

# Precancerous cervical lesion and associated factors among HIV-infected women on ART in Amhara Regional State, Ethiopia: A hospital-based cross-sectional study

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## Introduction

Cervical cancer is the second most common cancer in women.<sup>[1]</sup> Human papillomavirus (HPV) infection is a known cause of cervical, anal, vulva, vagina, and penis cancers as well as head and neck cancers.<sup>[2]</sup> Precancerous cervical lesions and cervical cancer are considered to be more aggravated and rapidly progresses in immune-compromised patient.<sup>[3]</sup> Cervical cancer is intersecting epidemic with human immunodeficiency virus (HIV) in sub-Saharan Africa where it has been the second most common cause of cancer-related death in women.<sup>[4]</sup> The high prevalence of precancerous cervical lesion among both male and female partners infected with HIV contributes for transmission of both HIV and HPV.<sup>[5]</sup>

A number of factors including health care, clinical, socioeconomic, reproductive, and behavioral-related factors

## ABSTRACT

**Objective:** Cervical cancer, which is caused by human papillomavirus, is one of the common cancers in women worldwide. The proportion of precancerous cervical lesion among HIV-infected women has not been investigated yet in this study area. The aim of this study was to determine the proportion of precancerous cervical lesion and associated factors among HIV-infected women on ART in Woldia and Dessie Hospitals, Amhara Regional State, Ethiopia.

**Methods:** A hospital-based cross-sectional study was conducted on 284 HIV patients. Data were collected using a structured questionnaire and visual inspection. Pap smear test was employed for confirmation of cancer. Descriptive statistics were used to summarize findings. A logistic regression model was considered to identify predictors of precancerous cervical lesions. Those variables with  $P < 0.05$  at a 95% confidence interval were considered as statistically significant.

**Results:** The overall proportion of precancerous lesion among HIV-infected women in this study was 9.9%. Among HIV-infected women age greater than 30 years old, single in marital status, commercial sex worker, had any other sexually transmitted infection, more than one sexual partner, more than two children and with vaginal wall abnormality were factors associated with the occurrence of precancerous cervical lesion.

**Conclusion:** The proportion of precancerous cervical lesion among HIV-infected women was low compared to some previous studies conducted among HIV-infected women in Ethiopia. Therefore, regular screening of HIV-infected women for precancerous cervical lesion is very important by giving especial consideration to identified associated factors.

**Keywords:** Precancerous cervical lesion, HIV-positive women, ART, Ethiopia

play a pivotal role to facilitate the HPV and HIV virus-mediated precancerous cervical lesion.<sup>[6]</sup>

Most of the time, HPV had caused precancerous cervical lesion and cancer in women and can be screened and treated easily before it will turn into invasive cancer.<sup>[7]</sup> However, most women in resource-poor countries do not have access to a screening program. Diagnosis and screening problem are a major challenge in developing countries. The actual coverage of cancer screening in developing countries is 19% compared to 63% in developed countries. To this end, 1% or less screening rate was observed in countries such as Bangladesh, Ethiopia, and Myanmar.<sup>[8]</sup> Visual inspection with acetic acid or with Lugol's iodine followed by biopsy and colonoscopy examination for cancer cases applied to improve the detection of precancerous cervical lesions. This technique was applied in most developing countries including Ethiopia which tried to apply a rational approach for screening

and subsequent management of precancerous cervical lesion in HIV-infected women.<sup>[9]</sup>

There are few studies conducted in Ethiopia regarding precancerous cervical lesion. However, the proportion of the precancerous cervical lesion and associated factors among HIV-positive women on antiretroviral therapy (ART) was not investigated before in the study area. Therefore, this study was aimed to determine the proportion of precancerous cervical lesion and associated risk factors among HIV-positive women on ART attending Woldia and Dessie Hospital, Ethiopia.

## Methods

### Study area, design, and period

An institutional-based cross-sectional study was conducted among HIV-positive women on ART in Woldia and Dessie referral hospitals, Amhara Regional State from February to March 2018. Even though precancerous cervical lesion screening service is present in many hospitals of Amhara Regional State, but these two hospitals were selected for this study because of high load of patients were utilizing the screening service compared to others. Woldia is located 520 km from the capital city of Ethiopia, Addis Ababa. The town is bounded by Lalibela town to the west, Kobo town to the north. Dessie referral hospital is found in South Wollo zone and is 400 km far from Addis Ababa. The town is bounded from the east Kombolcha and from the north Haik town. In Woldia Hospital, a total of 4350 HIV patients were on ART among whom 2078 of them were female. In Dessie Hospital, a total of 4210 HIV patients were on ART among whom 2294 were female.<sup>[10]</sup>

### Sample size and sampling techniques

The sample size was determined using a single population proportion formula using the prevalence of precancerous cervical lesion (22.1%) from a study conducted in Hawassa Hospital, Southern Ethiopia.<sup>[11]</sup> The final sample size for this study including 10% non-response rate was 291. The final sample size was allocated proportionally based on the number of HIV-infected female attending Woldia and Dessie Hospitals. We include 134,150 study participants from Woldia and Dessie Hospital, respectively. The study participants were selected consecutively until the required sample size was fulfilled.

### Data collection methods

#### *Face-to-face interview*

Data were collected by eight data collectors who had training on cervical cancer screening (three nurses and four midwifery and one gynecologist) using structured questionnaire adapted from previous literature.<sup>[11-13]</sup> The questionnaire contains sociodemographic characteristics, clinical factors, and behavioral factor.

#### *Visual inspection methods*

The visual inspection procedure was conducted by trained nurses and midwives working in the cancer screening and treatment centers of the hospitals. Unlubricated bivalve speculum was inserted into the vagina to visualize the cervix using a halogen focus lamp which was used to look the squamocolumnar junction (SCJ). Any excess mucus found in it was cleaned using a cotton swab. Then, a 5% acetic acid solution was applied to the cervix and the findings were reported within 1 min.<sup>[11,14]</sup> Precancerous cervical lesions were defined as being dense acetowhite lesions with well-defined margins which were observed within the vicinity of the transformation zone originating from the SCJ, or if the whole cervix or cervical growth turned white.<sup>[11,14]</sup> A suspicion of invasive cervical cancer (ICC) was defined as any cervical ulcer or growth being observed. The results of the visual inspection were classified as negative, positive, or suspicious for ICC according to the International Agency for Research on Cancer training manual. For uncertainty of the screening result, the nurses consulted a trained gynecologist for confirmed the diagnosis.

#### *Data quality control*

The questionnaire was translated into the local language and back-translated to the English language for its consistency. The questionnaire was pretested on 5% of the sample size in Kobo Hospital to ensure its consistency, completeness and appropriate modifications were made before the actual data collection. Data collectors were trained for 2 days on the data collection tool and the data collection procedure. The collected data were checked for completeness and consistency by the supervisors. Double data entry was done by two data clerks to check its consistencies.

#### *Method of data analysis*

The data were first coded, entered, and cleaned using Epi data statistical software version 3.1 and then exported into the Statistical Package for the Social Sciences version 22 software for analysis. Descriptive statistics such as percentages and mean and standard deviation were used to summarize findings. A logistic regression model was considered to identify predictors of precancerous cervical lesions. First, bivariate analysis was done between each independent variable and outcome variables. Those variables with  $P < 0.05$  at 95% confidence interval were regarded as statistically significant factors associated with the presence of precancerous cervical lesions.

#### *Ethics approval and consent to participate*

Ethical clearance was obtained from Haramaya University, College of Health and Medical Sciences, Institutional Health Research Ethics Review Committee. Permission was obtained from Woldia and Dessie Hospital. After the purpose and procedure of the research was explained, written, informed, and signed consents were taken from each study participants. The data were kept confidentiality. There was no direct payment

for participating in this study. Perhaps, treatment required following laboratory positive findings and VIA stage. The treatment was facilitated by investigators and given free of charges.

## Results

### *Sociodemographic characteristics*

A total of 284 HIV-infected women were enrolled in the study, with 97.6% response rate. The age range of the study participants was from 18 to 65 years with a mean age of 34.48 years (Standard deviation  $\pm$  9). Majority of study participants were urban dwellers (80.9%). Among the study participants, 40.2% and 40.1% of them were married and able to write and read, respectively. One hundred forty (49.3%) of them were orthodox and majority (78.9%) of them were from Amhara ethnic group. Seventy seven (27.1%) were commercial sex workers and 34.2% of participants were earning  $\leq$  17.86 USD/month [Table 1].

### **Reproductive, clinical, and behavioral characteristics**

Sixty-seven (23.6%) of the study participants were started practicing sex before 15 years of age. The large proportion (78.9%) of the study participants become pregnant at list once in their lifetime and 28.5% of them were  $>$  20 years of age at the time of their first pregnancy. One hundred thirteen (39.8%) participants had a history of abortion at least once in their lifetime. From the total study participants, about 70.4%, 29.9%, and 23.9% of the participants had CD<sub>4</sub> count  $>$ 200 cells/mm<sup>3</sup>, history of sexually transmitted infection (STI), and vaginal wall abnormality, respectively [Table 2].

### **Proportion and factor associated with precancerous cervical lesion**

The overall proportion of precancerous cervical lesion was 9.9% (95% CI: 6.3, 13.17). In bivariate logistic regression analysis, variables such as age, marital status, occupation, parity, any other STI, number of sexual partners, and vaginal wall abnormality were found significant ( $P < 0.05$ ) considered as a candidate for multivariate logistic regression analysis. Among which, age, marital status, occupation, parity, any other STI, number of sexual partner and vaginal wall abnormality were still found statistically significant in multivariate logistic regression analysis ( $P < 0.05$ ) [Table 3].

In multivariate analysis, those who were infected with any other STI were almost 5 times more likely to develop precancerous cervical lesion compared to STI non-infected individuals (AOR = 4.515; 95% CI: 1.496–13.602). Those who had vaginal wall abnormality were more than 4 times more likely to develop precancerous cervical lesion compared to individual who had normal vaginal wall (AOR = 4.242; 95% CI: 1.423–12.676). Individual who was commercial sex worker had almost 5 times was more likely to develop precancerous cervical lesion compared to a non-commercial sex worker

**Table 1:** Sociodemographic characteristics of human immunodeficiency virus-positive women on antiretroviral therapy in Woldia and Dessie Hospital, Amhara Regional State, North Ethiopia, 2018 ( $n=284$ )

Variables	Frequency (%)
Age (years)	
<30	139 (48.9)
>30	145 (51.1)
Resident	
Urban	230 (80.9)
Rural	54 (19.1)
Ethnicity	
Oromo	9 (3.2)
Amhara	224 (78.9)
Tigre	51 (17.9)
Religion	
Muslim	110 (38.7)
Orthodox	140 (49.3)
Protestant	34 (12.0)
Educational status	
Unable to read and write	114 (40.1)
Able to read and write	82 (28.9)
1–8 grades	63 (22.2)
9–12 grades	25 (8.8)
Marital status	
Married	116 (40.9)
Single	18 (6.3)
Widowed	65 (22.9)
Divorced/separated	85 (29.9)
Occupation	
Farmer	40 (14.1)
Non-employee	75 (26.4)
CSW	77 (27.1)
Merchant	92 (32.4)
Parity (children)	
<2	212 (74.6)
>2	72 (25.4)
Income	
In birr (international dollar)	
<500 (17.86)	97 (34.2)
500–1000 (17.86–35.72)	67 (23.6)
>1000 (35.72)	120 (42.2)

(AOR = 4.984; 95% CI: 2.15-9.965). Participants who had only one sexual partner were 88.9% less likely to develop precancerous cervical lesion compared to multiple sexual partners (AOR: 0.112; 95% CI: 0.029, 0.478). Individuals with age  $\leq$ 30 years old had 73.0% less likely to develop precancerous cervical lesion compared to individuals with age  $>$  30 years old (AOR: 0.270; 95% CI: 0.076, 0.973). Women having two or fewer numbers of children were 79.2% less

**Table 2:** Reproductive, clinical, and behavioral characteristics of human immunodeficiency virus-positive women on antiretroviral therapy in Woldia and Dessie Hospital, Amhara Regional State, North Ethiopia, 2018 (n=284)

Variable	Category	Frequency (%)
Age of the first sexual practices (years)	<15	67 (23.6)
	15–20	135 (47.5)
	Above 20	82 (28.9)
History of abortion	Yes	113 (39.8)
	No	171 (60.2)
Type of contraceptive used	Pills	29 (22.0)
	Injection (depo-provera)	47 (35.6)
	Others	56 (42.4)
First age of pregnancy (years)	15–17	73 (25.7)
	18–20	130 (45.8)
	Above 20	81 (28.5)
Current CD4 count ( cells/mm <sup>3</sup> )	<200	84 (29.6)
	>200	200 (70.4)
History STI	Yes	84 (29.2)
	No	200 (70.4)
Vaginal wall abnormality	Yes	68 (23.9)
	No	216 (76.1)
Number of sexual partners	1	110 (38.7)
	≥2	174 (61.3)
Smoking	Yes	11 (3.9)
	No	273 (96.1)
Alcohol	Yes	30 (10.6)
	No	254 (89.4)

STI: Sexually transmitted infection

likely to develop precancerous cervical lesion compared to women greater than two number of children (AOR: 0.208; 95% CI: 0.060, 0.704). Being single in marital status was almost 5 times more likely to develop precancerous cervical lesion compared to married individuals (AOR: 4.901; 95% CI: 1.246-10.284) [Table 3].

## Discussion

This study assessed the proportion of precancerous cervical lesion among HIV-positive women in Woldia and Dessie Hospital, North Ethiopia. Understanding the magnitude and factors contributed to precancerous cervical lesion among HIV-infected women on ART helps to identify the screening requirements and to take preventive measures. Precancerous cervical lesion reveals a significant public health problem among HIV-infected women unless special consideration taken.

The overall proportion of precancerous cervical lesion in this study was 9.9%. This is comparable with the previous studies conducted in Dar es Salaam, Tanzania (8.7%).<sup>[15]</sup> However, it is lower than findings from the study done in Debre Markos Hospital in Ethiopia (14.1%)<sup>[13]</sup> and Uganda (13.6%).<sup>[16]</sup> On the

other hand, it is higher than other previous studies conducted in Nigeria (6%),<sup>[17]</sup> Rwanda (5.9%),<sup>[18]</sup> and Cameroon (3.9%).<sup>[19]</sup> This discrepancy might be due to the difference in the level of awareness, availability of screening and treatment program, and social and economic variation of the people. However, all those studies were used in the same screening methods.

In this study, different factors were identified which can be associated with the precancerous cervical lesion. Those participants with more than one sexual partner had a high risk of precancerous cervical lesion. This is similar with the previous reports from South Ethiopia,<sup>[11]</sup> Debre Markos Hospital, Ethiopia,<sup>[13]</sup> Côte d'Ivoire,<sup>[20]</sup> and Swaziland.<sup>[21]</sup>

Those study participants who developed vaginal wall abnormality were more prone to develop a precancerous cervical lesion. This is in line with the previous study conducted in Nigeria.<sup>[17]</sup> The other factors were a history of STI. This finding is consistent with the previous studies conducted in Southern Ethiopia<sup>[11]</sup> and Western Kenya.<sup>[5]</sup>

This study showed that being commercial sex workers were at high risk having a precancerous cervical lesion. The finding is consistent with other studies conducted in Nigeria.<sup>[17]</sup> However, different from other studies conducted in Debre Markos Hospital, Ethiopia.<sup>[13]</sup> The possible reason for the difference might be the difference in the awareness level of sexual partners and/or the awareness level of commercial sex workers on the transmission and preventing methods of STI.

This study also revealed that women with the age of >30 years were more likely associated with the precancerous cervical lesion. This result is consistent with the previous studies conducted in Abuja, Nigeria, reported women<sup>[17]</sup> and Brazil revealed that precancerous cervical lesion was most likely associated with age < 34.<sup>[22]</sup>

This study showed that women with higher parity were more likely to have precancerous cervical lesion compared. This finding is consistent with the results from the previous studies conducted in Dar es Salaam, Tanzania,<sup>[15]</sup> Côte d'Ivoire,<sup>[20]</sup> and Debre Markos Hospital, Ethiopia.<sup>[13]</sup> This is due to repeated vaginal delivery might be exposed to HPV infection due to vaginal wall laceration which is conducive for cross contamination. However, in contrast, another study done in Rwanda indicated the risk of developing any cervical cancerous lesion decreased with increasing parity.<sup>[18]</sup>

The current study revealed that single participants were associated with the presence of precancerous cervical lesion compared to married individuals. This is in line with the study conducted Debre Markos Hospital, Northwest Ethiopia.<sup>[13]</sup> Moreover, in addition to this in Debre Markos Hospital, Ethiopia reported that being unmarried and widowed were also the risk factor for precancerous cervical cancer,<sup>[13]</sup> but not in the current study.

**Table 3:** Factors associated with precancerous cervical lesion among human immunodeficiency virus-positive women on antiretroviral therapy in Woldia and Dessie Hospital, Amhara Regional State, North Ethiopia, 2018 (n=284)

Variable	Category	Status of VIA		COR at 95% CI	P	AOR at 95% CI	P
		Positive	Negative				
Age (years)	<30	7 (5.0)	132 (95.0)	0.313 (0.129–0.762)	0.048	0.270 (0.076–0.973)	0.043
	>30	21 (14.5)	124 (85.5)	1		1	
Residence	Urban	19 (8.3)	211 (91.7)	0.45 (1.060–0.0191)	0.248		
	Rural	9 (16.7)	45 (83.3)	1			
Marital status	Widowed	7 (10.8)	58 (89.2)	1.105 (0.396–3.079)	0.052	2.134 (0.556–8.183)	0.270
	Single	6 (33.3)	12 (66.7)	5.524 (1.510–20.2027)	0.03	4.901 (1.246–10.284)	0.026
	Divorced	10 (11.8)	75 (88.2)	0.902 (0.324–2511)	0.05	0.790 (0.185–3.352)	0.748
	Married	5 (4.3)	111 (95.7)	1		1	
Occupation	CSW	20 (20.6)	57 (79.4)	5.251 (2.083–9.124)	0.001	4.984 (2.15–9.965)	0.001
	Non-CSW**	8 (3.9)	199 (96.1)	1		1	
Education	Unable to read and write	12 (10.8)	99 (89.2)	1.636 (0.588–4.532)	0.667		
	Able to read and write	10 (12.3)	71 (87.2)	1.901 (0.658–15.494)	0.272		
	Formal education (1–12 grades)	6 (6.8)	81 (93.1)	1			
Parity	<2 children	14 (6.6)	198 (93.4)	0.293 (0.132–0.650)	0.013	0.208 (0.060–0.704)	0.012
	>2 children	14 (19.4)	58 (80.6)	1			
Abortion	Yes	10 (8.8)	103 (91.2)	0.825 (0.366–1.859)	0.643		
	No	18 (10.5)	153 (89.5)	1			
Contraceptive	Injection	5 (10.6)	42 (89.4)	0.265 (0.078–1.893)	0.391		
	Others***	9 (16.1)	47 (83.9)	0.573 (0.190–1.733)	0.421		
	Pills	9 (31.0)	20 (69.0)	1			
History of STI	Yes	20 (23.8)	64 (76.20)	5.500 (3.150–17.854)	0.025	4.515 (1.496–13.602)	0.023
	No	8 (4.0)	192 (96.0)	1		1	
Number of sexual partners	1	6 (5.5)	104 (94.5)	0.209 (0.078–0.564)	0.003	0.112 (0.029–0.478)	0.003
	≥2	22 (12.6)	152 (87.4)	1		1	
Alcohol	Yes	6 (20.0)	24 (80)	0.274 (0.558–4.712)	0.068		
	No	22 (8.7)	231 (91.3)	1			
Vaginal wall abnormality	Yes	17 (25.0)	51 (75.0)	6.242 (2.741–14.078)	0.018	4.244 (1.423–12.676)	0.016
	No	11 (5.1)	205 (94.9)	1		1	
First age of sexual intercourse (years)	<15	7 (10.4)	60 (89.6)	0.899 (0.294–2.745)	0.852		
	15–20	12 (8.9)	123 (91.1)	0.750 (0.267–2.127)	0.604		
	>20	9 (10.9)	73 (89.1)	1			
Current CD4 count (cells/mm <sup>3</sup> )	<200	3 (3.6)	81 (96.4)	2.330 (0.095–5.206)	0.235		
	>200	25 (12.5)	175 (87.5)	1			
First age of pregnancy (years)	15–17	7 (9.6)	66 (90.4)	0.899 (0.294–2.745)	0.852		
	18–20	12 (9.2)	118 (90.8)	0.759 (0.267–2.157)	0.604		
	>20	9 (11.1)	72 (88.9)	1			
Smoking	Yes	1 (9.1)	10 (90.9)	1.830 (0.835–4.008)	0.331		
	No	27 (9.9)	246 (90.1)	1			
Income (Birr)	<500	7 (7.2)	90 (92.8)	2.119 (0.761–5.902)	0.351		
	500–1000	10 (14.9)	57 (85.1)	2.119 (0.698–6.430)	0.825		
	>1000	11 (9.2)	109 (90.8)	1			

\*\*Farmer, merchant, non-employed. \*\*\*IUCD, condom, and Norplant. CI: Confidence interval, COR: Crude odds ratio, AOR: Adjusted odds ratio

## Conclusion

The proportion of precancerous cervical lesion was low compared to the previous studies conducted in Ethiopia. Age >30, single

in marital status, a commercial sex worker in occupation, parity, had any other a STI, more than 1 sexual partner, more than two children and with vaginal wall abnormality were factors associated with occurrence of precancerous cervical lesion. Thus,

community mobilization, campaigns, and education program to bring behavioral change by giving special consideration for risk factors found associated with the precancerous cervical lesion. This will also increase awareness and utilization of cervical cancer screening in the study area.

## Authors' contributions

Tadesse Belayneh designed the study, participated in data collection, analysis, interpretation, and write-up, drafted the manuscript, and critically revised the manuscript. HM designed the study, participated in data collection, analysis, interpretation, and write-up, drafted the manuscript, and critically revised the manuscript. FW designed the study, participated in data collection, analysis, interpretation, and write-up, drafted the manuscript, and critically revised the manuscript. All authors read and approved the final manuscript.

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