Prevalence of human papillomavirus genotypes among women with cervical lesions in the Shaanxi Province of China

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ABSTRACT. This study aimed to investigate human papilloma virus (HPV) genotypes among women with cervical lesions in Shaanxi Province, China, to obtain information regarding cervical lesion prevention and treatment. The study included 4508 HPV-positive subjects; cervical swab specimens were collected and tested for HPV infection status and HPV genotypes using polymerase chain reaction and reverse dot-blot hybridization. Women positive for HPV with cervical lesions, including chronic cervicitis, cervical intraepithelial neoplasia, and cervical squamous cell carcinoma (SCC), were examined; HPV-positive women with no cervical lesions were controls. Data were pooled and weighted estimates have been presented. For women with no cervical lesions and positive for one HPV genotype, HPV 52, 16, 58, 81, 33, and 56 were the most common; for multiple-HPV genotype infection, HPV 16, 52, 6, 18, 58, and 66 were the most common. Collectively, HPV 16, 58, 52, 18, 33, and 81 were the most common in women with cervical lesions. HPV 16 comprised 26.71%
of single-genotype and 15.64% of multiple-genotype infections. The proportion of HPV-16-positive cases was 29.15%, which was the highest among all HPV genotypes (P < 0.01). Single-HPV genotype infection was the most common in cervical HPV infection (77.48%); infection with two HPV genotypes comprised 72.22% of multiple-genotype infections. The proportion of single-low-risk HPV genotype infections decreased with increase in cervical lesion severity; there were no single- or multiple-low-risk genotype HPV infections in cervical SCC patients. The proportion of multiple-genotype HPV infections with at least one high-risk genotype increased with cervical lesion severity.

Key words: HPV; Genotype; Chronic cervicitis; Cervical intraepithelial neoplasia; Cervical squamous cell carcinoma

INTRODUCTION

Human papillomavirus (HPV) is a double-stranded DNA virus with a genome of approximately 8 kb. HPV can infect epithelial tissues through micro-abrasions or other epithelial trauma and replicate in the basal cells of the stratified epithelium. HPV infection is usually subclinical, and persistent infection can lead to tissue damage, malignancy (Lowy and Schiller, 2006), and, ultimately, cervical cancer (Cuschieri et al., 2004). HPV infection is rather common in China and it is estimated that 70-80% of women will be infected at least once in their lifetime and 10-15% of the cases will turn into persistent infections (Steben and Duarte-Franco, 2007). With 130,000 newly diagnosed cervical cancer cases every year, which accounts for almost 50% of new cases in the world, China has become a country with a high morbidity rate for cervical cancer (Steben and Duarte-Franco, 2007). HPV has multiple genotypes and the prevalence of these genotypes is associated with distinct populations and regionality (de Sanjosé et al., 2007). Our study investigates the prevalence of HPV genotypes among women in the Shaanxi Province in China using polymerase chain reaction (PCR) and reverse dot-blot hybridization assay. Our results could provide valuable information regarding the prevention and treatment of cervical cancer.

MATERIAL AND METHODS

Study population and enrollment

Cervical specimens were collected from patients enrolled in the Shaanxi Province Breast Cancer and Cervical Cancer Screening Program, Shaanxi Province Opportunistic Screening Program, and the Shaanxi Provincial Tumor Hospital. Additional samples were obtained from physical examination specimens from various populations in Shaanxi. Selection criteria were as follows: permanent resident in Shaanxi Province; sexually active for at least a year; no history of cervical colonization or hysterectomy; no systemic infection or autoimmune diseases; no pelvic examination, intravaginal drug administration, or sexual activity 3 days before the examination; psychologically sound; and not pregnant. All specimens were tested for HPV genotypes; due to the nature of our study, HPV-negative subjects were not included. A total of 3987 women with cervical lesions were enrolled (age range, 19-69 years; median age, 43.96 years); 521 women positive for
HPV with no cervical lesions were enrolled as the control group (NC) (age range, 21-63 years; median age, 43.87 years). In addition, the study included 697 chronic cervicitis patients (age, 19-61 years; median age, 41.26 years). The cervical intraepithelial neoplasia (CIN) group consisted of 1543 cases (CIN I = 528, CIN II = 601, CIN III = 414), with an age range of 24-62 years and a median age of 43.33 years. The squamous cell carcinoma (SCC) group included 1747 cases (SCC stage I = 339, SCC stage II = 934, SCC stage III = 379, SCC stage IV = 95), with an age range of 26-69 years and a median age of 45.67 years. Cases of cervical adenocarcinoma, adenosquamous carcinoma, and undifferentiated carcinoma were excluded from this study. All diagnoses were confirmed by a pathologist. Within the SCC group, there were 409 well-differentiated tumors, 885 moderately differentiated tumors, and 453 poorly differentiated tumors. There were 1063 cases with no lymph node involvement and 684 cases with lymph node metastasis present.

Equipment and reagents

HPV genotype detection reagents were purchased from Ya Neng Biotechnology Company (Shenzhen, China). This reagent can detect 18 high-risk HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, 83) and 5 low-risk HPV genotypes (6, 11, 42, 43, 81). The Applied Biosystems® 7500 Real-Time PCR System (USA) was used for PCR experiments. The bio-safety cabinet (HFsafe-1200TE) was provided by Li Kang Science and Technology Company (Shanghai, China). The ultra-low temperature freezer (DW-86L386) was purchased from Haier Company (China). The hybridization oven (FYY-3) was provided by Xing Hua Company (Ya Neng Biotechnology Company). Nylon membranes (pore size = 0.45 μM, thickness 6.0 ± 0.5 mm) were purchased from Pall (USA).

Specimen collection and preservation

A speculum was inserted into the subject’s vagina, which helped spread the vagina open and allowed access to the cervix. Vaginal secretions were swabbed from the cervix and then a sample was collected from the outer opening of the cervix by scraping with an endocervical brush. The brush was rotated 4-5 times in the central opening of the cervix to obtain sufficient cells. The brush was then broken off and the tip of the brush was placed into a tube filled with preservative liquid. The tube was sealed, labeled, and stored at -80°C until further testing. DNA extraction (DNA extraction kit, Bioteck, Beijing), PCR amplification (PCR kit, Bioteck), hybridization, incubation, and color development were all performed according to the manufacturer instructions (Li et al., 2013). For analysis, blue dots were considered positive and HPV genotype analysis was done on a readout system. Experiments were performed with positive controls (genotyping sample) to ensure the quality of analysis.

Statistical analysis

Data were collected and analyzed with the SPSS 16.0 software (SPSS, Chicago, IL, USA). The Student t-test and the χ² test were used, and P < 0.05 was considered significant.

RESULTS

Table 1 shows the prevalence of single-genotype HPV infections in women with cervical lesions. The most common genotypes were HPV 52, 16, 58, 81, 33, and 56 for women with no
cervical lesions (NC group); HPV 16, 52, 81, 58, 6, and 43 for the chronic cervicitis group; HPV 16, 52, 58, 33, 18, and 31 for the CIN I group; HPV 16, 52, 58, 33, 18, and 56 for the SCC stage I group; HPV 16, 58, 52, 33, and 56 for the SCC stage II group; HPV 16, 58, 18, 52, 33, and 56 for the SCC stage III group; and HPV 16, 58, 18, 52, 33, and 52 for the SCC stage IV group. The most prevalent genotypes in single-genotype infection or single-high-risk genotype infection were HPV 16, 58, 52, 18, 33, and 56, and in single-low-risk genotype infections were HPV 51, 59, 81, 18, 58, 33, and 68 for the SCC stage III group; and HPV 16, 58, 52, 18, 33, and 56 for the SCC stage IV group.

Table 1. Prevalence of single-genotype HPV infections in women with cervical lesions.

<table>
<thead>
<tr>
<th>HPV genotype</th>
<th>Control (NC)</th>
<th>CIN I</th>
<th>CIN II</th>
<th>CIN III</th>
<th>CIN IV</th>
<th>SCC stage I</th>
<th>SCC stage II</th>
<th>SCC stage III</th>
<th>SCC stage IV</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>31</td>
<td>96</td>
<td>67</td>
<td>82</td>
<td>81</td>
<td>103</td>
<td>317</td>
<td>126</td>
<td>51</td>
<td>934 (33.71)</td>
</tr>
<tr>
<td>High</td>
<td>15</td>
<td>30</td>
<td>37</td>
<td>38</td>
<td>26</td>
<td>13</td>
<td>9</td>
<td>7</td>
<td>2</td>
<td>74 (2.69)</td>
</tr>
<tr>
<td>Overall</td>
<td>46</td>
<td>126</td>
<td>104</td>
<td>119</td>
<td>108</td>
<td>116</td>
<td>334</td>
<td>133</td>
<td>53</td>
<td>1008 (37.41)</td>
</tr>
</tbody>
</table>

Table 2 shows the prevalence of multiple-genotype HPV infections in women with cervical lesions. The most common genotypes were HPV 16, 52, 6, 18, 58, and 66 for the NC group; HPV 16, 52, 58, 18, 56, and 6 for the chronic cervicitis group; HPV 16, 58, 18, 56, 6, and 52 for the CIN I group; HPV 16, 58, 52, 81, 18, and 6 for the CIN II group; HPV 16, 52, 81, 58, 33, and 52 for the CIN III group; HPV 16, 52, 18, 58, 56, and 6 for the SCC stage II group; HPV 16, 81, 52, 58, 42, and 18 for the SCC stage III group; and HPV 16, 52, 81, 18, 52, and 42 for the SCC stage IV group. The most prevalent genotypes were HPV 16, 52, 58, 33, 18, and 6 for multiple-genotype infections; and HPV 81, 6, 43, 42, and 11 in multiple-low-risk genotype infections.

Table 3 shows the prevalence of single- or multiple-genotype HPV infections in women with cervical lesions. The proportion of multiple-genotype HPV infections was only 7.10% in the NC group, and no more than two genotypes were detected in one specimen. In the chronic cervicitis group, the proportion of patients with two genotypes was 9.88%, and at most 3 genotypes were detected in one specimen. In the CIN I, II, and III groups, the proportion of multiple-genotype HPV infections was 14.70, 16.98, and 23.91%, respectively. A maximum of 4, 5, or 6 genotypes were identified in one specimen in the CIN I, II or III groups, respectively. In the SCC stage I, II, III and IV groups, the proportion of multiple-genotype HPV infections was 29.79, 35.44, 41.69, and 44.21%, respectively. A maximum of 6, 7, 7 or 5 genotypes were identified in one specimen in the SCC stage I, II, III, or IV groups, respectively. The proportion of multiple-genotype HPV infections was
The proportion of multiple-genotype HPV infections in chronic cervicitis was not significantly different from that in the NC group (P > 0.05). The difference between the proportion of multiple-genotype HPV infections in SCC stage III and SCC stage IV was not significant (P > 0.05). However, this difference was significant between the chronic cervicitis or SCC group and the CIN group (P < 0.01).

Table 2. Prevalence of multiple-genotype HPV infections in women with cervical lesions (each subtype in the multiple infections was counted separately).

<table>
<thead>
<tr>
<th>HPV genotype</th>
<th>Control (NC)</th>
<th>Chronic cervicitis</th>
<th>CIN I</th>
<th>CIN II</th>
<th>CIN III</th>
<th>SCC stage I</th>
<th>SCC stage II</th>
<th>SCC stage III</th>
<th>SCC stage IV</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>11</td>
<td>24</td>
<td>46</td>
<td>18</td>
<td>29</td>
<td>37</td>
<td>123</td>
<td>58</td>
<td>23</td>
<td>381 (15.64)</td>
</tr>
<tr>
<td>31</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td>11</td>
<td>38</td>
<td>18</td>
<td>5</td>
<td>17</td>
<td>5</td>
<td>110 (4.52)</td>
</tr>
<tr>
<td>33</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>19</td>
<td>11</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>56 (2.38)</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>53</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>31 (1.31)</td>
</tr>
<tr>
<td>58</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>118 (4.94)</td>
</tr>
<tr>
<td>62</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>66</td>
<td>9</td>
<td>10</td>
<td>5</td>
<td>9</td>
<td>15</td>
<td>20</td>
<td>84</td>
<td>29</td>
<td>9</td>
<td>166 (6.95)</td>
</tr>
<tr>
<td>68</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>12 (0.47)</td>
</tr>
<tr>
<td>691</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>141 (5.92)</td>
</tr>
<tr>
<td>73</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>39 (1.68)</td>
</tr>
<tr>
<td>830</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

NC = no cervical lesions; CIN = cervical intraepithelial neoplasia; SCC = squamous cell carcinoma.

Table 3. Distribution of single- and multiple-genotype HPV infections in women with cervical lesions.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Single genotype</th>
<th>Two genotypes</th>
<th>Three genotypes</th>
<th>Four genotypes</th>
<th>Five genotypes</th>
<th>Six genotypes</th>
<th>Seven genotypes</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>521</td>
<td>484 (92.90)</td>
<td>37 (7.10)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100 (1.93)</td>
</tr>
<tr>
<td>Chronic cervicitis</td>
<td>697</td>
<td>629 (90.24)</td>
<td>53 (7.60)</td>
<td>15 (2.15)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100 (1.93)</td>
</tr>
<tr>
<td>CIN I</td>
<td>528</td>
<td>451 (85.42)</td>
<td>54 (10.23)</td>
<td>16 (3.03)</td>
<td>7 (1.33)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100 (1.93)</td>
</tr>
<tr>
<td>CIN II</td>
<td>681</td>
<td>499 (63.03)</td>
<td>175 (24.86)</td>
<td>17 (2.83)</td>
<td>61 (8.90)</td>
<td>4 (0.67)</td>
<td>0</td>
<td>0</td>
<td>100 (1.51)</td>
</tr>
<tr>
<td>CIN III</td>
<td>414</td>
<td>315 (75.69)</td>
<td>66 (15.68)</td>
<td>24 (5.80)</td>
<td>5 (1.21)</td>
<td>3 (0.72)</td>
<td>1 (0.24)</td>
<td>0</td>
<td>100 (1.93)</td>
</tr>
<tr>
<td>SCC stage I</td>
<td>339</td>
<td>238 (70.21)</td>
<td>68 (20.06)</td>
<td>22 (6.49)</td>
<td>6 (1.77)</td>
<td>4 (1.18)</td>
<td>1 (0.29)</td>
<td>0</td>
<td>100 (1.11)</td>
</tr>
<tr>
<td>SCC stage II</td>
<td>934</td>
<td>603 (64.56)</td>
<td>236 (25.37)</td>
<td>67 (7.17)</td>
<td>18 (1.93)</td>
<td>7 (0.75)</td>
<td>2 (0.21)</td>
<td>0</td>
<td>100 (2.05)</td>
</tr>
<tr>
<td>SCC stage III</td>
<td>275</td>
<td>175 (63.84)</td>
<td>90 (32.89)</td>
<td>20 (7.31)</td>
<td>7 (2.50)</td>
<td>4 (1.45)</td>
<td>2 (0.73)</td>
<td>0</td>
<td>100 (7.36)</td>
</tr>
<tr>
<td>SCC stage IV</td>
<td>95</td>
<td>53 (55.79)</td>
<td>29 (30.53)</td>
<td>9 (4.70)</td>
<td>3 (3.16)</td>
<td>1 (1.05)</td>
<td>0</td>
<td>0</td>
<td>100 (1.06)</td>
</tr>
<tr>
<td>Total</td>
<td>4508</td>
<td>3493 (77.48)</td>
<td>733 (16.26)</td>
<td>199 (4.41)</td>
<td>52 (1.15)</td>
<td>23 (0.51)</td>
<td>6 (0.13)</td>
<td>2 (0.04)</td>
<td>100 (1.93)</td>
</tr>
</tbody>
</table>

NC = no cervical lesions; CIN = cervical intraepithelial neoplasia; SCC = squamous cell carcinoma.

Table 4 showed the distribution of high- or low-risk genotype HPV infections among women with cervical lesions. The proportion of single-low-risk genotype HPV infections in the chronic cervicitis group (28.84%) was significantly higher than in any other group (P < 0.05). Single-high-risk genotype HPV infections were very common in all groups, but the proportion decreased with the stage of SCC (P < 0.05). The proportion of multiple-low-risk genotype HPV infections was low in all groups, with none occurring in the SCC group. However, multiple-high-risk genotype HPV infections increased with the severity of cervical lesions. The proportion of high-risk HPV infections was 1.92% in the NC group compared with 24.21% in the SCC stage IV group. The difference

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18.02% in the CIN I (I, II, and III combined) and 36.18% in the SCC group (stages I, II, III, and IV combined).
between the chronic cervicitis group and the NC group was not significant (P > 0.05) in terms of high-risk HPV infections, while this difference was significant between the chronic cervicitis group and the CIN group. The proportion of multiple-high-risk genotype HPV infections was significantly lower in the NC group than in the CIN or SCC groups (P < 0.01). The data for multiple-high- and low-risk genotype HPV infections showed the same trend as multiple-high-risk genotype HPV infections.

**DISCUSSION**

HPV infection is one of the confirmed pathogenic factors in cervical cancer (Tovar et al., 2008). HPV 16 and 18 can be found in most cervical cancers (Stanley et al., 2007) and more than 50% of cervical cancer patients are HPV 16 positive (Grce et al., 2010). However, the prevalence of HPV infections is distinctly different between countries, ethnicities, and even regions within the same country (Clifford et al., 2005). It has been widely reported that most HPV infections are cleared within 12 months and only a small number become persistent infections. High-risk genotype HPV infections are usually difficult to clear and can increase the risk of CIN III by 100- to 300-fold (Bekkers et al., 2004).

Regional disparities in HPV genotypes have come into focus as the etiology of cervical cancer develops because the prevalence of a particular HPV genotype could provide more information on the carcinogenicity and epidemiology of the virus in one specific region. Genotype screening on a large scale could detect the prevalence of HPV genotypes (single or multiple genotype; high-risk, low-risk or both) in infected people who are asymptomatic (Tovar et al., 2008; Li et al., 2014) and the genotypes prevalent in women with cervical lesions. There are already several reports on this subject in China (Li et al., 2009; Muhanmode and Liu, 2010; Yang et al., 2010) but the numbers of enrolled participants were small. Our study analyzed specimens from HPV-positive women with or without cervical lesions (N = 521 or 3987, respectively). Among women positive for a single genotype, the most common genotypes were HPV 52, 16, 58, 81, 33, and 56 for women with no cervical lesions (NC group); HPV 16, 52, 81, 58, 6, and 43 for the chronic cervicitis group; HPV 16, 52, 58, 33, 18, and 56 for the CIN group; and HPV 16, 58, 18, 52, 33, and 56 for the cervical SCC group. Our results show that the most prevalent genotypes for single-genotype infections were distinct in different groups. HPV 16 was the most common genotype for single-genotype infections in all groups except the NC group, and this finding is consistent with previous reports (Clifford et al., 2005; Sandri et al., 2009; Li et al., 2011). Other common genotypes were first identified in our previous studies (Sandri et al., 2009; Muhanmode and Liu, 2010; Yang et al., 2010; Li et al., 2009, 2011; Rao et al., 2012).
The most prevalent genotypes in single-genotype or single-high-risk genotype HPV infections were HPV 16, 58, 52, 18, 33, and 56, while in single-low-risk genotype HPV infections the most prevalent genotypes were 81, 6, 43, 42, and 11.

Among patients with multiple-genotype HPV infections, the most common genotypes were HPV 16, 52, 6, 18, 58, and 66 for women with no cervical lesions (NC group); HPV 16, 52, 58, 18, 56, and 6 for the chronic cervicitis group; HPV 16, 58, 52, 6, 81, and 18 for the CIN group; and HPV 16, 52, 58, 81, 18, and 6 for the cervical SCC group. Collectively, the most common HPV genotype in women with cervical lesions was HPV 16, which accounted for 37.54% (381/1015) of multiple-genotype HPV infections. The second and third most common high-risk genotypes were HPV 52 and 58, accounting for 19.31% (196/1015) and 17.93% (182/1015) of multiple-genotype infections, respectively (Zhang et al., 2009). HPV 52 and 58 are prevalent in Asia and play important roles in multiple-genotype infections (Trottier et al., 2006; Wu et al., 2006).

The most common genotypes overall were HPV 16, 52, 58, 18, 33, and 81, accounting for 75.73% (3414/4508) of HPV infections in all patients. This shows that the prevalence of HPV in Shaanxi Province is due to multiple-genotype infections. While it has been suggested that multiple-HPV genotype infections do not correlate with the severity of cervical lesions (Sandri et al., 2009), other studies have shown a positive correlation between the two factors (Tao et al., 2006). The proportion of single- and multiple-genotype infections was 92.90 and 7.10% in the NC group, 90.24 and 9.76% in the chronic cervicitis group, 81.98 and 18.12% in the CIN group, and 63.82 and 36.18% in the SCC group, respectively. Therefore, the proportion of multiple-genotype infections increased with the severity of cervical lesions while the proportion of single-genotype infections decreased (P < 0.01). We identified numerous genotypes in multiple-genotype HPV infections in our study, many of which differed from previous reports (Zhao and Zhang, 2009). Overall, the proportion of single- and multiple-genotype infections was 77.48 and 22.52%, respectively. These values are 20% higher than the findings reported by Bhatia et al. (2008) and 43% lower than the findings from Sandri et al. (2009). The overall incidence of double-genotype infections was 16.26% and the incidence of three or more genotype infections was 6.26%. The single-genotype infections were more common in HPV infection-related cervical lesions (P < 0.01). Moreover, there were fewer multiple-genotype infections with more than three genotypes in women with cervical lesions, contrary to previous reports (Li et al., 2012). Double-genotype infections accounted for 72.22% of all multiple infections and were the most common scenario in multiple infections.

Spinillo et al. (2009) found that multiple-genotype HPV infections could lead to the progression of cervical lesions. The risk of disease progression tripled with multiple-high-risk genotype infections compared to single-high-risk genotype infections. Our study found that the proportion of single-low-risk genotype HPV infections decreased with the severity of cervical lesions (P < 0.01) but the proportion of multiple-genotype infections with at least one high-risk genotype increased with the severity of cervical lesions (P < 0.01). These results were consistent with previous studies (Tao et al., 2006). Single-high-risk genotype infections were common in all groups, but the proportion of single-high-risk infections decreased with the advancement of SCC stage. These findings suggest that multiple-genotype HPV infections play a role in precancerous lesions and cervical cancer progression. We hypothesize that the immune system is unable to clear the HPV infection efficiently when dealing with multiple-HPV genotypes. However, further investigation is required to determine if different genotypes act synergistically during disease progression.

We also found that single- or multiple-low-risk genotype infections occurred mainly in the chronic cervicitis and CIN groups but not in the SCC group (P < 0.01). This suggests that low-risk
genotypes do not increase the risk of cervical cancer and are not crucial to its pathogenesis (Wang et al., 2010; Su et al., 2012). Furthermore, single-high-risk genotype HPV infections were the most common in the SCC group (63.82%), occurring at a higher rate than multiple-high-risk infections (18.60%) and multiple-high- and low-risk infections (17.57%) (P < 0.01). There was no significant difference between the proportions of multiple-high-risk infections and multiple-high- and low-risk infections (P > 0.05). All SCC specimens were positive for at least one high-risk genotype infection, which was not observed in the chronic cervicitis or CIN groups (P < 0.01). This confirms that high-risk HPV genotypes are a crucial factor in the pathogenesis of cervical cancer.

Conflicts of interest

The authors declare no conflict of interest.

REFERENCES


Human papillomavirus genotypes in China


