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Araştırma

VAN ŞEHRİNDEKİ KADINLARDA HUMAN PAPİLLOMA VİRUS (HPV) SIKLIĞI, TİPLERİ VE SİTOLOJİ SONUÇLARI

PREVALENCE, TYPOLOGY AND SMEAR CYTOLOGY RESULTS FOR HUMAN PAPILLOMA VIRUS (HPV) IN WOMEN OF THE CITY OF VAN

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ÖZET

Amaç: Van ilinde yapılan servikal smear ve hpv taramaları sonrasında, hpv pozitif çıkan olguların hpv tiplerini ve yaygınlığını belirlemek ayrıca bu olguların smear sonuçlarını değerlendirmek amaçlı geriye dönük bir araştırma yapılmıştır.

Hastalar ve Yöntem: Van ili KETEM (Kanser Erken Teşhis Tarama ve Eğitim Merkezi) Ağustos 2014 ve Temmuz 2015 tarihleri arasında 4243 olgunun servikal smear ve HPV taramaları yapılmış ve HPV pozitif çıkan olguların HPV tiplendirilmesi ve yaygınlığı ayrıca aynı olguların smear sonuçları incelenmiştir.

Bulgular: 4243 kadın tarandı. 3967 kişi HPV Negatif (93.5%),102 kişi HPV Pozitif(2.4%), 174 kişinin sonucu ise yetersiz materyal şeklindeydi. Buna göre HPV pozitifler incelendiğinde; sadece HPV 16 ile enfekte 16 kişi (15.69%), sadece HPV 18 ile enfekte 5 kişi (4.9%) enfekte iken HPV 16 ve 18'in beraber enfekte ettiği kişi yoktu.HPV 16 ve diğer tip HPV ile enfekte 10 kişi (9.8%), HPV 18 ve diğer tip HPV ile enfekte 1 kişi (0.98%) saptandı.Diğer tip HPV'lerle (31,33,35,39,45,51,52,56,58,59,68) enfekte kişi sayısı 70 (68.63%) idi. HPV pozitif kişilerin smear sonuçları incelendiğinde ise; 56 kişide non spesifik enfeksiyon(54.90%), 25 kişide LGSIL (24.51%), 4 kişide normal smear bulguları (3.92%), 8 kişide yetersiz material (3.92%) saptandı ayrıca hiç bir olguda ASGUS bulgusuna rastlanmadı.

Sonuç: Servikal sitoloji taramaları yaygınlaştırılmalı ve riskli olgular prekanseröz lezyonların ve servikal kanser yaygınlığının azalması için aşılanma programlanmalıdır.Tüm gelişmiş ülkelerde olduğu gibi ülkemizde de geniş çaplı çalışmalarda HPV'nin servikal kanserle ilişkisi gösterilmiştir.Ülke genelinde yapılan HPV DNA teşhisi ve anormal sitoloji sonuçlarının takibi ülke genelinde servikal kanser risk haritasının belirlenmesine yardımcı olacaktır ve bu erken safhada yakalanan hastaların başarılı bir şekilde tedavi olmasına imkan verecektir.

Anahtar Kelimeler: HPV DNA; Servikal Sitoloji; Servikal Kanser; HPV 16.

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ABSTRACT

Objective: Introducing and retrospectively determining cervical HPV types and prevalence of the women in VAN in order to detect smear findings in those with HPV positive.

Material and Method: Cervical HPV typology and prevalence determination of 4243 women scanned by VAN KETEM (Center for cancer early diagnosis, scanning and training) between the dates of August 2014 and July 2015; HPV-positive samples were retrospectively analyzed to determine smear results.

Findings: 4243 women were scanned. Smear results of 3967 of them were HPV-negative (93.5%), 102 of them were HPV-positive (2.4%) and 174 of them were inconclusive (4.1%). Accordingly, in samples with HPV-positive, only HPV type 16 was detected in 16 people (15.69%) while 5 people (4.9%) carried only HPV type 18. There were no samples carrying HPV type 16 and 18 together however, there were 10 people carrying HPV type 16 and other types (9.8%). There were 1 sample carrying HPV 18 and other types together (0.98%).Number of samples with other HPV types (31,33,35,39,45,51,52,56,58,59,68) was 70 (68.63%). When cytological examinations were made in HPV-positive samples, there were 56 nonspecific infections (54.90%), 25 LGSIL (24.51%), 0 ASC-US (0%), 4 normal smears (3.92%) and 8 cases were determined inconclusive (7.84%).

Results: Cervical cytology scanning programs must become more widespread and vaccination must be scheduled with women of risk group in order to decrease precancerous lesions and cervix cancer rates. Expanded and improved studies have demonstrated the HPV subtype cervical cancer and HPV relationship in the most developed countries as like as our country. While HPV DNA identification and abnormal cytology findings are followed by KETEMs throughout the country to assist creating the cervix cancer risk map, this will enable determination of new patients and successful treatment at early stages.

Key Words: HPV DNA; Cervical Cytology; Cervical Cancer; HPV 16.

INTRODUCTION

Cervical cancer is the second most common type of cancer among women worldwide and is one of the major reasons for deaths due to gynecological cancers. Based on the 2006 data of World Health Organization, it is reported that a total of 510.000 new cervix cancer cases were diagnosed across the globe and 288.000 of them died due to cervix cancer (1). According to a study in Turkey, published in 2003 by the Cancer Control Department of the Ministry of Health of the Republic of Turkey which can be seen as the closest data to represent the Turkish population, cervical cancer was the 10th in frequency in all women's cancers and its incidence was 4.76 per hundred thousand. According to this study's results; the incidence of cervical cancer in Turkey seems to be well below that of many countries which implement well-developed national screening programs (2).

In Turkey, studies on HPV infections are made in specific group and populations, so it is difficult to identify the real prevalence. However, when these studies were examined, it is assumed that the prevalence is between 2 to 6% (3-7).

Human papillomavirus (HPV) is considered as an etiological agent in many cancer types, notably anogenital and head-neck cancers (8-10). Today, there are over hundred types of HPV were determined; 40 of which infect the anogenital zone. It is determined that 15 of them (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68,73, 82) have high oncogenic risk, 3 types (26, 53, 66) have medium risk and 12 types (6, 11, 40, 42, 43, 44, 54, 61, 70, 72,81 and 89) have low risk (11,12). Cervix cancer is the seventh most prevalent cancer type of all cancer types and the second of all women cancer types (13). It is considered that infections resulting from oncogenic HPV types are involved in etiopathogenesis of almost all cervix cancer types and precancerous lesions (11, 14 and 15) and especially HPV types 16 and 18 may be accounted for 70% of all cervix cancers (11). In early diagnosis and treatment of cervix carcinoma and precancerous lesions, determination of HPV DNA and HPV typology are important in addition to cytological scanning tests (15). In determination of HPV DNA, the most specific and accurate methods are PCR and DNA amplification (12). In our study, HPV DNA's existence and HPV types were investigated in cervical swab samples of a specimen that was selected randomly in the city of VAN.

MATERIAL AND METHODS

During cervical smear cytology scanning study conducted by KETEM from August 2014 to April 2015 in the city of VAN, 4243 women were scanned. Cervical HPV test genotypology was performed in this study and smear results of 3967 of the cases were HPV-negative (93.5%), 102 of them were HPV-positive (2.4%) and 174 of the results were inconclusive (4.1%) (Figure 1).

In HPV-positive samples, cervical samples were cytologically examined as well as polymerase chain reaction (PCR) method for HPV typology was used. In HPV-negative samples, cervical cytology and HPV DNA examination were not conducted. Accordingly, in samples with HPV-positive, only HPV type 16 was detected in 16 women (15.6%) while 5 women (4.9%) carried

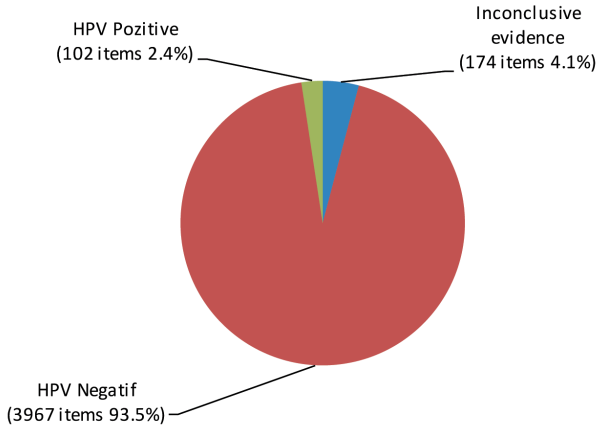

Figure 1 • HPV PCR results of 4243 cases scanned.

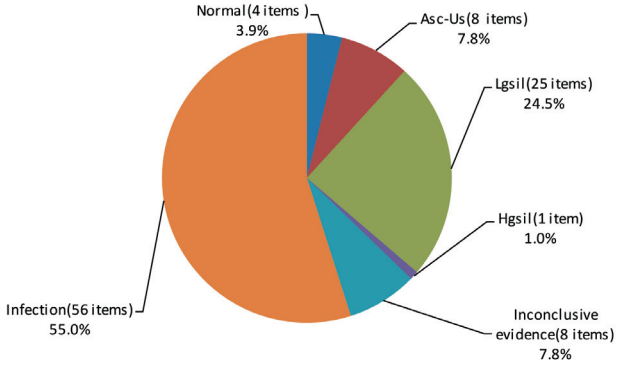

Figure 3 • Cytology results of cases with HPV PCR positive.

only HPV type 18. There were no samples carrying HPV type 16 and 18 together however, there were 10 people carrying HPV type 16 and other types (9,8%). There was no sample carrying HPV 18 and other types together. Number of samples with other HPV types (33, 33,35,39,45,51,52,56,58,59,68) was 70 (68.6%) (Figure 2).

When cytological examinations were made in HPV-positive samples, there were 56 nonspecific infections (55.0%), 25 LGSIL (24.5%), 1 HGSIL (1.0%), 8 ASC-US (7.8%), 4 normal smears (3.9%) and 8 cases were determined inconclusive (7.8%) (Figure 3).

DISCUSSION

Cervical cancer is the fourth most common type of cancer among women worldwide (16).The average age at diagnosis is 51 in cervical cancer patients, incidence peaking at two periods of age namely, 35–59 and 60–64 (17). Initiation of sexual intercourse at an early age, multiple sexual partners, low socioeconomic status, smoking, vitamin deficiency, and human papillomavirus (HPV) infection are well-established risk factors for cervical cancer (18, 19).

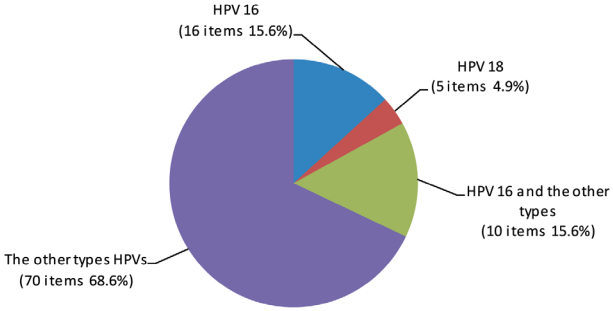

Figure 2 • HPV PCR positive cases by HPV types.

Genital HPV infection is the most prevalent STD in the world and HPV presence was detected in 99, 8% of all cervical cancer cases. HPV infection may cause anogenital condiloma, preinvasive cervical lesions and invasive cervical cancer (20-23). HPV has over 100 subtypes and over 15 of them (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66…) were found associated to cervical and other cancer types. Types 16 and 18 are the most high-risk HPV types and were isolated in almost 70% of all cervical cancer cases. Types 6 and 11 can only cause genital condiloma. Although 5-40% of women are infected with HPV, it is asymptomatic (23-26). In a study conducted by Kjaer et al., cervical cytological scanning results were evaluated in 11.617 cases and it was reported that 94% of women have normal cervical cytology; this rate was 93,5% in our study. 4,3% of women had LSIL and 1,6% had HSIL. HPV type 16 was reported as the most observed (6%) HPV subtype (27). This result matches on our findings in this study. HPV was determined in 53,2% of HSIL cases while HSIL wasn't detected in our study. In a study conducted by Bhatla et al. it was reported that 7,6% of women with normal cervical cytology; 42,3% of women in LSIL and 87,5% of HSIL cases had HPV (28). In a study where 644 HPV-positive patients were examined in İzmir region, it was reported that 546 cases had normal cervical cytology, 96 patients had abnormal cervical cytology and 78,3% of all HSIL cases had HPV infections (29).Based on the data obtained from International Association for Cancer Research (IARC), the most prevalent HPV genotypes observed in cervical cancers are: HPV16 (53%), HPV18 (15%), HPV45 (9%), HPV31 (6%) and HPV33 (3%). In a study of Munoz et al., HPV 16 was generally prevalent however; HPV 18 was especially prevalent in south eastern Asia countries (30).

The study conducted by P. Dursun, A. Ayhan et al. retrospectively examined 6388 patients admitted to 12 centers and for which smear and HPV analyses were conducted. Analyzed as a group, 25% of the patients were HPV-positive whereas in our study this rate was 3%. While HPV-positiveness in those having abnormal cytology was 57%, HPV-positiveness in normal pap test was 27%. HPV-positiveness was 37%, 9%, 27%, 20%, 22% and 41% for ASCUS, ASC-H, LSIL, HSIL, glandular abnormalities and squamous-cell carcinoma respectively. In our study, ASCUS rate was 8%, LSIL 24%, nonspecific infection rate was 55%. The most prevalent HPV types were HPV 16 (16%), HPV 18 (5%), HPV 16 with the other types (10%), HPV 18 with the other types (1%) and the other types HPV 68% (31).

According to the study conducted by Ozalp et al., 26 out of 615 patients (4%) were HPV-positive. 12 out of these 26 patients had HPV 16, 3 of them had HPV 18, 3 had HPV 51, 2 had HPV 6, 1 had HPV 52, 1 had HPV 33, 1 had HPV 16 and 31, 1 had HPV 6 and 52, 1had HPV 56 and 90, 1 had HPV 39 and 66.HPV DNA positive was found in four cervical cancer patient as well as 3 out of 4 patients with CIN III. HPV DNA was negative in 41 patients with the following cytological findings: 35 items ASCUS (5,6%), 4 items AGUS (0,6%), 2 items CIN I (0,3%). These 41 patients with abnormal cytological results were performed cervical biopsy accompanied with colposcopy, 3 items CIN I, 1 item CIN III and benign findings (inflammation, chronic cervicitis) were observed in others. In a study including 4122 cases, Bozkurt (32) reported chronic non-specific inflammation in 90.5%, ASCUS in 4%, HSIL 0.1% and squamous cell carcinoma in 0.2% of the samples. In a similar study Eroglu ***et al.*** (33) reported chronic non-specific inflammation in 79.6%, ASCUS in 0.5%, LSIL in 0.02%, HSIL in 0.02% and squamous cell carcinoma in 0.02% of the samples (34).

In another study conducted by P. Dursun et al., cervical cytologies of a total of 403 cases were examined. 93 of them (23%) presented abnormal cytological findings and 310 cases (77%) demonstrated normal cytology. 42% ASCUS, 46% LGSIL, 11% HGSIL was detected in 93 cases with abnormal cytology results. On the other hand, in the 36% group with abnormal smear findings, HPV was positive whereas in the group with normal cytology results, HPV detection rate was 20%. In cases with HPV-positive cases, ASCUS was 22%, LGSIL was 51% and HGSIL was 60%. HPV types that are the most prevalent types in cases with cytological abnormality were HPV 16 (35%), HPV 6(19%), HPV 18(9%) and other types (36%) (35).

In our study 4243 cervix samples were analyzed and 2.4% (102 cases) was detected as HPV-positive, 93.5% (3967 cases) were detected as HPV-negative and 4.1% was (174 cases) were found inconclusive. Analyzing these 102 samples with HPV-positive, it was reported that 15.69% had only HPV 16, 4.9% had only HPV 18, 9.8% had HPV 16 and other types, had HPV 18 and other types 0.98% and 68.63% had other types. Cytological examinations in these HPV-positive samples revealed LGSIL (24.51%), infections (54.90%), ASC-US (7.84%), Normal (3.92%) and inconclusive results (7.84%).

CONCLUSION

Although death rate of cervical cancer has dropped as a result of decrease in prevalence and early diagnosis following routine implementation of widespread cytological scanning programs; cervical cancer still continues to be a serious health problem. Cervical cytology scanning programs must become more widespread and vaccination must be scheduled with women of risk group in order to decrease precancerous lesions and cervix cancer rates. On the other hand, the approach to this disease would be inclusion of HPV vaccines in mandatory vaccination programs in Turkey, as it is the case in many developed countries, in order to eliminate this disease altogether in the future.

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