



## Analysis of High Risk HPV Subtypes Associated with Cervical Intraepithelial Neoplasia: A Single Centre Retrospective Study in the Mediterranean Region of Turkey

Servikal İntraepiteliyal Neoplazi ile İlişkili Yüksek Risk HPV Alt Tiplerinin Analizi: Türkiye'nin Akdeniz Bölgesinde Tek Merkezli Retrospektif Bir Çalışma

Dear Editor,

Various studies on the Human Papilloma Virus (HPV) types seen in our country have been conducted previously but they have been inadequate due to the insufficient number of patients as well as not representing a wide geographical area. Recently Dursun P. et al. conducted a multi-centered study on a large series of 6388 cases related to this issue and determined HPV positivity in 25% of the cases. In addition, this study investigated the incidence of HPV in patients with abnormal and normal cytology and the relationship between abnormal cytological findings and HPV types (1). HPV is known to play a role in precancerous and invasive lesions of the cervix and the incidence of these lesions is gradually increasing (2-6). We conducted an HPV subtype study in our region by investigating the presence of cervical precancerous lesions in cases examined for high-risk HPV DNA with the PCR method in the cervicovaginal cytology materials and found to be positive.

A total of 1137 patients whose cervicovaginal cytology specimens were obtained during routine gynecological examination at the Antalya Education and Research Hospital during 2012 and 2013 were retrospectively included in our study and the high-risk HPV DNA test was performed with the PCR method. Of the patients for which PCR was performed on the sample, the cervicovaginal cytology specimens of those found to have high-risk HPV DNA were stained with the Papanicolaou stain, evaluated with the microscope and investigated in terms of cervical precancerous lesions (ASCUS, SIL). We also determined the high-risk HPV subtype in cases found to have HPV and investigated the incidence.

The age range of the 1137 patients included in our study was 20-66 years. HPV DNA was detected in 36 cervicovaginal cytology materials and not found in 1101 patients where the presence of high-risk HPV DNA was investigated with PCR. When these 36 cases were evaluated in terms of precancerous lesions, 11 were found to have ASCUS, 20 L-SIL, 3 H-SIL and 2 reactive changes. HPV DNA positivity was 3.2% in cases studied with PCR, and ASCUS

was found in 30.6%, L-SIL in 55.6%, H-SIL in 8.3% and reactive changes in 5.5%. In total, 94.5% of the cases who were HPV DNA positive were observed to have a cervical precancerous lesion while 5.5% showed no precancerous lesion. High-risk HPV subtyping revealed that HPV type 16 was the most frequently observed type in all cases and 56, 51, 31, 59, 35, 52, 58, 18, 45, 39 and 33 were identified at decreasing rates. Accordingly, HPV types 16 and 56 were most common and type 33 least common among the cases. The most common types in the ASCUS group was 16 and 51 while type 16 was noted in all 3 cases with H-SIL (Table I).

In general, no cervical cancer was observed in cases diagnosed with ASCUS or L-SIL with cytology although HPV DNA was positive in most L-SIL cases (2,7). However, HPV DNA type determination in cases with abnormal cervical cytology is a predictive factor in terms of the presence of a high-grade cervical intraepithelial lesion (2). Studies on the incidence of HPV types have led to varied results. For example, types 16, 6 (8) and types 6, 11 (9) were most commonly seen in two studies conducted in our country while types 16, 6 were the most commonly seen types in the study of Dursun P et al., the most recent study on this subject (1). Studies from other countries have reported 16, 31 (10) 52, 16 (6) as the most common types. The relationship between intraepithelial lesions and HPV types has also been investigated, although the numbers are small. One study reported a significant correlation between abnormal cytological findings and type 16 (2). This finding is in consistent with the results of Dursun P et al (1). Similarly, type 16 was common in our study and the most common types were 16 and 51 in the ASCUS group, 16 and 56 in the L-SIL group while type 16 was seen in all 3 H-SIL cases. Type 16 was therefore seen in all three groups. The most common high-risk HPV types in the LSIL group, the largest group in our study, were types 16 and 56. It is interesting that only type 16 was seen in the HSIL group and Chiang YC et al. (11) have also reported a relationship between HSIL and types 16, 18. Various immunization methods are now present to prevent HPV infections and vaccines have

**Table I:** Relationship between microscopic diagnosis and HPV presence on cervical cytology and the subtype

Diagnosis/HPV type	16	18	31	33	35	39	45	51	52	56	58	59
ASCUS	4	1	1	-	1	1	-	3	2	2	1	-
LSIL	6	2	4	1	3	1	3	3	2	6	3	4
HSIL	3	-	-	-	-	-	-	-	-	-	-	-
Reactive	-	-	-	-	-	-	-	1	-	-	-	1
<b>Total</b>	13	3	5	1	4	2	3	7	4	8	4	5

ASCUS: Atypical Squamous Cells of Undetermined Significance.

LSIL: Low Grade Squamous Intraepithelial Lesion.

HSIL: High Grade Squamous Intraepithelial Lesion.

been shown to be particularly effective against HPV 16, 18 and 6, 11 strains. HPV type distribution varies according to the geographical region and it is important to know the variations regarding the efficacy of vaccination.

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## REFERENCES

- Dursun P, Ayhan A, Mutlu L, Çağlar M, Haberal A, Güngör T, Ozat M, Özgü E, Onan A, Taşkıran C, Güner H, Yetimlar H, Kasap B, Yüce K, Salman MC, Sayal B, Doğan S, Harma M, Harma M, Basaran M, Aydoğmuş H, Ergün Y, Sehirali S, Gültekin E, Köse S, Yildirim Y, Yenen M, Dede M, Alanbay I, Karaca R, Metindir J, Keskin L, Ustüner I, Avşar F, Yüksel H, Kirdar S. HPV types in Turkey: Multicenter hospital based evaluation of 6388 patients in Turkish Gynecologic Oncology Group Centers. *Türk Patoloji Derg.* 2013; 29:210-6.
- Jovanović AM, Dikić SD, Jovanovic V, Zamurovic M, Nikolic B, Krsic V, Rakic S, Stanimirovic B. Correlation of human papilloma virus infection with cytology, colposcopy and histopathological examination of the bioptic tissue in low- and high-grade intraepithelial lesions. *Eur J Gynaecol Oncol.* 2012; 33:512-6.
- Pientong C, Wongwarissara P, Ekalaksananan T, Swangphon P, Kleebkaow P, Kongyingyoes B, Siriaunkgul S, Tungsinmunkong K, Suthipintawong C. Association of human papillomavirus type 16 long control region mutation and cervical cancer. *Virology.* 2013; 10:30.
- Remschmidt C, Kaufmann AM, Hagemann I, Vartazarova E, Wichmann O, Deléré Y. Risk factors for cervical human papillomavirus infection and high-grade intraepithelial lesion in women aged 20 to 31 years in Germany. *Int J Gynecol Cancer.* 2013; 23:519-26.
- Pimentel VM, Jiang X, Mandavilli S, Umenyi Nwana C, Schnatz PF. Prevalence of high-risk cervical human papillomavirus and squamous intraepithelial lesion in Nigeria. *J Low Genit Tract Dis.* 2013; 17:203-9.
- Chen Q, Luo ZY, Lin M, Lin QL, Chen CY, Yang C, Xie LX, Li H, Zheng JK, Yang LY, Ju GZ. Prevalence and genotype distribution of human papillomavirus infections in women attending hospitals in Chaozhou of Guangdong province. *Asian Pac J Cancer Prev.* 2012; 13:1519-24.
- Arbyn M, Roelens J, Simoons C, Buntinx F, Paraskevaidis E, Martin-Hirsch PP, Prendiville WJ. Human papillomavirus testing versus repeat cytology for triage of minor cytological cervical lesions. *Cochrane Database Syst Rev.* 2013; 3:CD008054.
- Dursun P, Senger SS, Arslan H, Kuşçu E, Ayhan A. Human papillomavirus (HPV) prevalence and types among Turkish women at a gynecology outpatient unit. *BMC Infect Dis.* 2009; 9:191.
- Yavuzer D, Karadayı N, Erdağı A, Salepçi T, Baloğlu H, Dabak R. Serviks kanseri ve prekanseröz lezyonlarında PCR ile HPV tiplemesi. *Kartal EAH Tıp Dergisi.* 2009; 20:1-6.
- Milutin-Gasperov N, Sabol I, Halec G, Matovina M, Grce M. Retrospective study of the prevalence of high-risk human papillomaviruses among Croatian women. *Coll Antropol.* 2007; 31 Suppl 2:89-96.
- Chiang YC, Cheng WF, Chen YL, Chang MC, Hsieh CY, Lin MC, Chen CA. High-risk human papillomavirus, other than type 16/18, in predominantly older Taiwanese women with high-grade cervical preinvasive lesions. *Taiwan J Obstet Gynecol.* 2013; 52:222-6.