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Evaluation of Human Papilloma Virus Prevalence and Genotype Distribution in Bunyan State Hospital

Bünyan Devlet Hastanesinde İnsan Papilloma Virüsü Prevalansının ve Genotip Dağılımının Değerlendirilmesi

Nuri Çakır[1], Sinem Akça Keklikçioğlu[2]

[1] Bunyan State Hospital, Department of Microbiology, Kayseri, Türkiye
[2] Bunyan State Hospital, Department of Obstetrics and Gynecology, Kayseri, Türkiye

ABSTRACT

Aim: *Human papillomavirus (HPV) infection is the most common sexually transmitted infection and is known to cause cervical cancer. The World Health Organization (WHO) recommends HPV-DNA-based molecular tests as primary screening tests. In our study, we aimed to investigate the frequency and genotype distribution of HPV in women over the age of 18 who applied to our hospital's gynecology and obstetrics outpatient clinic and lived in our region.*

Materials and Methods: *1026 patients over the age of 18 who applied to the gynecology and obstetrics outpatient clinic of our hospital between 2022 and 2024 were included in the study. The results of patients whose cervical swab samples were taken, HPV DNA screening was performed, and whose laboratory results were known were evaluated retrospectively.*

Results: *HR-HPV positivity was detected in 32 (2.8%) of 1026 female patients included in our study. In positive patients, HPV16 positivity was detected in 1.4% of the patients, while HPV18 positivity was found in 0.9% and other 12 HR-HPV genotype positivity was found in 0.6%. It was observed that the highest number of applications and positive results were detected in 2024. It was reported that HPV16 positivity was the most common genotype in patients in all years.*

Conclusion: *: Prevalence studies provide important data in determining strategies to prevent HPV infection and its related cancers. In our country, screening programs need to be delivered to a wider audience and studies need to be carried out in this context.*

Keywords: *HPV screening, cervical smear test, HPV genotype distribution*

ÖZET

Amaç: *İnsan papilloma virüs (HPV) enfeksiyonu en yaygın cinsel yolla bulaşan enfeksiyondur ve serviks kanserine neden olduğu bilinmektedir. Dünya Sağlık Örgütü (WHO), HPV-DNA tabanlı moleküler testleri primer tarama testi olarak önermektedir. Çalışmamızda, hastanemiz kadın hastalıkları ve doğum polikliniğine başvuran ve bölgemizde yaşayan 18 yaş üstü kadınlarda HPV sıklığını ve genotip dağılımını araştırmayı amaçladık.*

Gereç ve Yöntemler: *2022- 2024 yılları arasında hastanemiz kadın hastalıkları ve doğum polikliniğine başvuran 18 yaş üstü 1026 hasta çalışmaya dahil edildi. Servikal fırça numunesi alınmış, HPV-DNA taraması yapılmış ve laboratuvar sonuçları belli olan hastalara ait sonuçlar retrospektif olarak değerlendirildi.*

Bulgular: *Çalışmamıza dahil edilen 1026 kadın hastanın 32'sinde (%2.8) HR-HPV pozitifliği saptandı. Pozitif hastalarda HPV16 pozitifliği hastaların %1.4'ünde tespit edilirken, HPV18 %0.9 ve diğer 12 HR-HPV genotipi pozitifliği ise %0.6 oranında bulundu. En fazla başvuru sayısının ve pozitif sonucun 2024 yılında tespit edildiği görüldü. Tüm yıllarda HPV16 pozitifliğinin hastalarda en fazla gösterilen genotip olduğu bildirildi.*

Sonuç: *HPV enfeksiyonu ve onunla ilişkili kanserlerin önlenmesinde uygulanacak stratejilerin belirlenmesinde prevalans çalışmaları önemli veriler sunmaktadır. Ülkemizde tarama programlarının daha geniş kitleye ulaştırılması ve bu kapsamda çalışmalar yapılması gerekmektedir.*

Anahtar Kelimeler: *HPV tarama, HPV genotip dağılımı, servikal smear testi*

Corresponding Author: Nuri Çakır, Kayseri City Hospital, Department of Internal Medicine, Kayseri, Türkiye ***Email:*** nuricakir@gmail.com

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INTRODUCTION

Human papillomavirus (HPV) infection is known to be the most common sexually transmitted disease worldwide, causes cervical cancer, which can result in death (1). The virus, which ranks fourth in incidence and mortality in the world, is becoming increasingly common with 604,000 new cases in 2020 (2). Cervical cancer ranks ninth among cancers and third among gynecological cancers seen among women in Turkey (3).

HPV positivity means the virus causes cervical cancer and/or persistent HPV infection (4,5). Although HPV infections are mostly acquired in young adulthood, some adults are also at risk of contracting new HPV infections (5-7). It has been reported that there are 228 different HPV gene types and 40 of them cause infections in the genital mucosa (8). The types of HPV that infect the genital mucosa and their high oncogenic potential are listed as high-risk [HR-HPV (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)] or low-risk [LR-HPV (HPV6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81)] (9). Another classification was made according to their carcinogenicity (potentially carcinogenic, possibly carcinogenic, low and high risk HPV genotype), and HPV 16 and HPV 18 are at the top of the classification with high risk (2).

HPV screening programs vary depending on the target populations of countries. According to the 2019 Turkey report of the Catalan Oncology Institute and the International Agency for Research on Cancer, HPV-related diseases are stated as 4.2%-67.8% and HPV types 16-18 (9). In the meta-analysis study the prevalence of high-risk HPV was found to be 33.7% in black adults, while it was 11.9% in Asian adults (10). According to the national report in Turkey in 2021, the incidence of cervical cancer caused by HPV is 5.93/100,000; the mortality rate was found to be 2.92/100,000 (11).

The World Health Organization (WHO) recommends HPV-DNA-based molecular tests as primary screening tests. A HPV screening program progressed in 2014 with a revised HPV-DNA and HPV genotype screening algorithm (12). After the first results were published, it was understood that different high-risk types were also detected in our country (13). Therefore, with our study, we aimed to retrospectively investigate the frequency of HPV and the genotype distribution of HPV16, HPV18 and other 12 HR-HPV pools in women over the age of 18 who applied to our hospital's gynecology and obstetrics outpatient clinic and lived in our region, and thus to present molecular epidemiological data of our region.

MATERIALS and METHODS

For this study, an application was made to the Kayseri City Training and Research Hospital ethics committee and approval was received dated 05.11.2024 and numbered 234.

Our study included 1058 patients over the age of 18 who applied to the gynecology and obstetrics outpatient clinic of our hospital and whose cervical brush samples were collected between January 1, 2022 and October 1, 2024. Our study was planned to retrospectively evaluate the results of people whose cervical brush samples were previously taken, HPV-DNA screening was performed, and whose laboratory results were known. Presence of pregnancy, current infection, previous surgery, cancer medication, immunosuppressive drug usage, previous cervical cancer diagnosis were the criteria for exclusion from the study. 32 patients were excluded from the study according to these criteria. Totally 1026 patients were included. Real time PCR technic was used for the HPV-DNA analysis giving qualitative results.

The samples were accepted as cervical brush samples in PreservCyt® solution, and all samples were delivered to the laboratory and kept in the laboratory at +2/+8°C until the studies were carried out. HPV genotyping was performed using the Cobas 4800 fully automatic analyzer (cobas® x480) and real-time PCR (Cobas® z 480) system in accordance with the manufacturer's instructions. After valid studies with the Cobas® 4800 system, three different results were obtained against 14 different high-risk HPV genotypes. These were: HPV16 alone, HPV18 alone, and 12 other HR-HPV pool (dHR-HPV) genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). In addition to the use of positive and negative controls in each study by the fully automated system, the presence of cellular status beta globin in the sample was detected as an internal control and the validity of all these data was checked by automatic analysis. The distribution of detected HPV genotypes was analyzed according to age groups and years. These results were obtained by retrospective scanning from the hospital data system.

RESULTS

HR-HPV positivity was detected in 32 (2.08%) of 1026 female patients aged 19-49 included in our study, as HPV16, HPV18 or one of the other 12 HR-HPV positivity results. While only a single dHR-HPV positivity was detected in all samples examined in our study, positivity was also detected with more than one HPV genotype in patients. When the distribution of patients in different age groups was examined, it was seen that the 30-39 age group was admitted to the hospital more than other age groups. When the distribution of HR-HPV positivity was examined by age groups, it was seen that positivity was most common in the 35-44 age group (Table 1). In positive patients, HPV16 positivity was detected in 1.4% of the patients, while HPV18 positivity was found in 0.9% and other 12 HR-HPV genotype positivity was found in 0.6%. When hospital admissions and HPV genotype positivity are examined by year, it is seen that the highest number of applications and positivity were detected in 2024. It was reported that HPV16 positivity was the most frequently demonstrated genotype in patients in all years (Table 2).

Table 1. HPV genotype distributions by age groups of patients.

Age	Negative (n / %)	HPV positive (n / %)	HPV16 (n / %)	HPV18 (n / %)	oHR-HPV (n / %)	HPV16/45 (n / %)
<25	41 / 100	-	-	-	-	-
25-29	206 / 100	-	-	-	-	-
30-34	229 / 91.8	5 / 2.1	2 / 0.81	3 / 1.2	-	-
35-39	238 / 94.1	14 / 5.7	6 / 2.4	5 / 2	1 / 0.4	2 / 0.8
40-44	151 / 93.4	10 / 6.2	5 / 2.9	2 / 1.1	1 / 0.5	2 / 1.1
45-49	161 / 98.1	3 / 1.8	2 / 1.2	-	1 / 0.6	-

HPV: *Human papillomavirus,* ***oHR-HPV:*** *other high risk HPV*

Table 2. HPV genotype distribution of patients by years

Years	Negative (n / %)	HPV positive (n / %)	HPV16 (n / %)	HPV18 (n / %)	oHR-HPV (n / %)	HPV16/45 (n / %)
2022	202 / 97.1	6 / 2.8	2 / 0.9	2 / 0.9	-	2 / 0.9
2023	390 / 96.9	12 / 3	4 / 10.2	2 / 0.5	6 / 1.5	-
2024	434 / 96.7	14 / 3.2	5 / 1.0	3 / 0.6	4 / 0.8	2 / 0.4
Total	1026 / 98.2	32 / 2.8	11 / 1	7 / 0.6	10 / 0.9	4 / 0.3

HPV: *Human papillomavirus,* ***oHR-HPV:*** *other high risk HPV*

DISCUSSION

Cervical cancers may be associated with HPV infections, especially HR-HPV and various HPV genotypes. In addition to HPV infections, other factors affecting the development of cervical cancer include age, hormonal contraceptive use, smoking and alcohol consumption (13).

There are similar studies on this subject in the literature. In the study of Mosmann et al. in 2021, they showed that there was an 18% HPV positivity rate as a result of screening (14). Jaworek et al. reported that they detected HPV-DNA in 21% of the samples in their 1198 cervical swab comparison study (15). In our study, it was observed that at least one HR-HPV genotype was detected in 32 of our patients (2.8%). HPV prevalence varies with age. The highest prevalence rate is seen between the ages of 20-24. The prevalence decreases in middle age groups, but an increase is observed in women aged 35-44 or 45-54 (we saw that positivity was most common in the 35-44 age group (Table 1). In the study of Smolarz et al. on 280 cervical samples in Poland, they reported that they detected HPV16 in 20%, HPV18 in 14%, and 12 other HR-HPVs in 33% (16). The study of Wang et al. in China with 5650 patients, the genotype distribution was 2.25% for HPV16, 0.5% for HPV18, and 9.15% for the other 12 HR-HPVs (17). In patients with abnormal cytology, the highest HPV type was HPV type 16 with 45.0%, followed by HPV type 18 with 20.0% (17). In our study, it is compatible with the most frequently encountered genotypes, with HPV16 at 46% and HPV18 genotype at 31%.

Although the distribution of HPV genotypes varies significantly around the world due to the patient's immuno-genetic factors, geographical characteristics, the use of different diagnostic methods and the fact that studies are generally conducted on a limited number of patient groups, it is stated that the most common type is HPV16, followed by different types. In our study, the most common genotype was found to be HPV16.

There are studies on HPV prevalence and genotype distributions in different geographical regions and time periods in our country (1,18-21). Peker et al. reported their resuls of İzmir Katip Çelebi University hospital datas as 18.6% HPV-DNA positive (1). Aydemir et al. reported their HPV-DNA positivity as 21.1%, Dursun et al. reported as 25% and Aydoğan et al.reported as 22.7% (18,20,21). The most comprehensive study in Turkey is the study conducted by Gültekin et al. (22). In this study containing data from more than one million patients included in the HPV-DNA screening program, it was stated that the prevalence for all HR-HPV types was 4.39% (22). HPV prevalence varies with age. The highest prevalence rate is seen between the ages of 20-24. Although the prevalence decreases in middle age groups, an increase is also observed in women aged 35-44 or 45-54 (1,19). The increase in older age groups in some regions may be associated with activated latent HPV infections. In our study, HPV prevalence was highest in the 35-44 group and was found to be compatible with the data in previous studies (19). Erickson et al. examined the relationship between age and HPV prevalence and it was reported that the detection of additional infection after the age of 30 was low, and HPV16 and 18 genotypes were most common in this age group. While the highest positivity rate for HPV16 is 27.3% in the 60-65 age group but no data was found in this age group in our study.

Conclusion

The HR-HPV DNA positivity rate in the patient group analyzed in our study was 2.8%. HPV positivity rates are increasing in young and older age groups. Prevalence studies provide important data in determining strategies to prevent HPV infection and its related cancers. We understand that HPV type 16 is a very important factor in terms of the frequency of precancerous lesions, that with national cancer screenings, many people are diagnosed at an early stage or while they still have a precancerous lesion, and how vital this is. Cervical cancer screening is recommended for women between the ages of 30 and 65 in every five years. In this context, it is necessary to make screening programs available to a wider audience and to carry out studies in this context in order to screen 20% of the target population every year.

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