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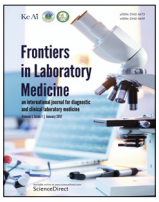

Prevalence and genotype distribution of human papillomaviruses in Sichuan, China

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ABSTRACT

Purpose: To research on infection rates of 18 HPV subtypes by recent years and the age-specific prevalence of HPV and provide a theoretical basis for the development of appropriate preventive care and constructing effective vaccine in Sichuan, China.
Methods: Cervical samples were collected from 48,170 women who underwent routine HPV screening, and HPV subtypes were detected by reverse membrane hybridization.
Results: From 2009 to 2016, the infection rate and the multiple infection rate of HPV were decreased year after year, the average rates were 25.6% (12320/48170) and 7.6% (3637/48170). The most common high-risk HPV subtypes were HPV-16 (17.8%, 2187/12320), followed by HPV-52 (17.4%, 2140/12320) and HPV-58 (12.4%, 1527/12320). HPV-16 (8.0%, 988/12320) also was the most prevalent subtype in the multiple infections. However, the infection rate of HPV-16 (25.1–16.9%) decreased from 2009 to 2016, whereas that of HPV-52 (6.8–26.1%) was obviously raised and ahead of HPV-16 in 2015 and 2016. The relationship curve between age and infection rate was a 'U' shape (two peaks at ≤25 group and ≥56 group, 30.2% and 29.8%, respectively; $\chi^2 = 302.382$, $P < 0.001$).
Conclusions: In Sichuan, the probability of women infected with HPV was very high. Due to the high infection rates of HPV-52 and HPV-58, the target of prophylactic vaccine design should include HPV-52 and HPV-58. Young and older women in Sichuan should conduct HPV testing and cervical cancer screening on a regular basis. In short, appropriate preventive care and constructing effective vaccine should be based on close monitoring of regional HPV.

Background

Cervical cancer is the second common cancer and the fourth leading cause of cancer death in females worldwide. In China, over 130,000 new cases are diagnosed every year. Molecular epidemiologic evidences clearly indicate that human papillomaviruses (HPV) is the crucial cause of cervical intraepithelial neoplasia and invasive cervical cancer. Subtypes of HPV are divided into low-risk and high-risk types according to their presumed oncogenic potential.[1] According to accumulated evidence, the major causative factor is persistent infection with high-risk HPV in the development of cervical intraepithelial neoplasia and invasive cervical cancer.[2] Moreover, high-risk HPV is also found to be a pathogenic factor associated with other cancers, such as vulva, vaginal, rectal and oral cancer.[3] But the distribution of HPV subtypes is different, both geographically and among populations. And data on HPV type-specific prevalence in different populations are important for elucidating the impact of HPV and constructing effective vaccine.

Objectives

There are few recent data on the distribution of HPV prevalence and type specificity in Sichuan. Therefore a more comprehensive study of HPV prevalence and type-specific distribution is necessary in Sichuan. Consequently, in this study, it reported the infection rates of 18 HPV subtypes in recent years and the age-specific prevalence of HPV, explored the trends and distribution of subtypes, and provided a theoretical basis for the development of appropriate preventive care and constructing effective vaccine.

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Study design

Study population

This cross-sectional study was conducted at the Key Laboratory of Bio-Resources and Eco-Environment, Chengdu, China. Seven hospitals in Chengdu and four hospitals of other areas were randomly selected as study sites (included Chengdu Western Hospital; The Affiliate Reproductive Hospital of Sichuan Genitalia Hygiene Research Center; Hospital of Chengdu Jinsha; Angel Women's & Children's Hospital; Chengdu Songziniao Sterility Hospital; Chengdu Medical College Attached Infertility Hospital; Nanchong City Shunqing District Maternal Health; Jiangyou County 305 Hospital; Yibin City Chuanrong Hospital; Wangcang County Peoples Hospital). Women who underwent routine HPV screening were eligible for inclusion. 48,170 women were included to this cross-sectional study from January 2009 to December 2016. All participants were required to have an intact cervix (e.g. no history of cauterization or surgical treatment), who were also informed of the anonymity and confidentiality of the study. This study was approved by the Ethics Committee of Sichuan University.

HPV genotyping

Cervical specimens were obtained from women by the cervical brush and placed in preservative buffer solution and stored at −20 °C. HPV genotyping was performed according to the manufacturer's instructions (Human papillomavirus genotyping kit, DaAn Gene, Guangzhou, China) through HPV DNA extraction, PCR amplification, hybridization, and gene chip analysis on a gene chip reading meter. The gene chip could identify 18 HPV genotypes, including 15 high-risk HPVs (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 58, 59, 66, 68, 83) and 3 low-risk HPVs (6, 11, 43).

Statistical analysis

The statistical calculations were performed by SPSS version 19 (IBM, Armonk, NY, USA). Chi-square test was used to check the results. P values less than 0.05 were considered significant.

Results

Total positive rate

From 2009 to 2016, HPV infection rate showed a gradual decline from 35.98% to 20.88%, with the average infection rate of 25.6% (Table 1, fig. 1). In addition, the multiple infection rate of HPV also showed a similar downward trend, from 10.5% to 6.0%, with the average multiple infection rate was 7.6%. On the other hand, the proportion of multiple infections in the total number of infections per year was basically stable at 27–35%, with the average proportion of 29.8%.

Multiple infections

In multiple infections of HPV, HPV-16 (8.0%, 988/12,320) was the most frequently detected (Table 2). HPV-52 (7.4%, 913/12,320) and HPV-58 (5.6%, 691/12,320) were still closely following HPV-16. In LR-HPV subtypes, HPV-6 (9.3%, 1149/12,320) was the most frequent subtype in multiple infections (fig. 2). On the other hand, the multiple infections proportion of each subtype had no significantly difference.

The prevalence rates of HPV-16, HPV-52 and HPV-58 in the total number of participants were 4.5%, 4.4% and 3.2%, respectively, which were higher than those of other subtypes. Infection rates of other subtypes were less than 2%.

Table 1
Statistics of HPV infection in 2009–2016.

	2009	2010	2011	2012	2013	2014	2015	2016	Total
Number of participants	820	1265	1681	2868	5491	7647	13864	14534	48170
Single infection	209	307	434	587	1096	1407	2442	2165	8647
Multiple infection (%)	86 (10.5)	147 (11.6)	204 (12.1)	317 (11.1)	515 (9.4)	524 (6.9)	1010 (7.3)	870 (6.0)	3673 (7.6)
Overall infection a (%)	295 (36.0)	454 (35.9)	638 (38.0)	904 (31.5)	1611 (29.3)	1931 (25.3)	3452 (24.9)	3035 (20.1)	12320 (25.6)
Multiple infection proportion b,%	29.2	32.4	32.0	35.0	32.0	27.1	29.3	28.7	29.8

a, Overall infection means the total of single infections and multiple infections.
b, In each year, the proportion of multiple infections in the total number of infections.

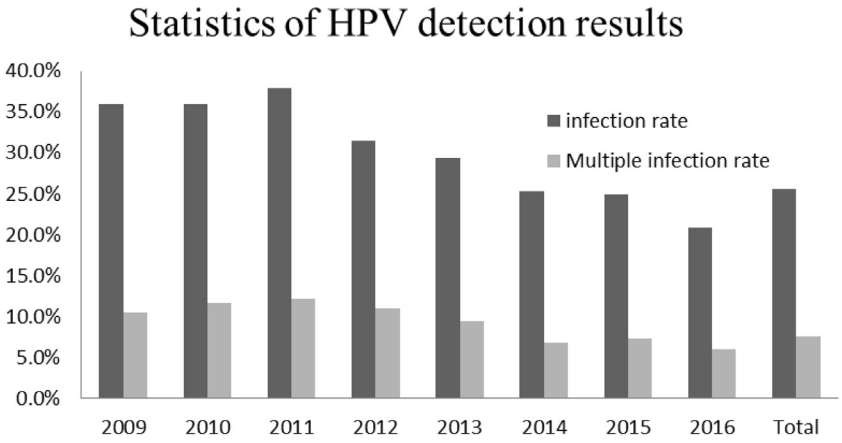

Fig. 1. Statistics of HPV detection results in 2009–2016.

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