Determinants of Human Papilloma Virus Infection in the Context of Bangladeshi Population: A Tertiary Hospital-based Study

Shirin Akter Begum[1], Tasfia Mahmud[2], Mehriban Amatullah[3], Md. Nurul Amin[4], Ashrafun Nessa[5]

Abstract

Background & Objective: Cervical cancer is a leading cause of female malignancy in Bangladesh, primarily driven by persistent high-risk Human Papillomavirus (HPV) infection. Understanding the sociodemographic and reproductive risk factors is essential for tailoring effective prevention and screening strategies. This study was undertaken to identify the risk factors associated with HPV infection and determine genotype distribution among women diagnosed with cervical precancerous and cancerous lesions in a tertiary hospital in Bangladesh. Methods: This descriptive cross-sectional study was conducted at the Colposcopy clinic, Department of Gynecological Oncology, Bangladesh Medical University (BMU), Dhaka, between August 2022 and July 2024. A total of 300 women presenting with positive screening results or clinical suspicion of malignancy with histologically confirmed cervical lesions, ranging from Cervical Intraepithelial Neoplasia (CIN) to invasive carcinoma, were purposively recruited from the colposcopy clinic. A comprehensive colposcopic evaluation was done and colposcopy-directed biopsies were obtained from all visualized abnormal areas. In instances where colposcopic findings were unremarkable despite positive screening, random four-quadrant biopsies of the transformation zone were performed to exclude occult disease. In clinically evident cases of cervical cancer, biopsies were collected directly from the primary tumor mass. Simultaneously, cervical specimens were collected for HPV-DNA testing from all screening-positive and suspected cancer cases. Molecular analysis was performed using the GenoFlow™ HPV Array Test Kit, which enabled the concurrent detection and identification of 33 HPV genotypes, including high-risk and low-risk variants, providing a detailed molecular profile of the viral burden in the study population. Results: The mean age of participants was 46.8 ± 11.2 years. HPV DNA was detected in 70.3% (n=211) & 29.7%(n=89) patients. Among HPV DNA positive cases (n=211) HPV-16 was the most prevalent genotype, present in 68.7%(n=145) of positive cases, followed by HPV-18 was 4.3%(n=9) and HPV-39 was 3.3%(n=7). Histopathology revealed that 58.3% (n= 175) of patients had invasive cancer, predominantly Squamous Cell Carcinoma 54.6%(n=164) & adenocarcinoma 3.7%(n=11). Low socioeconomic status was significantly associated with HPV positivity 64.5% (n=136) in the positive group vs. 37.5%(n=33) in the negative group;(p < 0.001) which was statistically significant. Passive smoking also showed a notable trend toward association 44.6%(n=134) where p = 0.072. While the majority of patients were multiparous 95%(n=287) and had early sexual debut 52.3%(n=157) at or below 15 years these factors did not reach statistical significance within this specific lesion-positive cohort. Conclusion: High-risk HPV-16 is the dominant driver of cervical lesions in the study population. Poverty is a significant risk factor for infection, likely due to limited healthcare access and awareness. To reduce the burden of cervical cancer, Bangladesh must prioritize high-coverage vaccination for adolescents while considering targeted vaccination for high-risk adults, alongside the implementation of primary HPV-DNA screening to detect infections before they progress to invasive malignancy.

Keywords: HPV, Cervical Cancer, Risk Factors, HPV-16, Bangladesh, CIN.

[1] Department of Gynecological Oncology, Bangladesh Medical University, Dhaka, Bangladesh, Email: Shirin.bsmmu@gmail.com

[2] Department of Pharmacology, Dr. Sirajul Islam Medical College, Dhaka, Bangladesh.

[3] Department of Obstetrics and Gynecology, Bangladesh Medical University, Dhaka, Bangladesh.

[4] Department of Research & Development Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh.

[5] Department of Gynecological Oncology, Bangladesh Medical University, Dhaka, Bangladesh.

Introduction

Cervical cancer remains one of the most common malignancies affecting women worldwide and continues to pose a significant public health challenge in low- and middle-income countries [1]. Despite being largely preventable, it accounts for substantial morbidity and mortality, particularly where organized screening and vaccination programs are limited [2]. Cervical precancerous lesions represent an intermediate stage in the progressive process of cervical carcinogenesis and offer a critical window for early detection and intervention [3].

Persistent infection with high-risk human papillomavirus (HPV) has been established as the principal etiological factor in the development of cervical cancer and its precursor lesions [4]. Among the high-risk HPV genotypes, HPV-16 and HPV-18 are responsible for the majority of invasive cervical cancers globally [5]. However, the distribution of HPV genotypes and the progression from infection to malignancy are influenced by several host, behavioral, and environmental factors. A targeted literature review recently highlighted that factors directly measuring sexual activity such as a higher number of sexual partners and younger age at first sexual activity are consistently associated with increased risk of infection [6]. Understanding these factors is essential for developing targeted prevention and control strategies [2].

Sociodemographic characteristics such as age, education level, and socioeconomic status have been shown to play an important role in HPV acquisition, persistence, and disease progression [7]. Women from lower socioeconomic backgrounds often face barriers to healthcare access, limited awareness of cervical cancer prevention, and delayed presentation, increasing their risk of advanced disease [8]. Reproductive and behavioral factors, including parity and sexual practices, have also been associated with HPV infection and cervical neoplasia. Furthermore, there is a clear association between smoking or tobacco chewing and HPV infection, while the impact of other factors like ethnicity, education, and marital status remains less consistent across different global contexts [6]. Additionally, lifestyle factors and alterations in the vaginal microenvironment may further contribute to HPV persistence and malignant transformation [9].

Although numerous studies have evaluated HPV prevalence and genotype distribution, there remains a relative paucity of comprehensive data examining the combined influence of sociodemographic and reproductive risk factors on HPV infection among women with cervical precancerous and cancerous lesions in tertiary care settings [10,11]. In particular, the influence of age shows an unclear pattern globally, though some evidence suggests older populations (e.g., >50 years) may be at higher risk. Such information is crucial for identifying high-risk groups and optimizing screening strategies, especially in resource-limited healthcare systems [12].

Therefore, the present study was conducted to assess the risk factors associated with HPV infection among women diagnosed with cervical precancerous lesions and cervical cancer in a tertiary care hospital. By identifying factors independently associated with HPV positivity, this study aimed to contribute to evidence-based planning of preventive measures, early detection strategies, and targeted public health interventions to reduce the burden of cervical cancer.

Methods & Materials

This descriptive cross-sectional study was conducted at the Colposcopy Clinic of the Department of Gynecological Oncology, Bangladesh Medical University (BMU), Dhaka, Bangladesh, from August 2022 to July 2024. Women with histologically proven cervical precancer and cancer constituted the study population. A total of 300 such women from the outpatient department and the colposcopy clinic of BMU were consecutively included in the study. Women who had previously received treatment for cervical precancer or cancer, and those with other concurrent gynecologic malignancies were excluded.

For the detection of precancerous lesions, a colposcopic examination was performed for all screening-positive women. The cervix was swabbed with 5% acetic acid and Lugol's iodine; vascular patterns were evaluated under a green filter followed by normal red light. Findings were assessed using the Swede score. Colposcopy-directed biopsies were taken from all visible abnormal areas. In cases of screening-positive but normal colposcopic findings, random biopsies were taken from four quadrants of the transformation zone. In suspected cases of cervical cancer, a biopsy was taken directly from the tumor. Simultaneously, HPV DNA testing was performed for all screening-positive and cancer cases. HPV testing was conducted on cervical samples using the **GenoFlow™ HPV Array Test Kit**. This kit utilizes Polymerase Chain Reaction (PCR) and "Flow-through" hybridization technology to detect 33 HPV types (including high-risk types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). The process included DNA extraction, PCR amplification, and hybridization with genotype-specific probes.

Sociodemographic, behavioral, clinical and reproductive data were collected using a pretested semi-structured questionnaire containing the variables of interest. In alignment with established global risk factors [6], the questionnaire captured data on:

- **Sociodemographic:** Age, education level, and income.
- **Behavioral Factors:** Smoking status, number of sexual partners, and age at first sexual activity.
- **Medical/Reproductive History:** Parity, Age at first delivery, history of prior abnormal screening test and use of contraceptives.

Data were analyzed using SPSS version 25. Descriptive statistics were done by means and standard deviations for quantitative data. And frequencies and corresponding percentages were performed for qualitative data. The distribution of demographic, behavioral, clinical and reproductive characteristics were studied among the study population. While inferential statistics (Chi-square, χ^2) evaluated the associations between HPV infection and the aforementioned risk factors. The level of significance was established at 5% and a p-value of < 0.05 was considered significant.

Results

Descriptive Statistics

The sampled population had a mean age of 46.8 ± 11.2 years, ranging from 23 to 77 years. Over 61%(n=183) of the respondents were 31 – 50 years old, 32.7% (n=98) > 50 years old with the remaining 6.3% (n=19) being older than 50. The educational background of the patients showed that the illiterate formed the main bulk 41.7%(n=125) followed by primary 31.7%(n=95), SSC 14.3%(n=43), HSC 7%(n=21), and graduate-level literates 5.3%(n=16). The monthly family income data suggest that a significant proportion 57%(n=171) of the patients was poor (monthly income below Taka 10000) followed by lower-middle class 31.3%(n=94) middle-class 7.3%(n=22) and rich 4.3%(n=13) (Table I).

The prevalence of suspected risk factors showed that while 12%(n=36) of the patients were tobacco chewers, only 4.7% (n=14) were smokers (together comprising 16.7% of the patients). On the other hand, passive smoker was 44.6%(n=134). Over two-thirds 68.7%(n=206) were used to using hormonal contraceptives. (Table-II & figure-1) Only 2.7%(n=8) patients had a family history of cervical cancer. (Figure-1).

Approximately two-thirds 63.7%(n=191) reported backache, 83% (n=248) vaginal discharge, 60%(n=179) vaginal bleeding, 37.3% (n=112) itching in the vaginal area, and over 40%(n=122) weight loss. About one-third 31% (n=93) of the respondents had experienced painful coitus and another one-third 32.7%(n=98) had post-coital bleeding. Over one-third 35.3%(n=106) reported

postmenopausal bleeding (Table III). Over half 52.3% (n=157) of the respondents had their 1st sexual intercourse at or below 15 years of age. The majority 93.7%(n=281) of the patients reported a single lifetime sexual partner. Over 95% (n=287) of the patients were multiparous (Table IV).

Out of 300 patients, 70.3%(n=211) were found to be HPV-DNA positive & 29.7%(n=89) were HPV DNA negative. (Table VII). The molecular study of the HPV-DNA showed that the isolated presence of genotype 16 was predominant 68.7%(n=145) followed by HPV18 genotypes were 4.3%(n=9) and HPV39 genotype was 3.3%(n=7). The single occurrences of various genotypes without 16, 18, and 39 were detected in 11.4% (n= 24) cases. While the presence of genotype 16 in association with other genotypes was found in 7.6% (n=16) cases, the simultaneous presence of multiple genotypes without HPV16 was found in 4.7% (n=10) cases. Thus, a total of 76.3% (n=161) cases out of 211 were infected with HPV16 either alone or in association with other genotypes. The rest 23.7% (n=50) with genotypes other than 16 (Table V).

Histopathological examination of biopsy materials taken from cervical lesions demonstrated that invasive cancer was the most prevalent finding 58.3% (n=175) followed by CIN1 19.7% (n=59) CIN2 10.4% (n=31), CIN3 9.3%(n=28) and CIS 2.3% (n=7). In terms of histological types of lesions, squamous cell carcinoma (SCC) formed the main bulk 54.6%(n=164) followed by high-grade lesions 22%(n=66), low-grade lesions 19.7%(n=59), and adenocarcinoma 3.7%(n=11) (Table VI).

Inferential Statistics

Nearly two-thirds 64.5%(n=136) of the HPV-DNA positive subjects were poor as opposed 37.5%(n=33) of the HPV-DNA negative subjects (p < 0.001) which was statistically significant. Women belonged poor social class are more likely to acquire HPV infection than their middle class and rich counterparts. Nearly half 48.8%(n=103) of the HPV-DNA positive women were passive smokers compared to 34.8%(n=31) of women with HPV-DNA negative. It indicates that passive smokers tend to be associated with HPV infection more frequently than the non-smokers (p = 0.072) (Table VII).

None of the reproductive features like age at first sexual intercourse, age at first delivery, number of sex partners, and parity were found to be associated with acquiring HPV infection. However, delivery at teen age (< 20 years) more often tends to be associated with acquiring HPV infection (p = 0.080). The presence of multiparous women was notably higher in the HPV-DNA positive group 94.3%(n=199) compared to that in the HPV-DNA negative group 98.9%(n=88) (p = 0.143) (Table VII).

Table I. Distribution of respondents by their demographic characteristics (n = 300)

Demographic characteristics	Frequency	Percentage
Age (years)		
≤ 30	19	6.3
31 – 50	183	61.0
> 50	98	32.7
Education		
Illiterate	125	41.7
Primary	95	31.7
SSC	43	14.3
HSC	21	7.0

Graduate plus	16	5.3
Monthly Income (Taka)		
≤ 10000 (Poor)	171	57.0
10000-25000 (Lower middle class)	94	31.3
25000-50000 (Middle class)	22	7.3
≥ 50000 (Solvent or Rich)	13	4.3

*Mean age = 46.85 ± 0.648 years; **range** = (23 – 77) yrs.

Table II. Distribution of respondents by their tobacco habituation & hormonal contraceptives-using behavior (n = 300)

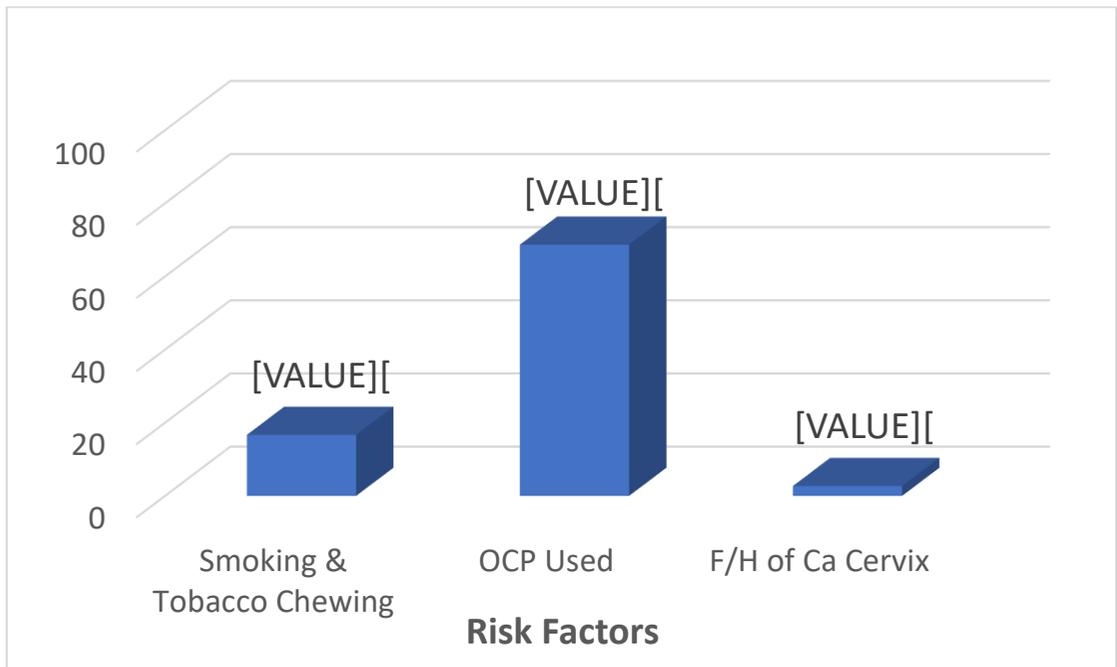| Behavioral and Genetical Factors		Frequency	Percentage
Smoking status			
Non-smoker		152	50.7
Smoker		14	4.7
Passive smoker		134	44.6
Tobacco chewing habit		36	12.0
Hormonal contraception used		206	68.7

Figure-1: Distribution of respondents by their risk factors: smoking, contraceptives use and family history cervical cancer.

Table III. Distribution of respondents by their presenting symptoms (n = 300*)

Symptoms	Frequency	Percentage
Backache	191	63.7
Irregular Vaginal bleeding	179	59.7
Painful coitus	93	31.0
Abnormal vaginal discharge	248	82.7
Itching in the vaginal area	112	37.3
Post-coital bleeding	98	32.7
Weight loss	122	40.7
Post-menopausal bleeding	106	35.3

*Total will not correspond to 100% for multiple responses

Table IV. Distribution of respondents by their reproductive features (n = 300)

Reproductive features	Frequency	Percentage
Age at 1st sexual intercourse		
≤15	157	52.3
16 – 30	143	47.7
Number of sex partners		
Multiple	19	6.3
Single	281	93.7
Parity		
Nullipara	13	4.3
Multipara	287	95.7

Table V. Distribution of respondents by their HPV DNA status

HPV DNA Profile	Frequency	Percentage
HPV-DNA Test (n = 300)		
Positive	211	70.3
Negative	89	29.7
HPV Genotypes (n = 211)		
16	145	68.7
18	9	4.3
39	7	3.3
Multiple genotypes with 16 predominant	16	7.6
Multiple genotypes without 16	10	4.7
Single occurrences of various genotypes	24	11.4

Table VI. Distribution of respondents by histopathological diagnosis (n=300)

HP Findings	Frequency	Percentage
Diagnosis		
CIN I	59	19.7
CIN II	31	10.4

CIN III	28	9.3
CIS	7	2.3
Invasive Cancer	175	58.3
Type of lesions		
Squamous cell carcinoma	164	54.6
Adenocarcinoma	11	3.7
Low-grade lesion	59	19.7
High-grade lesion	66	22.0

Table VII. Association of socioeconomic, and reproductive features and HPV infection

	HPV-DNA		
Reproductive features	Positive (n = 211)	Negative (n = 89)	**p-value**
Socioeconomic Status			
Poor	136(64.5)	33(37.5)	
Middle class	67(31.7)	51(58.0)	< 0.001
Rich	8(3.8)	4(4.5)	
Smoking status			
Smoker	10(4.7)	4(4.5)	
Passive-smoker	103(48.8)	31(34.8)	0.072
Non-smoker	98(46.5)	54(60.7)	
Age at 1st sexual intercourse			
≤ 15	83(39.3)	31(34.8)	0.463
16 – 30	128(60.7)	58(65.2)	
Age at 1st delivery			
≤ 20	179(84.8)	68(76.4)	0.080
> 20	32(15.2)	21(23.6)	
Number of sex partners			
Multiple	14(6.6)	5(5.6)	0.741
Single	197(93.4)	84(94.4)	
Parity			
Nullipara	12(5.7)	1(1.1)	0.143
Multipara	199(94.3)	88(98.9)	

*Data were analyzed using **Chi-square (χ^2)** Test and were presented as **n(%)**. Figures in the parentheses denote corresponding percentages.

Discussion

The findings of this study provide a comprehensive overview of the risk factors associated with Human Papillomavirus (HPV) infection among women with cervical precancerous and cancerous lesions in a tertiary care setting in Bangladesh. With an HPV positivity rate of 70.3% (n=211) among the symptomatic or screening-positive study population, our results underscore the significant burden of the virus and its strong association with cervical malignancy in the region. Consistent with global literature, HPV-16 was the most predominant genotype, identified in 76.3% (n=161) of all HPV-positive cases either as a single infection or in combination with other

types [5]. This aligns with previous research highlighting that HPV-16 and 18 are the primary drivers of cervical carcinogenesis worldwide [4]. While HPV vaccines are highly effective in preventing vaccine-type infections, their maximum protection is conferred when administered before exposure. However, the efficacy of vaccination in adults has been demonstrated in randomized clinical trials, suggesting that unvaccinated adults in our population could still benefit from "catch-up" strategies [6]. This is particularly relevant as adults remain at continuous risk for new HPV acquisition and subsequent disease [13]. Interestingly, while HPV-18 is typically the second most common type globally. In present study found HPV 18 was 4.3%(n=9) HPV-39 was 3.3%(n=7) to be relatively prominent after HPV-16. This variation emphasizes the importance of understanding local genotype distribution to optimize the impact of multi-valent HPV vaccines in the Bangladeshi context.

Our study revealed a significant association between socioeconomic status and HPV infection. Nearly two-thirds 64.5%(n=136) of HPV-positive subjects were from low-income backgrounds. This aligns with global observations confirming that women from lower socioeconomic strata face a disproportionate risk, likely due to limited access to healthcare, lack of awareness regarding preventive measures, and nutritional compromises that may facilitate viral persistence [7, 8]. Furthermore, the high rate of illiteracy 41.7%(n=125) among the participants suggests that educational barriers continue to hinder the success of cervical cancer screening programs [10]. Interestingly, while our study focused on a heterosexual female cohort, global data suggests that risk profiles vary significantly by sexual orientation and practice, with factors that directly measure sexual activity such as a higher number of sexual partners and younger age at first sexual activity consistently showing the strongest association with infection [6].

The mean age of 46.8 years and the high prevalence of invasive cancer 58.3%(n=175) suggest that many women present to tertiary facilities only at advanced stages of the disease. While the association between increasing age and infection often shows an unclear pattern globally. Some evidence suggests that populations older than 50 years may be at a higher risk compared to those under 50 years [6]. In the Bangladeshi context, this may be exacerbated by the lack of organized screening, leading to the high rate of invasive cancer observed in our study. While factors like early sexual debut (≤15 years) and high parity (95% multiparous) were frequent in our study population. They did not reach statistical significance as determinants for HPV positivity within this specific cohort. This may be due to the fact that the majority of our study population all having some form of cervical lesion, shared these baseline reproductive characteristics. Understanding these risk factors is vital for physicians to facilitate vaccination and screening decisions in non-adolescent cohorts [14].

However, we observed a notable trend regarding smoking. While active smoking was low (4.7%), the prevalence of passive smoking was high among HPV-positive women (48.8%) compared to HPV-negative women (p = 0.072). This supports the hypothesis that tobacco exposure, even second-hand, may impair the local immune response in the cervical transformation zone, aiding in the persistence of high-risk HPV [6, 9]. In our study, over two-thirds (68.7%) of participants used hormonal contraceptives. According to recent literature summaries, consistent condom use is associated with significantly decreased odds of HPV infection, whereas other contraceptive methods do not provide similar protection and may be associated with increased infection rates [6].

The histopathological data showed that squamous cell carcinoma (SCC) was the most common malignancy (54.6%). The significant presence of CIN1, CIN2, and CIN3 reinforces the concept that there is a critical "window of opportunity" for intervention [3]. Given the high prevalence of

HPV-16, strengthening primary prevention through vaccination and secondary prevention through HPV DNA testing is essential for reducing the morbidity observed in this study.

Conclusion

The study concluded that high-risk HPV infection, particularly genotype 16, is highly prevalent among women with cervical lesions in Bangladesh. Socioeconomic deprivation emerged as a primary risk factor for HPV positivity, while passive smoking and early delivery showed concerning trends. To reduce the burden of cervical cancer, Bangladesh public health strategies should prioritize:

- **Widespread HPV Vaccination:** Targeting young girls before sexual debut to provide protection against the most common HPV DNA genotypes identified (16 ,18 & 39).
- **Enhanced Screening:** Shifting toward HPV-based screening as a primary tool in tertiary and primary care settings to identify high-risk women earlier than visual inspection alone.
- **Targeted Advocacy:** Focused education for women in low-socioeconomic strata to overcome socio-educational barriers to care.

References

Yang D, Zhang J, Cui X, Ma J, Wang C, Piao H. Risk factors associated with human papillomavirus infection, cervical cancer and precancerous lesions in large-scale population screening. Frontiers in Microbiology. 2022 Jun 30; 13:914516.

Taye BT, Mihret MS, Muche HA. Risk factors of precancerous cervical lesions: The role of women's socio-demographic, sexual behavior and body mass index in Amhara region referral hospitals; case-control study. PloS one. 2021 Mar 26;16(3): e0249218.

Abera GB, Yebyo HG, Hailekiros H, Niguse S, Berhe Y, Gigar G, Asmelash T, Goba G. Epidemiology of pre-cancerous cervical lesion and risk factors among adult women in Tigray, Ethiopia. PloS one. 2023 Jan 6;18(1): e0280191.

Saldaña-Rodríguez P, Bahena-Román M, Delgado-Romero K, Madrid-Marina V, Torres-Poveda K. Prevalence and risk factors for high-risk human papillomavirus infection and cervical disorders: baseline findings from an human papillomavirus cohort study. Cancer Control. 2023 Sep 16; 30:10732748231202925.

Wabo B, Nsagha DS, Nana TN, Assob CJ. Prevalence and risk factors associated with precancerous cervical lesions among women in two cities in Cameroon. Pan African Medical Journal. 2022 Apr 6;41(1).

Del Pino M, Vorsters A, Joura EA, Doorbar J, Haniszewski M, Gudina IA, Kodjamanova P, Velicer C, Drury R. Risk factors for human papillomavirus infection and disease: A targeted literature summary. J Med Virol. 2024;96(2): e29420. doi: 10.1002/jmv.29420.

Merera D, Jima GH. Precancerous Cervical lesions and associated factors among women attending cervical screening at Adama Hospital Medical College, Central Ethiopia. Cancer management and research. 2021 Mar 3:2181-9.

Teklehaimanot DA, Mekuria AD, Dadi AF, Derseh BT. Precancerous lesion determinants in women attending cervical cancer screening at public health facilities in North Shoa Zone, Amhara, Ethiopia: an unmatched case-control study. BMC Women's Health. 2024 May 3;24(1):271.

Beyene T, Akibu M, Bekele H, Seyoum W. Risk factors for precancerous cervical lesion among women screened for cervical cancer in south Ethiopia: Unmatched case-control study. PLoS One. 2021 Jul 15;16(7): e0254663.

Getinet M, Taye M, Ayinalem A, Gitie M. Precancerous lesions of the cervix and associated factors among women of East Gojjam, Northwest Ethiopia, 2020. Cancer management and research. 2021 Dec 29:9401-10.

Temesgen MM, Alemu T, Shiferaw B, Legesse S, Zeru T, Haile M, Gelanew T. Prevalence of oncogenic human papillomavirus (HPV 16/18) infection, cervical lesions and its associated factors among women aged 21–49 years in Amhara region, Northern Ethiopia. Plos one. 2021 Mar 24;16(3): e0248949.

Tenkir L, Mamuye A, Jemebere W, Yeheyis T. The magnitude of precancerous cervical lesions and its associated factors among women screened for cervical cancer at a referral center in southern Ethiopia, 2021: a cross-sectional study. Frontiers in Global Women's Health. 2023 Aug 16; 4:1187916.

Velicer C, Zhu X, Vuocolo S, Liaw KL, Saah A. Prevalence and incidence of HPV genital infection in women. Sex Transm Dis.2009; 36:696-703.

Martínez-Gómez X, Curran A, Campins M, et al. Multidisciplinary, evidence-based consensus guidelines for human papillomavirus (HPV) vaccination in high-risk populations, Spain, 2016. EuroSurveill. 2019; 24:1700857.