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A Retrospective Analysis of Colposcopy Outcomes in High-risk HPV-positive Individuals Referred to Our Clinic

Kliniğimize Yönlendirilen Yüksek Riskli HPV Pozitif Hastaların Kolposkopi Sonuçlarının Retrospektif Analizi

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Abstract

Objective: Cervical cancer accounted for 2.4% of all newly diagnosed malignancies among women in Turkey, with approximately 1.588 new cases and 722 deaths reported in 2020. Current guidelines recommend a risk-based management approach in which women with high-risk human papilloma virus (HPV) positivity, regardless of cytology results, are often referred for colposcopic evaluation. This study aimed to compare our colposcopic biopsy findings in high-risk HPV-positive patients with the existing literature.

Method: This retrospective study included individuals referred to our tertiary care center between February 2024 and May 2025 due to high-risk HPV positivity, in line with current clinical guidelines. Data on patients' age, menopausal status, smoking habits, cytology results, HPV genotypes, and colposcopic biopsy outcomes were recorded and analyzed.

Results: A total of 180 patients were included. Notably, no cases of adenocarcinoma or invasive cervical cancer were detected. There were no statistically significant associations between age, menopausal status, smoking status, or HPV genotype and colposcopic biopsy outcomes (normal, CIN1, CIN2, CIN3). The only statistically significant finding was that CIN3 lesions were more frequently observed in women aged 51-65 years compared to other age groups (p=0.034).

Öz

Amaç: Türkiye'de serviks kanseri, kadınlarda yeni tanı konulan tüm malignitelerin %2,4'ünü oluşturmaktadır ve 2020 yılında yaklaşık 1,588 yeni olgu ile 722 ölüm bildirilmiştir. Güncel kılavuzlar, sitoloji sonucundan bağımsız olarak yüksek riskli insan papilloma virüsü (HPV) pozitifliği saptanan kadınların kolposkopi ile değerlendirilmesini öneren risk temelli bir yönetim yaklaşımını benimsemektedir. Bu çalışma, yüksek riskli HPV pozitif bireylerde elde ettiğimiz kolposkopik biyopsi bulgularını mevcut literatürle karşılaştırmayı amaçlamaktadır.

Yöntem: Bu retrospektif çalışmada, Şubat 2024 ile Mayıs 2025 tarihleri arasında yüksek riskli HPV pozitifliği nedeniyle üçüncü basamak sağlık merkezimize yönlendirilen hastalar, güncel klinik kılavuzlar doğrultusunda değerlendirildi. Hastaların yaşı, menopozal durumu, sigara kullanımı, smear sonuçları, HPV tipleri ve kolposkopik biyopsi sonuçları kaydedilerek analiz edildi.

Bulgular: Çalışmaya toplam 180 hasta dahil edildi. Önemli olarak, adenokarsinom ya da invaziv servikal kanser saptanmadı. Yaş, menopoz durumu, sigara kullanımı ve HPV tipleri ile kolposkopik biyopsi sonuçları (normal, CIN1, CIN2, CIN3) arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. Sadece 51-65 yaş grubundaki hastalarda CIN3 lezyonlarının diğer yaş gruplarına göre anlamlı düzeyde daha sık görüldüğü belirlendi (p=0,034).

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Abstract

Conclusion: Our colposcopic biopsy outcomes in high-risk HPV-positive patients were found to be consistent with the current literature.

Keywords: Cervical dysplasia, colposcopic biopsy, high-risk HPV positivity

Öz

Sonuç: Yüksek riskli HPV pozitif hastalarda elde ettiğimiz kolposkopik biyopsi sonuçları, mevcut literatür ile uyumlu bulunmuştur.

Anahtar kelimeler: Kolposkopik biyopsi, servikal displazi, yüksek riskli HPV pozitifliği

Introduction

Cervical cancer, a highly preventable malignancy by screening, resulted in the deaths of 4.138 women in the United States, averaging 11 fatalities per day, with half of the deceased aged 58 years or younger (1). Marked inequalities in the incidence and mortality rates of cervical cancer were noted. The highest incidence rates are observed in Sub-Saharan Africa, with 85% of fatalities occurring in underdeveloped nations worldwide (2). GLOBOCAN 2020 projections indicate that cervical cancer ranks as the fourth most prevalent disease among women globally, with over 604,000 new cases and 342,000 fatalities recorded in 2020 (3). Nearly 90% of cervical cancer deaths occur in resource-limited settings, underscoring global disparities in cancer prevention and care. Cervical cancer constituted 2.4% of all newly diagnosed malignancies in women in Turkey, with about 1.588 new cases and 722 fatalities reported in 2020 (3). The age-standardized incidence rate was 4.3 per 100,000 women, quite low in comparison to worldwide norms, presumably attributable to national cervical cancer screening initiatives aimed at women aged 30-65 years (4). Nonetheless, sustained efforts are required to enhance participation rates and adherence to follow-up, particularly among high-risk demographics. Girls aged 9 to 14 are incorporated into the immunization program in Turkey.

Persistent infection with high-risk human papillomavirus (HR-HPV), particularly HPV 16 and HPV 18, accounts for approximately 70% of cervical cancer cases (5). The early detection of cervical intraepithelial neoplasia (CIN) and the reduction of invasive cervical cancer have been significantly improved in countries with robust healthcare systems as a result of the implementation of HPV DNA testing and cytology-based screening programs. Current guidelines emphasize, a risk-based management approach, where women with positive HPV results, regardless of cytology status, are often referred for colposcopic evaluation (6).

Recent studies indicate that even women with normal cytology but positive HPV 16/18 genotypes carry a substantial risk of underlying high-grade lesions (CIN2+), with detection rates ranging from 10% to 40% (7). Consequently, colposcopy-guided biopsy remains the gold standard for evaluating HPV-positive women and confirming the presence of precancerous or cancerous lesions.

The aim of this study was to evaluate colposcopy-guided biopsy outcomes in patients referred to our clinic with high-risk HPV positivity and to examine their association with cervical cytology findings.

Materials and Methods

This retrospective analysis encompassed patients who received colposcopic biopsy at University of Health Sciences Turkey, Gaziantep City Hospital from February 2024 to May 2025. The study included patients who had a colposcopic assessment after being found to be cervical HPV positive for the first time. The criteria for exclusion were as follows: Possessed a history of surgical intervention for CIN or cervical carcinoma, radiation, or chemotherapy, and had undergone colposcopy without cervical biopsy. The study was approved by the Medical Ethics Committee of University of Health Sciences Turkey, Gaziantep City Hospital (approval no: 221/2025, date: 21.05.2025).

The cervical cytology analysis was carried out using the liquid-based cytology test. Expert pathologists analyzed the data and categorized them using the 2014 Bethesda system (8). The Bethesda technique was utilized for cytological evaluation, producing the subsequent results: negative for intraepithelial lesions or malignancy (NILM—normal), atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesion (ASC-H), low-grade intraepithelial lesion (LSIL), high-grade intraepithelial lesion (HSIL), atypical glandular cells (AGC), re-evaluation of insufficient cytology results was conducted. Kits from Qiagen were used to collect HPV DNA samples. The study included 14 carcinogenic HR-HPV types: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73 (9).

Colposcopic exams were performed in accordance with the 2020 American Society for Colposcopy and Cervical Pathology and Turkish Society of Gynecologic Oncology

Guidelines (10,11) and by gynecological oncologists. Cervical colposcopic examinations were performed using an EDAN C6A video colposcope (EDAN Instruments, Shenzhen, China) equipped with a green filter for enhanced visualization of vascular patterns. Multiple cervical biopsies were obtained from aberrant imaging locations. In the event of HR-HPV positive and the lack of concerning lesions in the colposcopic biopsy, a normal biopsy was conducted at positions 3, 6, 9, and 12. Endocervical curettage was performed in all patients who underwent colposcopic evaluation. The histopathology findings were categorized into four groups: Low-grade squamous intraepithelial lesions (comprising koilocytic changes, warts, and CIN I), high-grade squamous intraepithelial lesions [containing CIN II/III and carcinoma *in situ* (CIS)], chronic cervicitis or mucositis (inflammation), and no abnormality intraepithelial lesion or malignancy observed (normal).

Statistical Analysis

Statistical analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as number and percentage [n (%)]. Comparisons between categorical variables were performed using the chi-square test. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with CIN2+ lesions. Odds ratios and 95% confidence intervals were calculated. A p-value <0.05 was considered statistically significant.

Results

A total of 180 patients were referred to our clinic from family medicine units and other healthcare institutions (including private hospitals and secondary state hospitals) due to positive HPV test results. The mean age of the patients was 41.9±9.1 years. Among the study population, 80 (44.4%) patients were aged 30-40 years, 67 (37.2%) were aged 41-50 years, and 33 (18.5%) were aged 51-65 years. Overall, 44 (24.5%) patients were postmenopausal, and 56 (31.2%) were smokers. HPV16 was detected in 81 (45%) patients, HPV18 in 29 (16.1%) patients, and other high-risk HPV types in 40 (22.2%) patients. The distribution of other high-risk HPV types was as follows: HPV31 in 4 (2.2%), HPV33 in 6 (3.3%), HPV39 in 4 (2.2%), HPV45 in 4 (2.2%), HPV51 in 4 (2.2%), HPV52 in 4 (2.2%), HPV56 in 4 (2.2%), HPV58 in 4 (2.2%), and HPV68 in 6 (3.3%) patients.

Multiple HPV infection was detected in 30 (16.7%) patients. Dual HPV positivity included HPV16-18 in 8 (4.4%), HPV16-33 in 6 (3.3%), HPV31-33 in 5 (2.7%), HPV52-68 in 3 (1.6%), and HPV66-68 in 2 (1.1%) patients. Triple HPV positivity included HPV16-31-56 in 2 (1.1%), HPV39-45-53 in 1 (0.5%), HPV31-33-45 in 1 (0.5%), HPV31-33-66 in 1 (0.5%), and HPV52-66-68 in 1 (0.5%) patients. Cytology results showed that 127 (70.5%) patients had NILM, 32 (17.9%) had ASC-US, 9 (5%) had LSIL, 9 (5%) had HSIL, 2 (1.1%) had ASC-H, and 1 (0.5%) had AGC. Colposcopy-guided biopsy results revealed normal findings in 128 (71.1%) patients, CIN1 in 15 (8.3%), CIN2 in 9 (5%), and CIN3 in 28 (15.6%) patients. No cases of adenoCIS or invasive carcinoma were identified. The clinicopathologic characteristics of the patients are summarized in Table 1.

Table 1. Clinicopathologic characteristics of the patients

Patients characteristics	n=180	Percentage (%)
Age (mean ± SD), years old	41.9±9.1	
30-40 years	80	44.4
41-50 years	67	37.2
51-65 years	33	18.5
Menopausal status of patients		
Premenopause	136	75.5
Postmenopause	44	24.5
Patients' smoking status		
Non-smoker	124	68.8
Smoker	56	31.2
HR-HPV typing		
HPV16	81	45
HPV18	29	16.1
Non-16/18, HR-HPV	40	22.2
Multiple (dual) HPV Positivity	30	16.7
Cervical cytology		
NILM	127	70.5
ASC-US	32	17.9
LSIL	9	5
HSIL	9	5
ASC-H	2	1.1
AGC	1	0.5
Pathological biopsy result		
Normal	128	71.1
CIN 1	15	8.3
CIN 2	9	5
CIN 3	28	15.6

SD: Standard deviation, AGC: Abnormal glandular cells, AIS: Adenocarcinoma *in situ*, ASC-H: Atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesion, ASC-US: Atypical squamous cells—undetermined significance, CIN: Cervical intraepithelial neoplasia, HR-HPV: High-risk human papillomavirus, HSIL: High-grade intraepithelial lesion, LSIL: Low-grade intraepithelial lesion, NILM: Indicates negative for intraepithelial lesions or malignancy—normal or indicative of infection

The assessment of HPV types and colposcopic biopsy outcomes indicated that HPV16, HPV18, non-16/18 HR-HPV, and multiple HPV positivity were not significantly associated with the progression to severe cervical dysplasia (CIN2-3) (respectively, p=0.534, p=0.215, p=0.355, and p=0.285). The relationship between HPV positivity and colposcopic biopsy results is presented in Table 2.

The negative predictive value of cytology for detecting CIN2 or higher lesions (CIN2+) was 92.3%, whereas the positive predictive value was 100%. CIN2+ lesions were absent in 92.3% of patients with negative cytology results (NILM, ASC-US, LSIL), while CIN2+ lesions were detected in all patients with positive cytology findings (HSIL, ASC-H, AGC). Table 3 summarizes the relationship between cytology results and colposcopic biopsy findings.

When patients were categorized by age groups (30-40, 41-50, and 51-65 years), the detection rate of CIN3 was significantly higher in the 51-65 age group (p=0.034). The distribution of colposcopic biopsy outcomes according to age groups is shown in Table 4.

No statistically significant association was observed between menopausal status and colposcopic biopsy results (normal biopsy: p=0.554; CIN1: p=0.601; CIN2: p=0.577; CIN3: p=0.868). Similarly, smoking status was not significantly associated with colposcopic biopsy outcomes (normal biopsy: p=0.509; CIN1: p=0.424; CIN2: p=0.828; CIN3: p=0.433). These findings are summarized in Table 5.

Univariate and multivariate logistic regression analyses were performed to identify factors associated with CIN2+ lesions. None of the evaluated variables, including age, HPV16 positivity, multiple HPV infection, smoking status, and menopausal status, were independently associated with CIN2+ lesions (Table 6).

Table 2. Correlation among HPV subtypes and colposcopy-directed biopsy outcomes

Pathological biopsy results	HPV16 (n=81)	HPV18 (n=29)	Non-16/18 HR-HPV (n=40)	Multiple (dual) HPV positivity (n=30)	p-value*
Normal	54 (66.6%)	21 (72.4%)	32 (80%)	21 (70%)	0.534
CIN1	9 (11.1%)	1 (3.6%)	4 (10%)	1 (3.3%)	0.215
CIN2	3 (3.7%)	2 (6.8%)	1 (2.5%)	3 (10%)	0.355
CIN3	15 (18.6%)	5 (1.2%)	3 (7.5%)	5 (16.7%)	0.285

CIN: Cervical intraepithelial neoplasia, HR-HPV: High-risk human papillomavirus, *: p-values <0.05 were regarded as statistically significant
Univariate and multivariate logistic regression analysis were employed to assess independent variables linked to the outcomes

Table 3. Colposcopy biopsy results according to cytology (smear) results

Pathological biopsy results	NILM (n=127)	ASC-US (n=32)	LSIL (n=9)	HSIL (n=9)	ASC-H (n=2)	AGC (n=1)
Normal	105 (82.6%)	20 (62.5%)	3 (33.3%)	-	-	-
CIN1	8 (6.5%)	4 (12.5%)	3 (33.3%)	-		
CIN2	2 (1.5%)	3 (9.3%)	1 (11.1%)	2 (22.2%)		
CIN3	12 (9.4%)	5 (15.7%)	2 (22.2%)	7 (78.8%)	2 (100%)	1 (100%)

AGC: Abnormal glandular cells, ASC-H: Atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesion, ASC-US: Atypical squamous cells—undetermined significance, CIN: Cervical intraepithelial neoplasia

Table 4. Distribution of colposcopic biopsy outcomes by age categories

Pathological biopsy results	30-40 years (n=80)	41–50 years (n=67)	51-65 years (n=33)	p-value*
Normal	63 (78.7%)	48 (71.6%)	17 (51.5%)	0.214
CIN1	2 (2.5%)	9 (13.4%)	4 (12.1%)	0.391
CIN2	4 (5%)	2 (3.1%)	3 (9.1%)	0.420
CIN3	11 (13.8%)	8 (11.9%)	9 (27.3%)	**0.034**

CIN: Cervical intraepithelial neoplasia, *: p-values <0.05 were regarded as statistically significant

Table 5. Assessment of colposcopy outcomes based on patients' menopausal status and tobacco use			
Pathological biopsy results	**Premenopause (n=136)**	**Postmenopause (n=44)**	**p-value***
Normal	96 (70.5%)	32 (72.7%)	0.554
CIN1	10 (7.3%)	5 (11.4%)	0.601
CIN2	8 (5.9%)	1 (2.2%)	0.577
CIN3	22 (16.3%)	6 (13.7%)	0.868
The effect of smoking on colposcopic biopsy			
Pathological biopsy results	**Non-smoker (n=124)**	**Smoker (n=56)**	**p-value***
Normal	93 (75%)	35 (62.5%)	0.509
CIN1	12 (9.6%)	5 (9%)	0.424
CIN2	6 (3.4%)	3 (5.3%)	0.818
CIN3	15 (12%)	13 (23.2%)	0.433
CIN: Cervical intraepithelial neoplasia, *: p-values <0.05 were regarded as statistically significant			

Table 6. Univariate and multivariate logistic regression analysis for predictors of CIN2+ lesions						
Variable	**Univariate OR**	**95% CI**	**p-value**	**Multivariate OR**	**95% CI**	**p-value**
Age (years)	0.97	0.93-1.01	0.10	0.98	0.94-1.02	0.28
HPV16 positivity	1.68	0.79-3.55	0.18	1.52	0.70-3.31	0.29
Multiple HPV infection	1.94	0.90-4.19	0.09	1.73	0.78-3.84	0.17
Smoking status	1.53	0.77-3.05	0.22	1.41	0.69-2.90	0.34
Postmenopausal status	0.82	0.33-2.03	0.66	0.91	0.36-2.30	0.84
OR: Odds ratio, CI: Confidence interval. Cervical intraepithelial neoplasia (CIN)2+ was defined as cervical intraepithelial neoplasia grade 2 or higher. Variables included in the multivariate model were age, HPV16 positivity, multiple HPV infection, smoking status, and menopausal status. Statistical significance was defined as p<0.05, HPV: Human papillomavirus						

Discussion

Expertise in anatomy and histology is essential for the accurate performance of clinical colposcopy. Moreover, there are worldwide issues associated with standardizing language, facilitating ongoing training, executing quality assurance methods, and establishing enough infrastructure. According to the results of the study, we determined that our cervical colposcopic evaluation results based on HPV positivity were compatible with the current global and Turkey literature. The lack of adenoCIS and invasive malignancy was a pleasing finding.

The incidence rates of HPV types in our study align with the findings of extensive investigations completed in Turkey (9-11). Despite the absence of a statistically significant difference, current evidence identifies HPV16 as the predominant type associated with cervical dysplasia, particularly CIN2-3, and cervical cancer (12,13). Given that the likelihood of cervical dysplasia and cancer escalates with increased viral load, the literature reveals no statistically significant difference regarding HPV multiple positivity in relation to cervical cancer and cervical dysplasia when compared to other high-risk HPV types, specifically HPV16 and HPV18 (14,15). Furthermore, in contrast to previous claims in the literature, the probability of detecting CIN2 and more severe lesions was not increased in our patients who concurrently tested positive for HPV16-18. As previously shown in the literature, we established the sensitive predictive value of cervical cytology for CIN2 and higher lesions at 92% (16-18). In our study, similar to the study conducted in Turkey, the detection of CIN3 results was found to be high in women aged between 51 and 65 who underwent colposcopic biopsy and endocervical curettage (19).

While our analysis did not demonstrate a statistically significant disparity, we noted that the incidence of CIN3 biopsy findings was elevated in women who smoked and had colposcopic biopsy, consistent with existing literature (20). In accordance with the literature, no significant difference was seen in the identification of CIN2 and higher lesions between premenopausal and postmenopausal individuals when examining colposcopic biopsy data (21).

Study Limitations

The constraints of our study include the limited sample size and its retrospective design. In addition, the strength of our study is that it is a single-center study in which we determine our own practice.

Conclusion

The findings of our study are generally consistent with both global and Turkish literature. No significant association was observed between HPV genotype distribution and the detection of high-grade cervical lesions (CIN2+) in our cohort. The absence of adenoCIS and invasive cancer in our series may be related to the effectiveness of the national cervical cancer screening program.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Ethics Committee of University of Health Sciences Turkey, Gaziantep City Hospital (date: 21.05.2025, approval number: 221/2025).

Informed Consent: Informed consent was waived due to the retrospective design of the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Ş., G.G., M.G., Concept: E.Ş., G.G., M.G., S.G., Design: E.Ş., M.G., S.G., İ.T., Data Collection or Processing: E.Ş., G.G., M.G., İ.T., Analysis or Interpretation: E.Ş., İ.T., Literature Search:E.Ş., G.G., M.G., S.G., İ.T., Writing: E.Ş.

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