Original Article

# High-risk Human Papillomavirus (hrHPV) Prevalence and Genotype Distribution among Turkish Women

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## Abstract

**Purpose:** This study aimed to determine the rates of distribution of high-risk HPV (hrHPV) genotypes according to cervical smear samples and biopsy results in a large sample of Turkish women. **Methods:** The study was conducted with 4,503 healthy volunteer women aged 19-65 years. Samples of cervical smears were collected during the examination and liquid-based cytology was used for the Pap tests. The Bethesda system was used for reporting the cytology. High-risk HPV genotypes including HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 were investigated in samples. The study cohort was grouped according to age in decades, with comparisons made according to these age groups, Bethesda class, and cervix biopsy results. **Results:** Among all cases, 903 (20.1%) participants were positive for 1074 hrHPV-DNA genotypes. HPV-DNA positive cases were most common in the 30-39 age group (28.0%), followed by women under the age of 30 (38.5%). HPV genotypes were determined as, in order of frequency: Other hrHPV (n = 590, 65.3%), HPV16 (n = 127, 14.1%), Other HPV + HPV16 (n = 109, 12.1%), HPV 18 (n = 33, 3.6%), and Other HPV + HPV 18 (n = 32, 3.5%). Cervical smears were reported as ASCUS in 304 (6.8%) samples and high-grade squamous intraepithelial lesion (HSIL) in 12 (0.3%) of the samples. Biopsy demonstrated the presence of HSIL in 110 (12.5%) participants, with 644 (73.3%) negative cases. **Conclusion:** This showed an increasing incidence of Other HPVs besides the known importance of HPV 16 and 18 genotypes as risk factors for cervical cancer.

**Keywords:** Cervical cancer, high-risk HPV, human papillomavirus, pap smear

## Introduction

Cervical cancer is the second most common cancer in the world in women after breast cancer.[1] According to the Turkey Cancer Statistics Report, 2017, cervix uteri cancer ranks 9th in women with an incidence rate of 4.3/100,000 and a rate of 2.3% among all cancer types. In addition, according to this report, cervical cancer ranks first among Human Papillomavirus (HPV)-related cancers.[2]

The presence of different HPV types in the female genital system is associated with a number of diseases, such as condyloma, bowenoid papulosis, cervical, vaginal, and vulvar intraepithelial neoplasia, and carcinoma. High-risk HPV types are the major recognized risk factor for the development of cervical cancer. So, HPV types are divided into two groups: hrHPV and low-risk HPV (lrHPV). Hr HPV includes types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68, whereas lrHPV includes types 6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73, and 81.[3,4]

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Most cervical cancers are related to HPV (99.7%), with HPV16 with HPV 18 responsible for approximately 70% of these.[4,5] The prevalence of HPV in our country is between 1.5% and 32.1%.[3,5-7] The Pap test (Papanicolaou test, cervical cytology) is used in early diagnosis with high sensitivity, and hrHPV testing is the most effective among all available cervical screening tests. Cytological evaluation of cervical smear and simultaneous HPV testing is called a co-test and is the most accepted screening method in women over 30 years of age. As a consequence, HPV testing with cytology (co-test) was recommended as an efficient screening method and it provides early detection, and thus reduces the future risk of cervical cancer and related mortality. It thereby provides greater reassurance for screen-negative women than can be offered by cytology; as

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such, HPV testing provides for a safe extension of screening intervals.[8-10] According to the current recommendation of the U.S. Preventive Services Task Force (USPSTF), cervical cancer screening should begin at the age of 21 years. Cytology alone is recommended every 3 years between 21 and 29 ages of years. HPV (hrHPV) testing should start from the age of 30, and hrHPV testing with cytology (co-test) should be repeated every 5 years between 30-60 years. Under the age of 21 years, screening is not recommended.[9]

It is essential to examine the age groups known with the other risky HPV types, that there is only the quadrivalent vaccine in our country, and that the contact with the risk of transmission is reduced to the younger age group.[3,6] This study aimed to determine the rates of distribution of high-risk HPV (hrHPV) genotypes according to cervical smear samples and biopsy results in a large sample of Turkish women.

## Methods

This cross-sectional study was conducted among healthy volunteer women aged 19-65 years and carried out in the gynecology outpatient clinic of XXX University between 2016 and 2018.

Participants were selected from among volunteers, who did not have gynecological complaints, were not pregnant, were within the scope of screening, and were within the specified age range. In addition, participants with known HPV-related lesions in the genital, head, and neck region or who had received treatment for these lesions were excluded from the study. Patients with an active genitourinary infection, those whose last menstrual period had concluded less than 3 days previously, and those who had had sexual intercourse in the previous 48 hours were not included in the study.

Samples of cervical smears sent to the pathology laboratory for cytological examination were placed in a protective medium (BD SurePath™) and liquid-based cytology (LBC) was evaluated in the light microscope after preparation according to the manufacturer's recommendations. Samples were analyzed and reported according to the Bethesda System (2014).[8] Viral nucleic acid extraction and amplification in cervical swab samples were performed by the automated qualitative in-vitro testing system, Cobas 4800 HPV Test (Roche Molecular Systems, Pleasanton, CA). The results were evaluated qualitatively by the software program and the most common and oncogenic, 14 HPV genotypes (hrHPV) including HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 were investigated. While expressing the hrHPV results, the term 'Other hrHPV' was used except for HPV 16 and 18. The study cohort was grouped by age in decades. Comparisons were made according to these groups. Cervix biopsies were examined and classified as HSIL, Negative (negative for intraepithelial lesion and malignancy), and LSIL (low-grade squamous intraepithelial llesion) according to international criteria.[11]

SPSS 26.0 program was used in the analysis of the variables. The distribution of smear results by age group, biopsy, and HPV types was tested with the Fisher-Freeman-Halton test Monte Carlo Simulation technique, and column ratios were compared with each other. Bonferroni-corrected *P* value results were expressed. While quantitative variables were expressed as mean (standard deviation) and median (min-max) in the tables, categorical variables were shown as n (%). Variables were analyzed at a 95% confidence level, and a *P* value less than 0.05 was considered significant.

## Results

The mean age of the participants (n = 4503) was found to be (39.5 ± 9.3). The highest number of women included in the study were aged 30-39 (n = 1731, 38.4%), and the number of patients aged 60 years and over was the least (n = 107, 2.4%). Also, the rate of women under the age of 30 was 14.1% (n = 635). Among all cases, 903 (20.1%) participants were positive for 1074 hrHPV-DNA. HPV-DNA positive cases were most common in the age group of 30-39 (28.0%), followed by women under the age of 30 (38.5%). HrHPV-DNA was detected most frequently in women aged 30-39 with a rate of 38.4% followed by women under the age of 30 with a rate of 26.2% ($P > 0.050$). Among all age groups, Another hrHPV was detected more frequently than HPV 16 or 18, but no significant difference was found between age groups for frequencies ($P > 0.050$). While HPV16 was detected at the highest rate in women under 30 years of age at 25.5%, HPV18 was detected most frequently in women between 30-39 years of age at 8.2% ($P > 0.050$) [Table 1].

In cases under 30 years of age, Another HPV-DNA was found in only two (33.3%) of the 6 patients with HSIL as a result of cytology, while HPV 16 and 18 were not detected in any of the cases. Similarly, in all age groups, the rate of Other HPV-DNA positivity was found to be higher compared to that for HPV 16 and 18 in cases with HSIL according to smear samples. However, Other HPV-DNA positivity (27%) was similar to HPV 18 (7.0%) and significantly higher than HPV 16 (1.0%) in cases with HSIL in the 40-49 age group ($P < 0.001$). In the 50-59 age group with HSIL, Other HPV-DNA positivity (21.2%) was similar to HPV 16 (9.6%) and significantly higher than that for HPV 18 (5.8%) ($P = 0.001$) [Table 1].

hrHPV types in order of frequency were Other hrHPV (n = 590, 65.3%), HPV16 (n = 127, 14.1%), Other hrHPV + HPV16 (n = 109, 12.1%), HPV 18 (n = 33, 3.6%), and Other HPV + HPV 18 (n = 32, 3.5%). Of the cervical smear samples, 4,016 (89.2%) were found to be negative (negative for intraepithelial lesion or malignancy: NILM). Cervical smears were reported as ASCUS in 304 (6.8%) samples and HSIL in 12 (0.3%) of the samples. Of the 878 biopsies, conducted, HSIL was detected in 110 (12.5%) participants, with 644 (73.3%) cases negative [Table 2]. Another HPV (43.1%) was the most common in patients with HSIL in the biopsy, followed by HPV 16 (34.6%) and HPV 18 (8.4%) ($P > 0.050$).

ASCUS (atypical squamous cells of undetermined significance) was the most common cytological finding in all decades [Table 2]. In those participants under the age of 30, LSIL was the second

**Table 1: Smear results of HPV types (16,18 or Other) by age group**

| Age Class | HPV types | SmearResults | | | | | *P* |
|---|---|---|---|---|---|---|---|
| | | ASC-H *n* (%) | ASCUS *n* (%) | HSIL *n* (%) | LSIL *n* (%) | NILM *n* (%) | |
| <30 | HPV 16 | | | | | | 0.002[f] |
| | Negative | 0 (0)[a] | 34 (77.3)[b] | 2 (100)[bc] | 43 (86)[bc] | 484 (90.1)[c] | |
| | Positive | 2 (100)[a] | 10 (22.7)[b] | 0 (0)[bc] | 7 (14)[bc] | 53 (9.9)[c] | |
| | HPV18 | | | | | | 0.015[f] |
| | Negative | 1 (50)[a] | 42 (95.5)[bc] | 2 (100)[abc] | 46 (92)[c] | 524 (97.6)[b] | |
| | Positive | 1 (50)[a] | 2 (4.5)[bc] | 0 (0)[abc] | 4 (8)[c] | 13 (2.4)[b] | |
| | Diğer HPV | | | | | | <0.001[f] |
| | Negative | 0 (0)[ab] | 21 (47.7)[b] | 0 (0)[ab] | 13 (26)[a] | 411 (76.5)[c] | |
| | Positive | 2 (100)[ab] | 23 (52.3)[b] | 2 (100)[ab] | 37 (74)[a] | 126 (23.5)[c] | |
| 30-39 | HPV 16 | | | | | | <0.001[f] |
| | Negative | 3 (37.5)[a] | 86 (82.7)[b] | 1 (33.3)[ac] | 36 (73.5)[bc] | 1504 (96)[d] | |
| | Positive | 5 (62.5)[a] | 18 (17.3)[b] | 2 (66.7)[ac] | 13 (26.5)[bc] | 63 (4)[d] | |
| | HPV18 | | | | | | 0.003[f] |
| | Negative | 8 (100)[abc] | 98 (94.2)[bc] | 2 (66.7)[c] | 47 (95.9)[ab] | 1542 (98.4)[a] | |
| | Positive | 0 (0)[abc] | 6 (5.8)[bc] | 1 (33.3)[c] | 2 (4.1)[ab] | 25 (1.6)[a] | |
| | Diğer HPV | | | | | | <0.001[f] |
| | Negative | 5 (62.5)[ab] | 65 (62.5)[b] | 1 (33.3)[ab] | 21 (42.9)[a] | 1361 (86.9)[c] | |
| | Positive | 3 (37.5)[ab] | 39 (37.5)[b] | 2 (66.7)[ab] | 28 (57.1)[a] | 206 (13.1)[c] | |
| 40-49 | HPV 16 | | | | | | <0.001[f] |
| | Negative | 3 (100)[abcd] | 93 (93)[d] | 2 (50)[c] | 34 (89.5)[bd] | 1300 (97.4)[a] | |
| | Positive | 0 (0)[abcd] | 7 (7)[d] | 2 (50)[c] | 4 (10.5)[bd] | 35 (2.6)[a] | |
| | HPV18 | | | | | | 0.007[f] |
| | Negative | 3 (100)[abcd] | 99 (99)[cd] | 3 (75)[b] | 36 (94.7)[bd] | 1324 (99.2)[ac] | |
| | Positive | 0 (0)[abcd] | 1 (1)[cd] | 1 (25)[b] | 2 (5.3)[bd] | 11 (0.8)[ac] | |
| | Diğer HPV | | | | | | <0.001[f] |
| | Negative | 2 (66.7)[abc] | 73 (73)[c] | 1 (25)[b] | 15 (39.5)[b] | 1197 (89.7)[a] | |
| | Positive | 1 (33.3)[abc] | 27 (27)[c] | 3 (75)[b] | 23 (60.5)[b] | 138 (10.3)[a] | |
| 50-59 | HPV 16 | | | | | | <0.001[f] |
| | Negative | 4 (80)[a] | 47 (90.4)[a] | 1 (50)[a] | 6 (75)[a] | 471 (97.5)[b] | |
| | Positive | 1 (20)[a] | 5 (9.6)[a] | 1 (50)[a] | 2 (25)[a] | 12 (2.5)[b] | |
| | HPV18 | | | | | | 0.003[f] |
| | Negative | 5 (100)[ab] | 49 (94.2)[b] | 2 (100)[ab] | 7 (87.5)[b] | 481 (99.6)[a] | |
| | Positive | 0 (0)[ab] | 3 (5.8)[b] | 0 (0)[ab] | 1 (12.5)[b] | 2 (0.4)[a] | |
| | Diğer HPV | | | | | | 0.001[f] |
| | Negative | 3 (60)[a] | 41 (78.8)[a] | 2 (100)[ab] | 4 (50)[a] | 438 (90.7)[b] | |
| | Positive | 2 (40)[a] | 11 (21.2)[a] | 0 (0)[ab] | 4 (50)[a] | 45 (9.3)[b] | |
| 60≤ | HPV 16 | | | | | | 0.001[f] |
| | Negative | 2 (50)[a] | 3 (75)[a] | 1 (100)[ab] | 3 (75)[a] | 92 (97.9)[b] | |
| | Positive | 2 (50)[a] | 1 (25)[a] | 0 (0)[ab] | 1 (25)[a] | 2 (2.1)[b] | |
| | HPV18 | | | | | | 0.012[f] |
| | Negative | 3 (75)[a] | 4 (100)[ab] | 1 (100)[ab] | 3 (75)[a] | 94 (100)[b] | |
| | Positive | 1 (25)[a] | 0 (0)[ab] | 0 (0)[ab] | 1 (25)[a] | 0 (0)[b] | |
| | Diğer HPV | | | | | | <0.001[f] |
| | Negative | 1 (25)[a] | 3 (75)[ab] | 0 (0)[a] | 1 (25)[a] | 85 (90.4)[b] | |
| | Positive | 3 (75)[a] | 1 (25)[ab] | 1 (100)[a] | 3 (75)[a] | 9 (9.6)[b] | |
| Total | HPV 16 | | | | | | <0.001[f] |
| | Negative | 12 (54.5)[a] | 263 (86.5)[b] | 7 (58.3)[a] | 122 (81.9)[b] | 3851 (95.9)[c] | |
| | Positive | 10 (45.5)[a] | 41 (13.5)[b] | 5 (41.7)[a] | 27 (18.1)[b] | 165 (4.1)[c] | |
| | HPV18 | | | | | | <0.001[f] |
| | Negative | 20 (90.9)[ab] | 292 (96.1)[b] | 10 (83.3)[a] | 139 (93.3)[ab] | 3965 (98.7)[c] | |
| | Positive | 2 (9.1)[ab] | 12 (3.9)[b] | 2 (16.7)[a] | 10 (6.7)[ab] | 51 (1.3)[c] | |
| | Diğer HPV | | | | | | <0.001[f] |

*Contd...*

**Table 1: Contd...**

| Age Class | HPV Types | SmearResults | | | | | P |
|---|---|---|---|---|---|---|---|
| | | ASC-H *n* (%) | ASCUS *n* (%) | HSIL *n* (%) | LSIL *n* (%) | NILM *n* (%) | |
| | Negative | 11 (50.0)[ab] | 203 (66.8)[b] | 4 (33.3)[a] | 54 (36.2)[a] | 3492 (87.0)[c] | |
| | Positive | 11 (50.0)[ab] | 101 (33.2)[b] | 8 (66.7)[a] | 95 (63.8)[a] | 524 (13.0)[c] | |

Fisher FreemanHalton test (Monte Carlo); *Post Hoc* test: Bonferronicorrection. [abcde]Eachsubscriptletterdenotes a subset of Smearcategorieswhosecolumnproportions do not differsignificantlyfromeachother at the 0.5 level

**Table 2: An overwiew of age and smear results of HPV types**

| | Mean (SD.) | Median (min-max) |
|---|---|---|
| Age | 39.5 (9.3) | 39 (18-80) |
| | *n* | % |
| Age Class | | |
| <30 | 635 | 14,1% |
| 30-39 | 1731 | 38,4% |
| 40-49 | 1480 | 32,9% |
| 40-59 | 550 | 12,2% |
| 60≤ | 107 | 2,4% |
| Smear | | |
| ASC-H | 22 | 0,5% |
| ASCUS | 304 | 6,8% |
| HSIL | 12 | 0,3% |
| LSIL | 149 | 3,3% |
| Negative for intraepithelial lesion or malignancy (NILM) | 4016 | 89,2% |
| Biopsy | | |
| HSIL | 110 | 12,5% |
| Negative | 644 | 73,3% |
| LSIL | 124 | 14,1% |
| HPV Type | | |
| Negative | 3600 | 79,9% |
| 16 | 127 | 2,8% |
| 18 | 33 | 0,7% |
| Other | 590 | 13,1% |
| 16 and 18 | 4 | 0,1% |
| 16 and Other | 109 | 2,4% |
| 18 and Other | 32 | 0,7% |
| 16 and 18 and Other | 8 | 0,2% |

SD.:Standard Deviation

most detected lesion according to cervical cytology, and negative results were found in 50% (n = 13) and LSIL in 38.5% (n = 10) according to the biopsy results. In addition, no statistically significant association was found between cytology and biopsy results in this group. Cervix biopsy showed LSIL or HSIL in 0.03% of the cytology-negative cases in the 4th decade, whereas LSIL or HSIL was found in the biopsies in 1.8% of the cytology-negative cases in the 5th decade ($P < 0.001$). The distribution of biopsy reports and smear results of the participants according to decades are shown in Table 3 in detail.

The distribution of HPV-DNA positivity and smear results of the participants according to decades are shown in Table 4. Accordingly, the Other HPV group was most commonly found in cases with LSIL in cytology in all age groups. The rate was also significantly higher in patients under 30 years of age compared to that those with HPV 16 and 18 ($P < 0.001$). Of the cases with ASC-H (atypical squamous cells, cannot exclude HSIL) in cytology, while Other HPV frequency was found to be proportionally higher in those in their 4th, 5th, and 6th decades, HPV 16, on the contrary, was detected more often in the 3rd decade, ($P > 0.050$). The distribution of HPV types in those cases with HSIL in cytology was similar between age groups ($P > 0.050$).

## Discussion

The majority of the patients included in our study were negative for intraepithelial lesion or malignancy (NILM), and for hrHPV. hrHPV-DNA was detected most frequently in women aged 30-39. Other HPV-DNA positivity was higher compared to HPV 16 and 18 in total, and in HSIL and in LSIL in cytology. Other HPV types were the most common in HSIL in the biopsy, followed by HPV 16 and 18. The sample size in the study was sufficient compared to other clinical studies, except for those studies that present the results of ministry-supported HPV screening follow-ups.[12-14]

In order of frequency, the hrHPV types were as follows: Other hrHPV groups (including HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) and HPV16. In Gultekin *et al*.,[13,15] the most common top six HPV genotypes were HPV 16, 51, 31, 52, 56, and 18 at all age intervals and regions according to the Turkish national database HPV screening program, which includes four million females. Ghosh *et al*.[16] reported the Other HPV genotypes accounted for the greatest percentage of cytological diagnoses in all categories, and HPV genotype 16 accounted for the second-highest prevalence in all categories in 40,739 women in the Midwestern population of the US. de Sanjose *et al*.[4] reported the eight most common HPV types as 16, 18, 31, 33, 35, 45, 52, and 58 respectively in 8,977 HPV-DNA positive cervix cancers, obtained from 38 countries. They found that HPV types 16, 18, and 45 were the three most common types in each histological group (squamous cell carcinoma, adenocarcinoma, and adenosquamous cell carcinoma). They noted that the combined relative contribution of the eight most common HPV types was 8,196 of 8,977 cases (91%, 95%CI: 90–92). Together, HPV types 16, 18, and 45 were detected in 6,223 of 8,252 cases of squamous cell carcinoma (75%, 95%CI: 75–76). They reported that women infected with HPV 45 or HPV 18 were much younger than those infected with HPV 16 or any other HPV type as a single infection.[4] In the present study, hrHPV-DNA was detected most frequently in women aged 30-39 (38.4%) and under the age of 30 (26.2%). The rate of detection of Other hrHPV-DNA was higher than that

**Table 3: Biopsy results in age groups according to the smear test**

| Age Class | Biopsy | Smearresult | | | | | *P* |
|---|---|---|---|---|---|---|---|
| | | ASC-H *n* (%) | ASCUS *n* (%) | HSIL *n* (%) | LSIL *n* (%) | NILM *n* (%) | |
| <30 | | | | | | | 0.442 [f] |
| | HSIL | 0 (0) | 2 (11.1) | 1 (50) | 3 (11.5) | 14 (23.3) | |
| | Negative | 0 (0) | 10 (55.6) | 1 (50) | 13 (50) | 32 (53.3) | |
| | LSIL | 1 (100) | 6 (33.3) | 0 (0) | 10 (38.5) | 14 (23.3) | |
| 30-39 | | | | | | | <0.001[f] |
| | HSIL | 3 (50)[ab] | 11 (30.6)[b] | 2 (100)[a] | 8 (34.8)[ab] | 26 (13.5)[c] | |
| | Negative | 1 (16.7)[a] | 18 (50)[a] | 0 (0)[a] | 11 (47.8)[a] | 150 (77.7)[b] | |
| | LSIL | 2 (33.3)[a] | 7 (19.4)[ab] | 0 (0)[ab] | 4 (17.4)[ab] | 17 (8.8)[b] | |
| 40-49 | | | | | | | <0.001[f] |
| | HSIL | 1 (33.3)[abc] | 3 (7)[c] | 2 (100)[b] | 4 (16.7)[ac] | 17 (6.3)[ac] | |
| | Negative | 2 (66.7)[ab] | 27 (62.8)[b] | 0 (0)[b] | 10 (41.7)[b] | 230 (85.5)[a] | |
| | LSIL | 0 (0)[ab] | 13 (30.2)[b] | 0 (0)[ab] | 10 (41.7)[b] | 22 (8.2)[a] | |
| 50-59 | | | | | | | <0.001[f] |
| | HSIL | 1 (25)[ab] | 0 (0)[c] | 2 (100)[b] | 1 (12.5)[ac] | 8 (7.3)[ac] | |
| | Negative | 2 (50)[ab] | 19 (79.2)[bc] | 0 (0)[a] | 4 (50)[ab] | 95 (87.2)[c] | |
| | LSIL | 1 (25)[ab] | 5 (20.8)[b] | 0 (0)[ab] | 3 (37.5)[b] | 6 (5.5)[a] | |
| 60≤ | | | | | | | 0.042[f] |
| | HSIL | 0 (0)[ab] | 0 (0)[ab] | 1 (100)[b] | 0 (0)[ab] | 0 (0)[a] | |
| | Negative | 1 (50)[ab] | 2 (100)[ab] | 0 (0)[b] | 1 (50)[ab] | 15 (93.8)[a] | |
| | LSIL | 1 (50)[a] | 0 (0)[a] | 0 (0)[a] | 1 (50)[a] | 1 (6.3)[a] | |
| Total | | | | | | | <0.001[f] |
| | HSIL | 5 (31.3)[a] | 16 (13.0)[ab] | 8 (88.9)[c] | 16 (19.3)[a] | 65 (10.0)[b] | |
| | Negative | 6 (37.5)[abc] | 76 (61.8)[c] | 1 (11.1)[b] | 39 (47.0)[a] | 522 (80.7)[d] | |
| | LSIL | 5 (31.3)[ab] | 31 (25.2)[ab] | 0 (0.0)[bc] | 28 (33.7)[a] | 60 (9.3)[c] | |

Fisher FreemanHalton test (Monte Carlo); Post Hoc test: Bonferronicorrection. [abcde]Eachsubscriptletterdenotes a subset of Smearcategorieswhosecolumnproportions do not differsignificantlyfromeachother at the. 05 level

for other types, HPV16 was detected at the highest rate (25.5%) in women under 30 years of age and HPV18 was detected most frequently (8.2%) in women between 30-39 years of age. In all age groups, the rate of Other HPV-DNA positivity was found to be higher compared to that for HPV 16 and 18 in cases with HSIL according to smear samples. In the 40-49 age group, the rate for Other HPV-DNA positivity (27%) was significantly higher than that for HPV 16 (1.0%) in cases with HSIL, but in the 50-59 age group with HSIL, the rate for Other HPV-DNA positivity (21.2%) was significantly higher than that for HPV 18 (5.8%). Another HPV (43.1%) was the most common type in patients with HSIL in biopsy results, followed by HPV 16 (34.6%) and HPV 18 (8.4%). HPV 16 continues to be the most important HPV type for cervical cancer, with the importance of the Other HPV group increasing. The results show that the 14 different HPV genotypes included in the Other HPV group should be examined separately.

ASCUS was the most common cytological finding in all decades and Other HPV infections accompanied ASCUS higher compared to HPV 16 or 18.HSIL was detected in 12 (0.3%) of the cervical cytology samples and out of 878 biopsies, HSIL was detected in 110 (12.5%) patients. For those in their 5th decade, the rate of LSIL or HSIL confirmed with biopsy was significantly higher among cytology negative cases compared to that for those in their 4th decade. Cases with ASC-H infected with Other HPV groups were detected more frequently in those in the 4th, 5th, and 6th decades, but in the 3rd decade, HPV 16 was the most frequent. According to similar studies in the literature, HPV genotype 16 has the second-highest prevalence in all age categories and the highest prevalence in HSIL.[4,7,17] Furthermore, the decrease in the High-risk HPV detection rate and the increase in the rate of abnormal cytology is a trend that has been shown before with advancing age.[14,18,19] However, there is no detailed literature data, which would allow for a comparison and discussion of HPV types based on cytology reports for every age group.

The prevalence and distribution of genital HPV infection may vary depending on the sociocultural income of the sample, the investigation technique, and the suitability of the material. In studies even in different regions of our country, HPV DNA positivity rates vary. Previous studies have reported the prevalence of HPV to be between 2 and 44% in women. The highest prevalence of HPV is observed in women aged 20–24 years and it decreases with age.[3,5,16,18,20] HPV-DNA-positive cases were most common in the age group of 30-39, followed by women under the age of 30. But, the results of the present study are different from those in the literature, but, similar results were obtained in other studies conducted in our country. Dursun *et al*.[12] reported a significantly higher rate of HPV positivity in women under 30 years of age compared to that for women older than 30 (36.2% vs. 30.4%). The most likely reason for the differences

**Table 4: Frequencies of single or multiple HPV types in age groups according to smear results**

| Age | HPVType | SmearResults | | | | | P |
|---|---|---|---|---|---|---|---|
| | | ASC-H *n* (%) | ASCUS *n*(%) | HSIL *n* (%) | LSIL *n* (%) | NILM *n* (%) | |
| <30 | | | | | | | <0.001[f] |
| | Negative | 0 (0)[ab] | 18 (40.9)[b] | 0 (0)[ab] | 11 (22)[a] | 379 (70.6)[c] | |
| | 16 | 0 (0)[a] | 2 (4.5)[a] | 0 (0)[a] | 2 (4)[a] | 25 (4.7)[a] | |
| | 18 | 0 (0)[a] | 0 (0)[a] | 0 (0)[a] | 0 (0)[a] | 6 (1.1)[a] | |
| | Other | 0 (0)[abc] | 15 (34.1)[cd] | 2 (100)[de] | 28 (56)[be] | 93 (17.3)[a] | |
| | 16and18 | 0 (0)[ab] | 1 (2.3)[b] | 0 (0)[ab] | 0 (0)[ab] | 1 (0.2)[a] | |
| | 16andOther | 1 (50)[a] | 7 (15.9)[a] | 0 (0)[ab] | 5 (10)[ab] | 27 (5)[b] | |
| | 18andOther | 0 (0)[ab] | 1 (2.3)[ab] | 0 (0)[ab] | 4 (8)[b] | 6 (1.1)[a] | |
| | 16and18andOther | 1 (50)[a] | 0 (0)[b] | 0 (0)[ab] | 0 (0)[b] | 0 (0)[b] | |
| 30-39 | | | | | | | <0.001[f] |
| | Negative | 0 (0)[a] | 55 (52.9)[b] | 0 (0)[ab] | 13 (26.5)[a] | 1314 (83.9)[c] | |
| | 16 | 5 (62.5)[a] | 9 (8.7)[b] | 1 (33.3)[ab] | 7 (14.3)[b] | 37 (2.4)[c] | |
| | 18 | 0 (0)[a] | 1 (1)[a] | 0 (0)[a] | 1 (2)[a] | 9 (0.6)[a] | |
| | Other | 3 (37.5)[ab] | 26 (25)[b] | 1 (33.3)[abc] | 22 (44.9)[a] | 168 (10.7)[c] | |
| | 16and18 | 0 (0)[a] | 0 (0)[a] | 0 (0)[a] | 0 (0)[a] | 1 (0.1)[a] | |
| | 16andOther | 0 (0)[ab] | 8 (7.7)[b] | 0 (0)[ab] | 5 (10.2)[b] | 23 (1.5)[a] | |
| | 18andOther | 0 (0)[ab] | 4 (3.8)[b] | 0 (0)[ab] | 0 (0)[ab] | 13 (0.8)[a] | |
| | 16and18andOther | 0 (0)[abcde] | 1 (1)[de] | 1 (33.3)[c] | 1 (2)[be] | 2 (0.1)[ad] | |
| 40-49 | | | | | | | <0.001[f] |
| | Negative | 2 (66.7)[abc] | 70 (70)[c] | 0 (0)[b] | 11 (28.9)[b] | 1170 (87.6)[a] | |
| | 16 | 0 (0)[abcd] | 2 (2)[cd] | 1 (25)[b] | 2 (5.3)[bd] | 18 (1.3)[ac] | |
| | 18 | 0 (0)[abc] | 0 (0)[c] | 0 (0)[abc] | 2 (5.3)[b] | 9 (0.7)[ac] | |
| | Other | 1 (33.3)[abc] | 23 (23)[c] | 1 (25)[abc] | 21 (55.3)[b] | 119 (8.9)[a] | |
| | 16and18 | 0 (0)[ab] | 1 (1)[b] | 0 (0)[ab] | 0 (0)[ab] | 0 (0)[a] | |
| | 16andOther | 0 (0)[ab] | 4 (4)[b] | 1 (25)[b] | 2 (5.3)[b] | 17 (1.3)[a] | |
| | 18andOther | 0 (0)[abc] | 0 (0)[c] | 1 (25)[b] | 0 (0)[ac] | 2 (0.1)[ac] | |
| | 16and18andOther | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| 50-59 | | | | | | | <0.001[f] |
| | Negative | 2 (40)[ab] | 37 (71.2)[b] | 1 (50)[abc] | 1 (12.5)[a] | 428 (88.6)[c] | |
| | 16 | 1 (20)[ab] | 2 (3.8)[bc] | 1 (50)[a] | 2 (25)[a] | 8 (1.7)[c] | |
| | 18 | 0 (0)[ab] | 2 (3.8)[b] | 0 (0)[ab] | 1 (12.5)[b] | 2 (0.4)[a] | |
| | Other | 2 (40)[ab] | 7 (13.5)[bc] | 0 (0)[abc] | 4 (50)[a] | 41 (8.5)[c] | |
| | 16and18 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | 16andOther | 0 (0)[ab] | 3 (5.8)[b] | 0 (0)[ab] | 0 (0)[ab] | 4 (0.8)[a] | |
| | 18andOther | 0 (0)[ab] | 1 (1.9)[b] | 0 (0)[ab] | 0 (0)[ab] | 0 (0)[a] | |
| | 16and18andOther | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| 60≤ | | | | | | | <0.001[f] |
| | Negative | 0 (0)[a] | 3 (75)[bc] | 0 (0)[ac] | 1 (25)[ac] | 84 (89.4)[b] | |
| | 16 | 1 (25)[a] | 0 (0)[ab] | 0 (0)[ab] | 0 (0)[ab] | 1 (1.1)[b] | |
| | 18 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | Other | 2 (50)[ab] | 0 (0)[bc] | 1 (100)[a] | 2 (50)[ab] | 8 (8.5)[c] | |
| | 16and18 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | 16andOther | 0 (0)[ab] | 1 (25)[b] | 0 (0)[ab] | 0 (0)[ab] | 1 (1.1)[a] | |
| | 18andOther | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | 16and18andOther | 1 (25)[a] | 0 (0)[ab] | 0 (0)[ab] | 1 (25)[a] | 0 (0)[b] | |
| Total | | | | | | | <0.001[f] |
| | Negative | 4 (18.2)[a] | 183 (60.2)[b] | 1 (8.3)[a] | 37 (24.8)[a] | 3375 (84.0)[c] | |
| | 16 | 7 (31.8)[a] | 15 (4.9)[b] | 3 (25.0)[ac] | 13 (8.7)[bc] | 89 (2.2)[d] | |
| | 18 | 0 (0.0)[ab] | 3 (1.0)[ab] | 0 (0.0)[ab] | 4 (2.7)[b] | 26 (0.6)[a] | |
| | Other | 8 (36.4)[ab] | 71 (23.4)[b] | 5 (41.7)[ab] | 77 (51.7)[a] | 429 (10.7)[c] | |
| | 16and18 | 0 (0.0)[ab] | 2 (0.7)[b] | 0 (0.0)[ab] | 0 (0.0)[ab] | 2 (0.0)[a] | |
| | 16andOther | 1 (4.5)[ab] | 23 (7.6)[b] | 1 (8.3)[ab] | 12 (8.1)[b] | 72 (1.8)[a] | |

*Contd...*

**Table 4: Contd...**

| Age | HPVType | SmearResults | | | | | P |
|---|---|---|---|---|---|---|---|
| | | ASC-H *n* (%) | ASCUS *n*(%) | HSIL *n* (%) | LSIL *n* (%) | NILM *n* (%) | |
| | 18andOther | 0 (0.0)[ab] | 6 (2.0)[b] | 1 (8.3)[b] | 4 (2.7)[b] | 21 (0.5)[a] | |
| | 16and18andOther | 2 (9.1)[a] | 1 (0.3)[bc] | 1 (8.3)[ad] | 2 (1.3)[cd] | 2 (0.0)[b] | |

Fisher FreemanHalton test (Monte Carlo); *Post Hoc* test: Bonferronicorrection. [abcde]Eachsubscriptletterdenotes a subset of Smearcategorieswhosecolumnproportions do not differsignificantlyfromeachother at the ,05 level

in rates is the non-homogeneous distribution of age groups. On the other hand, it can be expected that the HPV positivity rate will decrease for younger age cohorts as a result of increased levels of social awareness, increased vaccination rates, and opportunities. But it has been reported in the recent literature that positivity rates will decrease with advancing age and the eradication of HPV infection.[10,21]

The sample size in this study seems to be sufficient, but when evaluated together with the subgroups, the number of cases is small in some groups. In addition, in the cytological evaluation, the number of cases is not homogeneous in distribution according to Bethesda classes or age groups. In addition, HPV vaccination status was not questioned. Therefore, this may be a reason for the proportionally greater presence of the Other HPV group in some age groups. In addition, the fact that the types in the Other HPV group could not be evaluated individually is another weakness of the study.

In this study, besides the known importance of HPV 16 and 18 genotypes as risk factors for cervical cancer, the increasing incidence of Other HPV demands attention. It may also contribute to the identification of hrHPV genotypes other than HPV 16 and 18 that can be included in the national screening program.

## Ethical approval

The study was approved by the Interventional Clinical Research Ethics Committee (Decision no: 09/138, Date: 30/04/2019).

## Patients' consent

Participants were included in the study after signing a voluntary consent form.


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Nil.


## Conflicts of interest

There are no conflicts of interest.

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