

Evaluation of HPV Screening Results Between 2017-2022 in Bursa Province

Bursa ili 2017-2022 Yılları Arası HPV Tarama Sonuçlarının Değerlendirilmesi

Salih METİN¹, Ahmet TİMUR¹

¹Bursa Provincial Health Directorate Public Hospitals Services Presidency, Bursa Türkiye

Yazışma Adresi / Correspondence:

Salih METİN

Bursa Provincial Health Directorate Public Hospitals Services Presidency, Bursa Turkey
E-mail : slhmtn@hotmail.com

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Salih METİN <https://orcid.org/0000-0003-1582-7900> slhmtn@hotmail.com

Ahmet TİMUR <https://orcid.org/0000-0002-6284-4677> dratimur@gmail.com

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Abstract

Introduction In our country, within the scope of the community-based cancer screening program in primary health care institutions, HPV and Pap smear tests are applied between the ages of 30 and 65 for cervical cancer screening, and is repeated every 5 years. This study aims to analyze the cervical cancer screening test results and define the prevalence of HPV genotypes in our province to provide preventive strategies for public health.

Materials and Methods In the study, cervical cancer screening tests taken between January 2017 and August 2022 in primary health care institutions and Cancer Early Diagnosis and Screening Training Centers (KETEM) in Bursa were evaluated using the Public Health Management Systems (HSYS) database.

Results A total of 118865 tests taken from women aged 30-65 years were evaluated for cervical cancer screening in primary care in Bursa province. The mean age of the women in the study was 46.19±9.06, and the prevalence of HPV was calculated as 5.6% in the samples taken. More than one HPV type was positive in some cases, and the most common type detected in the study was HPV16 (25.6%). A total of 89.6% of HPV were high-risk types. The frequency of abnormal cytological findings was 56.8% and high-risk HPV was 90.6% in the 30-44 age group; the frequency of abnormal cytological findings was 27.5% and high-risk HPV was 88.4% in the 45-54 age group and the frequency of abnormal cytological findings was 15.7% and high-risk HPV was 88.7% in the 55-65 age group and these were statistically significant (p=0.019 ve p=0.001).

Conclusion HPV screening and sampling in high-risk species for the early diagnosis of cervical cancer are an increasingly continuing strategy in our country and around the world. Despite the different frequencies of HPV types reported from many provinces of our country and around the world, HPV 16 and 18 are the most common factors to cause cancer increase the importance of HPV vaccination. Each region should conduct its own prevalence study, determine the most common cervical cytology, age group and HPV types to constitute the first step in determining the precautions for high risk populations.

Keywords HPV screening program, human papillomavirus, cervical cytology, pap smear,

Özet

Amaç Ülkemizde birinci basamak sağlık kuruluşlarında, toplumsal tabanlı kanser tarama programı kapsamında, kadın kanserleri arasında önemli bir yere sahip olan serviks kanserinin taranması amacıyla 30 ile 65 yaş aralığındaki kadınlara eş zamanlı HPV ve Pap-smear testi uygulanmakta ve her 5 yılda bir tekrarlanmaktadır. Bu çalışmanın amacı ilimizdeki servikal kanser tarama örneklerindeki HPV genotiplendirmesi ve sitolojik bulguların incelenmesi ve yüksek riskli tiplerin tespit edilerek toplum sağlığını korumak için önlem alınmasını sağlamaktır.

Gereç ve Yöntem Çalışmada Bursa geneli birinci basamak sağlık kuruluşları ve Kanser Erken Teşhis ve Tarama Eğitim Merkezlerinde (KETEM) serviks kanseri taraması amacıyla Ocak 2017- Ağustos 2022 arasında alınmış pap-smear ve HPV testleri Halk Sağlığı Yönetim Sistemleri (HSYS) veri tabanı kullanılarak değerlendirilmiştir.

Bulgular Bursa il genelinde birinci basamakta serviks kanseri taraması amacıyla 30-65 yaş aralığındaki kadınlardan alınmış 118865 tarama sonucu değerlendirilmiştir. Çalışmadaki kadınların yaş ortalaması 46,19±9,06 olup, alınan numunelerde HPV prevalansı %5,6 olarak hesaplanmıştır. Bazı olgularda birden fazla HPV tipi pozitif olmakla birlikte, çalışmada en sık tespit edilen tip HPV16 (%25,6) olarak bulunmuştur. HPV pozitif olguların %89,6'sı yüksek riskli HPV idi. 30-44 yaş grubunda anormal sitolojik bulgu saptanma sıklığı %56,8, yüksek riskli HPV saptanma sıklığı %90,6; 45-54 yaş grubunda anormal sitolojik bulgu saptanma sıklığı %27,5, yüksek riskli HPV saptanma sıklığı %88,4 ve 55-65 yaş grubunda anormal sitolojik bulgu saptanma sıklığı %15,7, yüksek riskli HPV saptanma sıklığı %88,7 olup yaş grupları arasında istatistiksel anlamlı fark mevcuttu (p=0,019 ve p=0,001).

Sonuç Kadınlar için önemli bir halk sağlığı sorunu olan serviks kanserinin erken teşhisi için HPV taraması, yüksek riskli türlerde biyopsi yapılması ülkemizde ve dünya genelinde artan şekilde devam etmektedir. Ülkemizin birçok ilinden ve dünya genelinden bildirilen HPV türlerindeki farklı sıklıklarına rağmen kansere yol açtığı bilinen HPV 16 ve 18 en sık görülen etken olması HPV aşısının önemini bir kat daha artırmaktadır. Her bölgenin kendi prevalans çalışmasını yapması en sık görülen servikal sitoloji, yaş grubu ve HPV etkenlerini belirlemesi riskli popülasyonlarda alınacak tedbirlerin belirlenmesinde ilk aşamayı oluşturmaktadır.

Anahtar Kelimeler

HPV tarama programı, insan papillomavirüs, pap smear, servikal sitoloji

INTRODUCTION

Cervical cancer constitutes 10% of cancer cases seen in women all over the world (1). Moreover, it is known to be the second most common cancer in women and the third most common cause of cancer-related deaths.

Human Papillomavirus (HPV) is detected in %10 of normal vaginal flora and does not cause carcinogenic changes. Besides this, it is clearly elucidated that it initiates oncogenic transformation and completes this transformation in 5-10 years in some cases. This transformation to cervical cancer is related to HPV genotype, age, sociodemographic features, multiple partners, poor hygiene, and other immunosuppressive conditions (1). Due to the long latency period and different effects on cancer, HPV genotyping became important in cervical cancer screening programs (2,3).

HPV genotypes are divided into two main groups as low risk and high-risk groups. While 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 genotypes are accepted as high-risk types, genotypes 6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73, 81 are accepted as low-risk types (4). Although high and low-risk types are accepted all over the world, the most common type that causes carcinogenesis changes regionally. For example, type 16 is claimed to be the most common type of carcinogenesis in Sub-Saharan Africa, and type 52 is claimed in Europe and America (2). This condition has attracted the attention of researchers to study the prevalence and subtype discrimination locally and regional studies have gained value.

Considering that cervical cancer is detected in nearly 530 thousand every year and 50% of these cases die, screening strategies draw attention worldwide. With the screening program for cervical cancer initiated by WHO in 2007, cervical cancer-related morbidity and mortality have tragically decreased worldwide. Then, all countries have integrated this screening program into their health systems. In 2009, screening of women between 30-65 years with HPV genotyping and pap-smear test every 5 years until two consecutive negative results are detected was accepted as our screening policy (5,6,7).

In this study, we aimed to analyze the cervical cancer screening test results and define the prevalence of HPV genotypes in our province.

MATERIAL and METHODS

The present study was approved by the ethics committee of Bursa City Hospital (decision number 2022-13/4) and written permission was taken from Bursa Provincial Health Directorate (barcode no 00175437745, date 07/10/2022).

According to 2021 TUIK data, the number of women between the ages of 30-65 living in Bursa is 766862. Within the scope of the community-based cancer screening program in primary health care institutions in our country, the HPV and Pap-smear test is applied to women between the ages of 30 and 65 and repeated every 5 years in order to screen for cervical cancer, which has an important place among female cancers. HPV Test and Pap-Smear Test are taken at the same time. For HPV test; a sample is taken with a DNA brush and placed in the DNA material tube. For Pap-Smear test; a sample is taken with a smear brush, spread on the lama (and a fixative spray is sprayed on it) and the slide is placed in the transport container. The samples taken are collected and sent to the HPV laboratory established in Ankara through the District Health Directorates. Evaluations are completed within 10 days after the samples are delivered to the laboratory. First, the HPV Test is evaluated. With the HPV test; 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 68, 70, 72, 73, 81, 82, 83, 84, 85, 89 types are studied. HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 types were evaluated as high-risk HPV types (HRHPV). When HPV is detected as positive, its cytology is evaluated with Pap-Smear test. If the HPV Test is negative in a healthy person, the screening program is continued with the test repeated every 5 years. Atypical Squamous Cells of Undetermined Significance (ASC-US), Low Grade Squamous Intraepithelial Lesion (LGSIL), Atypical Squamous Cells-cannot Exclude High-Grade Squamous Intraepithelial Lesion (ASC-H), Atypical Glandular Cells (AGC), and

Table 1. Evaluation of numerical characteristics of these in terms of this type between 1970-2021 in Turkey

	n	%	Mean age ± SD	Min-Max
HPV -	112240	94.4	46.30±9.06	30-65
HPV +	6625	5.6	44.41±8.82	30-65

Table 2. The distribution of HPV Types by Age Groups

HPV Type	Age Groups						Total	
	30-44		45-54		55-65		n	%
	n	%	n	%	n	%		
HPV16	996	27.8	479	23.7	221	21.7	1696	25.6
HPV51	520	14.5	295	14.6	153	15.0	968	14.6
HPV31	423	11.8	226	11.2	135	13.2	784	11.8
HPV52	386	10.8	216	10.7	98	9.6	700	10.6
HPV66	374	10.4	203	10.1	107	10.5	684	10.3
HPV53	294	8.2	209	10.4	124	12.2	627	9.5
HPV56	247	6.9	180	8.9	107	10.5	534	8.1
HPV68	264	7.4	166	8.2	84	8.2	514	7.8
HPV39	283	7.9	151	7.5	74	7.3	508	7.7
HPV18	260	7.2	121	6.0	71	7.0	452	6.8
HPV59	235	6.5	134	6.6	75	7.4	444	6.7
HPV58	205	5.7	129	6.4	84	8.2	418	6.3
HPV35	225	6.3	99	4.9	67	6.6	391	5.9
HPV45	176	4.9	91	4.5	29	2.8	296	4.5
Other	675	18.8	407	20.2	244	23.9	1326	20.0

*row percentage used

High Grade Squamous Intraepithelial Lesion (HGSIL) are grouped as “abnormal cytology”.

For the sample size of 5% HPV prevalence; 95% reliability was calculated as 1824 people with $\alpha=0.01$ margin of error. In the study, smear test of 118,865 samples taken between January 2017 and August 2022 for cervical cancer screening in primary health care institutions and KETEM in Bursa were evaluated using the Public Health Management Systems (HSYS) database.

Statistical analysis

The Shapiro-Wilk test was used to assess the distribution of variables. Thus, the continuous variables distributed normally, these variables were presented with mean \pm standard deviation. Categorical variables were expressed as frequency and percentages. Chi-square test was used to compare categorical data, and $p<0.05$ value was considered statistically significant. The analyses were performed with the SPSS 20.0 software.

RESULTS

In the present study, a total of 118865 cervical smear screening test results taken from women aged 30-65 years in

primary care between January 2017 and August 2022 across the province of Bursa were evaluated. The mean age of the participants was 46.19 ± 9.06 years, and the prevalence of HPV was 5.6% in the samples (Table 1).

More than one HPV types were positive in some cases. The most common type detected in our study was HPV16 (25.6%). The distribution of common HPV types by age group is shown in Table 2.

The cytological evaluations of those with positive HPV results were evaluated as 48% normal, 27.6% infection findings, 15.2% insufficient material, 6% ASCUS. The results are shown in Table 3.

Among all HPV-positive cases, the percentage of those with at least one HR-HPV subtype was found to be 89.6%. When this percentage was evaluated according to age groups, it was found to be 90.6% in the 30-44 age group, 88.4% in the 45-54 age group, and 88.7% in the 55-65 age group. There was a statistically significant difference in terms of HPV subtypes according to age groups ($p=0.019$) (Table 4).

When cytological examinations of HPV positive individuals were evaluated, 48% were normal, 27.6% had infe-

Table 3. Cervical Cytology Results

Cervical Cytology Results	n	%
Normal	3180	48.00
Infection findings	1831	27.62
Insufficient material	1005	15.20
ASCUS	399	6.02
LGSIL	175	2.64
ASC-H	20	0.30
AGC	14	0.21
HGSIL	1	0.01
Total	6625	100.00

ction findings, 15.2% were insufficient material, 6% were ASC-US, 2.6% were LGSIL, 0.3% were ASC-H, 0.2% were AGC, 0.01% were HGSIL. HR-HPV and LR-HPV of normal and abnormal cytology results are shown in Table 5. The distribution of cytology results according to HPV subtypes and ages is shown in Table 6. Abnormal cytology findings are seen in 43.8% of individuals infected with HR-HPV types, while this rate is 40.3% in individuals infected with LR-HPV types. The difference is not statistically significant ($p=0.113$). The rate of abnormal cytological findings in the 30-44 age group was 56.8%; 27.5% in the 45-54 age group; 5.7% in the 55-65 age group, and the difference between all groups is statistically significant ($p=0.001$) (Table 6).

DISCUSSION

The present study showed that HPV positivity rate was 5.6% in our province. In a study conducted in Adana in 2011, the positivity rate was 5.2% (8), in a study conducted in Sivas in 2014, the positivity rate was 6.4% (9), in a study conducted in Van in 2015, the positivity rate was 2.4% (10). In a study conducted in Amasya, the positivity rate was 4.2% (11), in a study conducted in Kayseri in 2018, the positivity rate was 4.16% (12), and in a study conducted in Çorum in 2019, the positivity rate was 3.5% (13).

In a study conducted on HPV results of 1 million women across Turkey in 2018, the positivity rate was 3.5% (7). In studies conducted on women with their sociodemographic structure and changing risk factors in many provinces, positivity rates ranging from 2.4-6.4% have been reported in the literature reported in our country since 2011. We attribute the fact that the HPV positivity rate in our study was found among the positivity rates reported in our country, because the cervical cancer screening target group was of similar age and sociodemographic structure. The prevalence of HPV in the general population varies geographically from country to country. The rates reported from studies conducted in the world vary within a wide margin between 2-44%. The lowest prevalence was reported in Asia while the highest prevalence was reported in Africa (8). Based on the largest population study conducted in our country, the prevalence of HPV is 3.5%, and it is among the countries with the lowest prevalence in the world (7). We attribute this to the fact that there is only one sexual partner socioculturally, that more than one sexual partner is not accepted by the society, and that HPV transmission is low.

In our study, the prevalence of HR-HPV was found to be 7.2%. This rate is higher than the rate of 3% previously reported from Adana in our country (8). In studies condu-

Table 4. HPV Subtypes according to Age Groups

Age groups	HPV subtype				X ²	P
	HR-HPV		LR-HPV			
	n	%	n	%		
30-44	3251	90.6	337	9.4	7.878	0.019
45-54	1784	88.4	234	11.6		
55-65	904	88.7	115	11.3		
Total	5939	89.6	686	10.4		

Table 5. The Distribution of Cytology Results According to HPV Subtype

Cervical Cytology Results	HPV subtype				TOTAL
	HR-HPV		LR-HPV		
	n	%	n	%	
Normal	2842	89.4	338	10.6	3180
Infection Findings	1659	90.6	172	9.4	1831
Insufficient Material	885	88.1	120	11.9	1005
ASC-US	363	91.0	36	9.0	399
LGSIL	156	89.1	19	10.9	175
ASC-H	20	100.0	0	0.0	20
AGC	13	92.9	1	7.1	14
HGSIL	1	100.0	0	0.0	1

cted in various countries of the world, the prevalence of HR-HPV was reported to be between 4.8-19.7% (14-16). Our study is consistent with the literature. The most common type among HR-HPVs is HPV 16 with a prevalence of 19.7%, which is similar to our country and literature (8, 14-16). The fact that the most dominant type is HPV 16, but the other types show variation in the ranking, shows how important geographical studies in HPV infections are. The fact that HPV 16 and 18 are the most common agents both in HR-HPVs and in the population with risky cytology reveals the importance of the vaccine containing 16 and 18 types against infections caused by HPV in women who are at risk of cervical cancer.

HPV DNA testing is recommended by many countries and official institutions such as WHO as primary prevention for cervical screening. In the study published by the cervical swab results of one million women in our country, HPV 16, HPV 51, HPV 31, and HPV52 were the four most common types (7). The four most common HPV agents in our study show similarities with this study, which includes a sample of the whole country.

In our study, cervical cytology was found to be 48% nor-

mal, 27.6% infectious, 15.2% insufficient material, 6% ASCUS, 2.6% LGSIL, 0.3% ASC-H, 0.21% AGC, 0.01% HGSIL. In a study previously reported from our country, cytology was reported as 36.2% normal, 17.9% infectious, 14.3% insufficient material, 18.8% ASCUS, 8.9% LGSIL, 1.3% ASC-H, 1.8% AGC, 0.9% HGSIL (17). We attribute the lower abnormal cytology in our study to the sociodemographic difference of the province where our study was conducted. In a study conducted in China, 5.5% abnormal cytology results were reported in pap-smear results (18). In a similar study conducted in Kayseri, the rate of abnormal cytology was reported to be 10.6%. The results of this study conducted in Kayseri and our study are similar (19), we attribute the similar results to the socio-cultural structure of Kayseri as a metropolis like Bursa and the fact that it was conducted in a large primary care-based sample.

When the cases with abnormal cytology were distributed according to age, it was found that the highest rate was between the ages of 30-44, and the number of patients with abnormal cytology decreased with advancing age. In a study reported from our country, it was reported that 39% of patients with abnormal cytology were in the 30-39

Table 6. The Distribution of cytology results according to HPV subtypes and ages

	CYTOLOGY				Total	X ²	p
	Normal		Abnormal				
	n	%	n	%			
HPV Subtype							
HR-HPV	2842	56.2	2212	43.8	5054	2.516	0.113
LR-HPV	338	59.7	228	40.3	566		
Total	3180	56.6	2440	43.4	5620		
Age Groups							
30-44	1766	55.5	1385	56.8	3151	15.002	0.001
45-54	1002	31.5	672	27.5	1674		
55-65	412	13.0	383	15.7	795		

age range (13). The excess of abnormal cytology in this age group suggested that the most common detection of HPV in the 4th decade may be due to the sexually active age.

CONCLUSION

HPV screening and sampling in high-risk species for the early diagnosis of cervical cancer are an increasingly continuing strategy in our country and around the world. Despite the different frequencies of HPV types reported from many provinces of our country and around the world, HPV 16 and 18 are the most common factors to cause cancer increase the importance of HPV vaccination. Each region should conduct its own prevalence study, determine the most common cervical cytology, age group and HPV types to constitute the first step in determining the precautions for high risk populations.

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