Proceedings of Anticancer Research, 2021, Volume 5, Issue 6
http://ojs.bbwpublisher.com/index.php/PAR
ISSN Online: 2208-3553
ISSN Print: 2208-3545

# Epidemiological Characteristics and Genotypes of Human Papillomavirus Infection in Mianyang

**Daping Song*, Min Min, Pingjing Guo, Xuemei Zhou**

The Third Hospital of Mianyang, Sichuan Mental Health Center, Mianyang 621000, Sichuan Province, China

***Corresponding author:** Daping Song, 809906@qq.com

**Abstract:** ***Objective:*** To investigate the epidemiological characteristics and genotypes of human papillomavirus (HPV) infection in Mianyang. ***Methods:*** The cervical samples of 27,040 patients, who visited the Department of Gynecology of The Third Hospital of Mianyang from January 2018 to January 2020, were collected. ***Results:*** The HPV-positive infection rate was 21.40% (5,787/27,040); the single HPV infection rate was 72.04% (4,169/5,787); the double HPV infection rate was 19.73% (1,142/5,787); the triple and above HPV infection rate was 8.22% (476/5,787); the top five high-risk HPV subtypes with the highest infection rates were HPV52, 16, 58, 53, and 51, while the top five low-risk HPV subtypes with the highest infection rates were HPV81, 42, 43, 6, and 11; there were significant differences in the HPV-positive infection rate, high-risk infection rate, low-risk infection rate, and multiple infection rate among different age groups ($P < 0.05$). ***Conclusion:*** The HPV infection rate in Mianyang was 21.4%, in which the majority of the cases were single infection; the high-risk HPV subtypes were HPV52, 16, 58, 53, and 51; the HPV-positive infection rate, high-risk infection rate, low-risk infection rate, and multiple infection rate were high in the middle but low at both ends in the context of age distribution; the top three age groups with the highest infection rates were 45-49, 40-44, and 30-34.

**Keywords:** HPV; Epidemiology; Gene subtype; Age

***Publication date:*** November 2021; ***Online publication:*** November 30, 2021

## 1. Introduction

In 2020, the global cancer statistics revealed that the incidence rate of cervical cancer was 600,000, ranking seventh and accounting for 3.1% of malignant tumors. Its mortality rate was 340,000, ranking ninth and accounting for 3.4% of malignant tumors. Persistent infection with human papillomavirus (HPV) is closely linked to the development of cervical cancer. HPV is a small, non-enveloped spherical double-stranded DNA virus, which has strong epitheliotropic property. This virus can infect the skin and mucosal surfaces, especially the vulva, reproductive system, anus, and oropharynx. It has been found that there are differences in its infection rate and subtype distribution among the female population in different regions, which may be related to geographical environment, lifestyle, and genetic inheritance [1-3]. Therefore, more local data are required to understand the epidemiological characteristics and subtype distribution of HPV infection among local women, so as to provide a basis for reference in local cervical cancer screening strategy, HPV vaccine coverage, clinical application, and efficacy evaluation. This study analyzed the infection rate and subtype distribution of 17 high-risk HPV subtypes and 6 low-risk HPV subtypes in 26,911 cases from cervical cancer screening.

## 2. Materials and methods

### 2.1. Inclusion criteria

The inclusion criteria were as follows: (1) patients from the Department of Gynecology of the Third Hospital of Mianyang in the age group of 20-60 and sexually active without any cervical cancer screening within the past 3 years; (2) HPV-PCR positive patients; (3) patients with no previous cervical cancer and history of hysterectomy; (4) non-pregnant and lactating women.

### 2.2. HPV detection

In order to collect the samples, HPV sampling brush was used. The procedure was carried out based on the following steps: gently pressing the brush in the cervical mouth, rotate the brush 3-4 times clockwise for 10 seconds; then, place the head of the cervical brush into the cell preservation liquid tube, and break the brush handle along the crease at the handle; following that, tighten the tube cap, proceed with specimen identification, and keep the cell preservation liquid tube in an upright position. The results from DNA extraction, template addition, PCR amplification, hybridization coloration, and analysis would show visible blue-violet dots if positive. According to the distribution map of HPV typing in the membrane strip, the subtypes were determined. Negative and positive controls were set as quality control points for each test. In this experiment, the Human Papillomavirus Genotyping (23 Types) Detection Kit (Yaneng Biotechnology (Shenzhen) Co., Ltd.) was used to design specific primers based on the genetic characteristics of HPV to amplify the target fragments of 23 HPV genotypes; the amplified products were hybridized with typing probes fixed on the membrane, including 17 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) and 6 low-risk types (6, 11, 42, 43, 81, 83). The HPV subtypes were determined according to the presence of hybridization signals.

### 2.3. Statistical analysis

The HPV-positive infection rate, the infection rate of various subtypes, and the rate of multiple infection were analyzed by Statistical Package for the Social Sciences (SPSS) software using chi-square ($\chi^2$) test. $P < 0.05$ indicates a statistically significant difference.

## 3. Results

### 3.1. HPV infection rate

The HPV infection rate of high-risk subtypes was 78.2% (6,287/8,040). The top five high-risk HPV subtypes with the highest infection rates were HPV52 (15.3%), 16 (10.6%), 58 (7.9%), 53 (7.2%), and 51 (6.4%). See **Table 1** for details.

**Table 1.** Distribution of high-risk HPV infection in patients (n = 8,040)

| | High-risk HPV | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Subtype | 52 | 16 | 58 | 53 | 51 | 68 | 56 | 59 | 18 | 33 | 39 | 66 | 31 | 35 | 45 | 73 | 82 | Total |
| Number of cases | 1229 | 856 | 634 | 581 | 518 | 445 | 315 | 287 | 277 | 270 | 200 | 192 | 175 | 136 | 95 | 39 | 38 | 6,287 |
| Proportion | 15.3% | 10.6% | 7.9% | 7.2% | 6.4% | 5.5% | 3.9% | 3.6% | 3.5% | 3.4% | 2.5% | 2.4% | 2.2% | 1.7% | 1.2% | 0.5% | 0.5% | 78.2% |

The HPV infection rate of low-risk subtypes was 21.8% (1,753/8040). The top five low-risk HPV subtypes with the highest infection rates of were HPV81 (8.2%), 42 (4.5%), 43 (3.9%), 6 (2.8%), and 11 (1.9%). See **Table 2** for details.

**Table 2.** Distribution of low-risk HPV infection in patients (n = 8,040)

| | Low-risk HPV | | | | | | |
|---|---|---|---|---|---|---|---|
| Subtype | 81 | 42 | 43 | 6 | 11 | 83 | Total |
| Number of cases | 657 | 358 | 315 | 227 | 155 | 41 | 1753 |
| Proportion | 8.2% | 4.5% | 3.9% | 2.8% | 1.9% | 0.6% | 21.8% |

### 3.2. Analysis of single HPV infection and multiple infection

The total positive rate of HPV infection was 21.40% (5,787/27,040), in which 4,169 (72.04%) of 5,787 HPV positive patients were single HPV infection. A total of 1,142 cases were double HPV infection, accounting for 19.73% (1,142/5,787); 476 cases were triple or more HPV infection, accounting for 8.22% (476/5,787). The cases were mainly single infection, accounting for 72.04%, and single low-risk HPV infection, accounting for 57.39%. Among those with double infection, the proportion of pure high-risk infection was the highest, accounting for 11.96%. Among those with triple and above infection, the proportion of mixed infection (high-risk + low-risk) was the highest, accounting for 5.30%. See **Table 3** for details.

**Table 3.** Composition ratio of single HPV infection and multiple infection in patients (n = 5,787)

| HPV | Number of cases | Constituent ratio | Positive rate |
|---|---|---|---|
| **Single infection** | **4,169** | **72.04%** | **15.42%** |
| High-risk | 848 | 14.65% | 3.14% |
| Low-risk | 3,321 | 57.39% | 12.28% |
| **Double infection** | **1,142** | **19.73%** | **4.22%** |
| Pure high-risk | 692 | 11.96% | 2.56% |
| High-risk + low-risk | 390 | 6.74% | 1.44% |
| Pure low-risk | 60 | 1.04% | 0.22% |
| **Triple infection and above** | **476** | **8.22%** | **1.76%** |
| Pure high-risk | 166 | 2.87% | 0.61% |
| Pure low-risk | 3 | 0.05% | 0.01% |
| High-risk + low-risk | 307 | 5.30% | 1.14% |
| **Total** | 5,787 | 100.00% | 21.40% |

### 3.3. HPV infection rates in different age groups

The 27,040 patients were divided into 14 groups according to their age: under 20 years old, 21-24 years old, 25-29 years old, 30-34 years old, 35-39 years old, 40-44 years old, 45-49 years old, 50-54 years old, 55-59 years old, 60-64 years old, 65-69 years old, 70-74 years old, 75-80 years old, and over 80 years old. The HPV positive infection rates in different age groups are shown in **Table 4**. Among them, 3.78% (1023/27,040) were 45-49 years old, 3.31% (894/27,040) were 40-44 years old, and 2.82% (763/27,040) were 30-34 years old, suggesting that there was a statistically significant difference in the HPV positive infection rate among different age groups (X2 = 212.218, $P < 0.05$). The infection rate was high in the middle and low at both ends in the context of age distribution. The top three age groups with peak infection rates were 45-49, 40-44, and 30-34.

**Table 4.** Age distribution and HPV infection of patients (n = 27,040)

| Age (years) | Positive rate | Negative rate | Total |
|---|---|---|---|
| < 20 | 50 (0.18%) | 87 (0.32%) | 137 (0.51%) |
| 20-24 | 304 (1.12%) | 870 (3.22%) | 1,174(4.34%) |
| 25-29 | 550 (2.03%) | 2,271 (8.40%) | 2,821(10.43%) |
| 30-34 | 763 (2.82%) | 3,231 (11.95%) | 3,994(14.77%) |
| 35-39 | 649 (2.40%) | 2,799 (10.35%) | 3,448(12.75%) |
| 40-44 | 894 (3.31%) | 3,508 (12.97%) | 4,402(16.28%) |
| 45-49 | 1,023 (3.78%) | 4,154 (15.36%) | 5,177(19.15%) |
| 50-54 | 742 (2.74%) | 2,386 (8.82%) | 3,128(11.57%) |
| 55-59 | 361 (1.34%) | 950 (3.51%) | 1,311(4.85%) |
| 60-64 | 203 (0.75%) | 457 (1.69%) | 660(2.44%) |
| 65-69 | 153 (0.57%) | 269 (0.99%) | 422(1.56%) |
| 70-74 | 55 (0.20%) | 136 (0.50%) | 191(0.71%) |
| 75-80 | 26 (0.10%) | 95 (0.35%) | 121(0.45%) |
| > 80 | 14 (0.05%) | 40 (0.15%) | 54(0.20%) |
| Total | 5,787 (21.40%) | 21,253 (78.6%) | 27,040(100%) |

### 3.4. Age distribution of high-risk infection, low-risk infection, and multiple infection

The positive rate, high-risk infection rate, low-risk infection rate, and multiple infection rate of different age groups are shown in **Table 5**. There were statistically significant differences in the high-risk infection rate ($X^2 = 31.138$, $P = 0.003$), low-risk infection rate ($X^2 = 32.629$, $P = 0.002$), and multiple infection rate ($X^2 = 116.940$, $P = 0.001$) of different age groups, suggesting that the high-risk, low-risk, and multiple infection rates of HPV in Mianyang are high in the middle and low at both ends in the context of age distribution and the top three age groups with peak infection rates are 45-49, 40-44, and 30-34.

**Table 5.** Age distribution of high-risk infection rate, low-risk infection rate, and multiple infection rate

| Age (years) | Positive rate | High-risk infection rate | Low-risk infection rate | Multiple infection rate |
|---|---|---|---|---|
| < 20 | 50 (0.86%) | 44 (0.90%) | 19 (1.18%) | 25 (1.55%) |
| 20-24 | 304 (5.25%) | 244 (5.00%) | 110 (6.84%) | 111 (6.86%) |
| 25-29 | 550 (9.50%) | 468 (9.60%) | 148 (9.20%) | 145 (8.96%) |
| 30-34 | 763 (13.18%) | 649 (13.31%) | 189 (11.75%) | 195 (12.05%) |
| 35-39 | 649 (11.21%) | 542 (11.11%) | 165 (10.26%) | 146 (9.02%) |
| 40-44 | 894 (15.45%) | 763 (15.65%) | 225 (13.99%) | 216 (13.35%) |
| 45-49 | 1023 (17.68%) | 846 (17.35%) | 284 (17.66%) | 241 (14.89%) |
| 50-54 | 742 (12.82%) | 616 (12.64%) | 224 (13.93%) | 231 (14.28%) |
| 55-59 | 361 (6.24%) | 303 (6.22%) | 103 (6.41%) | 111 (6.86%) |
| 60-64 | 203 (3.51%) | 181 (3.71%) | 54 (3.36%) | 82 (5.07%) |
| 65-69 | 153 (2.64%) | 136 (2.79%) | 55 (3.42%) | 73 (4.51%) |
| 70-74 | 55 (0.95%) | 47 (0.96%) | 21 (1.31%) | 25 (1.55%) |
| 75-80 | 26 (0.45%) | 24 (0.49%) | 8 (0.50%) | 13 (0.80%) |
| > 80 | 14 (0.24%) | 12 (0.25%) | 3 (0.19%) | 4 (0.25%) |

*Continued on the next page*

*Continued from previous page*

| Age (years) | Positive rate | High-risk infection rate | Low-risk infection rate | Multiple infection rate |
|---|---|---|---|---|
| Total | 5,787 (100%) | 4,875 (100%) | 1,608 (100%) | 1,618 (100%) |
| $X^2$ | 212.218 | 31.138 | 32.629 | 116.940 |
| *P* value | 0.001 | 0.003 | 0.002 | 0.001 |

## 4. Discussion

Cervical cancer is one of the most common malignant tumors of the female reproductive system. The incidence rate and mortality rate in recent years have been increasing year by year. In 2020, cervical cancer ranked fourth in both the incidence rate and mortality rate among women. It can be seen that the incidence of cervical cancer is shifting toward those of younger age. The persistent infection of high-risk HPV is closely related to the occurrence of cervical cancer. Therefore, the detection of HPV as an early screening method for cervical cancer has been widely promoted and applied. The early detection and treatment of HPV can effectively prevent the occurrence of cervical cancer.

Studies have found significant differences in the infection rates of HPV among women from different regions, which may be related to geographical environment, lifestyle, and genetic inheritance of the studied population [2,3]. The infection rate of HPV reported abroad is 20% to 25%, of which the infection rate of high-risk HPV accounts for 58%. The infection rates of HPV in different regions of China are as follows: 36.98% in Beijing, 31.84% in Shanghai, 31.50% in Chengdu, 26.54% in Changsha, and 11.02% in Shenzhen. In this study, the HPV infection rate, genotypes, infection mode, and age correlation of 27,040 patients in The Third Hospital of Mianyang were analyzed. The results showed that the total infection rate of HPV was 21.40% and the infection rate of high-risk HPV was 78.2%, which are consistent with the situation reported abroad. The cases in this group were mainly single infection, accounting for 72.04%. Single low-risk HPV infection accounted for 57.39%, while for double infection, the proportion of pure high risk was the highest, accounting for 19.73%. For triple and above infection, the proportion of high-low mixed infection was the highest, accounting for 5.30%. These are basically consistent with reports at home and abroad [4-6].

There are also regional differences in the distribution of HPV gene subtypes. People infected with different HPV subtypes have different risks of cervical cancer and precancerous lesions [6,7]. Globally, the top three high-risk HPV infections are HPV16, 18, and 31. In the Chinese population, the top three high-risk HPV infections are HPV16, 52, and 58. HPV52, 58, and 16 are the top three in South China and South Korea. In Beijing, the top three are HPV16, 52, and 33, while in Chengdu, the top three are HPV16, 52, and 58. In this research, the top three high-risk HPV subtypes based on their infection rates are HPV52, 16, and 58. This is consistent with the general situation among the Chinese population although there is a slight difference from foreign studies. In this study, HPV52 (15.3%) is the most common, while in foreign countries, HPV16 is the most common. Moreover, among the top three rankings globally, HPV52 is not included; rather, HPV31 is. This is not consistent with the general Chinese population. In this study, the infection rate of HPV31 accounted for only 2.2%, reflecting that this subtype is not common in this region. Therefore, this suggests that there are obvious regional differences in the distribution of HPV gene subtypes, which may be related to local climate, living habits, economic status, and genetic factors. At present, the nine-valent HPV vaccine on the market is aimed at HPV6, 11, 16, 18, 31, 33, 45, 52, and 58. The top five subtypes of high-risk HPV in this study are HPV52, 16, 58, 53, and 51. It can be seen from this that the vaccine does not cover for HPV53 and HPV51, ranking fourth and fifth, respectively, based on their infection rates in this region. Hence, a vaccine that is suitable for the local population needs to be developed, so as to more effectively prevent the occurrence and development of cervical cancer [7,8].

There are also age distribution differences in regard to HPV infection. Foreign studies have found that the HPV infection rate has a V-shaped distribution (low in the middle and high at both ends) with age. The lowest rate of infection was found to be among those age 30-34, while the peak infection rate was noted in two age groups: 20-24 and 40-49. The study carried out in Chengdu showed that the age distribution of HPV infection rate is consistent with foreign studies [9]. The lowest infection rate was found to be among those age 41-50, while the peak infection rate was noted in two age groups: ≤ 20 and > 50. This study found that there were significant differences in the positive infection rate ($X^2$ = 212.218, $P$ < 0.05), high-risk infection rate ($X^2$ = 31.138, P < 0.05), low-risk infection rate ($X^2$ = 32.629, P < 0.05), and multiple infection rate ($X^2$ = 116.940, P < 0.05) among different age groups, suggesting that the positive infection rate, high-risk infection rate, low-risk infection rate, and multiple infection rate of HPV infection in Mianyang are high in the middle but low at both ends based on age distribution; the top three age groups with peak infection rates were found to be 45-49 years old, 40-44 years old, and 30-34 years old. This is inconsistent with the literature reports at home and abroad [10]. The reason for this may be because women in the age group of 31-45 are sexually active; thus, the chance of HPV infection greatly increases; in addition, at this stage, women are more prone to developing early cervical cancer. Most women who usually drop by The Third Hospital of Mianyang for screening are of this age group; it can be appreciated that their cervical epithelium is already diseased. Young women and postmenopausal women have weak awareness of HPV screening; this may also be the reason that the infection rate is high in the middle and low at both ends in the context of age distribution. It has been reported that the reproductive immune system of young women who have sex prematurely is immature and the immunity of postmenopausal women has decreased. Therefore, these two groups are more likely to be infected with HPV. It is necessary to strengthen the health education for these two groups to improve their awareness of cervical cancer screening as well as realize early detection and timely treatment, in order to reduce the incidence rate and mortality of cervical cancer as well as precancerous lesions in these two groups.

In conclusion, this study provides data to support the research and development of vaccines that are suitable for the local population. In addition, it has been suggested that health education should be strengthened for young women and postmenopausal women to enhance their awareness of cervical cancer screening, so as to more effectively prevent the occurrence and development of cervical cancer in women in this region as well as reduce the incidence rate and mortality of cervical cancer and precancerous lesions.

## Disclosure statement

The authors declare that there is no conflict of interest.

## References


[1] Dong B, Sun P, Ruan G, et al., 2018, Type-Specific High-Risk Human Papillomavirus Viral Load as a Viable Triage Indicator for High-Grade Squamous Intraepithelial Lesion: A Nested Case-Control Study. Cancer Manage Res, 10: 4839-4851.

[2] Patti E, Rachel L, 2017, Natural History of HPV Infection Across the Lifespan: Role of Viral Latency. Viruses, 9(10): 267.

[3] Szymonowicz KA, Chen J, 2020, Biological and Clinical Aspects of HPV-Related Cancers. Cancer Biol Med, 17(4): 864-878.

[4] Wang Y, Lin W, Wu B, et al., 2018, Distribution and Related Factors of HPV High-risk Subtypes among HPV Positive Patients with Cervical Cancer Screening in Shenzhen from 2014 to 2016. Chinese Journal of Preventive Medicine, 52(5): 480-485.

[5] Wang Y, Chen Y, Zheng J, et al., 2020, Relationship between HPV-52 Infection and Cervical Squamous Epithelial Lesions in Shantou Women. Carcinogenesis, Teratogenesis & Mutagenesis, 32(4): 304-308.

[6] Li Y, Wang H, Zhang Y, et al., 2021, Correlation between Multi-Type Human Papillomavirus Infections and Viral Loads and the Cervical Pathological Grade. Int J Gynecol Obstet, 152: 96-102.

[7] Liu Y, Ang Q, Wu H, et al., 2020, Prevalence of Human Papillomavirus Genotypes and Precancerous Cervical Lesions in a Screening Population in Beijing, China: Analysis of Results from China's Top 3 Hospital, 2009-2019. Virol J, 17(1): 104.

[8] Li M, Du X, Lu M, et al., 2019, Prevalence Characteristics of Single and Multiple HPV Infections in Women with Cervical Cancer and Precancerous Lesions in Beijing, China. J Med Virol, 91: 473-481.

[9] Luo Z, Leng P, Liu X, et al., 2018, Epidemiological Characteristics of HPV Infection in Women in Chengdu and Its Relationship with Cervical Lesions. Journal of International Reproductive Health/Family, 37(1): 49-53.

[10] Yuan F, Xu P, He X, et al., 2020, Epidemiological Analysis of 37799 Cases of Cervical Human Papillomavirus in Deyang Area. Chinese Journal of Family Planning & Gynecology, 12(3): 56-59.