Original Article

Cervical Infection of Oncogenic Human Papillomavirus (HPV) Types in Beijing, China*

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Abstract

Objective This study was designed to determine the prevalence of oncogenic human papillomavirus (HPV) in cervical infections in Beijing, China, and to investigate the odds ratio (*OR*) of HPV single and multiple infections in abnormal cytology.

Methods A total of 19,018 specimens from outpatients in the department of obstetric and gynecology were collected. They were detected using high-risk HPV genotyping real-time polymerase chain reaction (PCR) kit and analyzed by ThinPrep cytology test for cervical pathological diagnosis. HPV prevalence, age-specific prevalence, and *OR* of each type of HPV in abnormal cytology were analyzed.

Results Overall, 19.1% (3,623/19,018) of the individuals were positive for HPV infection, 14.9% (2,833/19,018) were positive for a single HPV type, and 4.2% (790/19,018) were positive for multiple types. Among the 3,623 HPV-positive individuals, the most predominant HPV types were HPV52 (4.4%, 834/19,018), HPV16 (3.7%, 710/19,018), and HPV58 (3.4%, 644/19,018). The *OR* of multiple infections and single infection differed significantly among disease severities. The *OR* of dual infection was higher than that of each of the two single infection types, respectively.

Conclusion HPV prevalence in the outpatients was 19.1%, and the most predominant HPV types in the study were HPV52, HPV16, and HPV58. Women with multiple infectionswere more likely to have abnormal cytology.

Key words: Cervical cancer; HPV; TCT; LSIL; HSIL; Odds ratios

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INTRODUCTION

Cervical cancer (CC) is the second most common malignant disease and a leading cause of cancer mortality among women worldwide[1]. The causal link between human papillomavirus (HPV) infection and CC is now established beyond doubt. HPVs are small DNA viruses having a circular double-stranded DNA genome of approximately 8 kb, and they are classified on the basis of their genome DNA sequence. An HPV type has <90% similarity with other types at the

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nucleotide level[2-3].

Based on their association with CC and precursor lesions, HPVs can be grouped into high-risk, possible high-risk, and low-risk HPV types[4]. The high-risk HPV (HR-HPV) infection accounts for 43%-53% of patients with cervical intraepithelial neoplasia (CIN) in the western population[5-6]. HPV screening is strongly advised because of the important role of HPV in the development of CC and other associated diseases and its greater sensitivity and cost-effectiveness in detecting CC. Screening for HR-HPV may reduce the risk for CC. HPV16 and HPV18 are two predominant prevalent types associated with CC in western countries[7]. HPV prevalence data of some regions of China suggest that the distribution of HPV types is different in China[8-11].

Cervical coinfection with more than one HPV genotype is common. Nonetheless, it is unclear whether any two HPV types are more or less likely to be involved in a coinfection. The role played by coinfections with multiple HPV types in cervical neoplasia remains a difficult area of investigation. Some studies have shown that the risk for cervical precancerous lesions or invasive cancer in women infected with multiple HPV types is no greater than that in those with single-type infections, while some studies have shown that infection with multiple HPV types appears to act synergistically in cervical carcinogenesis[12-15]. With the increasing administration of HPV prophylactic vaccines, the mechanism behind multiple-type infections warrants further investigation, in light of the concern for HPV type replacement.

The purpose of this study was to investigate the prevalence of HR-HPVs and the frequency of single and multiple infections and to investigate the different risk of cervical lesion severity between HPV single and multiple infections. The interaction between different phylogenetic species in dual infection was also analyzed to assess the presence of any biological interactions between species that contribute to multiple-type infections.

MATERIALS AND METHODS

Subjects

A total of 19,018 patients were studied from January 2013 to July 2014 in the department of obstetric and gynecology at the Chinese PLA General Hospital in Beijing. All the 19,018 patients underwent high-risk HPV DNA quantitative measurement and biopsy. Among them, 17,790 individuals were diagnosed as normal, 959 patients were diagnosed with atypical squamous cells of undetermined significance (ASCUS), 93 patients were diagnosed with low-grade squamous intraepithelial lesion (LSIL), and 176 patients were diagnosed with high-grade squamous intraepithelial lesion (HSIL).

Pathological Examination

Cervical cytology was carried out by ThinPrep cytology test (TCT). Cytological diagnosis was made according to the Bethesda system classification. Histological diagnosis of the cervix was made according to the criteria proposed by the 7th edition of 'Obstetrics and Gynecology'. The biopsy of pathological sections was reviewed by senior physicians.

HPV Detection and Genotyping

DNA extraction and HPV genotyping were carried out using high-risk HPV genotyping real-time PCR kit (Shanghai ZJ Bio-Tech Co., Ltd) to detect the following HPV types: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. The lowest detection limit of the kit was 1×10^4 copies/mL. Amplification techniques performed on SLAN®-96P (Shanghai Hongshi Medical Technology Co., Ltd) were used for the quantitative estimation of HPV DNA copies.

Statistical Analysis

All statistical analyses were performed using SPSS statistical software version 19.0. The data were stratified by age (≤20 years, 21-25 years, 26-30 years, 31-35 years, 36-40 years, 41-45 years, 46-50 years, 51-55 years, 56-60 years, and ≥61 years). Chi-squared analyses were used for bivariate comparisons between age groups. $P<0.05$ was considered as statistically significant. Logistic regression was used to estimate the odds ratio (*OR*) with 95% confidence intervals to examine the association between HPV infection and CIN risk.

RESULTS

Prevalence of the Oncogenic Genotypes in the Cervical Samples

Real-time PCR quantification assays were used to investigate the frequency of type-specific HPV infection. Among the 19,018 patients, positive HPV test were obtained in 3,623 (19.1%, 3,623/19,018) patients, of whom 2,833 (14.9%, 2,833/19,018) were positive for a single HPV type and 790 (4.2%,

790/19,018) were positive for multiple types (Figure 1).

Overall, HPV52 had the highest prevalence (4.4%, 834/19,018), followed by HPV16 (3.7%, 710/19,018), HPV58 (3.4%, 644/19,018), HPV39 (2.7%, 518/19,018), and HPV51 (2.0%, 387/19,018). HPV18 had a prevalence of 1.3% (241/19,018) and was ranked seventh. In the 2,833 patients infected with single infection, the three most prevalence types were HPV52 (3.0%, 576/19,018), HPV16 (2.6%, 491/19,018), and HPV58 (2.2%, 416/19,018). In the 790 patients infected with multiple infections, the three most prevalence types were HPV52 (1.4%, 258/19,018), HPV39 (1.3%, 253/19,018), and HPV58 (1.2%, 228/19,018) (Figure 1). Among the multiple infections, 632 (80.0%, 632/790) had dual infections, 125 (15.8%, 125/790) had triple infections, 29 (3.7%, 29/790) had fourfold infections, and 4 (0.5%, 4/790) had fivefold infections.

The percentages of the single and multiple infections of each of the 13 typesare shown in Figure 2. Among the 13 oncogenic HPV types, HPV16 (69.2%, 491/710), HPV52 (69.1%, 576/834), and HPV18 (65.1%, 157/241) constituted the highest proportion of single infections and HPV68 (82.1%, 133/162), HPV39 (48.8%, 253/518), and HPV59 (42.9%, 90/210) constituted the highest proportion of multiple infections. HPV68, HPV39, and HPV59 belonged to Alpha genus seventh species (A7).

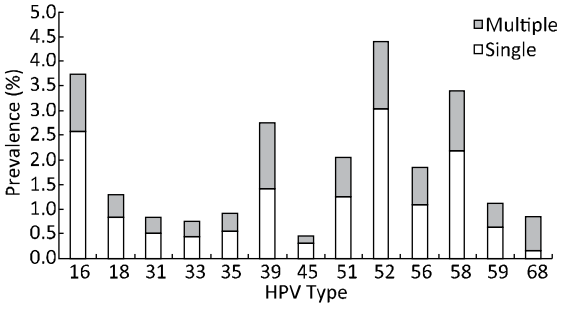

Figure 1. Prevalence of the 13 oncogenic HR-HPVs.

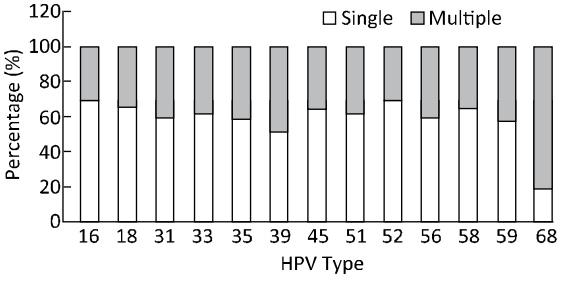

Figure 2. Single and multiple infection constituent ratios of each of the 13 oncogenic HPV types.

Age-specific Prevalence of HPV Infection

The prevalence of HPV infection was significantly different among the different age groups (χ^2=20.542, *P*=0.00847), ranging from 17.8% (171/961) in women aged ≥61 years to 24.1% (210/872) in women aged 21-25 years. Two peaks were observed for the prevalence of HPV infection, one for the group of women aged 21-25 years and the other for the group of women aged 56-60 years (20.3%, 196/967) (Figure 3). (The number of samples in the 20-year-old age group was too small for the analysis) .

The prevalence of single HPV infection was not significantly different among the different age groups (χ^2=8.3016, *P*=0.4046), ranging from 12.5% (120/961) in women aged ≥61 years to 17.1% (149/872) in women aged 21-25 years (Figure 3).

The prevalence of multiple HPV infections was significantly different among the different age groups (χ^2=42.726, $P=9.894\times10^{-7}$), ranging from 3.3% in women aged 36-40 years (102/2,529) and 41-45 years (109/2,746) to 7.0% (61/872) in women aged 21-25 years. Two peaks were observed for the prevalence of HPV infection, one for the group of women aged 21-25 years and the other for the group of women aged 56-60 years (5.5%, 53/967) (Figure 3).

Prevalence of HPV Infection in Different Cytological Diagnoses

The prevalence of HPV infections was significantly different among the different disease categories. The prevalence rates were 16.6% (2,946/17,790) in normal individuals, 48.6% (466/959) in patients with

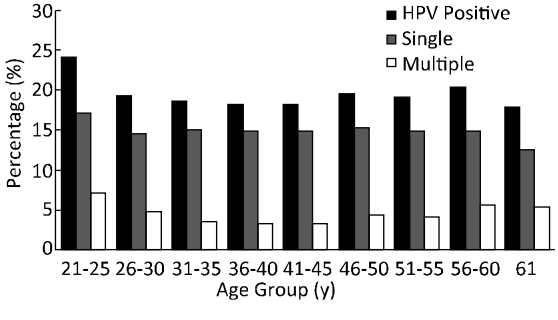

Figure 3. Age-specific prevalence of HPV infection.

ASCUS, 78.5% (73/93) in patients with LSIL, and 78.4% (138/176) in patients with HSIL.

The prevalence rates of single HPV infection were 13.2% (2,351/17,790) in normal individuals, 34.7% (333/959) in patients with ASCUS, 46.2% (43/93) in patients with LSIL, and 60.2% (106/176) in patients with HSIL. Thecytological diagnosis showed an increasing trend in the single HPV infection.

The prevalence rates of multiple HPV infectionswere 3.3% (595/17,790) in normal individuals, 13.9% (133/959) in patients with ASCUS, 32.3% (30/93) in patients with LSIL, and 18.2% (32/176) in patients with HSIL. The prevalence of dual infections ranged from 2.7% (480/17,790) in normal individuals to 23.7% (22/93) in patients with LSIL. The prevalence of triple infections ranged from 0.5% (89/17,790) in normal individuals to 7.5% (7/93) in patients with LSIL.

The prevalence rates of HPV infection in normal individuals and in patients with LSIL and HSIL were shown in Figure 4.

Relationship of HPV Infection with Risk of Abnormal Cytology

The risk of HPV infection and cervical lesions was investigated. Overall, the *OR* ranged from 4.76 (4.22-5.38) in ASCUS to 18.39 (12.85-26.33) in LSIL; HSIL showed an *OR* of 18.3 (14.07-23.81). *OR* showed an increasing trend in the single HPV infection, ranging from 4.26 (3.73-4.88) in ASCUS to 13.57 (9.02-20.43) in LSIL and to 17.61 (13.39-23.16) in HSIL. The *OR* of multiple infections ranged from 6.73 (5.61-8.08) in ASCUS to 37.42 (26.31-53.24) in LSIL; HSIL showed an *OR* of 21.01 (15.01-29.41).

In comparison to single infection, *ORs* in the multiple infections were 1.58 (1.27-1.96) in ASCUS, 2.76 (1.75-4.35) in LSIL, and 1.19 (0.80-1.79) in HSIL. In comparison to single infection, *ORs* in both dual infections and triple infections were all greater than 1. In general, multiple infections had a higher *OR* than that of single infection in all the categories, triple infections had a higher *OR* than that of dual infections in all the categories, and dual infection had a higher *OR* than that of single infection.

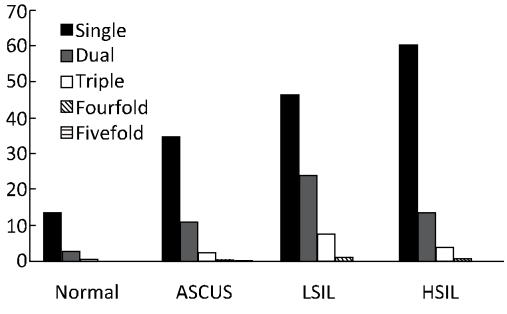

Figure 4. Prevalence of HPV infection in different cytology categories.

Incomparison to single infection, *ORs* of multiple infections of each of the oncogenic types were almost greater than that of single infection, except HPV16. When HPV16 alone was analyzed, women with single infection were more likely to have abnormal cytology with the highest *OR* associated with HSIL [70.60 (56.29-88.54)] in single infection than in multiple infections [56.17 (41.32-76.36)] (Table 1).

Pattern of Dual Infections and the Risk of Abnormal Cytology

Among the 632 dual-infection individuals, the most predominant types were HPV39 (30.2%, 191/632), HPV52 (27.8%, 176/632), and HPV58 (25.5%, 161/632). At the type level, A5 (HPV51) accounted for 16.8% (106/632), A6 (HPV56) accounted for 16.0% (101/632), A7 (HPV18, 39, 45, 59, 68) accounted for 68.7% (434/632), and A9 (HPV16, 31, 33, 35, 52, 58) accounted for 98.6% (623/632).

There were 68 combination types of 2 of the 13 HPV-type coinfections. The most predominant types were HPV39&68 (14.6%, 92/632), HPV16&52 (4.9%, 31/632), and HPV16&58 (4.7%, 30/632). There were a total of 10 types of dual coinfections with the number of individuals beyond 16, with the individual number of 457 (48.9%, 309/632) (Table 2).

According to the type of HPV species classification, the dual infections could be divided into eight types (A5+A6, A5+A7, A5+A9, A6+A7, A6+A9, A7+A7, A7+A9, and A9+A9). The most predominant types were A9+A9 (26.6%), followed by A7+A9 (25.8%), A7+A7 (16.6%), A6+A9 (11.1%), A5+A9 (10.4%), A5+A7 (4.6%), A6+A7 (3.2%), and A5+A6 (1.76%). The constituent ratio of the dual infections at species level showed that the dual infections including A5 accounted for 16.8% (106/632), A6 accounted for 16.0% (101/632), A7 accounted for 50.2% (317/632), and A9 accounted for 73.9% (467/632) of the dual infections.

The risk of HPV infection and cervical lesions was investigated in the eight types of dual coinfections. The *OR* for LSIL of A5+A6 was greater than that of A5 single and A6 single types. The *OR* of A5+A7 was greater than that of A5 single and A7 single types. A6+A7, A7+A7, and A9+A9 had greater *OR* than that of the single species, respectively (Table 3).

Table 1. HPV Infections and Cytology Result-all Odds Ratios in Comparison to Normal Infection Group

HPV Type		Single Infection				Multiple Infections			
		Normal	ASCUS	LSIL	HSIL	Normal	ASCUS	LSIL	HSIL
16	(*n*)	332	87	12	60	153	35	9	22
	(%)	1.9	9.1	12.9	34.1	0.9	3.6	9.7	12.5
	(*OR*)	1	**7.89 (6.36-9.78)**	**26.83 (16.59-43.37)**	**70.60 (56.29-88.54)**	1	**6.89 (4.97-9.55)**	**43.66 (27.19-70.09)**	**56.17 (41.32-76.36)**
18	(*n*)	134	19	1	3	55	15	6	8
	(%)	0.8	2.0	1.1	1.7	0.3	1.6	6.5	4.5
	(*OR*)	1	**4.27 (2.73-6.69)**	**5.54 (0.93-33.15)**	**8.75 (3.27-23.39)**	1	**8.21 (5.06-13.33)**	**80.97 (50.35-130.19)**	**56.82 (36.41-88.67)**
31	(*n*)	69	17	2	5	46	12	1	4
	(%)	0.4	1.8	2.2	2.8	0.3	1.3	1.1	2.3
	(*OR*)	1	**7.42 (4.69-11.74)**	**21.51 (7.73-59.84)**	**28.31 (15.09–53.09)**	1	**7.85 (4.57-13.5)**	**16.13 (3.61-72.19)**	**33.97 (17.39-66.34)**
33	(*n*)	63	16	1	6	36	14	1	3
	(%)	0.4	1.7	1.1	3.4	0.2	1.5	1.1	1.7
	(*OR*)	1	**7.65 (4.77-12.26)**	**11.78 (2.4-57.74)**	**37.2 (21.49-64.41)**	1	**11.71 (7.16-19.15)**	**20.62 (4.95-85.82)**	**32.55 (15.07-70.34)**
35	(*n*)	87	12	0	2	55	12	3	2
	(%)	0.5	1.3	0.0	1.1	0.3	1.3	3.2	1.1
	(*OR*)	1	**4.15 (2.37-7.29)**	NA	**8.98 (2.74-29.38)**	1	**6.57 (3.8-11.36)**	**40.48 (19.25-85.12)**	**14.2 (4.75-42.52)**
39	(*n*)	240	21	2	2	194	39	13	7
	(%)	1.3	2.2	2.2	1.1	1.1	4.1	14.0	4.0
	(*OR*)	1	**2.63 (1.7-4.08)**	**6.19 (1.73-22.15)**	**3.26 (0.85-12.53)**	1	**6.05 (4.43-8.28)**	**49.74 (33.09-74.76)**	**14.09 (7.56-26.26)**
45	(*n*)	47	5	0	2	26	3	1	0
	(%)	0.3	0.5	0.0	1.1	0.1	0.3	1.1	0.0
	(*OR*)	1	**3.2 (1.33-7.69)**	NA	**16.62 (5.73-48.22)**	1	**3.47 (1.13-10.7)**	**28.55 (7.55-107.98)**	NA
51	(*n*)	204	23	4	8	111	31	5	1
	(%)	1.1	2.4	4.3	4.5	0.6	3.2	5.4	0.6
	(*OR*)	1	**3.39 (2.24-5.14)**	**14.55 (6.43-32.94)**	**15.32 (8.58-27.35)**	1	**8.41 (5.97-11.84)**	**33.43 (17.86-62.57)**	**3.52 (0.54-22.81)**
52	(*n*)	505	60	5	6	199	42	6	11
	(%)	2.8	6.3	5.4	3.4	1.1	4.4	6.5	6.3
	(*OR*)	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	1	**6.35 (4.7-8.59)**	**22.38 (11.84-42.3)**	**21.59 (13.39-34.82)**
56	(*n*)	176	19	8	3	111	23	8	1
	(%)	1.0	2.0	8.6	1.7	0.6	2.4	8.6	0.6
	(*OR*)	1	**3.25 (2.06-5.12)**	**33.74 (19.99-56.93)**	**6.66 (2.39-18.55)**	1	**6.24 (4.18-9.31)**	**53.49 (33.41-85.64)**	**3.52 (0.54-22.81)**
58	(*n*)	362	38	7	9	169	41	7	11
	(%)	2.0	4.0	7.5	5.1	0.9	4.3	7.5	6.3
	(*OR*)	1	**3.16 (2.28-4.39)**	**14.35 (7.44-27.68)**	**9.71 (5.34-17.66)**	1	**7.3 (5.4-9.88)**	**30.74 (17.55-53.86)**	**25.43 (16.01-40.38)**
59	(*n*)	107	13	0	0	73	14	2	1
	(%)	0.6	1.4	0.0	0.0	0.4	1.5	2.2	0.6
	(*OR*)	1	**3.66 (2.12-6.3)**	NA	NA	1	**5.77 (3.46-9.63)**	**20.33 (7.22-57.25)**	**5.35 (0.9-31.82)**
68	(*n*)	25	3	1	0	105	19	7	2
	(%)	0.1	0.3	1.1	0.0	0.6	2.0	7.5	1.1
	(*OR*)	1	**3.61 (1.18-11.1)**	**29.69 (7.94-111.02)**	NA	1	**5.45 (3.5-8.48)**	**49.48 (29.92-81.83)**	**7.44 (2.2-25.2)**

Note. NA=not available; bold value indicates that *OR* does not include 1.0 ($P<0.05$).

All the *ORs* of the dual infections were greater than that of the single infection of the two types, respectively (Table 4).

DISCUSSION

In the current study, HPV52 had the highest prevalence (4.4%), followed by HPV16 (3.7%) and HPV58 (3.4%), while HPV18 (1.3%) was ranked seventh. Previous studies have suggested that HPV52 and HPV58 are two important HPV types associated with CC in China. The oncogenic HPV prevalence result in the current study was consistent with those of previous studies[7-14].

Table 2. Dual Infections in Different Cervical Disease Categories

Dual Infections	Normal	ASCUS	LSIL	HSIL	Total	Species
51&52	22	3	1	0	26	A5+A9
16&51	8	8	1	0	17	A5+A9
56&58	13	4	2	0	19	A6+A9
52&56	14	4	0	0	18	A6+A9
39&68	73	14	5	0	92	A7+A7
39&52	21	5	0	0	26	A7+A9
39&58	20	0	0	2	22	A7+A9
16&52	24	0	1	6	31	A9+A9
16&58	18	8	2	2	30	A9+A9
52&58	24	3	0	1	28	A9+A9

Table 3. HPV Infections and Cytology Result-all Odds Ratios of Dual Infections in Comparison to the Normal Group

HPV		Normal	ASCUS	LSIL	HSIL
A5 Single	(*n*)	315	54	9	9
	(*OR*)	1	3.39 (2.24-5.14)	14.55 (6.43-32.94)	15.32 (8.58-27.35)
A6 Single	(*n*)	287	42	16	4
	(*OR*)	1	3.25 (2.06-5.12)	33.74 (19.99-56.93)	6.66 (2.39-18.55)
A7 Single	(*n*)	553	61	4	7
	(*OR*)	1	3.32 (2.55-4.32)	5.37 (2.06-14.02)	4.94 (2.38-10.27)
A9 Single	(*n*)	1418	230	27	88
	(*OR*)	1	4.88 (4.2-5.68)	14.13 (9.08-21.99)	24.24 (18.62-31.57)
A5+A6	(*n*)	10	0	1	0
	(*OR*)	1	NA	74.22 (25.52-215.83)	NA
A5+A7	(*n*)	24	3	2	0
	(*OR*)	1	3.76 (1.23-11.54)	61.85 (27.61-138.54)	NA
A5+A9	(*n*)	47	16	2	1
	(*OR*)	1	10.25 (6.44-16.3)	31.58 (12.32-80.98)	8.31 (1.56-44.39)
A6+A7	(*n*)	14	5	1	0
	(*OR*)	1	10.75 (4.74-24.4)	53.01 (16.7-168.34)	NA
A6+A9	(*n*)	54	12	3	1
	(*OR*)	1	6.69 (3.87-11.56)	41.23 (19.67-86.42)	7.23 (1.31-40.03)
A7+A7	(*n*)	82	17	6	0
	(*OR*)	1	6.24 (3.93-9.92)	54.31 (32.23-91.51)	NA
A7+A9	(*n*)	127	23	2	11
	(*OR*)	1	5.45 (3.64-8.17)	11.69 (3.69-36.99)	33.83 (21.87-52.34)
A9+A9	(*n*)	122	30	5	11
	(*OR*)	1	7.4 (5.22-10.5)	30.42 (16.04-57.69)	35.22 (22.85-54.29)

Note. NA=not available.

The constituent ratio of each of the 13 oncogenic HPV types showed that HPV68 (82.1%), HPV39 (48.8%), and HPV59 (42.9%) constituted the highest proportion of multiple infections. HPV68, HPV39, and HPV59 belonged to Alpha genus seventh species (A7). Therefore, the dual infections including A7 may not occur randomly, whereas multiple-type infections occur more frequently than would be expected by chance alone.

As to each of the 13 HPV types, the *ORs* of multiple infections were all greater than that of the single infection, except HPV16 (Table 1). This was not consistent with previous studies.

Our results demonstrate that women with multiple infections were at a significantly increased risk for ASCUS, LSIL, and HSIL compared to those with single infections. Dual infections had a significantly increased risk for ASCUS, LSIL, and HSIL when compared with each of the two single types. Our results indicate that women with multiple infections are at a significantly increased risk for cervical disease compared to those with single infection.

Table 4. HPV Infections and Cytology Result-all Odds Ratios of Dual Infections (n>16) in Comparison to the Normal Group

Dual Infections	Normal	ASCUS	LSIL	HSIL	Species
51&52	1	**4.11 (1.35-12.52)**	**33.74 (9.36-121.58)**	NA	A5+A9
51-S	1	**3.39 (2.24-5.14)**	**14.55 (6.43-32.94)**	**15.32 (8.58-27.35)**	
52-S	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	
16&51	1	**30.11 (15.97-56.76)**	**92.78 (33.7-255.43)**	NA	A5+A9
16-S	1	**7.89 (6.36-9.78)**	**26.83 (16.59-43.37)**	**70.6 (56.29-88.54)**	
51-S	1	**3.39 (2.24-5.14)**	**14.55 (6.43-32.94)**	**15.32 (8.58-27.35)**	
56&58	1	**9.26 (3.68-23.3)**	**114.18 (56.8-229.56)**	NA	A6+A9
56-S	1	**3.25 (2.06-5.12)**	**33.74 (19.99-56.93)**	**6.66 (2.39-18.55)**	
58-S	1	**3.16 (2.28-4.39)**	**14.35 (7.44-27.68)**	**9.71 (5.34-17.66)**	
52&56	1	**8.6 (3.41-21.72)**	NA	NA	A6+A9
52-S	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	
56-S	1	**3.25 (2.06-5.12)**	**33.74 (19.99-56.93)**	**6.66 (2.39-18.55)**	
39&68	1	**5.77 (3.46-9.63)**	**50.84 (28.77-89.83)**	NA	A7+A7
39-S	1	**2.63 (1.7-4.08)**	**6.19 (1.73-22.15)**	3.26 (0.85-12.53)	
68-S	1	**3.61 (1.18-11.1)**	**29.69 (7.94-111.02)**	NA	
39&52	1	**7.17 (3.1-16.57)**	NA	NA	A7+A9
39-S	1	**2.63 (1.7-4.08)**	**6.19 (1.73-22.15)**	3.26 (0.85-12.53)	
52-S	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	
39&58	1	NA	NA	**39.06 (15.92-95.84)**	A7+A9
39-S	1	**2.63 (1.7-4.08)**	**6.19 (1.73-22.15)**	3.26 (0.85-12.53)	
58-S	1	**3.16 (2.28-4.39)**	**14.35 (7.44-27.68)**	**9.71 (5.34-17.66)**	
16&52	1	NA	**30.93 (8.37-114.28)**	**97.66 (62.22-153.28)**	A9+A9
16-S	1	**7.89 (6.36-9.78)**	**26.83 (16.59-43.37)**	**70.6 (56.29-88.54)**	
52-S	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	
16&58	1	**13.38 (7.03-25.46)**	**82.47 (38.82-175.21)**	**43.4 (18.04-104.43)**	A9+A9
16-S	1	**7.89 (6.36-9.78)**	**26.83 (16.59-43.37)**	**70.6 (56.29-88.54)**	
58-S	1	**3.16 (2.28-4.39)**	**14.35 (7.44-27.68)**	**9.71 (5.34-17.66)**	
52&58	1	**3.76 (1.23-11.54)**	NA	**16.28 (3.66-72.44)**	A9+A9
52-S	1	**3.58 (2.75-4.66)**	**7.35 (3.18-17)**	**4.64 (2.11-10.19)**	
58-S	1	**3.16 (2.28-4.39)**	**14.35 (7.44-27.68)**	**9.71 (5.34-17.66)**	

Note. NA=not available; bold value indicates that OR does not include 1.0 (P<0.05).

This study is a relatively large-scale epidemiological survey of HR-HPV prevalence in China, and the prevalence data of the 13 HPV types have reference value for the surveillance of HPV infection and CC control and prevention. There are still some limitations of this study that should be noted. The HPV genotyping kit used in this study can detect only 13 HPV types of all the known HPV types; hence, the prevalence of multiple infections may be underestimated to some extent. In addition, the analysis of interaction between the different types may be limited.

In summary, this study investigated the prevalence of the most predominant oncogenic HPV types (HPV52, HPV16, and HPV58) in women with normal and abnormal cytology. This study suggests that women with multiple-type HPV infections were more likely to have abnormal cytology than those with single HPV-type infections.

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