

# Predictors of Precancerous Cervical Lesions Among Women Screened for Cervical Cancer in Bahir Dar Town, Ethiopia: A Case–Control Study

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**Purpose:** Cancer of the cervix is the second most common cancer among women worldwide. Despite it is a serious public health problem in Sub-Saharan African countries including Ethiopia, formation on predictor of the precancerous cervical lesion is not well documented, particularly in the study area. This study aimed to identify the predictors of precancerous cervical lesions among women screened for cervical cancer in Bahir Dar town, North West Ethiopia, 2018/19.

**Patient and Methods:** Institution-based unmatched case–control study was conducted in selected health facilities in Bahir Dar town from November 15, 2018, to January 16, 2019. Data were collected from 102 cases and 305 controls using an interviewer-administered structured questionnaire and entered into Epi Data version 3.1, then export to SPSS version 23 for analysis. Variables with P-value  $\leq 0.2$  in the bivariate analysis were included in the multivariate logistic regression model. Odds ratio with 95% confidence interval was used to identify the predictors of precancerous cervical lesions.

**Results:** Women who initiated sexual intercourse before the age of 18 years (AOR = 1.68, 95% CI: 1.015–2.804), history of sexually transmitted infection (AOR = 1.74, 95% CI: 1.087–2.790) and two or more lifetime sexual partners (AOR=1.733, 95% CI: 1.069–2.810) were predictors for a precancerous cervical lesions.

**Conclusion:** This study confirms that the initiation of sexual intercourse before the age of 18 years, having history of sexually transmitted infection, and two or more lifetime sexual partners were determinants for precancerous cervical lesions. So that it should be focused on prevention through early detection and treatment of sexually transmitted infection with condom promotion. Women with a higher risk of precancerous lesions should also be encouraged to be screened more frequently for cervical cancer.

**Keywords:** precancerous cervical lesion, human papillomavirus, visual inspection with acetic acid

## Introduction

Globally, approximately 570,000 cases of cervical cancer and 311,000 deaths from the disease occurred in 2018. Cervical cancer was the fourth most common cancer in women, ranking after breast cancer, colorectal cancer, and lung cancer. Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries. Ethiopia accounts for 7095 newly diagnosed cervical cancer cases and 4732 cervical cancer deaths in 2012.<sup>1,2</sup>

Cervical cancer is cancer arising from the cervix, in which the cells of the cervix become abnormal and start to grow uncontrollably, forming a tumor. Approximately

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90% of intraepithelial neoplasm is attributed to human papillomavirus (HPV) infection.<sup>3</sup>

Visual Inspection with Acetic Acid (VIA) is one of the screening modality of the precancerous cervical lesion.<sup>4</sup> Screening with VIA in low-income countries is a commonly preferred method than Human Papilloma Virus (HPV) test and cytologic or Pap smear. This is because it does not need more advanced trained crypto-technicians or pathologists and other programmatic requirements.<sup>5</sup> In Ethiopia, screening uptake of women in the community is low<sup>6,7</sup> because of the lack of awareness of the community about cervical cancer risk factors and prevention methods.<sup>8–11</sup> In addition to these, screening uptake, as well as knowledge about cervical cancer risk factors and prevention, is also low among the health workers.<sup>12,13</sup>

Identifying predictors of the precancerous cervical lesion is important for planning more targeted screening programs to decrease the high morbidity and mortality of the disease in the country.<sup>14</sup> However, the predictor of precancerous cervical lesions among the general population in Ethiopia is not well identified. Studies conducted so far in Ethiopia are limited to assessing the cost and its predictors of cervical cancer treatment, prevalence, and predictors of Pap smear cervical epithelial cell abnormality, risk factors associated with invasive cervical carcinoma, knowledge about cervical cancer, HPV prevalence, prevalence and risk factors among Human Immune Deficiency Virus (HIV) positive women. Even a study done about the predictor was centrally located in Addis Ababa where most facilities available to prevent as well as to detect early.<sup>14,16–19</sup> The Ethiopian health sector development program IV (2010/11–2014/15) includes the prevention and control strategies of cancer.<sup>20</sup> We undertook this research to identify predictors of the precancerous cervical lesion to inform and strengthen the existing cervical cancer prevention and control programs in peripheral regions in the country. Besides, the study will inform health education about cervical cancer prevention and stimulate etiologic research about cervical precancerous lesions.

## Methods and Materials

### Study Area and Period

The study was conducted from November 15, 2018, to January 16, 2019, in Bahir Dar town (the capital city of the Amhara region) which is the second largest and populous region in Ethiopia, located approximately 565 km northwest of Addis Ababa capital city of Ethiopia. The total population of the town is 348, 778 of whom 179,849 (52%) are female. The town has one comprehensive specialized public hospital

serving approximately five million people within and outside the city, ten public health centers, ten public health posts, two private hospitals, seventeen private medium clinics, twelve junior private clinics, and five Non-Governmental organization (NGO) comprehensive health facilities. The study was conducted in selected health facilities that provide cervical cancer screening services at Felege Hiwot Comprehensive Specialized Hospital (FHCSH), Family Guidance Association of Ethiopia (FGAE) and Maris topes international Ethiopia.<sup>21</sup>

### Study Design

An institution-based unmatched case–control study design was conducted.

### Source Population

All women who utilized services from FHCSH, FGAE, and Maris topes international Ethiopia.

### Study Population

Cases – All women having positive cervical cancer screening result in FHCSH, FGAE and Maris topes international Ethiopia during the study period.

Controls – All women having negative cervical cancer screening result at FHCSH, FGAE, and Maris topes international Ethiopia during the study period.

### Sample Size Determination and Sampling Procedure

#### Sample Size Determination

Two population proportion sample size calculation formula was used to estimate the required sample size using Epi Info version 7 with the assumption of 95% CI, power =80% with case and control ratio of 1:3 which was taken from the previous study done in Adama, Ethiopia, 2017.<sup>22</sup> Based on the above assumptions the sample size became 378 (cases=95 and controls=283). By adding a 10% non-response rate, the final sample size was 415 (104 cases and 311 controls) (Table 1).

#### Sampling Procedure

Out of the 56 health facilities in Bahir Dar town, three of them were given cervical cancer screening services with VIA, which were FHCSH, FGAE and Mari stop International Ethiopia. Those health facilities were selected purposively due to the provision of cervical cancer screening using VIA regularly for all women. The total sample size was proportionally allocated to

**Table I** Shows Sample Size Determination for Study Participants in 2018/19

Variables	AOR	% of Cases	% of Controls	Required Sample of		Total Sample Size
				Cases	Controls	
Use of contraceptives	2.05831	74.5	58.7	95	283	378
History of STI	2.17	38.2	22.1	82	244	326
Age of 1st exposure to sexual intercourse > 15	3.727	45.5	18.3	29	85	114
Number of sexual partner	6.08336	58.2	21.1	17	50	67

each selected health facility based on average monthly client flow, as reviewed from the registration book. Finally, the case-control incidence density sampling method was used to select the study participants from each facility. Cases (positive visual inspection with acetic acid screens) enrolled consecutively as they were diagnosed to have precancerous cervical lesion until the required sample size was obtained. For each case, three controls (negative visual inspection with acetic acid screens) were selected consecutively from the same health facilities on the same day as soon as the cases were diagnosed (Figure 1).

For controls: women who are age 30–49 and negative VIA findings.

**Exclusion Criterion**

For both cases and controls, women who were critically ill and unable to respond during the data collection period were excluded.

**Dependent Variable**

Precancerous cervical lesion

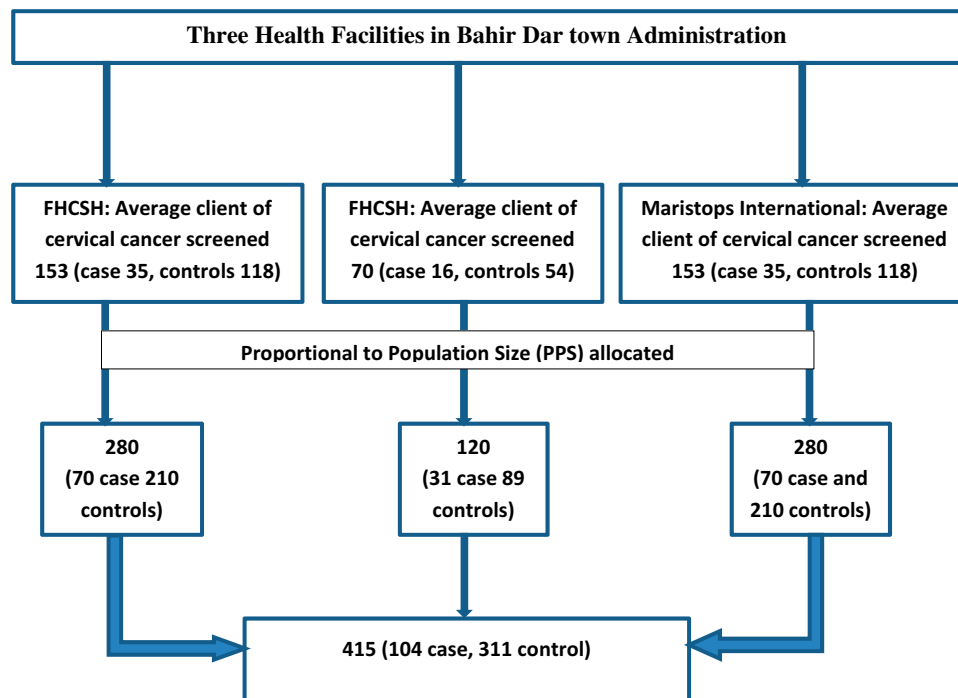
**Independent Variables**

Socio-Demographic Descriptive Variables

**Inclusion Criterion**

For cases: women who are age 30–49 and positive VIA findings.

- Age
- Residence
- Ethnicity



**Figure 1** Sampling procedure of predictor of precancerous cervical lesions among women screened for cervical cancer in Bahir Dar Town, Ethiopia, 2018/19.

- Marital Status
- Educational status
- Occupation
- Religion
- Income

#### Reproductive Related Factor

- use of contraception
- History of STI
- Age at menarche
- Early initiation of sexual intercourse
- Lifetime sexual partner
- HIV/AIDS result H IV/AIDS tested
- ART follow up
- Male circumcision
- Abortion
- Number of pregnancy
- Age of first birth
- Number of children
- Family history of cervical cancer

#### Hygienic Related Factor

- Sharing of underwear
- Genital hygiene practice

### Operational/Term Definitions

Case: A participant who had a precancerous lesion if a woman screened positive for VIA finding.<sup>6</sup>

Control: A participant who had a precancerous lesion if a woman screened negative for VIA finding.<sup>6</sup>

Multiple sexual partners: A woman who had two or more sexual partners in her lifetime.<sup>10</sup>

Early Age of sexual intercourse: Initiation of sexual intercourse below the age of 18 years.<sup>10</sup>

Sharing of underwear: women who sharing their pants from family, friends, and other relatives.<sup>10</sup>

Genital hygiene practice: vaginal washing practice per day.<sup>10</sup>

### Data Collection Procedures

A structured interviewer-administered questionnaire was prepared by reviewing similar articles. The questionnaire was prepared in English language, then translated to Amharic language and translated back to English to maintain its consistency.

The questionnaire included important issues like; socio-demographic information of the respondents, reproductive health-related variables, and other hygienic related factors.

Three diploma clinical nurse data collectors and one BSc supervisor in the health field were assigned. The data collectors had relatively similar working experience in cancer clinics. They were also had experience in data collection on the same issue in other areas of the country. Training was given for two days on the way of interviewing and filling the questionnaire.

According to the World Health Organization (WHO) guidelines for screening and treatment of precancerous lesions of cervical cancer prevention, the result can be interpreted as positive when an acetowhitish lesion with well-defined margins observed within the vicinity of the transformation zone, on the other hand, if the whole cervix turned white (visual inspection with acetic acid—positive).

The result would be negative when there is no acetowhitish lesion (visual inspection with acetic acid—negative); or suspicious for cancer when there is a visible ulcerative cauliflower-like ulcer, oozing and bleeding on touch. Women with findings of “suspicious” were not included in the study (N=8).

### Data Quality Assurance

The questionnaire was pre-tested on 5% of the sample in Debre Markos referral hospital before the actual data collection period. During the data collection, the principal investigator had made close supervision to support data collectors. All the collected data were reviewed by the principal investigator each day. The questionnaire was checked for completeness on a daily basis by the immediate supervisors.

### Data Analysis Procedures

Data were entered, cleaned, checked, edited, and coded into Epi Data version 3.1 and analyzed using SPSS version 23 statistical software. Categorical variables were summarized as frequencies and percentages. Bivariate and multi-variable logistic regressions were used to determine the association of dependent and independent variables. The statistical significance was declared at p-value <0.05.

### Ethics Approval and Consent to Participants

Bahir Dar University, College of Medicine and Health Science, Institutional Review Board with a protocol number of CMHS 0143/18-19 approved the study and ethical

clearance was obtained from this office. The study was conducted in accordance with the Declaration of Helsinki. A written letter was given to each health institution from Bahir Dar city administration health office. The respondents were informed about the purpose of the study, and written consent was obtained from the study subjects.

## Result

### Socio-Demographic Characteristics of Study Participants

A total of 407 women were participated in the current study with a response rate of 98%. The median age of the participants was 38 years  $\pm$  11 IQR years. Majority of the ethnicity and religions were Amhara 404 (99.3%) and Orthodox 390 (95.8%) respectively. A higher proportion of study participants 296 (72.7%) were married and 192 (63%) of participants were housewives. Majority of 261 (64.1%) participants had no formal education (Table 2).

### Sexual and Reproductive Health-Related Characteristics of Study Participant

The mean age of first sexual intercourse of the women was 16.4  $\pm$  4.1 SD years. Out of the participants more than half

of the women 258 (63.4%) had first sexual intercourse below the age of 18 years. Concerning women's sexual history, 235 (57.7%) had two or more sexual partners in their lifetime. About one hundred forty-one (34.6%) of women had a history of sexually transmitted diseases. Out of the participants, only 14 (3.4%) had history of oral contraceptive use for more than five years. Among the total participants 228 (56%) women had 4 and above history of pregnancy and (86%) women had a history of at least one childbirth, and 40.3% of women had a history of abortion. About 119 (29.2%) of participants have had menstruation before 15 years. Concerning participants' HIV/AIDS status, 61 (14.7%) were positive for HIV and only 3.2% participants had family history of cervical cancer (Table 3).

### Hygienic Related Characteristics of Study Participants

Among women participated in the study, only 13 (3.2%) women had history of sharing underwear from family, colleges, and relative. Concerning vaginal cleaning, out of the women participated, 375 (92.1%) of women washed or cleaned their vagina two or more times a day (Table 4).

**Table 2** Socio-Demographic Characteristics of Women Screened for Cervical Cancer in Bahir Dar, Ethiopia, 2018/19

Variables	Category	Frequency	Percent	Control (%)	Case (%)
Residence	Urban	186	45.7	138 (45.4)	48 (47.1)
	Rural	103	25.5	167 (54.75)	26 (25.5)
Age	30–34	221	54.3	77 (25.2)	54 (52.9)
	35–39	113	27.8	77 (25.2)	36 (35.5)
	40–44	68	16.7	50 (16.4)	18 (17.6)
	45–49	123	30.2	101 (33.1)	22 (21.6)
Marital status	Married	296	72.7	218 (71.8)	78 (76.5)
	Divorced	54	13.3	40 (13.1)	14 (13.7)
Educational status	No formal education	261	64.1	200 (65.6)	61 (59.8)
	Primary	43	10.6	28 (9.2)	15 (14.7)
	Secondary	33	8.1	27 (8.9)	6 (5.9)
	Collage and above	70	17.2	50 (16.4)	20 (19.6)
Occupation	Housewives	256	62.9	192 (63)	64 (62.7)
	Government employee	14	3.4	7 (2.3)	7 (6.9)
	Self-employee	137	33.7	106 (34.8)	31 (30)
Income	<1000	62	15.2	44 (14.4)	18 (17.6)
	1000–1999	113	27.8	87 (28.5)	26 (25.5)
	2000–2999	79	19.4	60 (19.7)	19 (18.6)
	3000–3999	36	8.8	27 (8.9)	9 (8.8)

**Table 3** Sexual and Reproductive Health-Related Character of Women Screened for Cervical Cancer in Bahir Dar, Ethiopia, 2018/19

Variable	Category	Frequency		Control (%)	Case (%)
		No	%		
Age at first sex	18 and above	149	36.6	119 (39)	30 (29.4)
	Less than 18	258	63.4	186 (61)	72 (70.6)
Age at menarche	Less than 15	119	29.2	88 (28.9)	31 (30.4)
	15 and above	288	70.8	217 (71.1)	71 (69.6)
HIV result	Negative	330	81.1	247 (84.9)	83 (83)
	Positive	61	15	44 (15.1)	17 (17)
STI	No	266	65.4	211 (69.2)	55 (53.9)
	Yes	141	34.6	94 (30.8)	47 (46.1)
Duration of oral contraceptive	1–5	67	16.5	52 (17)	15 (14.7)
	>5	14	3.4	11 (3.6)	3 (2.9)
	Not applicable	326	80	242 (79.3)	84 (82.4)
Life time sexual Partner	One	172	42.3	139 (45.6)	33 (32.4)
	Two or more	235	57.7	166 (54.4)	69 (67.6)
Male circumcision	Yes	407	100	305 (100)	102 (100)
Age at birth	Less than 18	138	38.5	98 (37.3)	40 (42.1)
	18–24	165	46.1	123 (46.8)	42 (44.2)
	25 and above	55	15.4	42 (16)	13 (13.7)
No of pregnancy	No	18	4.4	16 (5.2)	2 (2)
	1–3	161	39.6	119 (39)	42 (41.2)
	4 or more	228	56	170 (55.7)	58 (56.9)
Abortion number	No	243	59.7	186 (61)	57 (55.9)
	1–2	147	36.1	105 (34.4)	42 (41.2)
	3 and above	17	4.2	14 (4.6)	3 (2.9)
Number of children	No	53	13	43 (14.1)	10 (9.8)
	1–3	174	42	122 (40)	52 (51)
	4 or more	180	44	140 (45.9)	40 (39.2)
Family history of cervical cancer	No	398	96.8	299 (98)	99 (97.1)
	Yes	9	3.2	6 (2)	3 (2.9)

**Table 4** Hygienic Related Characteristics of Screened Women in Bahir Dar Town, Ethiopia, 2018/19

Variable	Category	Frequency		Control (%)	Case (%)
		No	%		
Sharing under wear	No	394	96.8	295 (96.7)	99 (97.1)
	Yes	13	3.2	10 (3.3)	3 (2.9)
Vaginal cleaning	One times day	32	7.9	22 (7.2)	10 (9.8)
	Two or more times a day	375	92.1	283 (92.8)	92 (90.2)

## Factors Associated with Precancerous Cervical Lesion

In Bivariable analysis, occupation, age at first sex, history of STIs, lifetime sexual partner, number of children and age of the respondents were found to have a p-value of  $\leq 0.2$ . To control the effect of other confounding factors they were entered into multivariable logistic analysis. In the multivariable analysis, initiation of sexual intercourse, having a history of STIs and multiple sexual partners were found to be a significant predictor

of precancerous cervical lesion in women with precancerous cervical cancer.

Women who had early initiated sexual intercourse before the age of 18 were 1.7 times more likely to have the lesion compared with those who initiated sexual intercourse at the age of 18 years and late (AOR = 1.68: 95% CI [1.02, 2.80]). Women who had history of STIs were 1.74 times more likely to have cervical precancerous lesions than those who had no history of STI (AOR = 1.74: 95% CI (1.09, 2.8)). Similarly, those having two or more lifetime sexual partners were 1.75 times higher to develop precancerous cervical cancer (AOR=1.75: 95% CI (1.09, 2.81)) (Table 5).

## Discussion

This study was intended to identify the predictor of precancerous cervical lesion.

In the current study, women who initiated first sexual intercourse before the age of 18 were at a higher risk for the development of precancerous cervical lesions compared with those who initiated 18 and late.

The finding of this study was consistent with studies done in Yirgalem zonal hospital, Debre Markos hospital and Adama in which women who had a history of early initiation of first sexual intercourse before 18 years and less were at higher risk to develop precancerous cervical lesion than those whose age is  $\geq 18$  years' age.<sup>16,22,23</sup>

The reason behind this may be during puberty, cervical tissue undergoes physiologic changes, transformation zone on the ectocervix becomes enlarged, and becoming exposed to HPV facilitate infection facilitating the development of dysplasia, a cervical squamous precancerous. This was supported by Rodriguez that culmination of transmission of HPV infection usually occurs early in the first year after the start of sexual intercourse. This is due to HPV infection is highly contagious and endemic in women who had sex the first time aged  $< 17$  years 2–3 times the risk for cancer compared with those having sex aged  $\geq 20$  years.<sup>24</sup>

However, the result of this study was different from the study done in Swaziland and Jimma where there was no difference among women who initiated first sexual intercourse early and late age. The possible explanation for the observed difference might be differences in sample size and the type of study design ie this study was case control while a study conducted in Swaziland and Jimma were cross-sectional studies.<sup>10,25</sup>

This study also showed that women who had a history of sexually transmitted infections were at a higher risk of developing precancerous cervical lesions. This result is comparable with a study done in Jimma, Swaziland and North Ethiopia which revealed that women who had a history of sexually transmitted infection were at a higher risk to develop precancerous cervical lesions

**Table 5** Multivariate Analysis of Selected Variables Among Study Participants of Bahir Dar, Ethiopia, 2018/19

Variable	Category	Control	Case	COR (95% CI)	Adjusted OR (95% CI)
Age	30–34	77 (25.2)	26 (25.5)	1.00	1.00
	35–39	77 (25.2)	36 (35.3)	1.3859 (0.764, 2.511)	1.393 (0.757, 2.563)
	40–44	50 (16.4)	18 (17.6)	1.066 (0.536, 2.144)	1.029 (0.503, 2.104)
	45–49	101 (33.1)	22 (21.6)	0.645 (0.340, 1.2144)	0.597 (0.307, 1.159)
Occupation	House wife	192 (63)	64 (82.7)	1.00	1.00
	Government employee	7 (2.3)	7 (6.9)	3.000 (1.014, 8.880)	2.549 (0.821, 7.913)
	Self-employee	106 (34.8)	31 (30.4)	0.877 (0.537, 1.432)	0.769 (0.430, 1.374)
Age at first sex intercourse	18 and above	119 (39)	30 (29.4)	1.00	1.00
	Less than 18	186 (61)	72 (70.6)	1.535 (0.946, 2.492)	1.687 (1.015, 2.804)*
Number of children	No	43 (14)	10 (9.8)	1.00	
	1–3	122 (40)	52 (51)	1.833 (0.856, 3.922)	2.702 (0.879, 8.310)
	4 or more	140 (45.9)	40 (39.2)	1.229 (0.567, 2.668)	0.791 (0.454, 1.378)
STI	No	211 (69.2)	55 (53.9)	1.00	1.00
	Yes	94 (30.8)	47 (46.1)	1.918 (1.212, 3.035)	1.741 (1.087, 2.790) *
Number of Lifetime sexual partner	One	139 (45.6)	33 (32.4)	1.00	1.00
	Two or more	166 (54.4%)	69 (67.6)	1.733 (1.069, 2.810)	AOR=1.75 CI (1.092, 2.807)*

Note: \*p-value  $< 0.05$ .

than women who had no history of sexually transmitted infection.<sup>10,25,26</sup> This might be due to Long-term inflammation caused by sexually transmitted diseases increases the risk of precancerous cervical lesions.

In contrary to this study, the result was different from the study done in Debre Markos and Mekelle hospitals. Sexually transmitted infection was not associated with the risk of precancerous cervical lesion development.<sup>16,19</sup> The possible explanation may be the population of Mekelle and Debre Markos were women who had known HIV-positive status. This might protect them from STIs (because of the perceived risk of STIs) due to awareness about opportunistic infection for HIV during follow up.

The current study also showed that women who had more than one-lifetime sexual partners were at a higher risk of developing precancerous cervical lesions than women who had only one-lifetime partner. The finding was comparable with a study conducted in Mekelle, Swaziland, and Yogyakarta that multiple sexual partners were a determinant factor for the development of precancerous cervical lesions.<sup>8,25,27</sup> This is because having multiple sexual partners exposes for HPV which increases the risk of developing precancerous cervical lesions. However, another studies done in Zimbabwe and Harare showed that having more than five sexual partners was found to be protective compared to having one sexual partner.<sup>28</sup> The difference may be as a result of sample size difference (180) in Zimbabwe compared (407) to the current study.

## Conclusion

This study confirmed that initiation of early sexual intercourse before the age of 18 years, having history of sexually transmitted diseases and history of two or more lifetime sexual partners were factors associated with precancerous cervical lesions. So that it should be focused on prevention through early detection and treatment of sexually transmitted infections with condom promotion. Women with a higher risk of precancerous lesions should also be encouraged to be screened more frequently for cervical cancer.

## Abbreviations

AOR, Adjusted Odds ratio; CI, Confidence Interval; CMHS, Collage of Medicine and Health Science; FGAE, Family Guidance Association of Ethiopia; FHCSH, Felege Hiwot Compressive Specialized Hospital; HIV, Human Immune Virus; HPV, Human Papilloma Virus; NGO, Non-Governmental Organization; SD, Standard Deviation;

SPSS, Statistical Package for Social Science; STI, Sexually Transmitted Infection.

## Data Sharing Statement

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

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## Author Contributions

JA: conceived the research idea and developed the proposal, participated in data collection and analysis, and drafted the paper. GA and AW: Enriched the concept and proposal write up, participated in data analysis and drafting of the manuscript, and critically reviewed the manuscript. GA: Prepared and critically reviewed the manuscript. Generally, all authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests.

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