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Factors Associated with Histopathological Examination Findings among HPV DNA Positive Women Attending at a Tertiary Cancer Hospital of Nepal

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ABSTRACT

Background

Cervical cancer remains a major public health concern in Nepal, particularly among women infected with high-risk human papillomavirus (HPV). Histopathological examination plays a critical role in diagnosing precancerous and cancerous cervical lesions. This study aimed to assess the histopathological findings and their associated factors among HPV DNA-positive women attending a tertiary cancer hospital in Nepal.

Methods

A hospital-based cross-sectional study was conducted among 78 HPV DNA-positive women aged 30–60 years who visited B.P. Koirala Memorial Cancer Hospital from July 2021 to June 2022. Data were collected using a structured questionnaire, medical records, and laboratory reports. Histopathological findings were categorized into normal, cervicitis, and cervical intraepithelial neoplasia (CIN I, II, III). Descriptive statistics, chi-square tests, and binary logistic regression were used for data analysis in SPSS version 16.

Results

Among the 39 HPV-positive women, (61.5%) had abnormal histopathological findings, with CIN III (18%) being the most common lesion, followed by CIN I (15.4%) and cervicitis (14.1%). HPV-16 and HPV-18 were the most frequently detected genotypes. Most sociodemographic and reproductive variables were not significantly associated with histopathological outcomes. However, Liquid-Based Cytology (LBC) results showed a significant association ($p < 0.001$) with histopathological findings.

Conclusions

A high proportion of HPV-positive women had precancerous cervical lesions, especially those infected with HPV-16 and HPV-18. The study underscores the importance of integrating HPV DNA testing with cytology and histopathological evaluation for early detection and management of cervical lesions in Nepal.

Keywords: HPV; histopathology; cervical cancer; CIN; cytology; Nepal.

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INTRODUCTION

Cervical cancer is one of the most common cancers among women. It is primarily caused by the Human Papilloma Virus (HPV), which is sexually transmitted. HPV types are classified into high-risk and low-risk, with high-risk types being more closely associated with cervical cancer.[1,2] High-risk HPV leads to abnormal cervical cytology and histopathological changes, eventually progressing to cancer.[3,4] HPV infection is detected in over 90% of squamous cell carcinomas and varies from 32% to 100% in adenocarcinomas.[5-14] HPV DNA testing shows high sensitivity for detecting cervical cancer and precancerous lesions.[15,16] HPV DNA-positive women show a 73% chance of abnormal histopathological findings, which is statistically significant.[17] Studies confirm HPV DNA as a more sensitive and reliable screening method than cytology.[16] It shows 94.6% sensitivity and 94.1% specificity for CIN I and II.[16] HPV 16 and 18 are the most aggressive high-risk types, often associated with HSIL and LSIL.[18,19] This study aims to assess abnormal histopathology in HPV 16 and 18 positive women.

METHODS

A hospital-based cross-sectional study was conducted at BP Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal, over a six-month period from July to December, 2024. The study consisted of HPV DNA-positive women attending the hospital during the study period. A total of 1,000 women participated, all of whom tested positive for HPV DNA through either self-collected or physician-collected samples and subsequently underwent histopathological examination. Women who did not undergo histopathological evaluation were excluded from the study. Ethical approval was obtained from the Nepal Health Research Council (Ref. No. 53/2024), and written informed consent was taken from each women before inclusion. Confidentiality and anonymity were strictly maintained throughout the data collection and analysis process. Data were collected using a structured questionnaire by trained health personnel. The questionnaire gathered information on socio-demographic characteristics, sexual and reproductive health history, behavioral factors such as smoking, and clinical findings. HPV DNA positivity was confirmed through laboratory analysis of cervical samples, and women who tested positive underwent histopathological examination of cervical tissue based on standard clinical protocols. The primary outcome variable was the histopathological examination finding, categorized as normal, precancerous lesions (CIN I, II, III), or cervical cancer. Independent variables included age, marital status, education level, parity, age at first sexual intercourse, contraceptive use, history of sexually transmitted infections (STIs), smoking status, and type of HPV detected. Data were first checked for completeness and entered into Microsoft Excel, then exported to statistical software such as SPSS 16 for analysis. Descriptive statistics including frequencies, percentages, means, and standard deviations were used to summarize participant characteristics. Bivariate analysis using the Chi-square test was conducted to explore associations between independent variables and histopathological findings. Variables with a p-value less than 0.05 in bivariate analysis were considered as statistically significant.

RESULTS

In 41 cases the result of HPV DNA was positive but 2 cases were defaulter. This research was carried out among 39 women after excluding defaulter. Out of 39 HPV DNA positive cases, 61.5% (n=24) were found to have precancerous lesions, while 38.5% (n =15) had normal cervical cytology. This indicates a high prevalence of precancerous changes among individuals testing positive for HPV DNA (Figure 1).

Among the 24 cases with precancerous lesions, CIN III was the most common type, observed in 54.17% (n = 13) of cases, followed by CIN I in 37.5% (n = 9). Both AIS and CIN II were observed in 4.17% (n = 1) of cases each. This suggests a substantial proportion of high-grade lesions among the HPV DNA-positive individuals (Table 1).

Among the 39 HPV DNA positive cases, LBC detected CIN III in 53.8% (n = 7) of cases that had

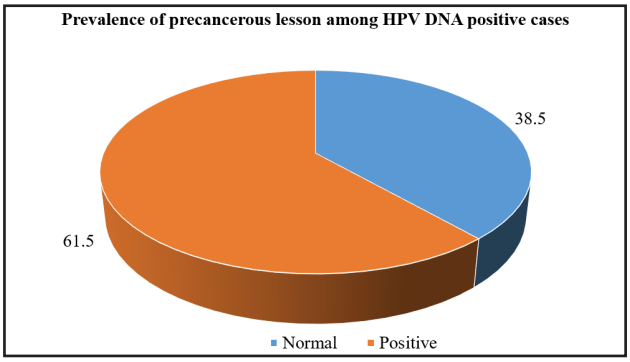

Figure 1. Prevalence of precancerous lesson among HPV DNA positive cases. (n=39)

Table 1. Type of precancerous lesion among positive cases. (n=24)

Type of precancerous lesion	Frequency (%)
AIS	1(4.17)
CIN I	9(37.50)
CIN II	1(4.17)
CIN III	13(54.17)

CIN III histopathology, indicating strong agreement for high-grade lesions. However, 1 case with a normal histopathological finding was also LBC positive. Lower-grade lesions like CIN I showed mixed results, with 5 cases being LBC negative and 4 being LBC positive. Notably, AIS was not detected in LBC-negative samples but was identified in 1 LBC-positive case (Table 2).

Table 2. Cross tabulation between histopathological finding with LBC. (n=39)

Histopathological finding	LBC result	
	Negative n(%)	Positive n(%)
Normal	14(53.8)	1(7.7)
AIS	0	1(7.7)
CIN I	5(19.2)	4(30.8)
CIN II	1(3.8)	0
CIN III	6(23.1)	7(53.8)

The analysis of sociodemographic and clinical factors in relation to histopathological outcomes revealed several findings. Age had no significant association with histopathological results ($p > 0.9$). Age at marriage showed no significant association ($p = 0.3$), though more positive cases (13%) were married before 15 years compared to normal cases. BMI also had no significant association ($p = 0.5$), but normal cases were slightly more likely to be overweight. Menopausal status showed no significant association ($p = 0.5$), with the majority being premenopausal in both groups. Occupation had no significant association ($p = 0.4$), and the distribution across jobs was similar for both groups. LBC result was significantly associated with histopathological outcomes ($p = 0.005$), with 50% of positive LBC cases showing positive histopathology compared to 6.7% in normal cases. The number of sexual partners showed no significant association ($p = 0.6$), and participation in screening was slightly higher among positive cases (58%) than normal cases (40%). Sexual bleeding had no significant association ($p = 0.14$), and marital status showed no significant association ($p > 0.9$), with most women in both groups married. Family history also showed no significant association ($p = 0.7$), but 21% of positive cases reported a family history of cervical cancer compared to 13% in normal cases (Table 3).

DISCUSSION

Definitely the infection of human papilloma virus is the key for the cervical cancer and proved by the many studies in the past and along with all those HPV most common are 16 and 18. Our study have shown that those with HPV16 and 18 positive all gone for histopathological examination out of 39 HPV 16 and 18 positive cases 24 (61.5%) were having precancerous lesion which indicates that high prevalence of HPV 16 and 18 in causing invasive cervical cancer. As our result study from Serbia also showing that highest percentage of the abnormal histological finding among the HPC 16and 18 of 86.41%. [19] One study has also shown that incidence of HPV 16 and 18 are with 77.7% association with the all kind of adenosquamous cervical cancer.[20] Not only HPV 16 and 18 are high prevalent to infection it is also associated with abnormal histological findings as well as cervical cancers.[9, 16, 20] among HPV positive cases 4.17% were AIS, 37.5% cases were CIN I ,4.17% were CIN II and 54.17 % were CIN III here we can see most prevalent were major grades of precancerous lesions. Similar, to us one study from India also showed patient with HPV positive have chronic cervicitis as well as precancerous lesion along

Table 3. Association between Histopathological result with selected sociodemographic variables. (n=39)				
Characteristic	**Overall (n = 39[1])**	**Histopathological result**		**p-value[2]**
		Normal (n = 15[1])	**Positive (n = 24[1])**	
Age (years)				
30-35	4 (10%)	1 (6.7%)	3 (13%)	>0.9
35-40	8 (21%)	3 (20%)	5 (21%)	
40-45	11 (28%)	4 (27%)	7 (29%)	
45-50	16 (41%)	7 (47%)	9 (38%)	
Age at marriage (Years)				
<15	3 (7.7%)	-	3 (13%)	0.3
≥15	36 (92%)	15 (100%)	21 (88%)	
BMI (Kg/m²)				
Underweight	17 (44%)	5 (33%)	12 (50%)	0.5
Normal	14 (36%)	6 (40%)	8 (33%)	
Obese I	7 (18%)	3 (20%)	4 (17%)	
Obese II	1 (2.6%)	1 (6.7%)	-	
Menopausal				
No	36 (92%)	13 (87%)	23 (96%)	0.5
Yes	3 (7.7%)	2 (13%)	1 (4.2%)	
Occupation				
Unemployed	4 (10%)	3 (20%)	1 (4.2%)	0.4
Farmer	9 (23%)	2 (13%)	7 (29%)	
Job	3 (7.7%)	1 (6.7%)	2 (8.3%)	
Worker	6 (15%)	3 (20%)	3 (13%)	
Others	9 (23%)	2 (13%)	7 (29%)	
Enterprise	8 (21%)	4 (27%)	4 (17%)	
LBC				
Negative	26 (67%)	14 (93%)	12 (50%)	0.005
Positive	13 (33%)	1 (6.7%)	12 (50%)	
Number of Partner				
Two	33 (85%)	12 (80%)	21 (88%)	0.6
Three	5 (13%)	3 (20%)	2 (8.3%)	
Four	1 (2.6%)	0 (0%)	1 (4.2%)	
Participate screening				
Yes	20 (51%)	6 (40%)	14 (58%)	0.3
No	19 (49%)	9 (60%)	10 (42%)	
Sexual bleeding				
Yes	2 (5.1%)	2 (13%)	0 (0%)	0.14
No	37 (95%)	13 (87%)	24 (100%)	
Marital status				
Married	37 (95%)	15 (100%)	22 (92%)	>0.9
Divorced	1 (2.6%)	0 (0%)	1 (4.2%)	
Widowed	1 (2.6%)	0 (0%)	1 (4.2%)	
Family history				
No	32 (82%)	13 (87%)	19 (79%)	0.7
Yes	7 (18%)	2 (13%)	5 (21%)	
[1] n (%)				
[2] Fisher's exact test; Pearson's Chi-squared test				

with cervical cancer which was statistically significant and comparable to negative cases.[17] though our study showing AIS in only 4.17% of cases in contrast to this study AIS more frequently found in the study done in USA.[20] study from china also showed HPV 16 and 18 positive cases are more prone to have CIN II and CIN III in that study they have also compared the HPV infection with liquid based cytology which

showed the even in normal cytology reported with HPV infection have shown abnormal histopathology with prevalence of 21.1%.[21]another study from the china have shown absolute risk of developing abnormal high grade lesions with HPV 16 and 18 is high in second one.[22] Not only absolute risk they have also found that overall prevalence of the abnormal histopathological lesion are high among the HPV 16 and HPV 18 regardless of individual infection if combined infection risk of CIN 3 is doubled.[22]

CONCLUSIONS

This study highlights a high prevalence (61.5%) of precancerous cervical lesions among HPV DNA-positive women, particularly those infected with high-risk HPV types 16 and 18. CIN III was the most commonly observed histopathological abnormality, indicating a significant burden of high-grade cervical intraepithelial neoplasia in this population. Although many socio-demographic and clinical variables, including age, BMI, age at marriage, and number of sexual partners, did not show statistically significant associations with histopathological outcomes, a significant association was found between Liquid-Based Cytology (LBC) results and histopathological findings. This underscores the potential value of using HPV DNA testing in conjunction with LBC for improved detection of cervical abnormalities. The findings emphasize the need for early screening and follow-up histopathological evaluation in HPV-positive women to ensure timely intervention and reduce the burden of cervical cancer in Nepal.

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