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Magnitude of precancerous cervical lesions induced by human papillomavirus subtypes 16 and 18 and associated factors among affected women

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Abstract. The present study aimed to assess the magnitude of precancerous cervical lesions induced by human papillomavirus (HPV) subtypes 16 and 18 and the associated factors among affected women. An institutional-based cross-sectional study was conducted among 337 women screened for cervical cancer using HPV and visual inspection with acetic acid tests. The results revealed that 14.2 and 13.9% of the respondents had HPV and precancerous cervical lesions, respectively. The mean age of the respondents was 36.7±9.1 years. Women in the age group of 56-65 years [adjusted odds ratio (AOR), 7.91; 95% confidence interval (CI), 1.95-32.09], age at first intercourse (AOR, 5.36; 95% CI, 1.58-18.13), history of sexually transmitted infections (STIs) (AOR, 3.52; 95% CI, 1.27-9.72), human immunodeficiency virus (HIV) positivity (AOR, 6.81; 95% CI, 1.99-23.54) and the number of sexual partners (AOR, 4.37; 95% CI, 1.15-17.3) were independent factors for the prevalence of HPV subtypes 16 and 18. Women in the age group of 56-65 years (AOR, 10.69; 95% CI, 2.24-50.93), history of STIs (AOR, 3.44; 95% CI, 1.35-8.78), HIV positivity (AOR, 16.7; 95% CI, 6.5-43.04) and multiple sexual partners (AOR, 3.29; 95% CI, 1.13-9.58) were key independent factors associated with the prevalence of precancerous cervical lesions induced by HPV subtypes 16 and 18. On the whole, the present study found a low prevalence of high-risk HPV infection and precancerous cervical lesions. Women aged >55 years, those who commenced sexual intercourse at an age <18 years, and women with a history of STIs, HIV and multiple sexual partners were factors for precancerous cervical lesions induced by HPV subtypes 16 and 18.

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Abbreviations: HIV, human immunodeficiency virus; HPV, human papillomavirus; IUCD, intrauterine contraceptive device; SCJ, squamocolumnar junction; STI, sexually transmitted infection; VIA, visual inspection with acetic acid

Key words: visual inspection with acetic acid, OncoE6TM Cervical Test, human papillomavirus, cervical lesion

Introduction

The uterine cervix has a simple columnar epithelium in the endocervix and a non-keratinized stratified squamous epithelium in the endocervix, with mucus-secreting glands in the lamina propria. The transformation zone, just outside the external ostium is prone to neoplasia caused by vaginal exposure (1).

The most prevalent type of cancer affecting the female reproductive system is cervical cancer, which is preceded by a protracted pre-invasive phase and is characterized microscopically by a spectrum of precancerous cervical lesions (2). The lesions may gradually progress to cervical cancer unless screened and treated early (3).

There is evidence to indicate that human papillomavirus (HPV) infection, age, the onset of sexual activity at a young age, multi-parity, having several sexual partners, the use of oral contraceptives, smoking, having a history of sexually transmitted infections (STIs) and human immunodeficiency virus (HIV) are all potential host variables (4). The primary cause of cervical cancer is HPV infection, which is sexually transmitted. Of note, two (subtypes 16 and 18) of the 150 HPV serotypes are oncogenic types. Often human immunity can spontaneously clear off the majority of HPV infections without treatment. However, in an immune deficiency state, the infection progresses into a cervical lesion. Finally, the lesion causes cervical cancer, unless it is detected and treated at an early stage.

Previous studies have demonstrated that 14% of global incidences and 18% of related deaths occur in Sub-Saharan African countries and 14-17% in Ethiopia (1,5-7). Moreover, studies performed in Arba-Minch and Gurage, Ethiopia have also demonstrated that the prevalence of high-risk

HPV infection and the development of precancerous cervical lesions was 17.3 and 27.7% respectively, which is a relatively high prevalence (8,9).

Contrary to other malignancies of the reproductive system, cervical cancer can be avoided by the early detection of a precancerous lesion through the screening and treatment of lesions. Any one of three techniques can be used to identify such lesions, namely the HPV deoxyribose nucleic acid test, pap smear and visual inspection with acetic acid (VIA) (10). At 1 min after applying acetic acid to the cervix, a well-defined aceto-whitish region forms, according to a positive VIA test result (3).

Improved screening coverage, vaccination accessibility, early cervical lesion treatment, and the identification and monitoring of risk factors are all critical for the management of the burden of cervical cancer. The aforementioned strategies significantly lower cervical cancer-related mortality and morbidity in settings with limited resources (11). In resource-constrained settings, the World Health Organization (WHO) 2013 cervical cancer guideline suggested routine screening for women of reproductive age using VIA or, where possible, HPV testing followed by cryotherapy treatment (12). The likelihood of unvaccinated HPV-negative women developing cervical cancer in the following 5 to 10 years is reduced, according to several studies, indicating that primary HPV testing is a crucial preventive measure, particularly for unvaccinated women (13).

Ethiopia began implementing preventive measures in September, 2010, and the national health strategy included the prevention and control of cervical cancer (10). Additionally, a pilot program to vaccinate schoolgirls against HPV genotypes 16 and 18 before they have their first sexual experience began in 2019 and included the Amhara region. Cervical lesions and HPV infection are widespread in the community despite the use of such preventive measures.

According to the Ethiopian cervical cancer treatment and prevention guidelines report, over the past 5 years, immense progress has been made including the introduction of HPV vaccination into the routine immunization program and the scale-up of national cervical cancer screening and treatment using the 'see and treat' approach (10). The vaccination program strengthens at each level of health institution in Ethiopia. Regional health bureaus planned to implement the routinization of HPV vaccination within regions. Woreda health offices of Amhara regional state play a crucial role in sharing information, mobilizing women for service and facilitating HPV vaccination for target girls. Health facilities administer HPV vaccination for eligible girls as per the national immunization schedule. Moreover, the school-based HPV vaccination program will be coordinated by the health extension worker at the community level, and eligible out-of-school girls will be referred to a health facility for vaccination. In addition to the required health facilities, media schools, and the Ministry of Health are also the most effective advocates for facilitating HPV vaccination. Currently, three types of HPV vaccination (bivalent, quadrivalent and nonavalent) are introduced in different countries. Ethiopia also used such vaccines to compact widely distributed HPV infection. The vaccine helps lower the prevalence of high-risk HPV strains responsible for these conditions. There is ample evidence to indicate that the aforementioned HPV bivalent vaccine protect against genotype 16 and18, the quadrivalent vaccine genotype 6, 11, 16 and 18 and the nonavalent which give protections five additional genotypes (31, 33, 45, 52 and 58) (10, 14-17).

Of note, there are data available regarding HPV infection in certain other countries. However, according to the authors' research, before the present study was conducted, only one related study had been conducted in Ethiopia 4 years prior (18). The objective of the present study was to ascertain the prevalence of infection with HPV subtypes 16 and 18, premalignant cervical lesions and associated variables among women undergoing cervical cancer screening in hospitals in East Gojjam Zone, Northwest Ethiopia. As a result, the present study provides information to the relevant authorities for designing intervention plans, such as health promotion and education regarding the management of cervical precancerous lesions. This could improve current cervical cancer preventive and control initiatives. The results of the present study may serve as the starting point for further research.

Patients and methods

A facility-based cross-sectional study design was conducted at two hospitals which are located in East Gojjam Zone, Ethiopia from February to April, 2021 Gregorian calendar (G.C) The sample size was calculated using a single population proportion formula. By considering the prevalence of HPV at 16% (4) with a 5% margin of error, 95% confidence level, and design effect of 1.5; the final sample size was 337. The final sample size was proportionated to the selected two hospitals [Debre Markos Comprehensive Referral Hospital (n=200) and Finote Selam Hospital (n=137)], which provide HPV testing and cervical cancer screening; these hospitals were selected from 11 public hospitals (one referral and ten primary hospitals) based on the lottery method (involves assigning a unique identifier to each member of the population, then randomly drawing identifiers to select the sample (19). The research catchment area of Debre Markos University includes a total of 11 hospitals (having equal chances to be selected as study settings); using the lottery method, the present study selected two hospitals for conducting the actual study setting. The screening women of reproductive age for HPV and cervical lesions using VIA in Ethiopia has been scaled up to all hospitals since 2018 (10).

Ethical clearance was obtained from the Ethics Committee of the School of Medicine, Debre Markos University (1874/02/2021). Moreover, permission was obtained from the East Gojjam Zone Health Department and managers of selected hospitals. The present study was carried out in accordance with the Declaration of Helsinki. Informed written consent was obtained from the study participants after being informed about the voluntary basis of participation. All methods used in the study were in line with the regulations and guidelines for the treatment of diseases in hospitals of East Gojjam. The confidentiality of patient information was protected.

Study population. Up until the required sample size was attained, women who had cervical cancer screening at selected hospitals were included in the study. However, to prevent unneeded discomforts linked to the endocervical swabs of the procedure, women with verified malignant tumors and pregnant women were excluded from the present study.

Data collection procedure and quality assurance. Data were collected using a pre-tested structured questionnaire that was created after reviewing other related studies and being modified following the objectives of this particular study (8,20-23). Data collectors received 2 days of training on data collection practices. The four supervisors were tasked with assessing the data collection, while the four BSc-qualified nurses who were certified in cervical screening and working in the gynecology ward in the selected hospitals were assigned to collect the data. The questionnaire was initially written in English before being translated into Amharic. All clients of the reproductive age group who were tested by routine VIA test were invited to participate in this study. After receiving verbal agreement from the clients in the healthcare institution, data were collected from them through face-to-face interviews.

A trained professional conducted the screening procedure following the cervical cancer and HPV infection screening protocol outlined in the guidelines (10). Prior to the actual data collection, the questionnaire was pre-tested among 5% of the study population in the Bichena Primary Hospital (Bichena, Ethiopia) to ensure its consistency and completeness, and appropriate modifications were performed.

Measurements and definitions. The following terms were used in the present study: i) Cervical precancerous lesions: These were used to denote dense aceto-white lesions with clearly defined edges that are found in the squamocolumnar junction (SCJ) transformation zone or if the entire cervix or a cervical growth has gone white. ii) Oncoprotein E6 HPV 16/18 testing: Women who participated in the study had their endocervical swabs taken by inserting the swab devices into the endocervix and rotating them three times in a counterclockwise direction. According to the manufacturer's instructions, the E6 HPV 16/18 oncoprotein detection lateral flow (LF) strip test (OncoE6™ Cervical Test; Arbor Vita Corporation) was used to identify the HPV types 16 and 18 in the cervical swabs. The test results were also interpreted following the manufacturer's guidelines (18). iii) Aceto-whitish: After applying 5% acetic acid to the cervix, a white patch appeared, possibly indicating a precancerous lesion (10,24). iv) Use of a contraceptive technique: This term was used in cases where contraceptives, such as such as oral contraceptive pills, an injection, an implant, or intrauterine contraceptive devices (IUCDs) were used for ≥1 month. v) Early sexual initiation: Engaging in sexual activity prior to turning 18 years of age. vi) Multi-parity: Having more than two offspring. vii) Multiple partners for sexual activity: Having sexual relations with two or more individuals at the same time. viii) Positive for VIA: There are dense aceto-whitish regions that are well-defined, distinct, and near to the SCJ (10). ix) Negative for VIA: The cervix of VIA, which is healthy and has stayed light and pink in color, has no aceto-white lesions (10).

Data processing and statistical analysis. The acquired data were coded, entered and cleaned using EpiData version 4.6 (EpiData Association) before being exported into the SPSS version 26 software (IBM Corp.) for analysis after being ensured to be complete. Socio-demographic factors and the prevalence of HPV subtypes 16 and 18 and precancerous cervical lesions were summarized using appropriate descriptive analysis techniques, such as percentages, summary statistics and crosstabulation. Bivariate and multivariate logistic regression analyses were used to assess the risk factors associated with the presence of HPV and precancerous cervix lesions. Multivariate logistic regression was used to reanalyze the variables in the bivariate logistic regression that yielded $P<0.25$. Variables yielding $P<0.05$ with a 95% confidence interval (CI) were deemed statistically significant throughout repeated logistic regression analyses and were linked to the presence of HPV and precancerous cervix lesions.

Results

Sociodemographic characteristics of the participants. A total of 337 women aged 25-65 years were enrolled in the present study, with a mean age of 36.7±9.1 years. The response rate of the study participants was 100%. Among the study participants, 153 (45.4%) were in the age group of 25-35 years. Of the total respondents, 314 (93.2%) were Orthodox Christian followers followed by protestants. Among the study participants, 328 (97.3%) of them were Amhara followed by Oromo. Of these respondents, 136 (40.4) and 201 (59.6%) of them resided in rural and urban areas, respectively. The majority of 254 (75.4%) were married and 191 (56.7%) were housewives and 135 (40.1%) were not attending formal education (Table I).

Reproductive health characteristics. Among the study participants, 229 (68%) of them used contraceptive methods. Of those participants who used contraceptives 28 (12.3%), 61 (26.6%), 93 (40.6%) and 47 (20.5%) were using IUCDs, implants, injectables and pills, respectively. The majority of the study respondents [183 (54.3%)] had an irregular menstrual history in terms of menstrual regularity. A total of 75 respondents reported having experienced postcoital bleeding in the past, whereas the remaining respondents had no such history. The majority of the study participants had given birth to >3 children, with a mean number of parity of 4.13±2.5 children (Table II).

Lifestyle and sexual behavior. Only 45 (13.4%) of the participants in the present study had ever undergone a cervical cancer screening. A total of 7 (2.1%) of the respondents had ever smoked, and 22 (6.5%) of them regularly consumed alcohol. In total, 150 of the respondents had their first sexual intercourse before the age of 18 years, while the remaining 187 (55.5%) did so when they were at least 18 years of age, with the mean age at their first sexual intercourse being 17.01±3.5 years. Of the study participants, 265 (78.6%) had never used condoms throughout their lifetime. A total of 103 (30.6%) of the study participants had a history of STIs and 113 (33.5%) of them had a husband who had a history of STIs. Of note, 54 (16%) of the responders who underwent HIV testing were HIV seropositive. As regards several sexual encounters, 180 respondents (53.5%) reported having more than two sexual partners, while the remainder did not (Table III).

Prevalence of infection with HPV subtypes 16 and 18, and precancerous cervical lesions. The proportion of infection with HPV subtypes 16 and 18, and VIA positivity was evenly distributed across the age groups, as indicated in Table IV,

Table I. Sociodemographic characteristics of the women in the present study (n=337) aged 25-65 years in the East Gojjam Zone, Northwest Ethiopia, 2021.

Variables and category	Number	Percentage	Mean ± SD
Age, years			
25-35	153	45.4	36.7±9.1
36-45	117	34.7	
46-55	38	11.3	
56-65	29	8.6	
Religion			
Orthodox	314	93.2	
Muslim	7	2.1	
Protestant	16	4.7	
Ethnicity			
Amhara	328	97.3	
Oromo	9	2.7	
Residence			
Urban	201	59.6	
Rural	136	40.4	
Marital status			
Married	254	75.4	
Single	23	6.8	
Widowed	21	6.2	
Divorced	39	11.6	
Educational status			
Diploma and higher	67	19.9	
Secondary grades (9-12)	51	15.1	
Primary grades (1-8)	84	24.9	
No formal education	135	40.1	
Occupation			
Housewife	191	56.7	
Daily laborer	38	11.3	
Merchant	42	12.5	
Governmental employee	66	19.5	

Table II. Reproductive characteristics of the women in the present study (n=337) aged 25-65 years in the East Gojjam Zone, Northwest Ethiopia, 2021.

Variables and category	No. of patients	Percentage	Mean ± SD
Contraceptive method used			
Yes	229	67.9	
No	108	32.1	
Type of contraceptive used			
IUCD	28	12.3	
Implant	61	26.6	
Injectables	93	40.6	
Pills	47	20.5	
Menstrual regularity			
Regular	154	45.7	
Irregular	183	54.3	
Post-coital bleeding			
Yes	75	22.3	
No	262	77.7	
Have given birth			
Yes	273	81	
No	64	19	
No. of births			
<2	41	15.1	4.13±2.5
≥2	232	84.9	

IUCD, intrauterine contraceptive device.

while older participants (46-55 years) had considerably higher HPV and VIA positivity rates. The prevalence of infection with HPV subtypes 16 and 18 and precancerous cervical lesions among women screened for cervical cancer was 14.2% with (95% CI, 10.7-18.1) and 13.9% with (95% CI, 11.83-19.54) (Table V). The prevalence of infection with HPV subtypes 16 and 18 among women with and without cervical lesions was 82.9 and 3.1%, respectively (Table V). Infections with HPV subtypes 16 and 18 were present in 3.2% of HIV-negative women and in 72.2% of HIV-positive women, respectively Table VI.

Factors associated with infection with HPV subtypes 16 and 18, and precancerous lesions of the cervix. Variables yielding P<0.25 following bivariate analysis were deemed confounding factors, and they were reanalyzed in multivariate logistic regression analysis to ascertain their association with precancerous cervix lesions. In multivariate logistic regression analysis, those variables yielding P<0.05 were significantly associated with infection with HPV subtypes 16 and 18, and precancerous lesions of the cervix.

Bivariate logistic regression. The bivariate logistic regression analysis identified several factors associated with infection with HPV subtypes 16 and 18, and precancerous cervical lesions. Bivariate logistic regression analysis revealed that age, commencing sexual intercourse at <18 years of age, the woman's of STIs, HIV positivity and having two or more sexual partners were significantly associated with infection with HPV subtypes 16 and 18 (Table VI). Moreover, age, women with a history of STI, HIV seropositivity, and the number of sexual partners of women were found to be associated with the development of precancerous cervical lesions (Table VII).

Multivariate logistic regression. As demonstrated in Table VI, all variables in the table have a P-value <0.25 in bivariate logistic regression and were re-analyzed in multivariate logistic regression analysis. Controlling for the effect of confounders in the age group of 56-65 years, commencing sexual intercourse at <18 years of age, the woman's history of STIs, being HIV seropositive, and having multiple sexual partners were found

Table III. Lifestyle and sexual behavior characteristics of the women in the present study (n=337) aged 25-65 years in the East Gojjam Zone, Northwest Ethiopia, 2021.

Variables and category	No. of patients	Percentage	Mean ± SD
Cervical cancer screening before			
Yes	45	13.4	
No	292	86.6	
Smoking history			
Yes	7	2.1	
No	330	97.9	
Alcoholic history			
Yes	22	6.5	
No	315	93.5	
Age at first sexual intercourse			
<18	150	45.5	17.01±3.5
≥18	187	55.5	
Condom use during sexual intercourse			
Yes	72	21.4	
No	265	78.6	
STIs			
Yes	103	30.6	
No	234	69.4	
Partner with STIs			
Yes	113	33.5	
No	224	66.5	
HIV			
Positive	54	16	
Negative	283	84	
More than two sexual partners			
Yes	180	53.5	
No	157	46.5	

HIV, human immunodeficiency virus; STI, sexually transmitted infection.

to be significantly associated with the presence of infection with HPV subtypes 16 and 18.

Women in the age group of 56-65 years were 7.9-fold more likely to be infected with HPV subtypes 16 and 18 as compared to the age group of 25-35 years. As regards the early initiation of sexual intercourse, those women who commenced sexual intercourse prior to 18 years of age were 5.3-fold more likely to develop high-risk HPV infections than their counterparts. Women who had a history of STIs were 3.52-fold more likely to have a high-risk HPV infection as compared to those who had no history of STIs [adjusted odds ratio (AOR), 3.52; 95% CI, 1.27-9.72]. Women who had a HIV-positive serostatus were 6.8-fold more likely to have a high-risk HPV infection compared to those who were HIV-negative (AOR, 6.8; 95% CI, 1.99-23.54). Women who had two or more lifetime sexual partners were 4.37-fold more likely to be infected with HPV subtypes 16 and 18 as compared to those who had less than two sexual partners (AOR, 4.37; 95% CI, 1.15-17.3) (Table VI).

In addition, as shown Table VII, there was a significant association between precancerous cervical lesions and the age group of 56-65 years (AOR, 10.69; 95% CI, 2.24-50.93), a history of STIs (AOR, 3.44; 95% CI, 1.35-8.78), being HIV seropositive (AOR, 16.7; 95% CI, 6.5-43.04) and multiple sexual partners (AOR, 3.29; 95% CI, 1.13-9.58).

Discussion

The present study assessed precancerous cervical lesions induced by HPV subtypes 16 and 18, and associated factors among women aged 25-65 years. The prevalence of infections with HPV subtypes 16 and 18, and precancerous cervical lesions was 14 and 13.9%, which was lower than that in the studies conducted by Leyh-Bannurah *et al* (9) (17.3%) and Teka *et al* (8) (27.7%). This disparity could be the result of the test provider's abilities and the length of the study time differing. The present study employed an antigen detection method, whereas others used a molecular detection method to detect many HPV types. Worldwide, HPV types 16 and 18 are the most prevalent and are responsible for the majority of anogenital HPV-related malignancies in women (25). The present study found a prevalence of HPV of 3.1% among women without cervical lesions, which is consistent with a previous study performed in Sudan (3.2%) (26), although markedly lower than that in other East African countries, such as Mozambique (40.3%) (27) and Kenya (41.4%) (7). In the present study, 82.9% of women with cervical lesions had HPV. This finding is higher than that from previous studies by Bekele *et al* (28), and Ameya and Yerakly (29) in Jimma (67.1%) and Hawasa (49.3%), Ethiopia, respectively.

The present study revealed that the prevalence of infection with HPV subtypes 16 and 18 among women with and without cervical lesions was 83.3 and 3.1%, respectively. This result revealed a high prevalence, suggesting that HPV subtypes 16 and 18 are strongly associated with cervical lesions, consistent with the literature (7,25) that these subtypes are high-risk and major contributors to cervical lesions. The prevalence of 3.1% also indicated a lower prevalence of HPV subtypes 16 and 18 in women without cervical lesions, supporting their role in the development of cervical lesions. Moreover, the Cohen kappa agreement test of the two test methods revealed the following: Substantial agreement between them (kappa value of 0.792 with a P-value 0.001). This result revealed that the two test methods are in strong concordance in detecting the presence or absence of infection with HPV subtypes 16 and 18. The P-value 0.001 signifies that the observed agreement is statically significant and highly unlikely to be due to chance; that reinforces the kappa value and concordance between the two test methods.

As regards precancerous cervical lesions, the prevalence in the present study was higher than that in studies carried out in Bahir Dar Northwest Ethiopia (14.3%) (30), Dessie Northeast Ethiopia 6.9%, Madagascar (11.3%) (31) and Malawi (12.4%) (31). This discrepancy may result from the different ages

Table IV. Proportion of infection with HPV subtypes 16 and 18 and precancerous cervical lesions among the women in the present study (n=337) aged 25-65 years in East Gojjam Zone, Northwest Ethiopia, 2021.

	HPV infection based on E6 16/18 antigen test		VIA cervical cancer screening	
Variables and categories	Positive, n (%)	Negative, n (%)	Positive, n (%)	Negative, n (%)
Age, years				
25-35	11 (7.2)	142 (92.8)	8 (5.2)	145 (94.8)
36-45	13 (11.2)	104 (88.9)	17 (14.5)	100 (85.5)
46-55	14 (36.8)	19 (65.5)	12 (31.6)	26 (68.4)
56-65	10 (34.5)	221 (65.5)	10 (34.5)	19 (65.5)
Education				
No formal education	29 (21.5)	106 (78.5)	29 (21.5)	106 (78.5)
Primary grades (1-8)	12 (14.3)	72 (85.7)	10 (11.9)	74 (88.1)
Secondary grades (9-12)	3 (5.9)	48 (94.1)	4 (7.8)	47 (92.2)
Diploma and above	4 (6)	63 (94)	4 (6)	63 (94)
Marital status				
Married	35 (13.8)	219 (86.2)	36 (14.2)	218 (85.8)
Single	2 (8.7)	21 (91.3)	1 (4.3)	22 (95.7)
Widowed	9 (42.9)	12 (57.1)	6 (28.6)	15 (71.4)
Divorced	2 (5.1)	37 (94.9)	4 (10.3)	35 (89.7)
Residence				
Rural	25 (18.4)	111 (81.6)	27 (19.9)	109 (80.1)
Urban	23 (11.4)	178 (88.6)	20 (10)	181 (90)

HPV, human papillomavirus; VIA, visual inspection with acetic acid.

Table V. Prevalence of infection with HPV subtypes 16 and 18 among the women in the present study (n=337) aged 25-65 years, with and without cervical lesions, in East Gojjam Zone, Northwest Ethiopia, 2021.

A, Prevalence of infection with HPV subtypes 16 and 18 and cervical lesions

Tissue type	No. of patients	HPV-positive, n (%)	HPV-negative, n (%)
Cervical lesions	47	39 (82.9)	8 (17.1)
No cervical lesions	290	9 (3.1)	281 (96.9)

B, Prevalence of infection with HPV subtypes 16 and 18 and precancerous cervical lesions

Variable	Percentage (%)	95% confidence interval
HPV subtypes 16 and 18	14.2	10.7-18.1
Precancerous cervical lesion	13.9	11.83-19.54

HPV, human papillomavirus.

of the study populations, the underlying prevalence of STIs, and the reproductive characteristics of the study participants.

The present study also assessed factors associated with the progression of high-risk HPV infection to precancerous cervical lesions among the study participants and the findings revealed that respondents in the age group of 56-65 years, those who commenced sexual intercourse at <18 years of age, women with STIs, being HIV seropositive, and having multiple sexual partners were predictors of chronic infection with oncogenic HPV subtypes and progression to cervical lesions. As regards cervical lesions, the age group of 56-65 years, a history of STIs, being HIV seropositive, and multiple sexual

Table VI. Multivariate logistic regression analysis of factors associated with infection with HPV subtype 16 and 18 among the women in the present study (n=337) aged 25-65 years in East Gojjam Zone, Northwest Ethiopia, 2021.

	HPV infection based on E6 16/18 antigen test				
Variables and category	Positive, n (%)	Negative, n (%)	COR (95% CI)	AOR (95% CI)	P-value
Age, years					
25-35	11 (7,2)	142 (92.8)	1	1	NS
36-45	13 (11.2)	104 (88.9)	0.47 (0.05-0.39)	2.24 (0.65-7.71)	0.19
46-55	14 (36.8)	19 (65.5)	0.23 (0.09-0.61)	4.49 (1.09-18.47)	0.06
56-65	10 (34.5)	289 (85.8)	1.10 (0.40-3.04)	7.91 (1.95-32.09)	0.01[a]
Residence					
Rural	25 (18.4)	111 (81.6)	0.07 (1.74-3.22)	1.33 (0.38-4.61)	0.64
Urban	23 (11.4)	178 (88.6)	1	1	NS
Educational status					
No formal education	29 (21.5)	106 (78.5)	0.23 (0.07-0.69)	0.34 (0.10-1.19)	0.65
Primary grades (1-8)	12 (14.3)	72 (85.7)	0.22 (0.06-0.78)	1.43 (0.25-8.04)	0.68
Secondary grades (9-12)	3 (5.9)	48 (94.1)	0.61 (0.29-1.27)	0.88 (0.17-4.39)	0.87
Diploma and above	4 (6)	63 (94)	1	1	NS
Use of contraceptives					
No	13 (12)	95 (88)	1	1	NS
Yes	35 (15.3)	194 (84.7)	0.75 (0.38-1.51)	1.61 (0.58-4.41)	0.35
Age at first intercourse					
<18	41 (24.7)	125 (75.3)	0.14 (0.05-0.34)	5.36 (1.58-18.13)	0.01[a]
≥18	7 (4.1)	164 (95.9)	1	1	
No. of births					
1-2	5 (15.6)	27 (84.4)	1	1	NS
3-4	26 (12.1)	188 (87.9)	0.19 (0.06-0.67)	0.31 (0.07-1.31)	0.11
>4	13 (48.1)	14 (51.9)	0.14 (0.06-0.35)	0.92 (0.17-4.93)	0.93
Abortion					
No	27 (11.2)	215 (88.8)	1	1	NS
Yes	21 (22.1)	72 (77.9)	0.44 (0.23-0.83)	0.51 (1.32-1.89)	0.51
Patient's history of STIs					
No	26 (11.1)	208 (88.9)	1	1	NS
Yes	22 (21.4)	81 (78.6)	0.46 (0.24-0.85)	3.52 (1.27-9.72)	0.02[a]
Partners history of STI					
No	28 (12.5)	196 (87.5)	1	1	NS
Yes	20 (17.7)	93 (82.3)	1.51 (0.86-2.81)	0.43 (0.03-5.64)	0.52
HIV serostatus					
Negative	9 (3.2)	274 (96.8)	1	1	NS
Positive	39 (72.2)	15 (27.8)	0.01 (0.01-0.03)	6.81 (1.99-23.54)	0.01[a]
No. of sexual partners					
<2	5 (3.2)	152 (96.8)	1	1	NS
≥2	43 (24.3)	134 (75.7)	9.55 (3.75-25.34)	4.37 (1.15-17.3)	0.03[a]

[a]Indicates statistically significant difference (P<0.05). HPV, human papillomavirus; HIV, human immunodeficiency virus; STI, sexually transmitted infection; COR, crude odds ratio; AOR, adjusted odds ratio; NS, not significant.

partners were factors significantly associated with the presence of a precancerous cervical lesions.

According to the findings of the present study, women between the ages of 56 and 65 years were 7.9-fold times more likely to be infected with HPV subtypes 16 and 18, and to develop precancerous cervical lesions than women between the ages of 25 and 35 years. This finding is consistent with the findings of other studies (6,22,32-34). This may be due to immune deficiency being predominant in women who are at an advanced age, causing multiple infections.

Table VII. Multivariate logistic regression analysis of factors associated with a precancerous cervical lesion among the women in the present study (n=337) aged 25-65 years in East Gojjam Zone, Northwest Ethiopia, 2021.

	VIA result				
Variables and category	Positive, n (%)	Negative, n (%)	COR (95% CI)	AOR (95% CI)	P-value
Age, years					
25-35	8 (5.2)	145 (94.5)	1	1	
36-45	17 (14.5)	100 (85.5)	3.08 (1.28-7.41)	3.24 (0.93-11.29)	0.65
46-55	12 (31.6)	26 (68.4)	8.36 (3.11-22.45)	5.59 (1.13-22.77)	0.06
56-65	10 (34.5)	19 (65.5)	9.53 (3.35-27.13)	10.69 (2.24-50.93)	0.01[a]
Age at first intercourse					
<18	36 (21.7)	130 (78.3)	0.18 (0.07-0.41)	0.34 (0.11-1.01)	0.65
≥18	11 (6.4)	160 (93.6)	1	1	
No. of births					
1-2	6 (18.8)	26 (81.3)	1	1	
3-4	27 (12.6)	187 (87.4)	0.62 (0.23-1.65)	0.43 (0.102-1.86)	0.26
>4	12 (44.4)	15 (55.6)	3.46 (1.07-11.14)	1.52 (0.28-8.28)	0.62
History of STIs					
No	24 (10.3)	210 (89.7)	1	1	
Yes	23 (22.3)	80 (77.7)	2.51 (1.34-4.71)	3.44 (1.35-8.78)	0.01[a]
HIV serostatus					
Negative	15 (5.3)	268 (94.7)	1	1	
Positive	32 (59.3)	22 (40.7)	25.98 (12.25-55.11)	16.7 (6.5-43.04)	0.01[a]
No. of sexual partners					
<2	6 (3.8)	152 (96.2)	1	1	
≥2	41 (23.2)	136 (76.8)	7.5 (3.12-18.42)	3.29 (1.13-9.58)	0.03[a]

[a]Indicates statistically significant difference (P<0.05). HPV, human papillomavirus; HIV, human immunodeficiency virus; STI, sexually transmitted infection; COR, crude odds ratio; AOR, adjusted odds ratio.

According to the present study, the average age of the first sexual activity of the participants was 17.01 years, which was closer to the average age of their first marriage, which was 16.8 years. This implies that women generally begin sexual intercourse after getting married for the first time. Approximately 150 respondents (44.5%) had their first sexual experience before 18 years of age. This higher prevalence of early initiation of sexual intercourse is due to early marriage in the country Ethiopia specifically in the present study setting is relatively common. The findings demonstrated that women who commenced sexual intercourse before the age of 18 years were 5.36-fold more likely to have chronic infection with HPV subtypes 16 and 18, and develop cervical lesions; this finding is consistent with that of other studies performed in different settings (8,35-38). This may be a result of the extended duration of HPV virus exposure and the slow onset of precancerous cervical abnormalities (39,40).

In the present study, precancerous cervical lesions were 1.5-fold more likely to occur in women with STI histories than in their counterparts. The findings of other studies support this finding (32,41-44). Co-infections with HPV and other STIs may be the reason for this connection. The present study was similar to studies from Zambia (45) and Rwanda (46), which revealed a higher prevalence of HPV subtypes 16 and 18 (72.2%) among HIV-positive women than among women without HIV (3.2%). Moreover, women who had a HIV-positive serostatus were 6.8-fold more likely to have precancerous cervical lesions compared to those who were HIV-negative. This finding is strongly supported by studies performed in Tanzania (47), Uganda (41) and Southern Ethiopia (8). This association may be due to HIV infection being an immune-suppressive disease that increases the likelihood of concurrent HPV infection (48).

STIs are a sign of having had unsafe sex, which is how genital human HPV is primarily transmitted. Concurrent to this, the present study found a slightly higher prevalence of HPV infections among women who had a history of STIs (12.5%) than those who had not (17.7%). Moreover, having multiple sexual partners had a 11.5-fold higher odds of cervical lesions. These findings are consistent with the findings of other studies by different authors in different countries (8,20,33,38,44,49,50). The possible explanation is due to the incidence of having multiple sexual partners, which increases the likelihood of acquiring HPV infection, which in turn, causes cervical cancer. It was also found that the early initiation of sexual intercourse, HIV infection, STIs and

multiple sexual partners were significantly associated with a precancerous cervical lesion.

In the present study, the necessary factors were examined as much as possible as the study made use of primary data. The principal investigator supervised the daily data collection activity. The questionnaire was pretested and required modification was made. The response rate was 100%.

The present study had some limitations however, which should be mentioned. The present study, which employed a cross-sectional study design and involved women examined for HPV subtypes (16 and 18) and precancerous cervical lesion, did not demonstrate a cause-and-effect relation. The findings of the present study cannot be applied to the general population of Ethiopia as it was limited to Debre Markos Comprehensive Referral Hospital and Finote Selam Hospital. Moreover, the present study employed a method to confirm HPV protein for only some of the serotypes. This selective confirmation may introduce bias and limit the generalizability of the findings. The lack of comprehensive serotype confirmation could affect the accuracy of prevalence estimates and associations with cervical lesions.

In conclusion, the present study identified a relatively low prevalence of infection with HPV subtypes 16 and 18 and precancerous cervical lesions. This may be a result of the poor sensitivity of VIA and the exclusion of pregnant women with cervical cancer who were also carrying a child. According to the present study, testing for HPV and VIA combined, increases the early identification of women who are at a high risk of cancerous lesions and who require effective cervical cancer screening programs. The present study revealed that the age group of 55-65 years, the use of oral contraceptives, a history of STIs, being HIV positive and having multiple sexual partners are factors independently associated with the presence of infection with HPV subtypes 16 and 18, and with the progression of this infection to precancerous cervical lesions.

Therefore, the use of outreach cervical cancer screening programs to encourage more women to participate in screening is required. Moreover, it is advised that all women who are >55 of age and who have a history of STIs, HIV and several sexual partners should be screened for cervical cancer. Health professionals should provide health education regarding prevention and management principles of cervical cancer. Healthcare professionals and the public need to be educated about the combined benefits of HPV and VIA testing. Moreover, pre-teens and teens need to be encouraged to become vaccinated against HPV. Parents also need to be educated about the benefits of HPV vaccinations. In addition, strong policies and guidelines need to be developed for the prevention and control of cervical precancerous lesions. Furthermore, a wider range of studies is also warranted in order to understand VIA-positive results in women infected with HPV.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MG, MJ, HB, TB and EF were involved in the drafting of the project. MG, GA and BA were involved in the reviewing and editing of the project. MG, AA, BA, TB and MJ were involved in the study methodology. MG, MJ, EF, HB, TB and GA were involved in the investigative aspects of the study. MJ, TB, HB, AA and EF supervised the study. MG, MJ, AA, TB and EF were involved in the formal analysis. MG, AA, BA and EF were involved in the writing of the original draft of the manuscript. MG, MJ and TB were involved in the writing, reviewing and editing of the manuscript. All authors contributed to manuscript revision and have read and approved the final version of manuscript. MG and TB confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Ethical clearance was obtained from the Ethics Committee of the School of Medicine, Debre Markos University (1874/02/2021). Moreover, permission was obtained from the East Gojjam Zone Health Department and managers of selected hospitals. The present study was carried out in accordance with the Declaration of Helsinki. Informed written consent was obtained from the study participants after being informed about the voluntary basis of participation. All methods used in the study were in line with the regulations and guidelines for the treatment of diseases in hospitals of East Gojjam. The confidentiality of patient information was protected.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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