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ORIGINAL RESEARCH

# Analysis of genotype and age distribution of cervical human papillomavirus infection in Futian District, Shenzhen, China

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**Abstract**

Our study aims to understand the prevalence of cervical HPV (Human papilloma virus) infection, different subtypes causing infection and age distribution characteristics of women in Futian District, Shenzhen, China, to provide a reference for effective local prevention and treatment of HPV and targeted development and application of the HPV vaccine. Information on HPV results, age and HPV genotypes infected were collected and retrospectively analysed among women who attended the free cervical cancer screening programme conducted by the Shenzhen Futian District Government between 01 January 2016 and 31 December 2022 at our gynaecology outpatient clinics and medical check-up centres. There were 2792 positive cases among 27,738 females in Futian District, Shenzhen, with a positivity rate of 10.07%. Types 52, 58, 16, 68, 51, 39, 18, 31 and 33 were the top 9 infected genotypes in Futian District, Shenzhen, China. The high prevalence of these three genotypes, HR-HPV (High-risk human papilloma virus) types 68, 51 and 39, in the region is an important finding. Age-related differences in HPV infection rates were considerable, with the bimodal peak of the infection rate curve occurring in the age ranges of 30–34 and 60–65. The distribution of cervical HPV infection types in each region is unique, and different age groups have their susceptibility to different HPV genotypes. Geographical and age specificity should be considered in the therapeutic usage of vaccinations.

**Keywords**

Human papillomavirus; Genotype distribution; Age distribution; Cervical cancer

## 1. Introduction

Cervical cancer is the second most serious malignancy threatening women's health, second only to breast cancer in terms of incidence. Human papillomavirus is the culprit of cervical cancer [1]. More than 450 distinct HPV genome types have been discovered [2], which can be classified as high-risk or low-risk according to their carcinogenic potential [3]. Chronic HR-HPV infection is necessary for the development of cervical cancer [4–6]. Currently, primary prevention (HPV vaccination) and secondary prevention (cervical cancer screening) are the most important means of preventing cervical cancer in China. HPV infection has been shown in previous studies to be highly geographic- and age-specific [7]. The prevalence and genotype distribution of HPV infection in women varies considerably by country and even by region and by age [8, 9]. The absence of pertinent epidemiological data not only has a negative impact on public health but may also prevent the development of vaccines that are both specific and efficient. Therefore, it is essential to study the prevalence and genotype distribution of HPV infection in different regions. Few studies on the genotype distribution and age specificity of HPV infection in the region have been reported in China. Therefore, this paper analyses the HPV infection status and age distribution of 27,738 women who underwent free HPV screening at our hospital from 01 January 2016 to 31 December 2022, with the aim of providing an important reference for the precise prevention and treatment of cervical cancer and the targeted development and application of HPV vaccines locally.

## 2. Objects and methods

### 2.1 Study subjects

HPV test results and age information were collected from women who underwent free government HPV screening at the Gynecology Outpatient Clinic and Health Screening Centre of Shenzhen Hospital (Futian) of Guangzhou University of Chinese Medicine from 01 January 2016 to 31 December 2022. Among the collected HPV data, there were 151 cases of missing age data because some women's age information was not filled in or not entered into the system, resulting in their age data not being found in the system. The main age of free HPV screening was 30–65 years, and the actual age of the tested women was 21–76 years, with a mean of 43.40 ± 8.460 years. Among them, 349 patients were <30 years old, 4481 patients were 30–34 years old, 5177 patients were 35–39 years old, 5268 patients were 40–44 years old, 5489 patients were 45–49 years old, 3817 patients were 50–54 years old, 1991 patients were 55–59 years old, 998 patients were 60–65 years old, and 16 patients were >65 years old. The sample sizes of <30 and >65 years were excluded from the analysis of age-related specificity because they were small, not representative of the overall age group, and not within the free screening age range.

#### 2.1.1 Diagnostic criteria

Cervical HPV infection was diagnosed by detection of high-risk and low-risk HPV types in cervical cells by second-generation hybridization capture (HC-II), with a positive result for either type. HR-HPV infection was diagnosed as positive for any of the high-risk subtypes, and LR-HPV (Ligh-risk human papilloma virus) infection was diagnosed as a low-risk subtype infection only. Monoinfection, where only one HPV type was present in a specimen, and multiinfection, where two or more HPV infections were present in a specimen. Those who tested negative for HR-HPV and LR-HPV in cervical cells were diagnosed as HPV-negative.

#### 2.1.2 Inclusion criteria

Inclusion criteria were as follows: age ≥30 years, ≤65 years, sexually active; met diagnostic criteria for cervical HPV infection or HPV-negative; conscious and not cognitively impaired; and agreed to cooperate with this investigation.

#### 2.1.3 Exclusion criteria

Exclusion criteria were as follows: people with mental or neurological conditions who were unwilling or unable to cooperate; with other serious primary medical or surgical diseases; and those who were unable to cooperate with this survey.

### 2.2 Research methodology

#### 2.2.1 Sample collection methods

The method was performed by our specialist gynaecologists. The vaginal speculum fully exposed the cervix, and after wiping excess secretion with a large sterile cotton swab, the head of the cervical brush was slowly placed at the opening of the cervix, and the brush was gently rotated clockwise for 6 to 10 turns. After removing the cervical brush, it was quickly placed in a specimen bottle containing a specially prepared cell preservation solution, and the cap was screwed tightly. A unique barcode indicating the name, age and time of testing of the screened person was attached before being sent for HPV testing.

#### 2.2.2 Detection methods

The assay instrument was BGIseq200, an independent platform of China Shenzhen Huada Gene Technology Co. Detection of 16 genotypes using second-generation high-throughput sequencing assays. The principle is to use hybridization complementation technology to capture the target DNA sequence onto a probe, followed by PCR (Polymerase Chain Reaction) amplification and sequencing. There were 14 high-risk types (16, 18, 52, 58, 56, 31, 33, 35, 39, 45, 51, 59, 66, 68) and 2 low-risk types (6, 11).

### 2.3 Statistical processing

Data analysis was performed using SPSS (Statistical Product and Service Solutions) version 27 which is produced by IBM (International Business Machines Corporation) Corporation in Armonk, New York and the chi-square test or Fisher's exact test was used. $p < 0.05$ was considered a statistically significant difference.

## 3. Results

### 3.1 Genotype distribution of HPV infection

A total of 27,738 cases were collected from women who participated in free cervical HPV screening in Futian, Shenzhen, China, with 2792 HPV-positive cases. The overall positivity rate was 10.07% (2792/27,738). The nine most common genotypes were 52 (n = 696, 24.93%), 58 (n = 404, 14.47%), 16 (n = 395, 14.15%), 68 (n = 233, 8.35%), 51 (n = 213, 7.63%), 39 (n = 207, 7.41%), 18 (n = 192, 6.88%), 31 (n = 156, 5.59%) and 33 (n = 149, 5.34%). All 16 HPV types tested were predominantly single infected (Fig. 1). The five most common genotypes for mono-infection were type 52 (n = 517, 18.52%), type 16 (n = 309, 11.07%), type 58 (n = 298, 10.67%), type 68 (n = 170, 6.09%) and type 39 (n = 141, 5.05%). The five most common genotypes for multiple infections were types 52 (n = 179, 6.41%), 58 (n = 106, 3.80%), 51 (n = 88, 3.15%), 16 (n = 86, 3.08%) and 39 (n = 66, 2.36%). Four of the five genotypes commonly found in single and multiple infections are the same, HPV types 52, 16, 58 and 39.

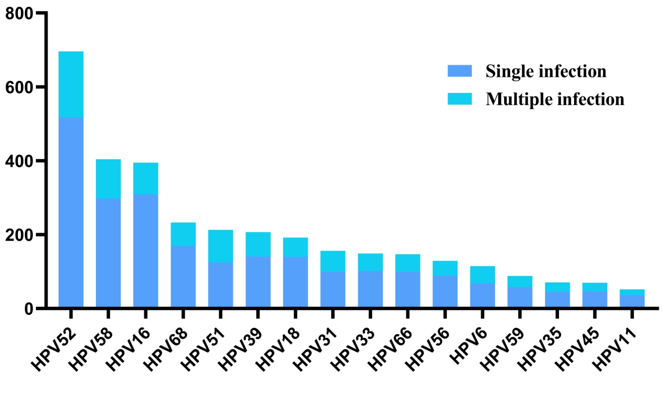


**FIGURE 1. Prevalence of different HPV genotypes.** HPV: Human papillomavirus.

### 3.2 HPV infection by age group

As shown in Table 1, of the 27,222 patients aged between 30 and 65 years, 2759 were positive, representing an overall infection rate of 10.14%. The age groups were divided into 7 groups: 30–34, 35–39, 40–44, 45–49, 50–54, 55–59 and 60–65 years old, with significant differences in HPV prevalence between age groups ($\chi^2 = 45.666$, $p < 0.001$).

**TABLE 1. Age distribution of HPV infection.**

| Age (yr) | Total cases | Positive cases No. (%) | HR-HPV No. (%) | LR-HPV No. (%) | Single infection No. (%) | Multiple infection No. (%) |
|---|---|---|---|---|---|---|
| 30–34 | 4481 | 490 (10.94) | 468 (10.44) | 22 (0.49) | 402 (8.91) | 88 (1.96) |
| 35–39 | 5177 | 453 (8.75) | 437 (8.44) | 16 (0.31) | 395 (7.63) | 58 (1.12) |
| 40–44 | 5268 | 526 (9.98) | 508 (9.64) | 18 (0.34) | 449 (8.52) | 77 (1.46) |
| 45–49 | 5489 | 541 (9.86) | 532 (9.69) | 9 (0.16) | 462 (8.42) | 79 (1.44) |
| 50–54 | 3817 | 396 (10.37) | 383 (10.03) | 13 (0.34) | 331 (8.67) | 65 (1.70) |
| 55–59 | 1992 | 199 (9.99) | 190 (9.54) | 9 (0.45) | 153 (7.68) | 46 (2.31) |
| 60–65 | 998 | 154 (15.43) | 151 (15.13) | 3 (0.30) | 126 (12.63) | 28 (2.81) |
| Total | 27,222 | 2759 (10.14) | 2669 (9.80) | 90 (0.33) | 2318 (8.52) | 441 (1.62) |

*HPV: Human papillomavirus; HR: High-risk human papilloma virus; LR: Ligh-risk human papilloma virus.*

Figs. 2,3 show that the prevalence of HPV infection and HR-HPV infection in all age groups exhibited a roughly "U-shaped" curve, with two age groups, 30–34 and 60–65 years, showing double peaks of the curve. The highest prevalence of HPV infection (15.43%) and HR-HPV infection (15.15%) was in people aged 60–65 years; the 35–39 age group was the trough of the two curves, with the lowest HPV prevalence in this age group at 8.75%; HR-HPV also had the lowest prevalence at 8.44%. The prevalence of HPV infection and HR-HPV infection among people aged 40–59 years fluctuates between 9.86%~10.37% and 9.54%~10.03%, respectively, roughly the same as the overall infection rate. A decreasing trend in HR-HPV prevalence among 35–39-year-olds can be identified when compared to 30–34-year-olds. The prevalence of LR-HPV infection was stable across all age groups, fluctuating between 0% and 0.49%, well below the overall prevalence of 10.04%.

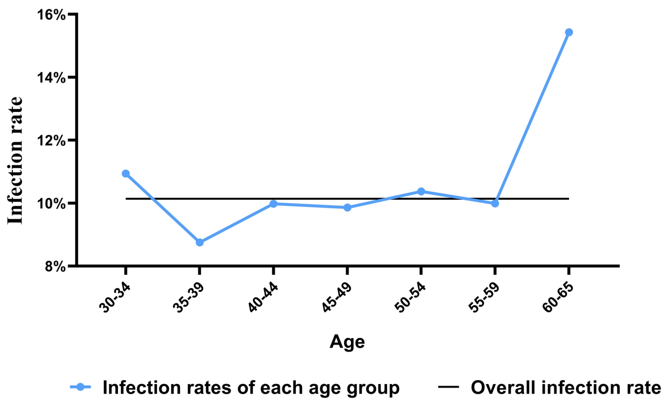


**FIGURE 2. HPV infection rates and age-specific prevalence.**

Fig. 4 demonstrates that all age categories of women had a high prevalence of the three genotypes HR-HPV 52, 58 and 16, with HR-HPV 52 being the most common. HR-HPV types 58, 16 and 18 had the highest prevalence in women aged 50–54 years. In addition to the three genotypes HR-HPV 52, 58 and 16, which are commonly found, HR-HPV 33, 66, 59 and LR-HPV 11 are more likely to be found in people aged 35–39 years, HR-HPV 39 and 45 are more likely to be found in people aged 40–44 years, and HR-HPV 31, 51, 56 and 35 are

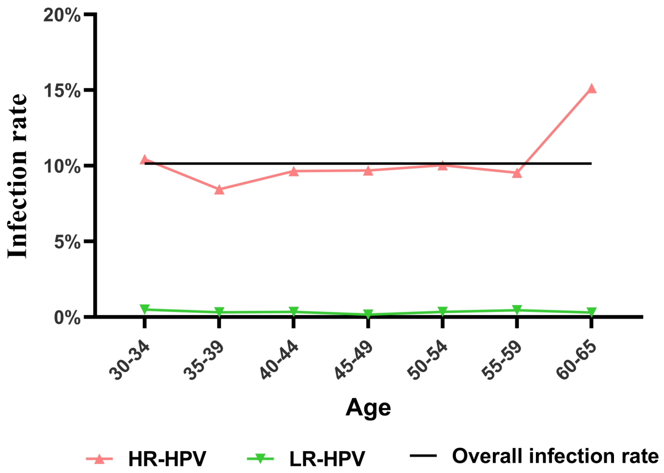


**FIGURE 3. Age-specific prevalence of HR and LR-HPV genotypes.** HPV: Human papillomavirus; HR-HPV: High-risk human papilloma virus; LR-HPV: Ligh-risk human papilloma virus.

the most prevalent in people aged 55–59 years. LR-HPV type 6 is generally uncommon; however, it is more prevalent in the 30- to 34-year-old age group than in other age groups.

## 3.3 Age distribution of single and multiple infections

When examining the age distribution characteristics of single and multiple infections collectively and the difference between age and single and multiple infections was statistically significant ($\chi^2$ = 14.458, $p$ = 0.025) (Fig. 5). HPV infections were predominantly single infections in all age groups, and the rates of single and multiple infections were lower than the overall rates in all age groups, except for the 60–65-year-old group, where the rate of single infections (n = 126, 12.63%) was higher than the overall rate. The rate of single and multiple infections was the highest of all age groups for women aged 60–65 years, and the rate of multiple infections tended to increase progressively with age in those aged 35 years and over.

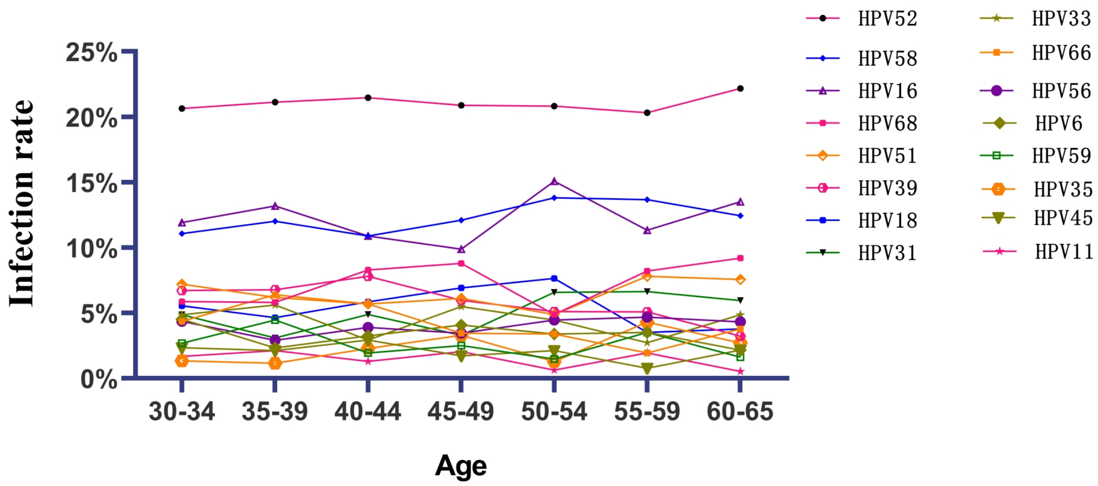


**FIGURE 4. Genotype distribution of HPV in each age group.** HPV: Human papillomavirus.

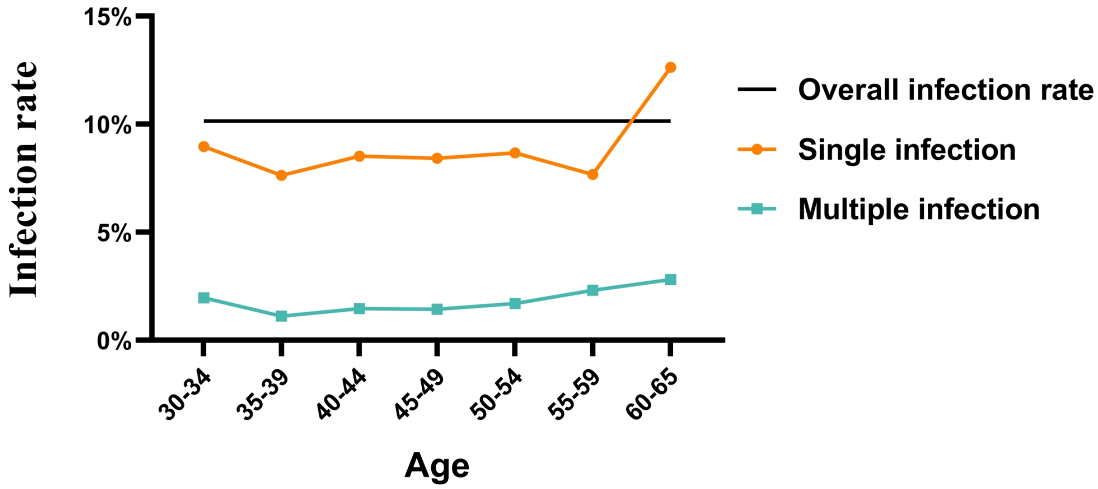


**FIGURE 5. Age-specific distribution of single and multiple infections.**

## 4. Discussion

Numerous studies have demonstrated that HPV cervix infection is a common factor in virtually all cases of cervical cancer [10]. Despite free government-led cervical cancer screening, the incidence and mortality rates of cervical cancer remain at high levels [11]. Reliable data estimates that the number of new cases of cervical cancer in China will reach 111,820 and 61,579 deaths from cervical cancer in 2022 [12]. The prevalence of HPV infection varies significantly among populations in different regions; therefore, it is necessary to study the prevalence, genotype and age distribution of HPV infection in women in the region, which can provide a reference for the precise prevention and treatment of HPV and the targeted development and application of the HPV vaccine in the local area.

In this study, the overall HPV infection rate in Futian District, Shenzhen, was 10.07%, which was lower than that in other regions in China, such as 22.97% in Northwest China [13], 16.95% in Northeast China [14], and 22.7% in Beijing, China [15], and slightly higher than that in Longgang District, which is also located in Shenzhen, at 8.2% [16]. Some studies have shown that the five most prevalent HPV genotypes in China are 52, 16, 53, 58 and 51 [17], with Guangdong Province, China being the 52, 16 and 58 types [18]. According to this research, the nine most prevalent HPV genotypes in the Futian district of Shenzhen were, in the following order: 52, 58, 16, 68, 51, 39, 18, 31 and 33. This shows that the prevalence of HPV infection and the different HPV genotypes that women may carry differ geographically. The causes might be attributed to different economic conditions, cultural norms, hygiene practices, sexual behaviours, and demographic movements in each location [19]. Therefore, prevention and treatment of HPV infection should be balanced with geographical causes.

With the inclusion of a large sample size, we found significant differences in the prevalence of HPV infection between age groups ($\chi^2 = 45.666$, $p < 0.001$), and the relationship between HPV genotype distribution and age was also revealed. A "U-shaped" curve of infection rates was derived for different age groups. The two groups of people aged 30–34 and 60–65 are the twin peaks of the U-shaped curve. Women of all ages typically had the three genotypes HR-HPV 52, 58 and 16, with HR-HPV 52 being the most prevalent. Although the frequency of infection is not particularly high overall, LR-HPV type 6 is more prevalent in the 30- to 34-year-old age group than in other age groups. The infection rate in the 30–34 age group is a peak in the curve, considering that women in this age group are mostly of childbearing age, sexually active, and may have poor sexual habits and multiple sexual partners [20, 21]. Women in this age group also have stressful lives and are responsible for providing for their families [22]. The information presented above serves as a reminder of the need to educate women of reproductive age about the dangers of HPV infection to prevent and cure cervical cancer. HR-HPV types 52 and 68 are more likely to be found in people aged 60–65 years. The prevalence of HPV infection in women aged 60–65 years in this paper is the highest of all age groups and is an area of a high prevalence of single and multiple infections. This is because fewer women in this age group participate in cervical cancer screenings, their reproductive tracts shrink after menopause, the test itself causes substantial discomfort, and there are misunderstandings about science. The majority of women who get screening at this age already have reproductive tract conditions, which causes a greater likelihood of positive. It has been suggested that if HR-HPV is not cleared before menopause, there is a greater likelihood of progression to cervical cancer after menopause [23]. As a result, it appears that our scientific education and older women's cancer prevention initiatives need to be strengthened. Our findings suggest that age specificity should be taken into account in HPV treatment since different genotypes have distinct susceptibilities at various ages.

The success of prevention and treatment has been established in several nations throughout the globe, giving women hope that HPV vaccine and cervical cancer screening may prevent women from developing HPV and lead to the eradication of cervical cancer. To date, four HPV vaccines are available in China, including Cinchonin, Cervarix, Gardasil-4 and Gardasil-9. Sinecure and Cervarix are bivalent vaccines that protect against HPV types 16 and 18; Gardasil-4 is a quadrivalent vaccine that protects against HPV types 6, 11, 16 and 18. Gardasil-9, a nine-valent vaccine, primarily offers protection against HPV types 6, 11, 16, 18, 52, 58, 31, 33 and 45. Epidemiological studies have shown that the nine-valent vaccine has a preventive effect of 90.4%–100% [24], while the bivalent and quadrivalent vaccines have an effectiveness rate of 50%–82% for the prevention of cervical lesions [25, 26]. According to studies, China has an extremely low HPV vaccine coverage rate of just 6%, particularly for those under the age of 18. The place of residence, capita household income/month, individual self-efficacy and family health had a significant impact on HPV vaccination [27]. In this study, the nine most common HPV genotypes in the Futian area of Shenzhen were 52, 58, 16, 68, 51, 39, 18, 31 and 33. The high prevalence of these three HR-HPV genotypes, 68, 51 and 39, in the region was an important finding, but the existing vaccine did not cover these three types. HR-HPV types other than HR-HPV 16 and 18 are associated with 70% of cervical cancers, while other types of HR-HPV can cause 10%–20% of cervical cancers [28]. To lower the prevalence of HPV infection in women in Futian District, Shenzhen, China, and subsequently lower the prevalence of cervical cancer in the area, HPV vaccinations for HPV types 68, 51 and 39 should be developed and included in the future HPV vaccine.

## 5. Conclusions

Different age groups also have their distinct susceptibilities to various HPV genotypes, and each location has its own distinctive distribution of the various cervical HPV infection types. The therapeutic use of immunizations should take geographic and age specificity into account.

## AVAILABILITY OF DATA AND MATERIALS

Not applicable.

## AUTHOR CONTRIBUTIONS

BFS—designed the study and carried it out; HYX, XDL, RM, HML, GHH, RHS and DWM—supervised the data collection, analysed the data, interpreted the data, prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the medical Ethics Committee of Shenzhen Hospital (Futian) of Guangzhou University of Chinese Medicine (Approval no. KS-2022091-1).

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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