DOI:10.34084/bshr.1455863 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

http://dergipark.org.tr/tr/pub/bshr

Investigation of Human Papillomavirus (HPV) Frequency and Genotype Analysis in Cervical Samples

Servikal Örneklerde Human Papilloma Virüs (HPV) Sıklığının Araştırılması ve Genotiplerinin Analizi

Yeliz Çetinkol, Selahattin Ünlü, Melahat Gürbüz, Cengiz Demir

Afyonkarahisar University of Health Siences Faculty of Medicine, Department of Medical Microbiology, Afyonkarahisar, Türkiye

ORCID ID: Yeliz Çetinkol: https://orcid.org/0000-0003-4940-4498, Selahattin Ünlü: https://orcid.org/0009-0002-9185-0109 Melahat Gürbüz: https://orcid.org/0000-0001-6290-1216, Cengiz Demir: https://orcid.org/0000-0002-5569-886X

***Sorumlu Yazar / Corresponding Author:** Yeliz Çetinkol , **e-posta / e-mail:** dryelizcetinkol@gmail.com

Geliş Tarihi / Received : 20-03-2024 **Kabul Tarihi / Accepted:** 03-04-2024 **Yayın Tarihi / Online Published:** 30-04-2024

Çetinkol Y., Ünlü S., Gürbüz M., Demir C. Investigation of Human papillomavirus (HPV) frequency and genotype analysis in cervical samples, J Biotechnol and Strategic Health Res. 2024;8(1):50-57

Abstract

Aim Human Papillomaviruses (HPVs) are double-stranded DNA viruses belonging to the Papillomaviridae family. There is ample evidence demonstrating the association of Human Papillomavirus (HPV) with cervical carcinoma. This study aimed to investigate the presence of HPV DNA in cervical swab samples and determine the HPV genotypes in positive samples.

Material and Method The three-year results of cervical swab samples sent to the Medical Microbiology Laboratory of Afyonkarahisar Health Sciences University Faculty of Medicine Hospital for screening for HPV DNA presence between January 1, 2020, and December 31, 2022, were retrospectively evaluated in this study. HPV genotyping was performed using the cobas 4800 (cobas® x480) fully automated system (Roche Diagnostics, Indianapolis, USA) for extraction, and the samples were analyzed using the Real-time PCR (cobas® z 480) system following the manufacturer's instructions.

Results HPV-DNA was detected in 415 out of a total of 4960 patients (8.4%), while 4545 (91.6%) tested negative. Evaluation of HPV positivity revealed that the highest positivity rates were observed in HR-HPV at 68%, HPV 16 at 17.3%, and HPV 16 combined with HR-HPV at 8.2%. HPV-DNA positivity was highest at 38% in the 35-44 age group, while it was lowest at 3.4% in patients under 25 years old.

Conclusion The aim of our study is to contribute to the data of our region and our country by determining the HPV incidence and common subtypes in our region, and to collect data that can guide vaccine studies. Thus, vaccination programs, alongside screening programs, will serve to restrict the spread of infection in at-risk populations and prevent HPV-related cancers.

Keywords Cervical cancer, HPV-DNA, *Human papillomavirus*

Özet

Amaç *Human Papilloma virüsler çift zincirli DNA yapısında olup papillomavirüs ailesindendirler. Human Papilloma Virüs (HPV)'ün servikal karsinomla bağlantılı olduğunu gösteren birçok kanıt bulunmaktadır. Bu çalışmada servikal sürüntü örneklerinde HPV-DNA varlığı araştırılmış ve pozitif bulunan örneklerin HPV genotiplerinin saptanması amaçlanmıştır.*

Gereç ve Yöntem *Bu çalışmada 1 Ocak 2020 ile 31 Aralık 2022 tarihleri arasında Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıp Fakültesi Hastanesi Tıbbi Mikrobiyoloji Laboratuvarına HPV-DNA varlığının taranması amacıyla gönderilen servikal sürüntü örneklerine ait üç yıllık sonuçlar retrospektif olarak değerlendirilmiştir. HPV genotiplendirmesi için ekstraksiyon işlemi cobas 4800 (cobas® x480) (Roche Diagnostics, Indianapolis, ABD) tam otomatize cihazı ile yapılmış ve numuneler Real-time PCR (cobas® z 480) sistemi kullanılarak üretici firma direktifleri doğrultusunda çalışılmıştır.*

Bulgular *HPV-DNA, incelenen toplam 4960 hastanın 415'inde (%8.4) pozitif, 4545'inde (%91.6) ise negatif saptanmıştır. HPV pozitifliği açısından değerlendirildiğinde en yüksek pozitifliğin sırasıyla %68 oranında HR-HPV, %17,3 oranında HPV 16 ve %8,2 oranında HPV 16 ve HR-HPV birlikte pozitifliği olduğu görülmüştür. HPV-DNA pozitifliği en fazla %38 ile 35-44 yaş grubunda görülürken, en az %3,4 ile 25 yaş altı hasta grubunda bulunmuştur.*

Sonuç *Çalışmamızın amacı, bölgemizdeki HPV görülme sıklığı ve yaygın alt tiplerinin belirlenmesi ile bölge ve ülkemiz verilerine katkı sağlamak, ayrıca aşı çalışmalarına yol gösterebilecek verilerin toplanmasıdır. Tarama programları ile birlikte yürütülecek olan aşı programları, risk altındaki bu popülasyonda enfeksiyonun yayılması için sınırlayıcı olacak ve HPV ile ilişkili kanserlerin önlenmesini sağlayabilecektir.*

Anahtar Kelimeler *Servikal kanser, HPV-DNA, Human papillomavirüs*

INTRODUCTION

Human papillomavirus (HPV) is a small, double-stranded DNA virus capable of replicating in skin and mucosal epithelial cells. Its genome, consisting of double-stranded circular DNA of approximately 8 kb, encodes oncoproteins (E1, E2, E4, E5, E6, E7) involved in virus replication and cell transformation, as well as late proteins (L1, L2) forming the capsid structure.[1] HPV oncoproteins play a significant role in tumor formation in cervical cancer (CC). Humoral immune response against the major capsid protein (L1) is generated during HPV infection, which is considered an indicator of past or current infection.[2]

Additionally, integration of the HPV genome into the host cell results in overexpression of E6 and E7 oncoproteins, which play a role in the transformation and progression of cervical and other HPV-related cancers.[3] Due to its genome structure and tropism for human epithelial tissues, there are more than 200 HPV genotypes classified into five different genera (alpha, beta, gamma, Mu, and Nu) based on their life cycles and infection causes.[4]

When assessing oncogenic risks, HPV types are categorized into low, intermediate, and high-risk groups. HPV 6, 11, 42, 43, and 44 are classified as low-risk, causing benign cervical lesions and condylomas without malignancy. The intermediate-risk group includes HPV 31, 33, 35, 51, and 52, which are implicated in malignant transformation, although this remains to be conclusively established.[5] The high-risk (HR-HPV) group primarily consists of HPV 16, 18, 45, and 56, which trigger neoplastic transformations. Moreover, 15 HPV types within the alpha genus, including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82, are classified as 'HR' types, possessing oncogenic properties and causing anogenital cancers. HPV 16 is responsible for approximately 55% of cervical cancer cases, while HPV 18 accounts for 15% of cancer cases.[6]

HR-HPV infection is particularly common in sexually active young women, but most infections are transient and self-limiting, often showing no clinical symptoms. However, approximately 10% of women have HR-HPV infection and are at risk for CC and its precursors. HPV infection has been reported to increase the risk of high-grade squamous intraepithelial lesion (HSIL) by 250 times.[7] Hence, HPV infections become highly significant. It is still unclear which genotypes are most likely to emerge in HPV infections. Age is considered a significant factor associated with HPV infection, but the relationship between age and persistent HPV infection is still debatable. Examining specific genotypes of HPV infection is crucial for reducing HSIL and guiding the prevention and treatment of CC. In this study, we aimed to determine the prevalence of HPV infection and identify HPV genotypes in women attending our hospital to optimize prevention strategies for CC and provide references for the development of HPV vaccines.

MATERIALS and METHODS

The study was approved by the Ethics Board of the Faculty of Medicine of Afyonkarahisar Health Sciences University (Decision no. 447-2023/10).

This study included cervical brush samples obtained from women aged 18 and over who attended the gynecology and obstetrics outpatient clinic at Afyonkarahisar Health Sciences University Faculty of Medicine Hospital for the purpose of screening for the presence of HPV-DNA between January 1 and December 31, 2022. Samples sent in BD SurePath solution (BD Company, Sparks, Maryland, USA) were stored in a refrigerator at +4°C until the day of analysis. HPV genotyping was performed using the cobas 4800 (cobas® x480) automated system (Roche Diagnostics, Indianapolis, USA), and samples were processed according to the manufacturer's instructions using the Real-time PCR (cobas® z 480) system. Qualitative results were reported separately for oncogenic HPV types HPV16 and HPV18, while for other HR-HPV types (including HPV31, 33, 39, 45, 51, 56, 58, 59, 66, and 68), genotypic discrimination was not performed and reported.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics 23 (SPSS Inc., Chicago, USA) software. Values with a normal distribution were analyzed using the independent samples t-test method. Fisher's exact test was used for comparisons of categorical variables between groups. Data were presented as percentages (%), means, standard deviations (±), and numbers (n), and a p-value of <0.05 was considered statistically significant.

RESULTS

Of the total 4960 patients whose HPV DNA was investigated, 415 (8.4%) were found to be positive, while 4545 (91.6%) were negative. The mean age of the women included in the study was 42.6 ± 9.7 years (range: 18-86 years). The mean age of those with HPV DNA positive results across all age groups was 40.9 ± 10.8 years (range: 18-76 years), while the mean age of those with negative results was 42 ± 9.6 years (range: 20-75 years). When the samples with positive HPV DNA were examined according to their genotypes, it was observed that the highest positivity rates were 68% for HR-HPV, 17.3% for HPV 16, and 8.2% for HPV 16 + HR-HPV, respectively (Table 1).

Table 1. Distribution of HPV Genotypes in HPV DNA Positive Samples

HPV Genotypes	HPV DNA Positive	
	n	%
Type 16	72	17.3
Type 16 + HR-HPV	34	8.2
Type 16 + Type 18	5	1.2
Type 16 + Type 18 + HR-HPV	2	0.5
Type 18	9	2.2
Type 18 + HR-HPV	11	2.6
HR-HPV	282	68
Total	415	100

To determine differences in age distribution, samples were divided into separate age groups: under 25 years old, 25-34, 35-44, 45-54, and 55 years and older. HPV prevalence was calculated according to age. The frequency distribution of HPV genotypes in age groups was generally observed to be HR-HPV, HPV16, and HPV18, along with HR-HPV positivity. Significant differences in mean ages for HPV genotypes were not detected among the five different age groups (p>0.05). The highest HPV-DNA positivity rate according to age groups was found in the 35-44 age group (38%), followed by the 45-54 (22.7%) and 25-34 (21.4%) age groups (Table 2).

Table 2. Distribution of HPV Genotypes by Age Groups n (%)

HPV Genotypes	**Under 25 years**	**25-34 years**	**35-44 years**	**45-54 years**	**55 years and older**
Type 16	3 (0,7)	16 (3,9)	26 (6,3)	13 (3,1)	14 (3,4)
Type 16 + HR-HPV	1 (0,2)	3 (0,7)	13 (3,1)	11 (2,7)	6 (1,4)
Type 16 + Type 18	0 (0,0)	1 (0,2)	2 (0,5)	1 (0,2)	1 (0,2)
Type 16 + Type 18 + HR-HPV	0 (0,0)	1 (0,2)	0 (0,0)	0 (0,0)	1 (0,2)
Type 18	0 (0,0)	4 (1)	3 (0,7)	2 (0,5)	0 (0,0)
Type 18 + HR-HPV	3 (0,7)	4 (1)	3 (0,7)	0 (0,0)	1 (0,2)
HR-HPV	7 (1,7)	60 (14,5)	111 (26,7)	67 (16,1)	37 (8,9)
Total n (%)	**14 (3,4)**	**89 (21,4)**	**158 (38)**	**94 (22,7)**	**60 (14,5)**

The highest number of tests belonged to the year 2022, with 2305 samples, followed by 1849 samples in 2021 and 806 samples in 2020. The positivity rates for the years 2020, 2021, and 2022 were found to be 9.4%, 8.4%, and 7.9%, respectively. The positivity rate between years was examined and 2020 was found to be statistically significant compared to other years. ($p<0.05$) (Table 3).

Table 3. HPV genotype rates by years n (%)

Year	Positive	Type 16	Type 16 + HR-HPV	Type 16 + Type 18	Type 16 + Type 18 + HR-HPV	Type 18	Type 18 + HR-HPV	HR-HPV
2020	76 (18,3)	16 (3,9)	5 (1,2)	0 (0,0)	0 (0,0)	2 (0,5)	1 (0,2)	52 (12,5)
2021	155 (37,3)	26 (6,3)	13 (3,1)	3 (0,7)	0 (0,0)	6 (1,5)	6 (1,5)	101 (24,3)
2022	184 (44,4)	30 (7,2)	16 (3,9)	2 (0,5)	2 (0,5)	1 (0,2)	4 (1)	129 (31,1)
Total	**415**	**72 (17,3)**	**34 (8,2)**	**5 (1,2)**	**2 (0,5)**	**9 (2,2)**	**11 (2,7)**	**282 (68)**

*p<0.05 was considered statistically significant

DISCUSSION

HPV is the most common sexually transmitted viral infection worldwide, affecting both women and men. Approximately 85% of women and 95% of sexually active men become infected with HPV at some point in their lives. Nearly all sexually active individuals become infected with HPV within the first few years of sexual activity, with almost half of them being infected with HR-HPV types. HPV is responsible for nearly all cervical cancers and plays a significant role in various non-cervical cancers, including anal (90%), vaginal (75%), oropharyngeal (70%), vulvar (69%), and penile (63%) cancers. While more than 50% of the morbidity and mortality of vaginal and penile cancer cases occur in Asia, vulvar cancer is more predominant in Europe.[8] On the other hand, cervical cancer, with an estimated 604,127 new cases and 341,831 deaths in 2020, became the second most common cancer type among individuals aged 15 to 44 worldwide.[9] Regions such as India, Eastern Europe, Latin America, and sub-Saharan Africa have the highest rates of infection.[10]

In screening, in addition to searching for HPV-DNA, Pap smear tests are also used for the detection of precancerous lesions and HPV infection. The combined use of both methods is referred to as "co-testing".[11] The World Health Organization, the American College of Obstetricians and Gynecologists (ACOG), and the American Cancer Society (ACS) recommend screening tests every three years for women aged 21-65, with more frequent screening recommended for immunocompromised women.[12] Effective cervical screening requires scaling surveillance-based programs, population-based screening studies, and survey-based methods to support elimination strategies, as well as encouraging women to participate in screening programs and ensuring regular screenings.

The frequency of HPV varies globally, with higher rates observed in developing regions. Approximately 90% of deaths related to cervical cancer occur in low- and middle-income countries. Studies compiled from women known to be cytologically healthy have shown HPV prevalence to be around 24% in sub-Saharan Africa, 33.6% in East Africa, and even higher in Latin America.[9] The highest prevalence of HPV among women is observed in Asian regions, particularly in East Asia (China) and South Central Asia (India), where nearly half of the women (57.7% and 44.7%, respectively) are carriers. In South Africa, 42.2% of women have been identified as HPV carriers. When average values are examined, HPV infection rates are higher in developing regions (42.2%) compared to developed regions (22.6%).[13]

Studies have shown that HPV infection varies significantly across different regions. The prevalence of persistent HR-

HPV infection has been reported as 36.1% in the United States[14] and between 26.9% to 38.8% in Europe.[15]

In a study conducted by Pedroza-Gonzalez et al. in Mexico, they evaluated the association between HPV infection with high-risk viruses and the likelihood of developing cervical cancer, finding a 72.9% association. In this study, the prevalence of HPV infection was determined to be 74.4%, with the most dominant HR-HPV types reported as 18 (13.95%), 31 (10.85%), and 16 (9.3%).[16] A study in Denmark reported a prevalence of 31.4%,[17] while in Korea, it was 12.4%.[18] According to a meta-analysis from 2013, the global prevalence was estimated to be 43%, whereas a study conducted in 2023 reported a prevalence of 29.4%.[19] When examining studies conducted in our country, Gültekin M., et al. found an HPV-DNA rate of 4.36%, while Yerlikaya et al. reported a slightly lower rate of 4.9%, compared to our study.[20,21] On the other hand, Peker BO., et al. reported a higher HPV-DNA presence rate of 18.6%, Alacam S., et al. found a rate of 36.3%, and Yakut S., et al. reported a rate of 18.4%, indicating higher rates compared to our study.[22,23,24] In our study, cervical samples were evaluated for the molecular detection of HPV, and the overall HPV infection rate was found to be 8.4% among the analyzed patients. When compared to other studies, the frequency reported in our research was found to be lower than both the global prevalence of 29.4% and the rate in developing regions (42.2%). These results are thought to be explained by the relatively closed nature of our country and especially the Afyon region, higher rates of monogamous relationships, and a later age of sexual debut. These findings shed light on the epidemiological profile of HPV infection in our region and emphasize the importance of understanding regional variations in HPV prevalence for effective public health interventions.

The distribution of HPV genotypes varies significantly among different geographical regions and ethnic groups. In a study by Liang HY., et al., HPV 16 was found to be the most commonly observed genotype, followed by HPV 58, 52, 18, 33, 31, 59, 39, 68, and 45.25 Liu J., et al. reported in 2020 that HPV 58 and 53 were the most persistent genotypes, followed by HPV 52, 16, and 39.[26] Meanwhile, Zhao M., et al. detected an HPV prevalence of 29.4% in their study, with the most prevalent genotypes being HPV 16 (35%), HPV 52 (28.2%), HPV 58 (27.1%), HPV 18 (26%), HPV 33 (24.4%), HPV 31 (23.4%), HPV 59 (21.9%), HPV 39 (19.5%), HPV 68 (16.6%), and HPV 45 (15.1%).[27] In a study conducted by Zhang J., et al., the HPV prevalence in China was reported as 84.4%, highlighting variations in the distribution of HPV types among different regions.[28] Other studies conducted in China have also reported a high prevalence of HPV 52 among women aged 15 to 94 in different regions.[29] Conversely, in Sweden, lower prevalences of HPV 52 and HPV 58 were found. The prevalence of HPV 45, belonging to the HR-HPV group, was relatively high in European countries, particularly in Sweden, where it was found to be 7%.[30] A global study reported an HPV 45 prevalence of 11.6%.[31] However, the prevalence of HPV 45 is lower in Asia, with rates as low as 0.5% in China[32] and 2.2% in India.[33] In a study conducted in Sub-Saharan Africa, the detected genotypes were classified in order of prevalence as follows: HPV 16 (18%), HPV 35 (10.1%), HPV 52 (10%), HPV 18 (9.7%), HPV 45 (6.8%), HPV 51 (6.6%), HPV 58 (6.4%), HPV 56 (6.20%), HPV 33 (6.1%), HPV 31 (5.9%), HPV 39 (4.2%), HPV 68 (4%), HPV 59 (3.4%), HPV 66 (2.2%), HPV 62 (0.3%), and HPV 61 (0.1%).[34] In our study, when the samples with positive HPV DNA were examined according to genotypes, it was observed that the highest positivity rates were 68% for HR-HPV, 17.3% for HPV 16, and 8.2% for HPV 16+HR-HPV, respectively.

Epidemiological studies have shown that the main HPV types causing cancer are primarily HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. Despite the fact that these results represent crucial considerations for HPV vaccination, current vaccines do not fully cover all genotypes associated with HPV-related diseases, even though they prevent most HPV infections.[35,36] Molina-Pineda et al.[37] reported a prevalence of 11.5% for HPV 59 in cervical cancer patients,

and HPV 59 has been identified in the top five genotypes of HPV infection in various regions worldwide, including Ghana, China, and Switzerland.[27] Additionally, although HPV 51, HPV 53, HPV 56, and HPV 68 are known to be associated with cervical intraepithelial neoplasia 1 (CIN 1) at a rate of 31% and with cervical intraepithelial neoplasia 2 (CIN 2) at a rate of 26%, HPV 68, which is among the 14 HPV genotypes not covered by the 9-valent vaccine, has an infection prevalence of 9.3%.38 Schlecht et al. found a high prevalence of HPV 68 in unvaccinated individuals in their 2021 study.[39] The importance of studies investigating HPV genotype distributions becomes evident in this context.

In a study conducted in Turkey in 2019, HPV 16 was reported to be present in 36.9% of cases, while HPV 18 was found in 13.9% of cases.[40] In the study by Aydoğan S., et al., the highest positivity was observed in HPV 16 at 41.8%, followed by HPV 51 at 12.7%. HPV 18 was detected in 11.8% of cases.[41] Yakut S., et al. found HPV 16 positivity in 4.5% of women with HPV positivity, HPV 18 positivity in 1.8%, and positivity for the other 12 HR-HPV genotypes at a rate of 12.1%.[24] Similarly, in a study conducted in Turkey in 2022, HPV 16 was found in 3.3% of cases, HPV 18 in 0.7%, and HR-HPV in 11.9%, with a positivity rate of 2.5% for multiple HPV types.[22] In a large-scale study conducted in Turkey in 2020, which included over 4 million patients, HPV type 16 was the most commonly detected type across all age groups and geographical regions, followed by types 51, 31, 52, 56, and 18.[20] In our study, HPV DNA genotyping was performed on the patients included in our research. The most frequently detected HR-HPV group was found in 68% of cases, followed by HPV 16 at 17.3% and HPV 18 at 8.2% (Table 1). The occurrence of three types of HR-HPV in two patients (0.5%) was observed, while the rate of patients with two types of HPV together was 12%. Our findings are generally consistent with the data from Turkey and globally, although there are significant variations in HPV types both within our country and internationally. The relationship between age and HPV infection remains controversial in studies conducted to date. Some studies have reported that a lower age is associated with an increased risk of infection.[42] Tounkara F., et al. reported that patients under 30 years old and over 50 years old have a higher likelihood of experiencing persistent HPV infection, emphasizing the need to pay particular attention to these age groups during follow-up. This study highlighted the widespread prevalence of HR-HPVs in individuals aged 18 to 30, making them particularly vulnerable to developing cervical cancer at the population level.[43]

Studies have reported variations in the relationship between HPV prevalence and age. It has been observed that prevalence is high among individuals aged 20-24, decreases in middle-aged groups, and then increases again in women over 35.[44] In our study, HPV prevalence was highest in the 35-44 age group at 38%, while it was 21.4% and 22.7% in the 25-34 and 45-54 age groups, respectively (Table 2). HPV prevalence in the middle age group was found to be higher compared to the literature. This may be attributed to the fact that in our country and region, the sexually active life occurs at older ages.

In their study, Wheeler BS., et al. frequently found HPV 16 and 18 in the group aged 30 and above.[45] Salazar KL., et al. reported a high frequency of multiple HPV genotype infections.46 In our study, the most common HR-HPV genotypes were detected in all age groups, particularly HPV 16 and HPV 16 with HR-HPV positivity predominated in the group aged 30 and above. Multiple HPV infections such as HPV 16 with HR-HPV were more commonly observed in the 35-44 age group.

Cervical cancer screenings have been significantly disrupted worldwide and in our country due to the COVID-19 pandemic. In our study, a notable decrease in the number of tests was observed for the year 2020 compared to the following years, and it was noted that the number of patients with HPV DNA positivity increased over the years. The highest HPV DNA positivity rate was observed

in 2022, reaching 44.4%. Upon examining the data for all years, it was found that besides HR-HPV types, HPV 16 (17.3%) and HPV 16 with HR-HPV co-positivity (8.2%) followed in frequency.

CONCLUSION

Special attention is required for the mortality and morbidity caused by HPV infection and its associated cervical cancer. Primarily, screening for early detection of cancer, uninterrupted implementation of vaccination programs, and the application of effective treatment protocols are crucial. These three fundamental aspects are part of the comprehensive surveillance program strategies at national or local levels by the World Health Organization to reduce cervical cancer due to public health concerns. The goal of the strategy is to achieve targets by 2030, especially in low and low-middle-income countries. This includes screening 70% of adults at the age of 35, repeating screening at the age of 45, and ensuring that 90% of girls are fully vaccinated with HPV vaccine by the age of 15.[47] Studies have shown that vaccines are highly effective in preventing precancerous lesions and invasive cancer infections caused by HPV infections.[48] Particularly in developing countries, the high mortality and prevalence rates of cervical cancer have reached alarming levels.

High rates of HPV-DNA have been detected in almost every age group included in our study. Vaccination programs, along with screening programs, will serve as a constraint against the spread of infection in this at-risk population, potentially preventing HPV-related cancers. It is believed that nationwide HPV DNA screening studies and vaccination programs targeting HPV infections will be highly effective in reducing the prevalence of cervical cancer.

Ethics Approval

The study was approved by the Ethics Board of the Faculty of Medicine of Afyonkarahisar Health Sciences University (Decision no. 447-2023/10).

Peer-review

Externally and internally peer-reviewed.

Authorship Contributions

Concept: Y.Ç., C.D., S.Ü., M.G Design: Y.Ç., C.D., S.Ü., M.G., Data Collection or Processing: Y.Ç., C.D., S.Ü., M.G., Analysis or Interpretation: Y.Ç., C.D., S.Ü., M.G., Literature Search: Y.Ç., C.D., S.Ü., M.G., Writing: Y.Ç., C.D., S.Ü., M.G.

Conflict of Interest

No conflict of interest was declared by the authors.

Funding

The authors declared that this study received no nancial support.

Informed Consent

Informed consent was not obtained since it was a retrospective archive scan.

References

1. Gülçin, A. L. P. İnsan Papillomavirusunun Genomik Yapısı ve Proteinleri. Mikrobiyol Bul. 2012; 46(3), 507-515.
2. Cuzick J, Bergeron C, von Knebel DM, et al. New technologies and procedures for cervical cancer screening. Vaccine. 2012; 30(Suppl 5):F107–F116.
3. Williams VM, Filippova M, Soto U, et al. HPV-DNA integration and carcinogenesis: Putative roles for inflammation and oxidative stress. Vol. 6, Future Virology. NIH Public Access. 2011; p. 45–57.
4. Doorbar J., Quint W., Banks L., et al. The biology and life-cycle of human papillomaviruses. Vaccine. 2012; 30:F55–F70.
5. Tulay P., Serakinci N. The role of human papillomaviruses in cancer progression. J. Cancer Metastasis Treat. 2016; 2:201.
6. Graham S.V. The human papillomavirus replication cycle, and its links to cancer progression: A comprehensive review. Clin. Sci. 2017;131:2201–2221.
7. Huh WK, Ault KA, Chelmow D, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. Gynecologic Oncology. 2015;136:178–182.
8. Jain M, Yadav D, Jarouliya U, et al. Epidemiology, Molecular Pathogenesis, Immuno-Pathogenesis, Immune Escape Mechanisms and Vaccine Evaluation for HPV-Associated Carcinogenesis. Pathogens. 2023;12(12):1380.
9. Bruni L., Albero G., Serrano B., et al. Human Papillomavirus and Related Diseases in the World. Summary Report 22 October 2021. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre); Barcelona, Spain: 2023.
10. Forman D., de Martel C., Lacey C.J., et al. Global burden of human papillomavirus and related diseases. Vaccine. 2012;30:F12–F23.
11. Johnson, C.A., James, D., Marzan, A., et al. Cervical cancer: an overview of pathophysiology and management. In Seminars in oncology nursing. 2019; 35, 2, pp. 166-174.
12. World Health Organization. WHO Guideline for Screening and Treatment of Cervical Pre-Cancer Lesions for Cervical Cancer Prevention: Use of mRNA Tests for Human Papillomavirus (HPV) World Health Organization; Geneva, Switzerland: 2021.
13. Tan S.C., Ismail M.P., Duski D.R., ve ark. Prevalence and type distribution of human papillomavirus (hpv) in malaysian women with and without cervical cancer: An updated estimate. Biosci. Rep. 2018;38:BSR20171268.
14. Bennett R, Cerigo H, Coutlée F, et al. Incidence, persistence, and determinants of human papillomavirus infection in a population of Inuit women in northern Quebec. Sexually Transmitted Diseases. 2015; 42: 272–278.
15. Schmeink CE, Massuger LF, Lenselink CH, et al. Prospective follow-up of 2,065 young unscreened women to study human papillomavirus incidence and clearance. International Journal of Cancer. 2013;133:172–181.
16. Pedroza-Gonzalez A, Reyes-Reali J, Campos-Solorzano M, et al. Human papillomavirus infection and seroprevalence among female university students in Mexico. Hum Vaccin Immunother. 2022;18(1): 2028514.
17. Stensen S, Kjaer SK, Jensen SM, et al. Factors associated with type-specific persistence of high-risk human papillomavirus infection: a population-based study. International Journal of Cancer. 2016;138:361–368.
18. Ingabire C, Lim MK, Won YJ, et al. Human papillomavirus genotype-specific persistence and potential risk factors among korean women: results from a 2-year follow-up study. Cancer Research and Treatment. 2018;50:813–822.
19. Rositch AF, Koshiol J, Hudgens MG, et al. Patterns of persistent genital human papillomavirus infection among women worldwide: a literature review and meta-analysis. International Journal of Cancer. 2013;133:1271–1285.
20. Gultekin M, Dundar S, Keskinkilic B, ve ark. How to triage HPV positive cases: Results of four million females. Gynecol Oncol. 2020;158(1):105-11.
21. Yerlikaya H., Filiz O, Murat, A. ve ark. Servikal Örneklerde Human Papillomavirüs Genotiplendirme ve Sitopatoloji Sonuçlarının Değerlendirilmesi. Dicle Tıp Dergisi. 2023; 50(2), 235-244.
22. Peker BO, Müderris T, Gül Yurtsever S, ve ark. Servikal fırça örneklerinde insan papilloma virüs prevalansı ve genotip dağılımı; üç yıllık analiz. Turk Mikrobiyol Cemiy Derg. 2022;52(3):168-174.
23. Alacam S, Bakir A. Human papillomavirus prevalence and genotype distribution in cervical swab samples in Istanbul, Turkey. J Infect Dev Ctries. 2021;15(8):1190-6.
24. Yakut S, Gareayaghi N, Yıldız Zeyrek F ve ark. Bir üniversite hastanesine başvuran kadın hastalarda yüksek riskli hpv sıklığı ve genotip dağılımı sonuçlarının 3 yıllık retrospektif analizi. Turk Mikrobiyol Cemiy Derg. 2023;53(4):272-277.
25. Liang HY, Chen XH, Zhang SW. Relationship between persistent infection of high-risk HPV and occurrence of cervical lesions. China Modern Doctor. 2017;55:52–55,58.
26. Liu, J., Shi, Y., Wang, L., et al. Epidemiology and persistence of cervical human papillomavirus infection among outpatient women in Heilongjiang province: A retrospective cohort study. Journal of Medical Virology. 2020; 92(12), 3784-3792.
27. Zhao M, Zhou D, Zhang M, et al. Characteristic of persistent human papillomavirus infection in women worldwide: a meta-analysis. PeerJ. 2023;11:e16247.
28. Zhang J, Cheng K, Wang Z. Prevalence and distribution of human papillomavirus genotypes in cervical intraepithelial neoplasia in China: a meta-analysis. Arch Gynecol Obstet. 2020;302:1329–1337.
29. Zhang H., Zhang S. Prevalence and genotype distribution of human papillomavirus infection among female outpatients in Northeast China: a population-based survey of 110,927 women. Archives of Gynecology and Obstetrics. 2023;308(1), 35-41.
30. Lagheden C, Eklund C, Lamin H, et al. Nationwide comprehensive human papillomavirus (HPV) genotyping of invasive cervical cancer. British Journal of Cancer. 2018;118:1377–1381.
31. Pirog EC, Lloveras B, Molijn A, et al. HPV prevalence and genotypes in different histological subtypes of cervical adenocarcinoma, a worldwide analysis of 760 cases. Modern Pathology. 2014; 27:1559–1567.
32. Jing L, Zhong X, Zhong Z, et al. Prevalence of human papillomavirus infection in Guangdong Province, China: a population-based survey of 78, 355 women. Sexually Transmitted Diseases. 2014;41:732–738.
33. Munjal K, Adamson CS, Rajendran V, et al. Human papillomavirus type distribution in invasive cervical cancers from Madhya Pradesh: implications for vaccination programs in central India. International Journal of Gynecological Pathology. 2014;33:531–536.
34. Tchouaket MCT, Kaè AC, Semengue ENJ, et al. Variability of High-Risk Human Papillomavirus and Associated Factors among Women in Sub-Saharan Africa: A Systematic Review and Meta-Analysis. Pathogens. 2023 Aug 11;12(8):1032.
35. De Oliveira CM, Fregnani J, Villa LL. HPV vaccine: updates and highlights. Acta Cytologica. 2019;63:159–168.
36. De Martel C, Plummer M, Vignat J, et al. Worldwide burden of cancer attributable to HPV by site, country and HPV type. International Journal of Cancer. 2017;141:664–670.
37. Molina-Pineda A, López-Cardona MG, Limón-Toledo LP, et al. High frequency of HPV genotypes 59, 66, 52, 51, 39 and 56 in women from Western Mexico. BMC Infectious Diseases. 2020;20:889.
38. Ma M, Zhu J, Yang Y, et al. The distribution and pathogenic risk of non-9-valent vaccine covered HPV subtypes in cervical lesions. Cancer Medicine. 2022;11:1542–1552.
39. Schlecht NF, Diaz A, Nucci-Sack A, et al. Incidence and types of human papillomavirus infections in adolescent girls and young women immunized with the human papillomavirus vaccine. JAMA Network Open. 2021;4:e2121893.
40. Muderris T, Afsar I, Yıldız A, ve ark. HPV genotype distribution among women with normal and abnormal cervical cytology in Turkey. Rev Esp Quimioter. 2019;32(6):516-24.
41. Aydoğan S, Yazhan A, Taş EE, ve ark. The presence and distribution of high risk HPV types in simultaneous cervical cytology samples. Turk Hij Den Biyol Derg, 2018; 75(1): 13-20
42. Rosa MI, Fachel JMG, Rosa DD, et al. Persistence and clearance of human papillomavirus infection: a prospective cohort study. American Journal of Obstetrics and Gynecology. 2008;199(617):e611-617.
43. Tounkara FK, Téguété I, Guédou FA, et al. Type-specific incidence, persistence and factors associated with human papillomavirus infection among female sex workers in Benin and Mali, West Africa. International Journal of Infectious Diseases. 2021;106:348–357.
44. Erickson BK, Alvarez RD, Huh WK. Human papillomavirus: what every provider should know. Am J Obstet Gynecol. 2013;208(3):169-75.
45. Wheeler BS, Rositch AF, Poole C, et al. Patterns of incident genital human papillomavirus infection in women: A literature review and metaanalysis. Int J STD AIDS. 2019;30(13):1246-56.
46. Salazar KL, Zhou HS, Xu J, et al. Multiple Human papilloma virus infections and their impact on the development of high-risk cervical lesions. Acta Cytol. 2015;59(5):391-8.
47. Nishimura H., Yeh P.T., Oguntade H., et al. Hpv self-sampling for cervical cancer screening: A systematic review of values and preferences. BMJ Glob. Health. 2021;6:e003743.
48. Deshmukh AA, Suk R, Shiels MS, et al. Incidence trends and burden of human papillomavirus-associated cancers among women in the United States, 2001-2017. J Natl Cancer Inst. 2021;113(6):792-6.