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CLINICAL ARTICLE

Characteristics of HPV prevalence in Sichuan Province, China

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ABSTRACT

Objective: To investigate the distribution of HPV subtypes and analyze variation in infection trends during a 6-year period in Sichuan Province, China. *Methods:* A cross-sectional observational study was conducted at a center in Chengdu between January 1, 2009, and December 31, 2014. Patients with at least one type of cervical disease confirmed by histology and cytology were eligible for inclusion. Cervical specimens were tested for the presence of high-risk and low-risk HPV subtypes by reverse membrane hybridization. *Results:* Among 10 682 participants, 3370 women (31.5%) were infected with HPV. The most frequently detected high-risk genotypes were HPV16 (n = 791; 27.1%), HPV58 (n = 476; 16.3%), HPV33 (n = 273; 9.4%), HPV52 (n = 244; 8.4%), and HPV18 (n = 201; 6.9%). The most frequently detected low-risk genotype was HPV6 (n = 703; 40.8%). The detection rates of HPV33 (from 7.9% to 10.2%) and HPV58 (from 14.0% to 16.7%) increased over the 6-year period, whereas those of HPV16 (from 32.3% to 24.9%) and HPV18 (from 10.0% to 6.2%) decreased. The prevalence of HPV infection was highest among women aged 21–25 years ($\chi^2 = 191.189$; $P < 0.001$). *Conclusion:* HPV58 and HPV33 were the most prevalent subtypes in Sichuan. Changes in the prevalences of infection with different HPV subtypes have been identified.

1. Introduction

Cervical cancer is the third most common malignancy recorded among women worldwide [1]. Approximately 500 000 new cases of cervical cancer are diagnosed every year, and the disorder causes 250 000 deaths; more than 85% of all patients are from low-income countries [2,3].

Cancer of the cervix is associated with infection by certain subtypes of HPV [4]. Convincing epidemiological evidence indicates that HPV is important in the development of this cancer; indeed, the risk of cervical cancer is 50-fold higher among women infected with HPV than among their uninfected counterparts [5,6].

Genital subtypes of HPV are divided into low-risk and high-risk groups according to their presumed oncogenic potential. HPV subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 83 are considered high risk [7]. By contrast, HPV subtypes 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, and 81 are considered to pose low or no oncogenic risk [7].

The distribution of HPV subtypes differs considerably both geographically and among populations [8]. Thus, effective vaccine constructs will necessarily have to be specialized for local populations; targeting highly prevalent HPV antigens in regions where they are distributed is a major consideration in vaccine design [9], and when studying HPV distributions and sequence variability in a given population.

Comprehensive study of HPV epidemiology is necessary in Sichuan Province, China, owing to its large population. Consequently, the aim of the present study was to investigate HPV subtype distribution and infection trends in this region.

2. Materials and methods

A cross-sectional observational study was conducted at the Key Laboratory of Bio-Resources and Eco-Environment, Chengdu, China, between January 1, 2009, and December 31, 2014. Women with visible cervical lesions and/or HPV-related diseases (e.g. cervical intraepithelial neoplasia) were eligible for inclusion. The present study was approved by the Ethics Committee of Sichuan University. All participants provided informed consent before sample collection.

Women presenting for cervical screening underwent histology and cytology evaluations for the identification of any cervical disease. Cervical specimens were collected from participants and placed in a preservative buffer solution and stored at –20°C. HPV genotyping was performed using the Human Papillomavirus Genotyping Kit for 23

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Table 1
Prevalence of HPV infection by age group.[a]

Age, y	Number of participants (n = 10 682)	Positive test result (n = 3370)	Negative test result (n = 7312)	Proportion within age group with positive test result, %
≤20	702 (6.6)	318 (9.4)	384 (5.3)	45.3
21–25	2705 (25.3)	1038 (30.8)	1667 (22.8)	38.4
26–30	2573 (24.1)	761 (22.6)	1812 (24.8)	29.6
31–35	1647 (15.4)	437 (13.0)	1210 (16.5)	26.5
36–40	1395 (13.0)	359 (10.7)	1036 (14.2)	25.7
41–45	943 (8.8)	244 (7.2)	699 (9.6)	25.9
46–50	450 (4.2)	126 (3.7)	324 (4.4)	28.0
51–55	133 (1.2)	32 (0.9)	101 (1.4)	24.1
≥56	134 (1.3)	55 (1.6)	79 (1.1)	41.0

[a] Values given as number (percentage) or percentage, unless indicated otherwise.

Types (Yaneng Bioscience, Shenzhen, China), which exploits chip technology to identify 23 different HPV genotypes in one reaction (18 high-risk and 5 low-risk subtypes). Viral DNA was extracted, amplified by PCR, and genotyped according to the manufacturer's instructions; negative and positive control samples were included in each experiment.

The data were analyzed using SPSS version 19 (IBM, Armonk, NY, USA). Patients were divided into age groups. Values were expressed as number and percentage. The Pearson χ^2 test was used to confirm the results. $P < 0.05$ was considered statistically significant.

3. Results

Of the 10 682 patients enrolled, 3370 (31.5%) had positive test results for HPV infection. High-risk genotypes detected were HPV16 (n = 791; 27.1%), HPV58 (n = 476; 16.3%), HPV33 (n = 273; 9.4%), HPV52 (n = 244; 8.4%), HPV18 (n = 201; 6.9%), HPV56 (n = 191; 6.6%), HPV66 (n = 134; 4.6%), HPV31 (n = 123; 4.2%), HPV59 (n = 93; 3.2%), HPV68 (n = 78; 2.7%), HPV51 (n = 72; 2.5%), HPV35 (n = 63, 2.2%), HPV53 (n = 58; 2.0%), HPV45 (n = 34; 1.2%), HPV73 (n = 29; 1.0%), HPV39 (n = 30; 1.0%), HPV83 (n = 20; 0.7%), and MM4 (n = 5; 0.2%). Low-risk genotypes detected were HPV6 (n = 703; 40.8%), HPV11 (n = 505; 29.3%), HPV43 (n = 403; 23.4%), HPV42 (n = 112; 6.5%), and HPV44 (n = 1; 0.1%).

The number of different HPV subtypes detected per patient were one (n = 2416; 71.7%), two (n = 706, 20.9%), three (n = 184, 5.5%), four (n = 50; 1.5%), five (n = 10, 0.3%), and six (n = 4; 0.1%). Most patients with more than one subtype of HPV harbored both high-risk and low-risk viruses (n = 549; 57.5%); 307 (32.2%) patients were infected with only high-risk subtypes and 98 (10.3%) patients were infected with only low-risk subtypes.

The highest HPV infection rate was found in the 21–25 year age group ($\chi^2 = 191.189$; $P < 0.001$) (Table 1). However, the prevalence in this age group did decrease between 2009 and 2014 (Fig. 1). However, the proportion of HPV infections seen among patients aged 26–30 years and 31–35 years increased. The highest within-group HPV infection rates were detected in the groups aged 20 years or younger (Table 1).

Trends in the HPV subtypes detected were assessed by year (Table 2). The high-risk subtypes HPV16 and HPV58 ranked as the first and second most frequently detected, irrespective of year. The prevalence of HPV33, HPV42, HPV43, and HPV58 increased between 2009 and 2014, whereas the detection rates of HPV6, HPV11, HPV16, and HPV18 decreased. The rates of mixed infections seemed to fluctuate (Table 3).

4. Discussion

The present study found that 31.5% of women with cervical diseases studied in Sichuan Province, China, were infected with at least one subtype of HPV. Epidemiology studies indicate that approximately 2%–20% of healthy women worldwide have detectable levels of HPV DNA in their cervical tissue [6]. The higher rate recorded in the present study might reflect the design, which aimed to select only women with active cervical disease. Indeed, other studies have shown that smoking habits, number of sexual partners, history of sexually transmitted diseases, and abnormal cervical cytology collectively increase HPV infection risk [10].

The distribution of HPV subtypes exhibits regional differences, with different HPV subtypes conferring varying risks of cervical cancer [11]. In a meta-analysis that included 14 595 patients with invasive cervical carcinoma and 7094 patients with precancerous lesions of the uterine cervix, the most common HPV subtypes were found to be 16, 18, 31, 33, 35, 45, 52, and 58 [12]. Furthermore, HPV subtypes 16, 18, 33, 45, 52, and 58 were more frequently detected in Asia than elsewhere in the world [13]. The present study indicated that the prevalences of some high-risk HPV subtypes in Sichuan Province differ from those elsewhere—e.g. HPV33 was more common in Sichuan than in Liaoning [9] and Shanxi [14], and HPV52 was more common than in Beijing [15].

In the present study, the detection rate of some HPV subtypes (33, 42, 43 and 58) had risen over time, whereas the detection rate of other HPV subtypes (6, 11, 16, and 18) had fallen. In China, which could still be considered a low-income country, most HPV screening programs aim to detect only HPV subtypes 6, 11, 16, and 18. Current vaccines target only these four HPV subtypes, which might be the causal mechanism underpinning increased infection rates with HPV33 and HPV58 in China. In

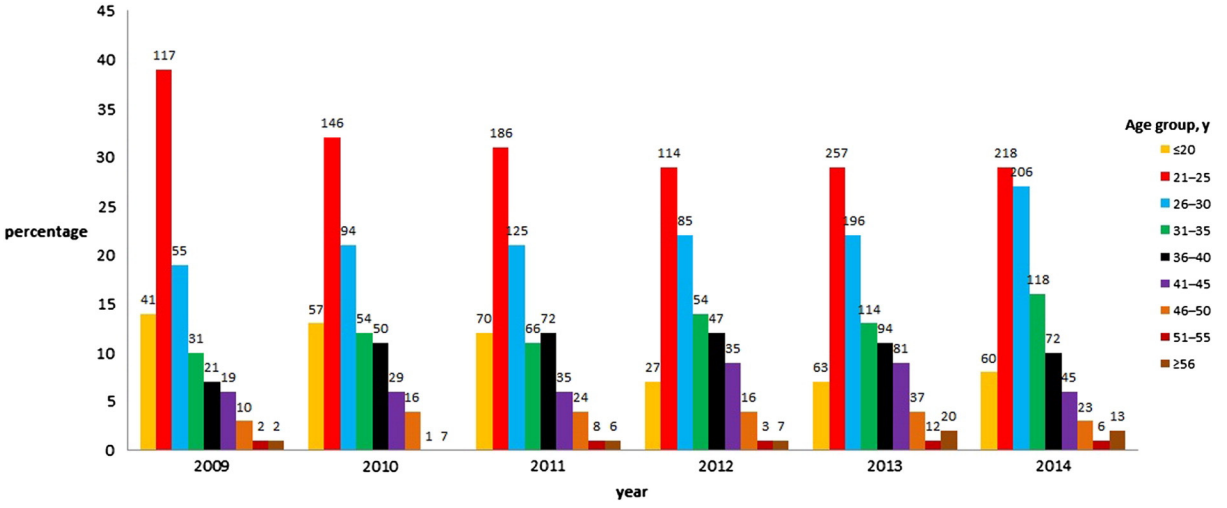

Fig. 1. The prevalence of HPV infection among the different age groups, by year. The number of positive test results for each age group is shown on top of the bars.

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