The clinical significance of HPV screening in premalignant cervical lesions

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Summary

Purpose: We evaluated the clinical significance of human papilloma virus (HPV) screening in premalignant cervical lesions. *Methods:* This prospective study was performed at Dicle University, School of Medicine, Department of Obstetrics and Gynecology, from January 2009 to June 2009. A total of 60 cases were evaluated. Thirty cases had premalignant cervical lesions. The prevalence of HPV was analyzed by polymerase chain reaction and types determined by Hybrid Capture II. The cases that had premalignant cervical lesions were evaluated with colposcopy. Statistical analyses were carried out by using the statistical packages for SPSS version 12.0 for Windows (Chicago, IL, USA). *Results:* Of all the cases, those with premalignant cervical lesions had higher prevalence of HPV DNA. The cases that had high oncogenic HPV type had more abnormal colposcopic findings. *Conclusion:* Premalignant cervical lesions should be evaluated by cervical cytology, colposcopy, HPV DNA screening and cervical tissue sampling. In this way, development of cervical cancer can be prevented.

Key words: Premalignant; Cervical; Lesion; HPV; Clinical significance.

Introduction

Premalignant cervical lesions (atypical squamous cells of undetermined significance – ASCUS, high-grade squamous intraepithelial lesions – HSIL, and low-grade squamous intraepithelial lesions – LSIL) have been considered to be preventable lesions of the cervix, caused by persistent human papilloma virus (HPV) infection [1, 2]. Exfoliative cytology, used to detect invasive and in-situ carcinomas of the uterine cervix, was first demonstrated by Papanicolaou and Traut [3]. When premalignant lesions have been detected in exfoliative cytology, HPV testing is used in the secondary assay with good sensitivity and a high negative predictive value (NPV), and colposcopy directed biopsies of suspicious areas should be taken for final diagnosis [4, 5]. HPV testing parameters include polymerase chain reaction (PCR), and Hybrid Capture II (HCII) assay [6]. In a recent study, 6.7% of cases of HSIL or cancer were found by histology, and 39.5% of patients had high-risk HPV. The sensitivity of HPV testing for high-grade dysplasia was 89.2%, and specificity was 64.1% [7].

In the present study the prevalence and types of HPV and colposcopic findings of premalignant cervical lesions were evaluated.

Material and Methods

This prospective study was performed at Dicle University, School of Medicine, Department of Obstetrics and Gynecology, from January 2009 to June 2009. A total of 60 cases were evaluated. The cases had normal cytology (n = 30, 50%) and premalignant cervical lesions (n = 30, 50%).

Cervical exfoliative cytology was made by the conventional method and samples were taken for HPV DNA testing by using reverse hybridization-based (GenID HPV) screening apparatus. The cases had premalignant cervical lesions assessed by colposcopy (Leisegang® OptiK™ light-emitting diode (LED) colposcopes) and of the cases that had abnormal colposcopy findings, colposcopy directed biopsies were taken.

The mean and standard deviation (SD) were calculated for continuous variables. Normality of variables was analyzed by the Kolmogorov-Smirnov test. The chi-square test and Student's t-test evaluated associations between the categorical and continuous variables. Two-sided p values were considered statistically significant at $p < 0.05$. Statistical analyses were carried out by using the statistical package for SPSS 12.0 for Windows (Chicago, IL, USA).

Results

Sixty women were evaluated in this study. The demographic and clinical characteristics of the cases are shown in Table 1. Mean ages were 38.90 ± 9.58 and 37.70 ± 7.52 in the study and control group, respectively. Sixteen patients (26.66%) were smokers and 40 (66.6%) women used hormonal contraceptives. Mean ages at sexual debut were 19.46 ± 3.03 and 20.75 ± 5.03 years, respectively, in the study and control groups which were not statistically different ($p = 0.237$).

In the study group, 50% of the cases had high-risk (HR) HPV, 20% had low-risk (LR) HPV, and in 18% of the cases HPV was not detected. In the control group, 33.3% of the cases had HPV DNA. Patients with normal cytology had significantly less prevalence of HPV than the premalignant cervical lesion group ($p < 0.001$). The incidence of HPV DNA increased by advancing age, and 38 (63.33%) of the cases were patients aged 35 and older.

Abnormal colposcopy findings (acetowhite epithelium,

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Table 1. — *Demographic and clinical characteristics of the cases*.

	Group with normal Pap smear (n = 30)	Group with premalignant Pap smear (n = 30)	*p*
Age (years)	37.70 ±7.52	38.90 ± 9.58	0.592
Age at sexual debut (years)	20.75 ± 5.03	19.46 ± 3.03	0.237
HPV (+)	10 (33.3%)	21 (70%)	< 0.001
HR-HPV	9 (30%)	15 (50%)	< 0.001

HR-HPV: High-risk human papilloma virus, $p < 0.05$ is accepted as statistically significant.

punctuation, mosaicism, leukoplakia, iodine-negative epithelium, and atypical vessels) were present in 83.3% of the cases in the premalignant cervical lesion group, and of these cases 15 (50%) had HR-HPV, six (20%) LR-HPV, and nine (30%) had HR-HPV in the control group ($p < .001$). In the premalignant cervical lesion group with HPV, 40.9% of the cases had two to three abnormal colposcopy findings.

Discussion

Premalignant cervical lesions are considered to be the leading cause of cervical cancer. The ability to detect and treat premalignant lesions of the cervix has reversed the natural history of cervical cancer [8]. Therefore, investigators always stress the importance of early detection and treatment of these lesions. Persistent infection of the female genitalia by oncogenic HPV types is the major cause of the premalignant and invasive cancer of the uterine cervix [1].

Age of patients with premalignant cervical lesions is an important factor for detection of HPV. Baseman *et al*. reported that that the prevalence of HPV infection increases with decreasing age [9]. However in our study, the majority of cases where HPV was detected were older than 35 years of age, which is related to the traditional sexual mores of patients in our region.

In different studies, an increasing ratio of HPV with ages at sexual debut has been reported. Derchain *et al*. [10], found the HPV prevalence to be higher in young women with early sexual debut, but on the contrary O'Keefe *et al*. [11] found no association with age at sexual debut and HPV. We also did not find any association between early sexual debut and HPV prevalence in our study.

In another study the overall HPV prevalence was reported as 81.0%, 72.9%, and 14.4%, respectively, in women with HSIL, LSIL, and normal cytology/histology [12]. This prevalence was 85%, 76% and 33.3% respectively, in our study.

Carta *et al*. [13] reported the incidence of abnormal colposcopic findings in premalignant cervical lesions as 83.4% in their study. We found a similar rate for colposcopic findings in the premalignant cervical lesion group.

In conclusion, we found high-risk HPV infection to be highly and positively associated with the severity of premalignant cervical lesions. It should never be forgotten that exfoliative cytology is not a diagnostic method, but when combined with colposcopy and HPV DNA testing, will bring about early detection of premalignant cervical lesions and thus prevention of invasive cancer.

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