Prevalence characteristics of cervical human papillomavirus (HPV) genotypes in the Taizhou area, China: a cross-sectional study of 37 967 women from the general population

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ABSTRACT

Objectives High-risk human papillomaviruses (hrHPVs) are highly prevalent worldwide, and HPV genotypes differ between geographical regions; however, sexually transmitted HPV may lead to cervical carcinogenesis. The objective of this cross-sectional study was to estimate the prevalence characteristics of cervical HPV genotypes in Taizhou, Southeast China.

Setting and participants A population-based sample of 37 967 eligible women (median age: 41.6; range: 15–90 years) visiting the Taizhou ENZE Medical Center in Taizhou (2012–2016) was analysed. HPV genotyping was performed on the collected specimens using a GP5+/bioGP6+-PCR/MPG assay by Luminex 200, which simultaneously identifies 27 different HPV genotypes and the β-globin gene (internal control).

Results The overall HPV infection rate was 22.8% in the Taizhou-based population, and the prevalence of high-risk HPV, low-risk HPV and mixed high-risk and low-risk HPV infection was 14.2%, 5.7% and 3.0%, respectively. The most prevalent genotypes were HPV52 (19.7%), HPV16 (11.9%), HPV58 (11.5%), HPV39 (7.2%), HPV16 (6.6%) and HPV56 (5.6%). The rate of multiple-type HPV infection was 5.7% in the whole population, and the HPV52+58, HPV16+52 and HPV16+18 mixed genotypes were most common in women with multiple infections. The age-specific HPV prevalence showed a bimodal curve, with a first peak below the age of 21 years (41.6%), followed by a second peak in the age group of 56–60 years (28.5%). Moreover, the HPV infection rate differed significantly between the outpatient and physical examination groups (24.0% vs 19.5%, p<0.0001). Further data comparisons showed that the distribution of HPV genotypes varied markedly between the two groups.

Conclusions Data from this study could be valuable for HPV-based cervical cancer screening efforts in certain areas, support the local vaccination programme in the Taizhou region and facilitate future diagnosis and treatment of HPV diseases.

BACKGROUND

Cervical cancer is the second most commonly diagnosed cancer and the third leading cause of cancer deaths among women in low-income countries. Persistent infection of high-risk human papillomavirus (hrHPV) is necessary for the development of high-grade cervical intraepithelial neoplasia (CIN2/3) and invasive cervical cancer (ICC). To date, more than 170 types of HPV can infect the anogenital epithelium, of which at least 12 are classified as ‘high risk’ because of their high carcinogenic potential; sexually transmitted HPV may lead to cervical carcinogenesis. HPV16/18 are well-known oncogenic genotypes; additionally, HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 are also closely associated with cervical cancer.

Other HPV types are classified as ‘low-risk’ genotypes (lrHPV), as they are associated with benign or low-grade changes in cervical cells, such as genital warts. The hrHPV prevalence among women attending routine cervical
screening has been shown to correlate well with cervical cancer incidence rates based on independently obtained HPV prevalence data as well as findings on the worldwide cervical cancer burden.

The current hrHPV testing algorithm is designed to serve as an additional approach for triaging atypical squamous cells of unknown significance (ASCUS) results or cotesting with cervical cytology in clinical practice. Recently, the Food and Drug Administration (FDA) in America approved hrHPV testing as an option for primary screening, and these tests use HPV16 and HPV18 genotyping along with a cocktail test of 12 other hrHPV genotypes. Based on the results of clinical trials, the high negative predictive value of hrHPV testing is sufficient to reassure a woman of an extremely low risk of CIN3+ or cancer for 5 years. In addition to the HPV screening strategy, HPV vaccination has been shown to be an effective programme against HPV infection and has been recently implemented in most western countries. However, HPV vaccination programmes have not been implemented in the Taizhou region.

As high-risk HPV genotypes are highly prevalent worldwide, HPV genotypes differ by geographical region, and sexually transmitted HPV may lead to cervical carcinogenesis, we conducted this study to establish a foundation for HPV-based screening in a specific area to support the local vaccination programme in Taizhou. The objective of this cross-sectional study was to investigate the characteristics of the distribution of HPV genotypes among women living in Taizhou.

MATERIALS AND METHODS

Ethics statement
This study was approved by the Institutional Medical Ethics Review Board of Taizhou Hospital in Zhejiang Province. Informed consent was obtained from the participants. For participants aged younger than 18 years, consent forms were signed by parents. Confidentiality was ensured during the data collection process, which was completed by Taizhou Hospital. Data were analysed anonymously.

Study population
The current Taizhou Area HPV study is a cross-sectional and large-scale study of Taizhou women conducted from 2012 to 2016. Between December 2012 and February 2016, a total of 42707 consecutive women ranging in age from 15 to 90 years underwent HPV testing in the Taizhou ENZE Medical Center, which includes Taizhou Hospital, Taizhou Maternity Hospital, Taizhou Central Hospital, Luqiao Hospital and a Health Management Center. The study population was divided into four age groups (<21, 21–29, 30–65 and >65 years) according to the American Cancer Society guidelines for cervical cancer screening.
The average age of the outpatient group was 40.7 years (SD: 10.1, range: 15–90 years): most outpatients were aged 30–65 years (83.2%). Of the 6705 (24.0%) women with HPV infection analysed, a single HPV type was detected in 4946 (17.7%), and multiple types were observed in 1759 (6.3%). Moreover, women in the physical examination group had a median age of 44.3 years (SD: 9.3, range: 21–82 years), and most women were aged 30–65 years (93.6%). Of the 1964 (19.5%) women with an HPV infection, a single HPV type was detected in 1530 (15.2%), and multiple types were observed in 434 (4.4%).

The baseline characteristics of the study population are shown in table 1.

### Table 1 Baseline characteristics of the study population

| Characteristics          | Outpatients | Women receiving physical examinations |
|--------------------------|-------------|---------------------------------------|
| All participants         | 27,899      | 10,068                                |
| Age (years)              |             |                                       |
| Median, years (SD)       | 40.7 (10.1) | 44.3 (9.3)                            |
| Range                    | 15–90       | 21–82                                 |
| Age group (years)*       |             |                                       |
| <21                      | 264         | 0.9 (0.8 to 1.1)                      |
| 21–29                    | 4023        | 14.4 (14.0 to 14.8)                   |
| 30–65                    | 23,221      | 83.2 (82.8 to 83.7)                   |
| >65                      | 391         | 1.4 (1.3 to 1.5)                      |
| HPV                      | 6,705       | 24.0 (23.5 to 24.5)                   |
| High risk†               | 4,278       | 15.3 (14.9 to 15.8)                   |
| Low/undetermined risk‡   | 1,527       | 5.5 (5.2 to 5.7)                      |
| Mixed types§             | 900         | 3.2 (3.0 to 3.4)                      |
| Multiple infection       |             |                                       |
| No                       | 4,946       | 17.7 (17.3 to 18.2)                   |
| 2 HPV types              | 1,271       | 4.6 (4.3 to 4.8)                      |
| 3 HPV types              | 360         | 1.3 (1.2 to 1.4)                      |
| 4 HPV types              | 93          | 0.3 (0.3 to 0.4)                      |
| 5 or more HPV types      | 35          | 0.1 (0.1 to 0.2)                      |

*According to the 2012 American Cancer Society guidelines for cervical cancer screening.
†Includes HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68.
‡Includes HPV types 6, 11, 26, 40, 42, 43, 44, 53, 55, 56, 61, 73, 81, 82 and 83.
§Mixed high-risk and low-risk HPV infection.

The overall HPV infection rate was 22.8% (8669/37,967, 95% CI 22.4% to 23.3%) in the Taizhou-based population. Between the outpatient group and the physical examination group, the HPV infection rate differed significantly (24.0% vs 19.5%, p<0.0001). Among all HPV-positive women, the prevalence of hrHPV, lrHPV and mixed high-risk and low-risk HPV (defined ‘mixed HPV’) infections was 14.2% (5382/37,967, 95% CI 13.8% to 14.5%), 5.7% (2149/37,967, 95% CI 5.4% to 5.9%) and 3.0% (1138/37,967, 95% CI 2.8% to 3.2%), respectively.

Multiple HPV genotypes with high-risk and/or low-risk HPV genotypes were found in 5.7% (2193/37,967, 95% CI 5.5% to 6.0%) of the overall population and 25.3% (2193/8669, 95% CI 24.4% to 26.2%) of the women with HPV infection. Of the women with multiple HPV infections, 843 (38.4%), 212 (9.7%) and 1138 (51.9%) were infected with hrHPV, lrHPV and mixed HPV genotypes, respectively. Moreover, 73.3% (1608/2193, 95% CI 71.5% to 75.2%) were infected with two types; the most common combinations were 52+58 (49 cases), 16+52 (33 cases) and 16+18 (29 cases). Additionally, 19.4% (426/2193, 95% CI 18.7% to 20.3%) of the infected women had three types, the most common combinations were 16+52+58 (seven cases) and 16+52+68 (five cases). Finally, 5.3% (117/2193, 95% CI 4.4% to 6.3%) had four types, and 1.9% (42/2193, 95% CI 1.3% to 2.5%) had more than five types of infection.

Among the 37,967 women (age range from 15 to 90 years, mean age 41.6±10.0 years), we examined the HPV prevalence in 5-year periods to assess the age trends in relation to HPV infection in more detail. The age...
distribution of HPV infection showed a bimodal curve in overall HPV prevalence, as shown in figure 1. The prevalence of total HPV exhibited its first peak below the age of 21 years (41.6%, 95% CI 35.7% to 47.5%) and decreased thereafter until the age of 56 years (28.5%, 95% CI 26.5% to 30.5%), where it peaked a second time. Notably, outpatients in the older age group (56–60 years) presented the highest HPV infection rate (34.7%, 95% CI 31.9% to 37.5%).

**Distribution characteristics of HPV genotypes**

Overall, HPV52 was the most prevalent genotype (19.7%, 95% CI 18.8% to 20.5%), both alone and in combination with other types, followed by HPV16 (11.9%, 95% CI 11.2% to 12.6%), HPV58 (11.5%, 95% CI 10.8% to 12.2%), HPV39 (7.2%, 95% CI 6.6% to 7.7%), HPV18 (6.6%, 95% CI 6.0% to 7.1%) and HPV56 (5.6%, 95% CI 5.1% to 6.1%). For low-risk/undetermined-risk HPV genotypes, HPV53 was the most common type, with an overall prevalence of 7.8% (95% CI 7.2% to 8.4%), followed by HPV81 (7.5%, 95% CI 6.8% to 8.3%), HPV61 (7.0%, 95% CI 6.5% to 7.6%), HPV43 (5.9%, 95% CI 5.2% to 6.6%), HPV66 (4.0%, 95% CI 3.6% to 4.4%) and HPV44 (3.8%, 95% CI 3.4% to 4.2%). The prevalences of HPV genotypes in the overall population, outpatients and women receiving a physical examination are shown in table 2.

Regarding the population-based distribution of hrHPV, the top six genotypes were analysed in both outpatients and women receiving a physical examination. HPV52 was the most frequent high-risk type (20.3%) in the outpatient population, followed by 16 (13.0%), 58 (11.8%), 39 (7.9%), 18 (6.7%) and 56 (5.9%). However, six different types were the most common in the physical examination population: HPV52 (17.4%), 58 (10.4%), 16 (8.2%), 39 (7.7%), 18 (6.1%) and 51 (4.9%). For low-risk/undetermined-risk HPV genotypes, HPV81 (7.2%) was the most common genotype in outpatients, followed by 53 (7.0%), 61 (6.8%), 45 (5.8%), 06 (4.2%) and 44 (3.5%), whereas HPV53 (10.3%) was the most frequent genotype in the physical examination population, followed by 81 (8.3%), 61 (7.9%), 45 (6.2%), 55 (5.0%) and 44 (4.8%).

The distribution of the top three HPV genotypes was also determined on the basis of age (table 3). For hrHPV, HPV16, 52 and 58 were the most prevalent among all of the age groups in outpatients and in the physical examination population, with the exception of the age group of 21–29 years, in which HPV52, 39 and 18 were the most common genotypes. For low-risk/undetermined-risk HPV genotypes, HPV06 was the leading genotype in younger age groups (ie, age groups <21 and 21–29 years), while in the older group (ie, 46–65 years), HPV53, 61 and 81 were the most prevalent lrHPV type. The presence of any HPV genotype was also significantly more frequently identified in younger rather than older women (p<0.001).

**DISCUSSION**

This article described a cross-sectional and large-scale study on the prevalence of HPV genotypes in Taizhou, Zhejiang Province, Southeast China. To date, to the best of our knowledge, there has been very little research on the population-based epidemiology of high-risk and low-risk HPV in different female age groups from both outpatients and women receiving physical examinations. HPV detection is currently an effective way to screen for cervical cancer. Knowledge of the distribution of HPV genotypes in population-based women will enable the evaluation of the potential efficacy of next-generation HPV prophylactic vaccines. All of the study specimens were collected before the approval of HPV vaccines in Taizhou.

Compared with region-based data on the Chinese population, the hrHPV-positive rate (17.2%) found in...
| HPV genotypes* | Overall population (n=37 967) | Outpatients (n=27 899) | Women receiving physical examinations (n=10 068) |
|----------------|-----------------------------|------------------------|-----------------------------------------------|
|                | Single infection (n=6476)   | Multiple infections (n=2193) | Overall infections (n=8669) | Single infection (n=1530) | Multiple infections (n=434) | Overall infections (n=1964) |
| High-risk HPV   |                             |                        |                                |                             |                          |                                |
| 52             | 1082 (12.5)                 | 623 (7.2)              | 1705 (19.7)                     | 850 (12.7)                  | 513 (7.7)                 | 1363 (20.3)                   | 232 (11.8) | 110 (5.6) | 342 (17.4) |
| 16             | 659 (7.6)                   | 372 (4.3)              | 1031 (11.9)                     | 559 (8.3)                   | 311 (4.6)                 | 870 (13.0)                   | 100 (5.1)  | 61 (3.1)  | 161 (8.2) |
| 58             | 605 (7.0)                   | 393 (4.5)              | 998 (11.5)                      | 469 (7.0)                   | 325 (4.8)                 | 794 (11.8)                   | 136 (6.9)  | 68 (3.5)  | 204 (10.4) |
| 39             | 366 (4.2)                   | 255 (2.9)              | 621 (7.2)                       | 277 (4.1)                   | 193 (2.9)                 | 470 (7.0)                    | 89 (4.5)   | 62 (3.2)  | 151 (7.7) |
| 18             | 306 (3.5)                   | 262 (3.0)              | 568 (6.6)                       | 225 (3.4)                   | 224 (3.3)                 | 449 (6.7)                    | 81 (4.1)   | 38 (1.9)  | 119 (6.1) |
| 56             | 240 (2.8)                   | 247 (2.8)              | 487 (5.6)                       | 184 (2.7)                   | 210 (3.1)                 | 394 (5.9)                    | 56 (2.9)   | 37 (1.9)  | 93 (4.7)  |
| 51             | 234 (2.7)                   | 197 (2.3)              | 431 (5.0)                       | 179 (2.7)                   | 156 (2.3)                 | 335 (5.0)                    | 55 (2.8)   | 41 (2.1)  | 96 (4.9)  |
| 33             | 200 (2.3)                   | 208 (2.4)              | 408 (4.7)                       | 167 (2.5)                   | 173 (2.6)                 | 340 (5.1)                    | 33 (1.7)   | 35 (1.8)  | 68 (3.5)  |
| 59             | 201 (2.3)                   | 182 (2.1)              | 383 (4.4)                       | 160 (2.4)                   | 150 (2.2)                 | 310 (4.6)                    | 41 (2.1)   | 32 (1.6)  | 73 (3.7)  |
| 68             | 182 (2.1)                   | 190 (2.2)              | 372 (4.3)                       | 137 (2.0)                   | 146 (2.2)                 | 283 (4.2)                    | 45 (2.3)   | 44 (2.2)  | 89 (4.5)  |
| 66             | 166 (1.9)                   | 155 (1.8)              | 321 (3.7)                       | 131 (2.0)                   | 132 (2.0)                 | 263 (3.9)                    | 35 (1.8)   | 23 (1.2)  | 58 (3.0)  |
| 31             | 144 (1.7)                   | 115 (1.3)              | 259 (3.0)                       | 119 (1.8)                   | 102 (1.5)                 | 221 (3.3)                    | 25 (1.3)   | 13 (0.7)  | 38 (1.9)  |
| 35             | 88 (1.0)                    | 96 (1.1)               | 184 (2.1)                       | 70 (1.0)                    | 80 (1.2)                  | 150 (2.2)                    | 18 (0.9)   | 16 (0.8)  | 34 (1.7)  |
| 45             | 66 (0.8)                    | 72 (0.8)               | 138 (1.6)                       | 48 (0.7)                    | 54 (0.8)                  | 102 (1.5)                    | 18 (0.9)   | 18 (0.9)  | 36 (1.8)  |
| Low-risk/undetermined-risk HPV |                     |                        |                                |                             |                          |                                |                     |
| 53             | 366 (4.2)                   | 309 (3.6)              | 675 (7.8)                       | 247 (3.7)                   | 225 (3.4)                 | 472 (7.0)                    | 119 (6.1)  | 84 (4.3)  | 203 (10.3)|
| 81†            | 185 (3.9)                   | 172 (3.6)              | 357 (7.5)                       | 116 (3.4)                   | 126 (3.7)                 | 242 (7.2)                    | 69 (5.0)   | 46 (3.3)  | 115 (8.3) |
| 61             | 330 (3.8)                   | 281 (3.2)              | 611 (7.0)                       | 229 (3.4)                   | 226 (3.4)                 | 455 (6.8)                    | 101 (5.1)  | 55 (2.8)  | 156 (7.9) |
| 43†            | 121 (2.5)                   | 160 (3.4)              | 281 (5.9)                       | 76 (2.3)                    | 120 (3.6)                 | 196 (5.8)                    | 45 (3.3)   | 40 (2.9)  | 85 (6.2)  |
| 06             | 188 (2.2)                   | 156 (1.8)              | 344 (4.0)                       | 155 (2.3)                   | 129 (1.9)                 | 284 (4.2)                    | 33 (1.7)   | 27 (1.4)  | 60 (3.1)  |
| 44             | 187 (2.2)                   | 144 (1.7)              | 331 (3.8)                       | 130 (1.9)                   | 107 (1.6)                 | 237 (3.5)                    | 57 (2.9)   | 37 (1.9)  | 94 (4.8)  |
| 55             | 139 (1.6)                   | 171 (2.0)              | 310 (3.6)                       | 85 (1.3)                    | 121 (1.9)                 | 211 (3.1)                    | 54 (2.7)   | 45 (2.3)  | 99 (5.0)  |
| 11             | 99 (1.1)                    | 114 (1.3)              | 213 (2.5)                       | 82 (1.2)                    | 104 (1.6)                 | 186 (2.8)                    | 17 (0.9)   | 10 (0.5)  | 27 (1.4)  |
| 42             | 96 (1.1)                    | 102 (1.2)              | 198 (2.3)                       | 70 (1.0)                    | 85 (1.3)                  | 155 (2.3)                    | 26 (1.3)   | 17 (0.9)  | 43 (2.2)  |
| 82             | 111 (1.3)                   | 85 (1.0)               | 196 (2.3)                       | 92 (1.4)                    | 70 (1.0)                  | 162 (2.4)                    | 19 (1.0)   | 15 (0.8)  | 34 (1.7)  |
| 40             | 62 (0.7)                    | 69 (0.8)               | 131 (1.5)                       | 48 (0.7)                    | 52 (0.8)                  | 100 (1.5)                    | 14 (0.7)   | 17 (0.9)  | 31 (1.6)  |
| 83             | 42 (0.5)                    | 43 (0.5)               | 85 (1.0)                        | 30 (0.4)                    | 35 (0.5)                  | 65 (1.0)                     | 12 (0.6)   | 8 (0.4)   | 20 (1.0)  |
| 26             | 8 (0.1)                     | 7 (0.1)                | 15 (0.2)                        | 8 (0.1)                     | 7 (0.1)                   | 15 (0.2)                     | 0 (0.0)    | 0 (0.0)   | 0 (0.0)   |

Continued
the present study was lower than the rates reported in a meta-analysis that summarised Chinese data for Haikou (31.9%), Guangdong (20.0%), Chongqing (27.3%), Jinan (25.7%) and Shanghai (22.6%), but was similar to the rates in Hangzhou (19.9%) and Nanchang (18.4%), which is another region in Southeast China. In China, the prevalence of hrHPV varied from 9.9% in Beijing to 31.9% in Haikou because of the different economic conditions, cultural diversity, genetic variations, HPV vaccine awareness and different lifestyles. Notably, the rate of awareness of HPV vaccination was only 16.0% in China, but was found to range from 67.1% to 71.3% in Western countries. The Advisory Committee on Immunization Practices (ACIP) recommends bivalent HPV vaccines, quadrivalent HPV vaccines and 9-valent HPV vaccines (9vHPV) for routine vaccination. In China, the most urgent public health issue is increasing HPV vaccination coverage and improving completion of the vaccination schedule.

Consistent with the data generated by Chinese population-based investigations, HPV16, 52 and 58 were found to be the predominant hrHPV types, but these results differed from those of a meta-analysis that summarised global reports, in which HPV16, 18 and 45; HPV16, 18 and 33 and HPV16, 18 and 58 were most commonly detected. In our population, HPV52 and 58 accounted for 31.2% of the infections, representing common types among Asian populations, and this rate was markedly higher than the global rate of 14.0%. We found that the rate of HPV52+58 infection was significantly increased in outpatients compared with women receiving physical examinations (32.1% vs 27.8%, p<0.001). The relatively high contribution of HPV52 and 58 to high-grade cervical lesions in East Asia has been previously reported, but HPV18, with an infection rate of 6.6%, is less common. Compared with women receiving physical examinations, the HPV16, 31, 33 and 52 infection rates were significantly increased in outpatients (p<0.05). These findings indicated that in addition to HPV16 and HPV18, an HPV vaccine in Taizhou should include HPV31, 33, 52 and 58 genotypes. Notably, the ACIP has recommended 9vHPV, which contains HPV6, 11, 16, 18, 31, 33, 45, 52 and 58 virus-like particles and is suitable for the Taizhou population.

The age-specific HPV distribution presents a bimodal curve, with the first peak below the age of 21 years (just after sexual debut), a lower prevalence plateau at middle ages and a variable rebound at older ages (≥56 years). Figure 1 shows high infection rates (41.6%) in younger age groups and a gradual decline to a plateau in middle-aged women, which reflects the natural history of HPV infections. The detection of HPV in women has been found to start consistently with a peak immediately after the onset of sexual relations, usually from 15 years of age, and to reach a prevalence of up to 80% among younger women, mostly transient infections that can be cleared within 1 or 2 years. In our population, we observed a less steep second peak in the older age group of those
| HPV status | Outpatients | 30–65 y | 46–65 y | >65 y | Women receiving physical examinations | 30–65 y | 46–65 y | >65 y |
|-----------|-------------|---------|---------|-------|--------------------------------------|---------|---------|-------|
|           | n=264       | n=4023  | n=15108 | n=8113 | n=391                               | n=495   | n=5178  | n=4249 |
| HPV+      | 111 (42.0)  | 937 (23.3) | 3384 (22.4) | 2189 (27.0) | 84 (21.5) | 89 (18.0) | 959 (18.5) | 882 (20.8) | 34 (23.3) |
| Multiple  | 49 (18.6)   | 301 (7.5)  | 746 (4.9)  | 627 (7.7)  | 36 (9.2)  | 17 (3.4)  | 187 (3.6)  | 213 (5.0)  | 15 (10.3)  |
| hrHPV     | 77 (29.2)   | 743 (18.5) | 2572 (17.0) | 1723 (21.2) | 69 (17.6) | 66 (13.3) | 640 (12.4) | 606 (14.3) | 29 (19.9)  |
| High-risk HPV* | 52 | 18 (16.2) | 208 (22.2) | 683 (20.2) | 435 (19.9) | 19 (22.6) | 17 (19.1) | 165 (17.2) | 152 (17.2) | 8 (23.5) |
|           | 16 (14.4)   | 127 (13.6) | 421 (12.4) | 288 (13.2) | 18 (21.4) | 7 (7.9)  | 83 (8.7)  | 69 (7.8)  | 2 (5.9)    |
|           | 58 (15.3)   | 97 (10.4)  | 354 (10.5) | 312 (14.3) | 14 (16.7) | 5 (5.6)  | 85 (8.9)  | 108 (12.2) | 6 (17.6)   |
|           | 39 (10.8)   | 79 (8.4)   | 230 (6.8)  | 147 (6.7)  | 2 (2.4)  | 11 (12.4) | 75 (7.8)  | 61 (6.9)  | 4 (11.8)   |
|           | 18 (10.8)   | 71 (7.6)   | 215 (6.4)  | 143 (6.5)  | 8 (9.5)  | 8 (9.0)  | 50 (5.2)  | 60 (6.8)  | 1 (2.9)    |
|           | 56 (7.2)    | 46 (4.9)   | 182 (5.4)  | 148 (6.8)  | 10 (11.9) | 8 (9.0)  | 46 (4.8)  | 36 (4.1)  | 3 (8.8)    |
|           | 51 (5.4)    | 71 (7.6)   | 156 (4.6)  | 99 (4.5)   | 3 (3.6)  | 6 (6.7)  | 49 (5.1)  | 39 (4.4)  | 2 (5.9)    |
|           | 33 (7.2)    | 51 (5.4)   | 155 (4.6)  | 119 (5.4)  | 7 (8.3)  | 1 (1.1)  | 32 (3.3)  | 33 (3.7)  | 2 (5.9)    |
|           | 59 (7.2)    | 55 (5.9)   | 145 (4.3)  | 99 (4.5)   | 3 (3.6)  | 1 (1.1)  | 34 (3.5)  | 35 (4.0)  | 3 (8.8)    |
|           | 68 (4.5)    | 38 (4.1)   | 126 (3.7)  | 108 (4.9)  | 6 (7.1)  | 3 (3.4)  | 38 (4.0)  | 45 (5.1)  | 3 (8.8)    |
|           | 66 (7.2)    | 40 (4.3)   | 127 (3.8)  | 82 (3.7)   | 6 (7.1)  | 1 (1.1)  | 26 (2.7)  | 29 (3.3)  | 2 (5.9)    |
|           | 31 (2.7)    | 29 (3.1)   | 103 (3.0)  | 77 (3.5)   | 9 (10.7) | 1 (1.1)  | 19 (2.0)  | 17 (1.9)  | 1 (2.9)    |
|           | 35 (2.7)    | 17 (1.8)   | 71 (2.1)   | 55 (2.5)   | 4 (4.8)  | 1 (1.1)  | 10 (1.0)  | 19 (2.2)  | 4 (11.8)   |
|           | 45 (2.7)    | 16 (1.7)   | 55 (1.6)   | 26 (1.2)   | 2 (2.4)  | 0 (0.0)  | 15 (1.6)  | 19 (2.2)  | 2 (5.9)    |
| Low-risk/undetermined-risk HPV* | 53 | 8 (7.2) | 59 (6.3) | 232 (6.9) | 168 (7.7) | 5 (6.0) | 8 (9.0) | 104 (10.8) | 88 (10.0) | 3 (8.8) |
|           | 81† | 4 (7.7) | 34 (7.4) | 111 (6.6) | 91 (8.0) | 2 (4.5) | 7 (10.8) | 56 (8.1) | 50 (8.3) | 2 (11.1) |
|           | 61 | 6 (5.4) | 48 (5.1) | 218 (6.4) | 176 (8.0) | 7 (8.3) | 4 (4.5) | 61 (6.4) | 90 (10.2) | 1 (2.9) |
|           | 43† | 5 (9.6) | 27 (5.9) | 88 (5.2) | 72 (6.3) | 4 (9.1) | 3 (4.6) | 48 (6.9) | 32 (5.3) | 2 (11.1) |
|           | 06 | 23 (20.7) | 63 (6.7) | 128 (3.8) | 66 (3.0) | 3 (3.6) | 4 (4.5) | 34 (3.5) | 22 (2.5) | 1 (2.9) |
|           | 44 | 6 (5.4) | 29 (3.1) | 131 (3.9) | 68 (3.1) | 3 (3.6) | 3 (3.4) | 44 (4.6) | 47 (5.3) | 0 (0.0) |
|           | 55 | 4 (3.6) | 18 (1.9) | 100 (3.0) | 87 (4.0) | 2 (2.4) | 2 (2.2) | 46 (4.8) | 50 (5.7) | 1 (2.9) |
|           | 11 | 11 (9.9) | 45 (4.8) | 75 (2.2) | 51 (2.3) | 4 (4.8) | 2 (2.2) | 14 (1.5) | 10 (1.1) | 1 (2.9) |
|           | 42 | 5 (4.5) | 12 (1.3) | 72 (2.1) | 66 (3.0) | 0 (0.0) | 2 (2.2) | 23 (2.4) | 18 (2.0) | 0 (0.0) |
aged 56–60 years (28.5%), which is a similar trend to those observed in Central America, Southeastern Asia and Western Africa.\textsuperscript{24} The slight increase in the HPV infection rate in older women (aged >246 years) might reflect the persistence of HPV or the reactivation of latent HPV around menopause,\textsuperscript{25} resulting from hormonal interactions with the HPV life cycle, viral characteristics and host susceptibility.\textsuperscript{26}

In the present study, multiple HPV infections were detected in 26.2% of the outpatients and were more frequent in younger women (aged <21 years). These findings are consistent with the results of Mejlhe\textsuperscript{o} et al\textsuperscript{27} and support the fact that greater sexual activity in younger women may be associated with the transmission of multiple HPV types. We also found that the rate of multiple HPV infections increased in the older age group (aged >65 years). The most common two-type combinations were HPV52+58 (49 cases), HPV16+52 (33 cases) and HPV16+18 (29 cases). It is still controversial that coinfection increases the risk of progression to cancer.\textsuperscript{28} Recently, Salazar et al\textsuperscript{29} reported that women infected with multiple HPV infections were at a lower risk of high-risk cervical lesions compared with their single-genotype infection counterparts, suggesting a possible cross-protection triggered by multiple infections.\textsuperscript{30} In contrast, Chaturvedi et al\textsuperscript{31} reported that women infected with multiple HPV infections were at significantly increased risk of CIN2+ when compared with those with single-genotype infections.

In addition to carcinogenesis, anogenital warts are a global public health problem that affects young men and young women and are mainly caused by two lrHPV types, HPV06 and 11.\textsuperscript{32} In our outpatients, the HPV06 (20.7%) and 11 (9.9%) infection rates significantly increased in younger women (<21 years). This highlights the importance of considering HPV6-related and HPV11-related diseases (genital warts) when assessing the potential benefits of preventive interventions such as HPV vaccination programmes.

In summary, the HPV prevalence and distribution of HPV type varied significantly in different female age groups between outpatients and women receiving physical examinations. The data from this study could be valuable for HPV-based cervical cancer screening efforts and could aid in the future vaccination, screening, diagnosis and treatment of HPV diseases.

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was signed by the parents of each participant

Patient consent For those patients aged younger than 18 years, the consent form
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