups. The chi-square test was used to compare categorical variables for comparisons between different age groups, and differences were considered statistically significant when the p-value was less than 0.05.

Results

Overall HPV infection status

Through a retrospective analysis of HPV testing results from January 2017 to April 2023, it was found that the infection rate of HR-HPV was 18.40% (8962/47423). A total of 15 h-HPV subtypes were detected in this study (Fig. 1A), with HPV 52 at 5.4%, HPV 58 at 3.1%, HPV 16 at 2.7%, HPV 51 at 2%, HPV 39 at 1.7%, HPV 56 at 1.6%, HPV 66 at 1.4%, HPV 68 at 1.3%, and HPV 59 at 1.2%. Notably, HPV 18 ranks tenth, which differs from previous studies. Earlier research indicated that HPV 18 is the second most common type causing cervical cancer, accounting for 65% of all cases [18]. In double infection cases, the most common combinations were HPV 52 + 58, followed by HPV 52 + 16 and HPV 58 + 16 (Fig. 1B). The results indicate that HPV 52 has the highest infection rate in Shanghai and tends to be co-infected with other subtypes.

HR-HPV infection status among different age groups

The HPV test results were divided into five age groups, and the infection rate for each group was calculated (Fig. 2). The results showed that HPV infection rates ranged from 15.1 to 24.94%, in the following order from lowest to highest: Group 3 (G3) (14.73%), Group 2 (G2) (16.97%), Group 5 (G5) (17.71%), Group 4 (G4) (18.01%), and Group 1 (G1) (24.94%), with Group 1 (G1) showing the highest infection rate. The differences in HPV infection rates among the age groups were statistically significant ($P < 0.05$). A peak in HPV infection was observed in women under 30 years old, with higher infection rates also found in the 50–59 and ≥ 60 age groups. Furthermore, significant differences in the infection rates of 13 high-risk HPV subtypes (HPV 16, 18, 31, 39, 45, 51, 52, 56, 58, 59, 66, and 82) were observed among the different age groups (Table 1).

Overall distribution of single, double, and multiple HPV infections

In this study, a single high-risk HPV infection was the most common, accounting for 73.7% of all positive cases. Dual infections comprised 18.4%, while multiple infections accounted for 7.9% (Table 2). When high-risk HPV infections were categorized by age, Group 1 (G1) (< 30 years) had the highest rate of single HPV infection (16.62%), followed by Group 4 (G4) (50–59 years) (14.39%), Group 2 (G2) (30–39 years) (13.59%), Group 5 (G5) (≥ 60 years) (12.74%), and Group 3 (G3) (40–49 years) (12.21%). The highest dual infection rate was also observed in Group 1 (G1) (< 30 years) (5.91%), with the lowest rate in Group 3 (G3) (2.3%). Among multiple infections, Group 1 (G1) (< 30 years) again showed the highest infection rate (3.3%). Similar to single infections, Group 1 (G1) (< 30 years) demonstrated the highest rate of multiple infections (Table 2). The five most common high-risk HPV genotypes, HPV 52, HPV 58, HPV 16, HPV 51, and HPV 39, were prevalent across single, dual, and multiple infections (Table 3).

Proportion of patients with different infection severity and distribution of HPV genotypes

Based on the severity of infection, this study categorized patients into mild, moderate, and severe infection groups. Mild infections were the most common, accounting for 67.5% of all positive cases, moderate infections comprised 31.3%, and severe infections accounted for 1.1% (Fig. 3A). In mild infections, HPV 52, HPV 58, HPV 16, HPV 51, and HPV 39 were predominant, whereas moderate infections were primarily associated with HPV

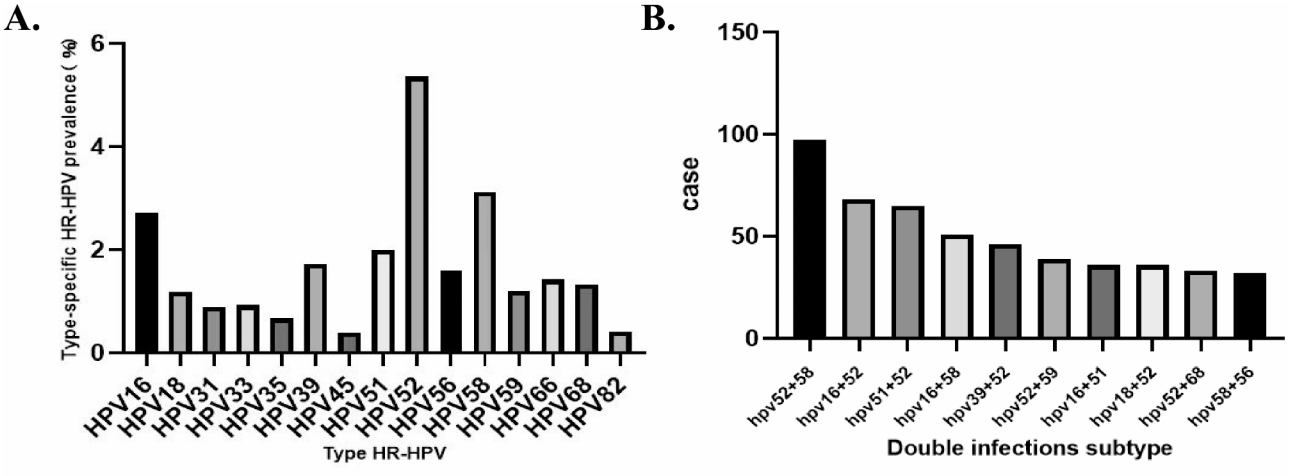

Fig. 1 Retrospective analysis of HPV subtypes and infection rates among 47,423 women in Shanghai. Note: **(A)** Proportion of patients infected with 15 h-HPV subtypes among the 47,423 women. **(B)** Top 10 subtype combinations in cases of dual infections

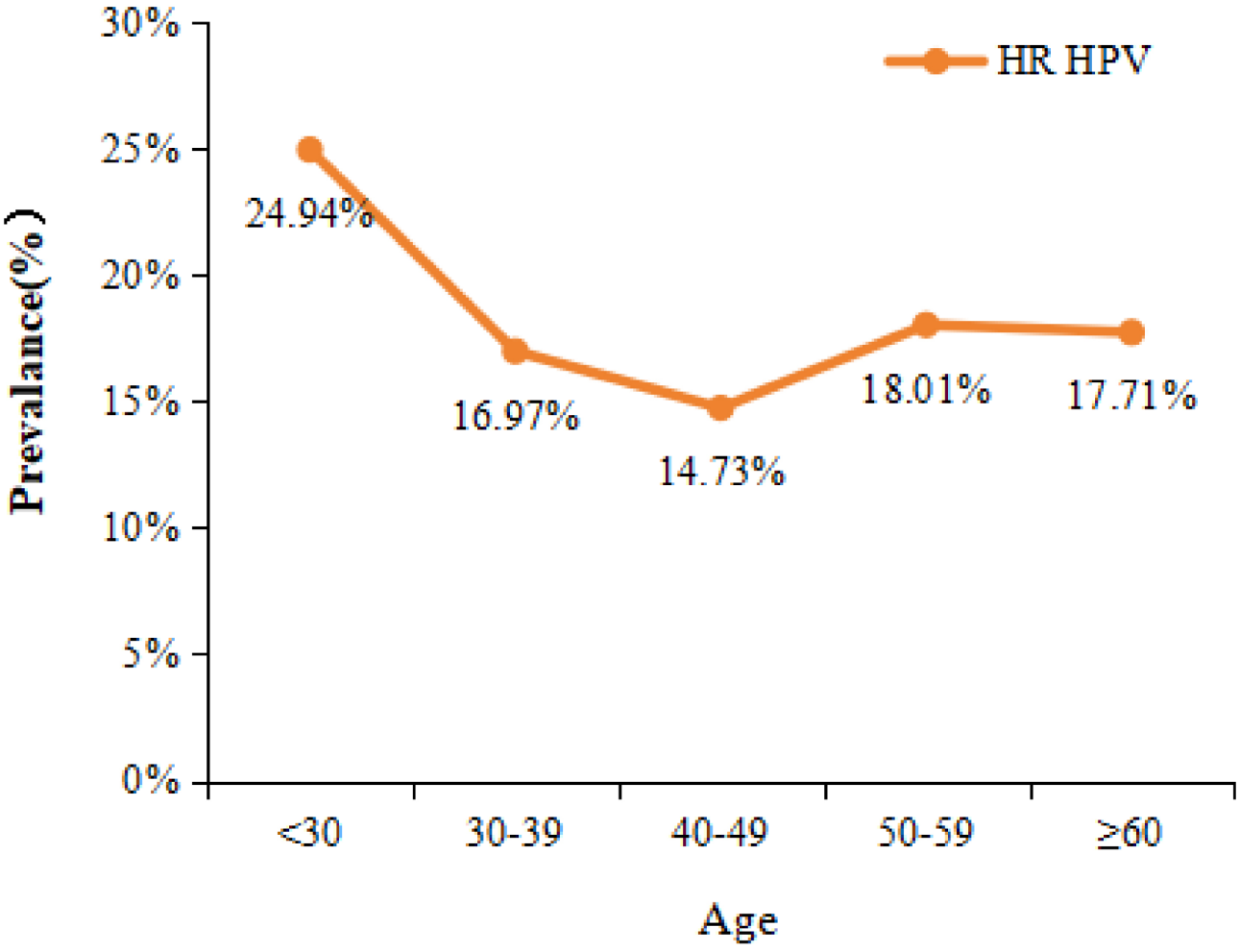

Fig. 2 HPV Infection Rates among Women in Five Age Groups (< 30 years, 30–39 years, 40–49 years, 50–59 years, and ≥ 60 years)

Table 1 Infection status of 13 subtypes of HR-HPV in different age groups

HPV hypotype	< 30 (*n* = 10254)	30–39 (*n* = 13682)	40–49 (*n* = 11495)	50–59 (*n* = 6629)	≥ 60 (*n* = 5363	x^2	*P*	Gamma value
hpv82	93(0.91%)	50(0.37%)	26(0.23%)	14(0.21%)	10(0.19%)	57.238	< 0.001	0.421
hpv68	183(1.78%)	165(1.21%)	109(0.95%)	99(1.49%)	76(1.42%)	3.066	0.080	0.065
hpv66	235(2.29%)	157(1.15%)	137(1.19%)	69(1.04%)	75(1.4%)	26.608	< 0.001	0.161
hpv59	241(2.35%)	158(1.15%)	86(0.75%)	50(0.75%)	36(0.67%)	108.810	< 0.001	0.338
hpv58	450(4.39%)	383(2.80%)	237(2.06%	226(3.41%)	182(3.39%)	12.216	< 0.001	0.085
hpv56	248(2.42%)	170(1.24%)	123(1.07%)	101(1.52%)	114(2.13%)	3.908	0.048	0.078
hpv52	749(7.30%)	649(4.74%)	480(4.18%)	350(5.28%)	314(5.85%)	18.242	< 0.001	0.078
hpv51	348(3.39%)	256(1.87%)	153(1.33%)	90(1.36%)	99(1.85%)	71.725	< 0.001	0.223
hpv45	71(0.69%)	49(0.36%)	35(0.3%)	12(0.18%)	18(0.34%)	20.034	< 0.001	0.259
hpv39	275(2.68%	208(1.52%)	146(1.27%)	102(1.54%)	84(1.57%)	30.428	< 0.001	0.156
hpv35	84(0.82%)	72(0.53%)	59(0.51%)	58(0.87%)	45(0.84%)	0.853	0.356	-0.022
hpv33	115(1.12%)	112(0.82%)	89(0.77%)	59(0.89%)	62(1.16%)	0.021	0.884	0.019
hpv31	161(1.57%)	95(0.69%)	77(0.67%)	42(0.63%)	49(0.91%)	23.507	< 0.001	0.192
hpv18	205(2.00%)	161(1.18%)	78(0.68%)	89(1.34%)	32(0.6%)	52.286	< 0.001	0.233
hpv16	471(4.59%)	288(2.10%)	227(1.97%)	153(2.31%)	151(2.82%)	49.461	< 0.001	0.164

Table 2 The prevalence of single, double, and multiple HPV subtypes at different ages

HPV infection	G1 (< 30 years) (*n* = 10254)	G2 (30–39 years) (*n* = 13682)	G3 (40–49 years) (*n* = 11495)	G4 (50–59 years) (*n* = 6629)	G5(≥ 60 years) (*n* = 5363)	Total	*P* value
HPV	2651 (25.85%)	2393 (17.49%)	1736 (15.10%)	1218 (18.37%)	964 (17.98%)	8962 (100%)	< 0.001
Single HPV	1704 (16.62%)	1860 (13.59%)	1404 (12.21%)	954 (14.39%)	683 (12.74%)	6605 (73.7%)	< 0.001
Double HPV	606 (5.91%)	397 (2.90%)	264 (2.30%)	202 (3.05%)	178 (3.32%)	1647 (18.37%)	< 0.001
Multiple HPV	341 (3.33%)	136 (0.99%)	68 (0.59%)	62 (0.94%)	103 (1.92%)	710 (7.9%)	< 0.001

Note: G1 = Group 1, G2 = Group 2, G3 = Group 3, G4 = Group4, G5 = Group 5

Table 3 The distribution proportion of different HPV subtypes in single, double, and multiple HPV infections

HPV subtype	Single infection		Double infections		Multiple infections	
	Positive no	95%CI	Positive no	95%CI	Positive no	95%CI
hpv_16	720	1.52(1.41–1.63)	341	0.72(0.64–0.8)	235	0.5(0.43–0.56)
hpv_18	282	0.59(0.53–0.66)	158	0.33(0.28–0.39)	127	0.27(0.22–0.31)
hpv_31	211	0.44(0.39–0.5)	110	0.23(0.19–0.28)	103	0.22(0.18–0.26)
hpv_33	212	0.45(0.39–0.51)	136	0.29(0.24–0.33)	90	0.19(0.15–0.23)
hpv_35	152	0.32(0.27–0.37)	106	0.22(0.18–0.27)	61	0.13(0.1–0.16)
hpv_39	416	0.88(0.79–0.96)	223	0.47(0.41–0.53)	178	0.38(0.32–0.43)
hpv_45	74	0.16(0.12–0.19)	59	0.12(0.09–0.16)	52	0.11(0.08–0.14)
hpv_51	467	0.98(0.9–1.07)	272	0.57(0.51–0.64)	212	0.45(0.39–0.51)
hpv_52	1634	3.45(3.28–3.61)	556	1.17(1.08–1.27)	357	0.75(0.68–0.83)
hpv_56	350	0.74(0.66–0.82)	209	0.44(0.38–0.5)	198	0.42(0.36–0.48)
hpv_58	852	1.8(1.68–1.92)	380	0.8(0.72–0.88)	248	0.52(0.46–0.59)
hpv_59	268	0.57(0.5–0.63)	175	0.37(0.31–0.42)	132	0.28(0.23–0.33)
hpv_66	347	0.73(0.66–0.81)	177	0.37(0.32–0.43)	154	0.32(0.27–0.38)
hpv_68	319	0.67(0.6–0.75)	188	0.4(0.34–0.45)	127	0.27(0.22–0.31)
hpv_82	76	0.16(0.12–0.2)	49	0.1(0.07–0.13)	69	0.15(0.11–0.18)
hpv_6 + 11	247	0.52(0.46–0.59)	168	0.35(0.3–0.41)	155	0.33(0.28–0.38)

52, HPV 58, HPV 16, HPV 51, and HPV 66. Severe infections were mainly linked to HPV 58, HPV 16, HPV 51, HPV 66, and HPV 18 (Fig. 3B).

Relationship between different HPV genotype infections and the proportion of mild, moderate, severe infections, and age

To better understand the relationship between different HPV genotypes and age, we compared the proportions of mild, moderate, and severe infections over five years (2017–2022) for different HPV genotypes. The results indicate that, with increasing time, the proportions of moderate infections compared to mild infections for HPV 82, HPV 68, HPV 66, and HPV 59 (Fig. 4). Further analysis of the proportions of moderate/severe infections revealed an increasing trend in the infection rates of HPV 59, HPV 33, and HPV 35 over time (Fig. 5A). Regarding the relationship between HPV genotypes and age, patients with moderate to severe HPV 59 infections were younger compared to those with mild infections, while HPV 33 and HPV 35 did not show a clear age-related trend (Fig. 5B).

Discussion

In China, due to insufficient vaccine coverage and inadequate HPV screening, especially in rural and underdeveloped areas, the prevalence of cervical diseases remains relatively high [19–21]. The prevalence and genotype distribution of HPV vary in different regions and living environments [22–24]. Understanding the prevalence and genotype distribution of HPV in Shanghai is crucial for developing prevention measures and strategies to eliminate cervical cancer [25].

In this retrospective analysis, the overall positivity rate of HR-HPV was 18.4%. Similar studies in other Chinese cities have reported comparable HPV infection rates. However, the HPV infection rate in this analysis was higher than that of Uyghur women in Xinjiang (9.15%) [26], but lower than that of women in Shaanxi Province (30.21%) [27], Beijing (21.0%) [28] and Chongqing (19.9%) [29]. These variations suggest that differences in geographical conditions and economic development may lead to variations in HPV infection rates. Studies have shown that in Shanghai, China, the age-specific prevalence of HPV infection exhibits two peaks—one in the

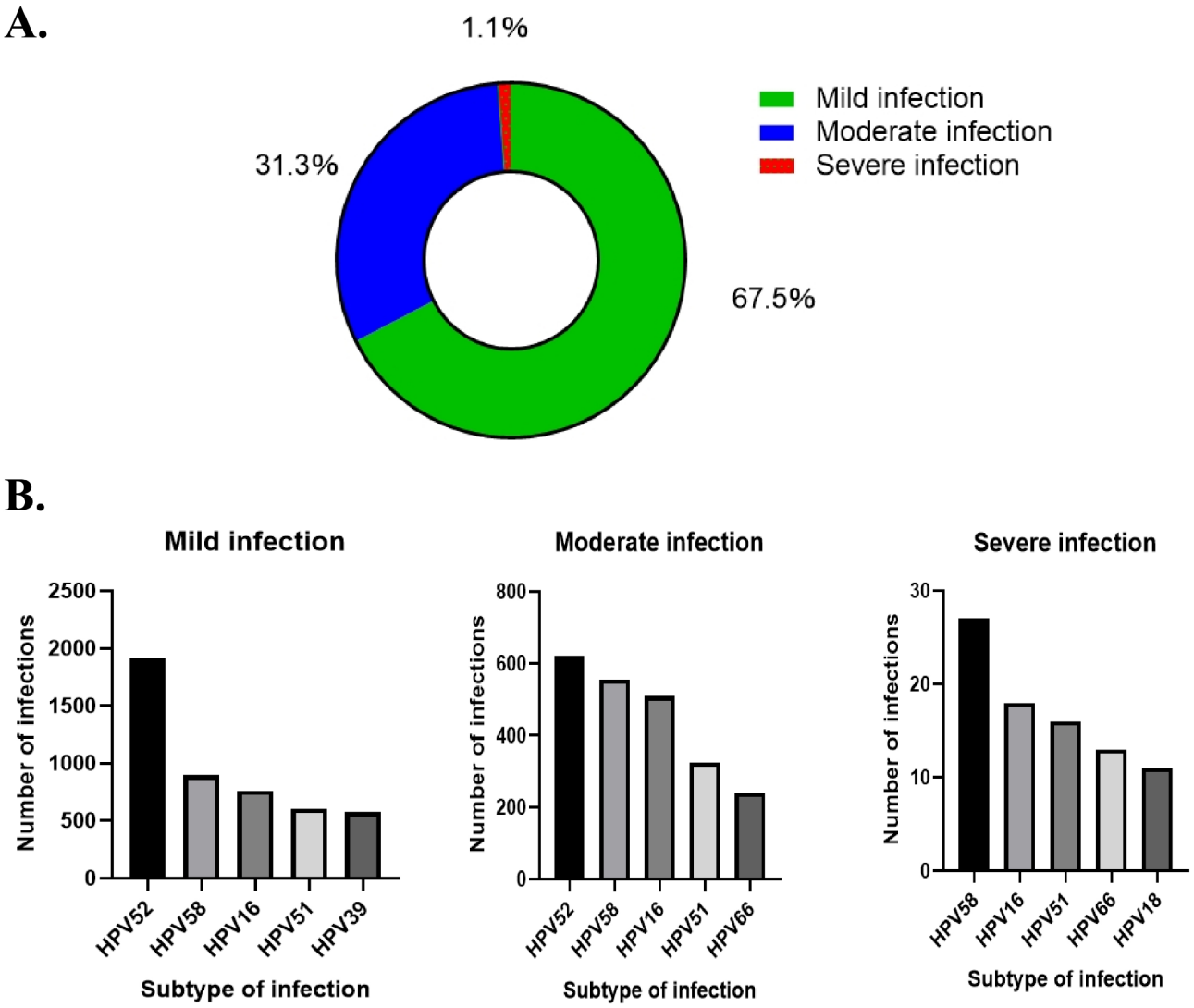

Fig. 3 Proportion of HPV infections and distribution of HPV genotypes among patients with different infection severities (mild, moderate, and severe). Note: **(A)** Proportion of HPV infections among patients with different infection severities (mild, moderate, and severe). **(B)** Distribution of different HPV genotypes among patients with different infection severities (mild, moderate, and severe)

age group over 55 years and another in the group under 25 years [30]. This finding is highly consistent with the conclusions of our study, which also revealed that HPV infection rates typically follow an age-specific pattern, with a peak observed among women under 30 years. The higher prevalence in younger women may be attributed to more frequent sexual activity and having multiple sexual partners. However, it is worth noting that although young women are more susceptible to HPV infection, their immune systems can generally clear transient infections, reducing the risk of cervical lesions [31]. Factors influencing the natural clearance of HR-HPV include smoking history, contraceptive methods, pregnancy, childbirth, age at first sexual intercourse, number of sexual partners, immune status, viral load, age, and HPV genotype [32].

It is noteworthy that the study found a second peak in HPV infection rates among women aged 50–59 and 60 and above. This phenomenon may be explained by the long latency period of HPV infection and the reactivation of the virus under conditions of immune system decline (such as menopause or aging) [33, 34]. Therefore, efforts to prevent cervical cancer should consider the age-specific nature of HPV infection, emphasizing the importance of HPV vaccination for adolescents and regular cervical cancer screening for women aged 30 and above.

Analysis of single, double, and multiple HPV infections shows that single infections are the most common, accounting for the majority of cases. The study also emphasizes the importance of studying the impact of multiple infections on cervical cancer risk, as multiple infections may persist longer and confer stronger

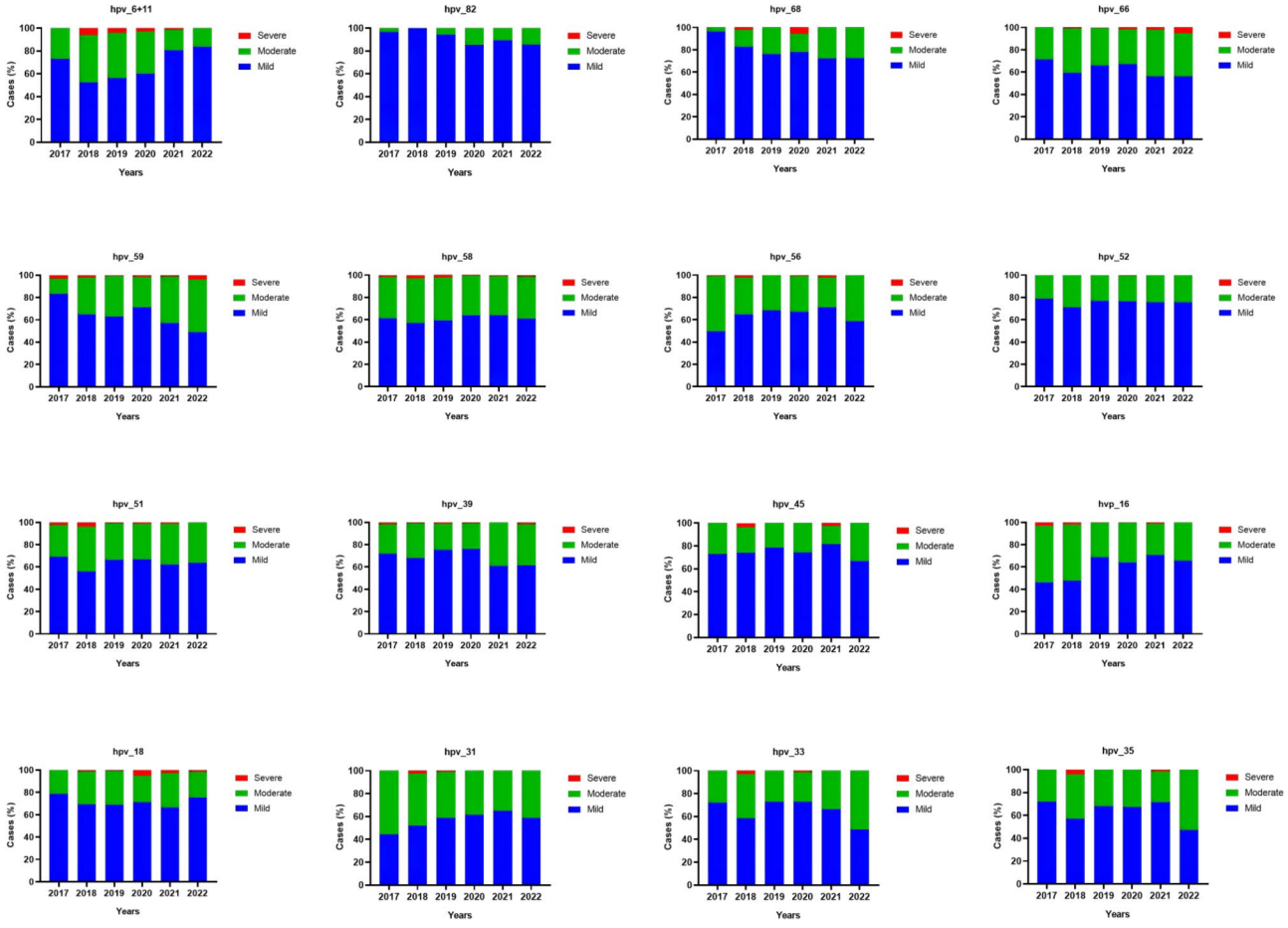

Fig. 4 Changes in the proportion of infection severities (Mild, Moderate, or Severe) among patients with different HPV denotypes from 2017 to 2022

resistance to self-immunity. However, some studies suggest that single HPV infections may lead to a higher risk of cervical cancer due to competition or balance between various HPV subtypes. In this study, the prevalence of single HPV infections was higher than that of double and multiple infections. It is worth noting that HPV52 and its related subtypes were prominent in all infection categories, highlighting the clinical significance of HPV52 in the region.

Compared to other regions of mainland China, there are differences in the distribution of HPV genotypes [35–37]. Studies have shown that the most common HPV genotypes in Jinshan District, Shanghai, are HPV52, HPV16, HPV58, HPV51, HPV53, and HPV68 [38]. This finding aligns closely with the results of our study, which identified HPV51, HPV39, HPV16, HPV52, HPV56, and HPV58 as the most prevalent high-risk genotypes in Xuhui District. Furthermore, analysis of moderate to severe infections indicates an increasing trend in HPV59, HPV33, and HPV35, emphasizing the importance of monitoring these subtypes. The study highlights the need for future vaccine development to consider regional variations in HPV genotype distribution to potentially enhance prevention strategies. However, it acknowledges that vaccine efficacy data specific to these regional genotypes are currently limited, necessitating further research.

The clinical value of this study lies in its potential contribution to refining cervical cancer prevention and screening strategies, particularly in urban populations. However, its retrospective nature and lack of inclusion of socioeconomic or behavioral factors necessitate cautious interpretation of its broader applicability. By analyzing the HPV infection rate and genotype distribution in Shanghai, we can more accurately identify groups needing additional attention, especially the peak groups of age-specific infections. For example, promoting HPV vaccination and regular screening for cervical cancer for women under 30 and above 50 can effectively reduce the incidence of cervical cancer. Additionally, the study highlights the potential link between multiple HPV infections and the risk of cervical lesions, providing valuable clues for future clinical interventions.

However, This study has notable limitations. Firstly, its retrospective design and reliance on hospital-based data may introduce selection bias and affect generalizability

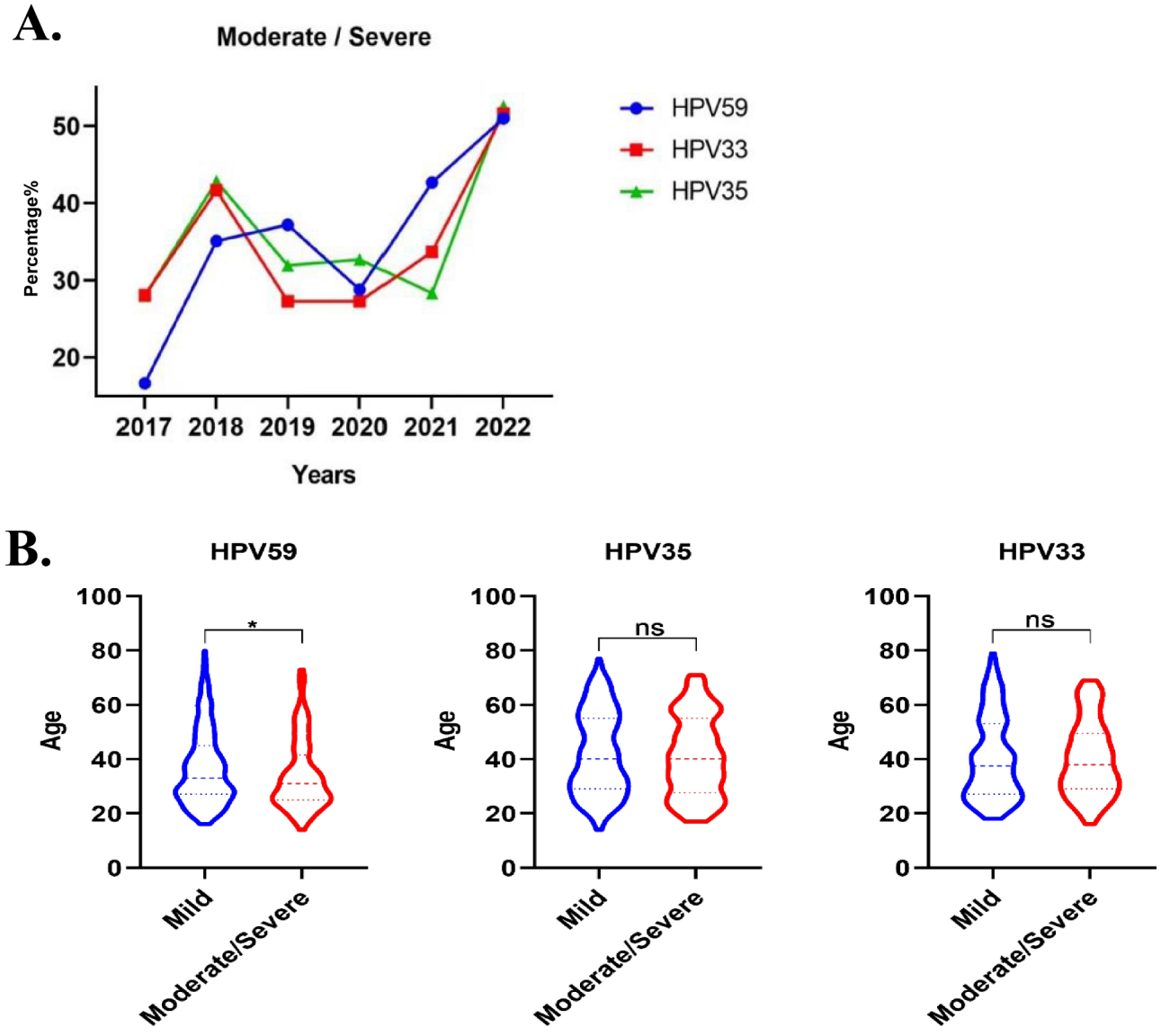

Fig. 5 The relationship between different HPV genotypes (HPV59, HPV33, and HPV35) and the proportion of moderate to severe cases and patient age. Note: **(A)** Proportion of patients with moderate and severe infections in HPV 59, HPV 33, and HPV 35 genotypes showing an increasing trend over time; **(B)** Relationship between HPV 59, HPV 33, HPV 35 genotypes and age

to the broader population. Additionally, the exclusion of socioeconomic, lifestyle, and behavioral factors from the analysis limits the ability to assess their influence on HPV prevalence. Furthermore, the absence of cytological and pathological follow-up data restricts the study's ability to correlate HPV infections with clinical outcomes, which are critical for validating the significance of identified trends.

Future research prospects should include more extensive and in-depth studies to fill existing knowledge gaps. For example, future studies could consider incorporating a wider range of geographic and population groups to more comprehensively assess the epidemiological characteristics of HPV infections. Additionally, studies should consider using prospective designs to reduce data collection biases and enhance the accuracy and reliability of research results. Furthermore, there should be an increase in research on the natural history of HPV infections, particularly in exploring the mechanisms of viral clearance and the development process of cervical cancer. Finally, considering the development of HPV vaccines, monitoring and studying newly emerging HPV genotypes and genotypes not covered by existing vaccine coverage is crucial, as this will facilitate future vaccine updates and strategy adjustments.

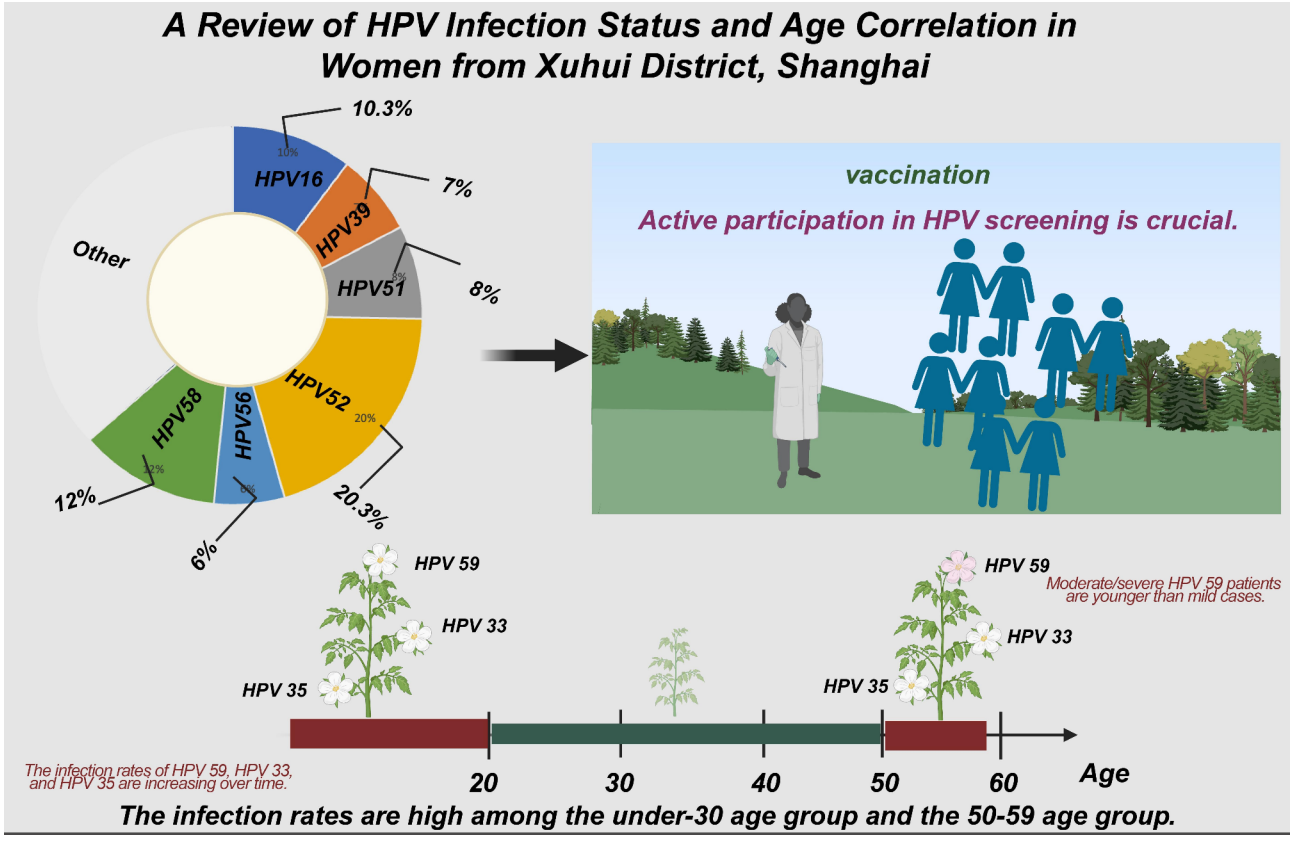

Fig. 6 Conceptual Illustration of HPV Infection Rate and Genotype Distribution among Females in Xuhui District, Shanghai

Conclusion

This study identified HPV 52, 58, 16, and 51 as the main HR-HPV genotypes among females in Xuhui District, Shanghai (Fig. 6). Notably, HPV 59, 33, and 35 demonstrated an increasing trend in moderate to severe infections, with HPV 59 having a higher tendency in younger age groups and a higher likelihood of co-infection with other types. These findings offer preliminary insights for guiding cervical cancer screening and HPV vaccine strategies in the region. However, the absence of clinical outcome validation and consideration of behavioral and demographic factors underscores the need for further comprehensive research to fully understand HPV epidemiology and its implications for public health interventions. However, the study has limitations and further research incorporating cytological and pathological results is needed for a comprehensive understanding.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12985-025-02663-4 .

Supplementary Material 1

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None.

Author contributions

Han Liu, Mingming Jiang, and Jiaying Wu contributed equally to data collection, analysis, and initial drafting of the manuscript. Yue Dai and Minyi Xu conducted statistical analyses and contributed to data interpretation. Lei Wang and Muyuan Ji supervised the study, provided critical feedback, and contributed to the manuscript's final revision. All authors reviewed and approved the final manuscript.

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Data availability

The raw data used in this study, including those presented in the article and supplementary materials, can be obtained by contacting the corresponding authors directly. Further inquiries regarding the data may be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Shanghai Eighth People's Hospital (No. 2023-061-21) and individual consent for this retrospective analysis was waived.

Competing interests

The authors declare no competing interests.

Conflict of interest
The author declares no conflict of interest.

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References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.
2. Nasreen S, Lone AR, Manzoor A, et al. Carcinoma cervix: a single institute experience from Kashmir, Northern India. J Cancer Res Ther. 2023;19(5):1407–11. https://doi.org/10.4103/jcrt.jcrt_203_22.
3. Okunade KS. Human papillomavirus and cervical cancer [published correction appears in J Obstet Gynaecol. 2020;40(4):590. Doi: 10.1080/01443615.2020.1713592]. J Obstet Gynaecol. 2020;40(5):602–8. https://doi.org/10.1080/01443615.2019.1634030.
4. de Sanjosé S, Diaz M, Castellsagué X, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis. 2007;7(7):453–9. https://doi.org/10.1016/S1473-3099(07)70158-5.
5. Han Y, Li Q, Ling C et al. HPV-Induced MiR-21 Promotes Epithelial Mesenchymal Transformation and Tumor Progression in Cervical Cancer Cells through the TGFβ R2/hTERC Pathway. Contrast Media Mol Imaging. 2022;2022:6297694. Published 2022 Sep 1. https://doi.org/10.1155/2022/6297694
6. Na J, Li Y, Wang J, Wang X, Lu J, Han S. The correlation between multiple HPV infections and the occurrence, development, and prognosis of cervical cancer. Front Microbiol. 2023;14:1220522. Published 2023 Jul 28. https://doi.org/10.3389/fmicb.2023.1220522
7. Aldarmahi A, Alzahrani H, Alqutub S, Alzahrani F. Exploring the attitudes and practices of female doctors towards cervical cancer screening in primary health care centers. J Med Life. 2023;16(5):773–81. https://doi.org/10.25122/jml-2022-0344.
8. Li J, Huang R, Schmidt JE, Qiao YL. Epidemiological features of human papillomavirus (HPV) infection among women living in Mainland China. Asian Pac J Cancer Prev. 2013;14(7):4015–23. https://doi.org/10.7314/apjcp.2013.14.7.4015.
9. zur Hausen H. Papillomaviruses and cancer: from basic studies to clinical application. Nat Rev Cancer. 2002;2(5):342–50. https://doi.org/10.1038/nrc798.
10. Espinoza H, Ha KT, Pham TT, Espinoza JL. Genetic Predisposition to Persistent Human Papillomavirus-Infection and Virus-Induced Cancers. Microorganisms. 2021;9(10):2092. Published 2021 Oct 3. https://doi.org/10.3390/microorganisms9102092
11. Gross G. Genitoanal human papillomavirus infection and associated neoplasias. Curr Probl Dermatol. 2014;45:98–122. https://doi.org/10.1159/000358423.
12. Wu EQ, Liu B, Cui JF, et al. Prevalence of type-specific human papillomavirus and pap results in Chinese women: a multi-center, population-based cross-sectional study. Cancer Causes Control. 2013;24(4):795–803. https://doi.org/10.1007/s10552-013-0162-8.
13. Yuan XW, Li YJ, Qiu Q, Luo ZY, Zhao XF. Prevalence and genotype distribution of human papillomavirus among 9945 women from the Nanhai area of Foshan. BMC Infect Dis. 2019;19(1):71. https://doi.org/10.1186/s12879-019-3687-y. Published 2019 Jan 18.
14. Zhou YX, Ma XH, Wang TT, Qu XL, Zhang XQ. Analysis of age-specified and genotype distribution of HPV multiple infections in the Chinese population. Sci Rep. 2024;14(1):2678. https://doi.org/10.1038/s41598-024-53271-1. Published 2024 Feb 1.
15. Hampson IN, Oliver AW. Update on effects of the prophylactic HPV vaccines on HPV Type Prevalence and Cervical Pathology. Viruses. 2024;16(8):1245. https://doi.org/10.3390/v16081245. Published 2024 Aug 2.
16. Jin J, Li S, Huang H, et al. Development of human papillomavirus and its detection methods (review). Exp Ther Med. 2024;28(4):382. https://doi.org/10.3892/etm.2024.12671. Published 2024 Jul 31.
17. Dalstein V, Riethmuller D, Prétet JL, et al. Persistence and load of high-risk HPV are predictors for development of high-grade cervical lesions: a longitudinal French cohort study. Int J Cancer. 2003;106(3):396–403. https://doi.org/10.1002/ijc.11222.
18. Santos GRBD, Cunha APA, Batista ZDS, et al. HPV 18 variants in women with cervical cancer in Northeast Brazil. Braz J Infect Dis. 2023;27(1):102734. https://doi.org/10.1016/j.bjid.2022.102734.
19. Oyouni AAA. Human papillomavirus in cancer: infection, disease transmission, and progress in vaccines. J Infect Public Health. 2023;16(4):626–31. https://doi.org/10.1016/j.jiph.2023.02.014.
20. Rahangdale L, Mungo C, O'Connor S, Chibwesha CJ, Brewer NT. Human papillomavirus vaccination and cervical cancer risk [published correction appears in BMJ. 2023;383:p2901. Doi: 10.1136/bmj.p2901]. BMJ. 2022;379(e070115). https://doi.org/10.1136/bmj-2022-070115. Published 2022 Dec 15.
21. Nelson CW, Mirabello L. Human papillomavirus genomics: understanding carcinogenicity. Tumour Virus Res. 2023;15:200258. https://doi.org/10.1016/j.tvr.2023.200258.
22. Yang X, Li Y, Tang Y, et al. Cervical HPV infection in Guangzhou, China: an epidemiological study of 198,111 women from 2015 to 2021. Emerg Microbes Infect. 2023;12(1):e2176009. https://doi.org/10.1080/22221751.2023.2176009.
23. Wang T, Luan L, Deng J, et al. Prevalence and human papillomavirus (HPV) genotype distribution in Suzhou, China. Hum Vaccin Immunother. 2023;19(2):2241309. https://doi.org/10.1080/21645515.2023.2241309.
24. Li X, Xiang F, Dai J et al. Prevalence of cervicovaginal human papillomavirus infection and genotype distribution in Shanghai, China. Virol J. 2022;19(1):146. Published 2022 Sep 12. https://doi.org/10.1186/s12985-022-01879-y
25. Zhao C, Zhao Y, Li J, Li M, Shi Y, Wei L. Opportunities and challenges for human papillomavirus vaccination in China. Hum Vaccin Immunother. 2024;20(1):2329450. https://doi.org/10.1080/21645515.2024.2329450.
26. Wang WL, Han CL, Ma J, et al. Status of high-risk HPV virus infection in Xinjiang region and its relationship with cervical lesions. Chin J Reprod Health. 2024;35(3):279–82.
27. Yu YQ, Fu SL, Xu HF, et al. Systematic review of HPV type infection rates in Chinese mainland women undergoing health examinations and distribution of HPV types in the 9-valent vaccine. Cancer Prev Treat. 2019;32(2):103–13.
28. Gao J, Gao X, Zhou JL, et al. Analysis of newly reported HIV-1 infections and epidemiological characteristics in Tongzhou District, Beijing, 2021–2022. Chin J Virol. 2024;14(1):37–41. https://doi.org/10.16505/j.2095-0136.2024.1006.
29. Zhang H, Zhang Z, Hu GL et al. Sexual behavior characteristics of MSW and current status of HIV and syphilis infections in Yuzhong District, Chongqing. In: Chongqing Society of Preventive Medicine. Proceedings of the Fourth Session of the Fourth Council and Academic Annual Meeting of Chongqing Society of Preventive Medicine. Chongqing Yuzhong District CDC Tuberculosis and AIDS Department; 2022:9. https://doi.org/10.26914/c.cnkihy.2022.052884
30. Ruan Y, Li H, Liu M, et al. A retrospective analysis of human papillomavirus (HPV) prevalence and genotype distribution among 25,238 women in Shanghai, China revealed the limitations of current HPV-based screening and HPV vaccine. Cancer Epidemiol. 2023;84:102372. https://doi.org/10.1016/j.canep.2023.102372.
31. Zhang L, Shi X, Zhang Q, et al. HPV-16 E7-Specific Cellular Immune Response in Women with Cervical Intraepithelial Lesion contributes to viral clearance: a cross-sectional and longitudinal clinical study. Front Immunol. 2022;12:768144. https://doi.org/10.3389/fimmu.2021.768144. Published 2022 Jan 13.
32. Saldaña-Rodríguez P, Bahena-Román M, Delgado-Romero K, Madrid-Marina V, Torres-Poveda K. Prevalence and risk factors for high-risk human papillomavirus infection and cervical disorders: baseline findings from an human papillomavirus Cohort Study. Cancer Control. 2023;30:10732748231202925. https://doi.org/10.1177/10732748231202925.
33. Tsoukas C. Immunosenescence and aging in HIV. Curr Opin HIV AIDS. 2014;9(4):398–404. https://doi.org/10.1097/COH.0000000000000077.
34. Ellwanger JH, Kulmann-Leal B, Ziliotto M, Chies JAB. HIV infection, chromosome instability, and Micronucleus formation. Viruses. 2023;15(1):155. https://doi.org/10.3390/v15010155. Published 2023 Jan 4.

35. Arbyn M, Simon M, Peeters E, et al. 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. Clin Microbiol Infect. 2021;27(8):1083–95. https://doi.org/10.1016/j.cmi.2021.04.031.
36. Zhang S, Xu H, Zhang L, Qiao Y. Cervical cancer: Epidemiology, risk factors and screening. Chin J Cancer Res. 2020;32(6):720–8. https://doi.org/10.21147/j.issn.1000-9604.2020.06.05.
37. Li Z, Liu P, Wang Z et al. Prevalence of human papillomavirus DNA and $p16^{INK4a}$ positivity in vulvar cancer and vulvar intraepithelial neoplasia: a systematic review and meta-analysis [published correction appears in Lancet Oncol. 2023;24(5):e192. doi: 10.1016/S1470-2045(23)00178-X]. Lancet Oncol. 2023;24(4):403–414. https://doi.org/10.1016/S1470-2045(23)00066-9
38. Yu Y, Liu HL, He CF, et al. Prevalent characteristics of human papillomavirus infection in 29,508 women in Jinshan District, Shanghai. Taiwan J Obstet Gynecol. 2022;61(6):971–6. https://doi.org/10.1016/j.tjog.2022.07.007.

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