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PRE-CANCEROUS CERVICAL LESION USING VISUAL INSPECTION WITH ACETIC ACID AMONG WOMEN ATTENDING ANTI-RETROVIRAL THERAPY IN TIGRAY HOSPITALS, NORTHERN ETHIOPIA.

[1]Haftom Gebrehiwot W/aregay, [2]*Sheeba Kumari and [3]Yemane Berhane

[1]Assistant Professor of Reproductive and Maternal Health Department of Midwifery, College of Health Sciences, Mekelle University, Ethiopia.
[2]Lecturer, Departmentof Nursing, College of Health Sciences, Mekelle University, Ethiopia.
[3]Assistant Professor of Reproductive and Maternal Health, Department of Nursing, College of Health Sciences, Adigrat University, Ethiopia.

*Corresponding Author: Sheeba Kumari Lecturer,

Departmentof Nursing, College of Health Sciences, Mekelle University, Ethiopia.

ABSTRACT

Background: Cervical cancer is one of the leading causes of death for middle-aged women in the developing world, yet it is almost completely preventable if precancerous lesions are identified and treated in a timely manner. Despite this fact, very few women receive screening and testing services in developing countries including Ethiopia. **Methods**: A facility based cross sectional studies both quantitative and qualitative methods were conducted from April to June/2015 at Tigray Public hospitals. Data were checked, coded and entered to Epi-info version 7, and exported to SPSS version 20 for analysis and multiple logistic regression model was used to identify factors associated with the outcome variable. The transcribed and translated qualitative data was triangulated and thematically described. **Results:** A total number of 88 (20.2 %(95% CI = 13%, 29%) human subjects had positive Visual Inspection with Acetic acid test among four hundred thirty five (435) HIV infected women. Having ever history of sexually transmitted disease (AOR=4.04, 95%CI: 2.19, 7.44), Age at first birth less than 18 years (AOR=3.36, 95%CI: 1.79, 6.32), Having more than one lifetime sexual partner (AOR=2.91, 95%CI: 1.13, 7.52),and Base line CD4 count less than 200cells/mm3 before HAART (AOR=7.51, 95%CI: 3.58, 15.68) were factors associated with precancerous cervical lesion. **Conclusions:** The magnitude of precancerous Cervical Lesion is high.Ever history of sexually transmitted disease, Age at first birth less than 18 years, having more than one lifetime sexual partner and Base line CD4 count less than 200cells/mm3 before HAART were factors associated with precancerous cervical lesion. Thus, therefore, screening for Cervical Intraepithelial Neoplasia is recommended for all women with HIV.

KEYWORDS: Cervical cancer, VIA, Precancerous Cervical Lesion, & HIV.

INTRODUCTION

Cervical cancer is a cancer arising from the cervix, which is due to the abnormal growth of cells that have the ability to invade other part of the body. It is almost always caused by Human Papilloma virus (HPV), specifically two strains HPV 16 and HPV 18. Other risk factors include giving birth to many children, smoking, using oral contraceptives for long time, low immune system and first sexual intercourse initiation at early age. Cervical cancer screening is a way to detect abnormal cervical cells, including precancerous cervical lesions, as well as early cervical cancers[1].

Cervical cancer is the second most prevalent cancer among women, with an estimated 530,232 new cases and 275,008 deaths globally each year. According to a World Health Organization 2004 report, cervical cancer is the most prevalent cancer in Africa and Southeast Asia, although it occurs only in women. Moreover, other developing countries with insufficient medical services carry a heavier burden of cervical cancer because of the lack of accessible screening services.[2, 3]

Cervical cancer trend is significantly reduced in high income countries due to early diagnosis and treatment. And because of poor access to quality screening and treatment service, the trend is increasing in developing countries[4]. Cervical cancer is the commonest cancer affecting reproductive organ and also, leading cause of death from cancer among women. It was estimated that 20.9 million women were at risk of developing cervical cancer in Ethiopia with an estimated 4648 and 3235 annual number of new cases and deaths respectively[2, 5]. HIV infection and cervical cancer are major public

health problems facing women in Ethiopia. More than half a million women are estimated to be infected with HIV and at risk of developing cervical cancer. Cervical cancer ranks as the 2nd most frequent cancer among women in Ethiopia. Therefore, this study is aimed to assess the magnitude of precancerous cervical lesions among HIV positive women.

METHODS AND MATERIALS
Study Setting
This study was conducted from April to June/2015 in Tigray region. Mekelle is capital city of Tigray Regional State and is located in the Northern part of Ethiopia, at 783 km from the capital city, Addis Ababa. According to projected central statistical agency of Ethiopia, the region have one referral hospital, fourteen hospitals and more than 200 health centers served the society.

Study Design and Source Population
Facility based cross sectional study design containing mixed methods both quantitative and qualitative was employed. HIV positive women who were visiting ART clinic and screened for PCCL were study participants.

Sample Size Determination and Sample Procedure
The sample size for quantitative was calculated using single population proportion formula (P=22%), confidence level of 95 and margin of error 4% and 5% significance level. Considering 5% possible non-response rate the total sample size was =435 HIV positive clients.[7]

The sample procedure was taken from all Hospitals that were found in Tigray region, four of them were selected by simple random sampling technique. The sample size was proportionally allocated to each selected health facility. Then study subjects were selected by using systematic sampling method. For the qualitative design purposive sampling method was employed.

Data Collection and Procedures
Structured questionnaire which was prepared in English and translated to the local language Tigrigna were used to collect data through face-to-face interview. In addition Patients' ART follow up charts were reviewed. FGD were also employed to collect a data for qualitative purposes. Experienced data collectors and supervisors were used to gather the data.

The Specific Procedure of data collection was inserting bivalve speculum into the vagina and visualized the cervix using a halogen focus lamp to identify the Squamo-Columnar Junction through cleaning using a cotton swab, a five percent acetic acid solution was applied to the cervix for visual inspection with acetic acid. Then the Precancerous lesions finding was visible just one minute after application.

Data Processing and Analysis
Data were coded, entered and cleaned. Data analysis was carried out using SPSS version 20 software package. Simple descriptive statistics and the magnitude of association between the different variables in relation to the outcome variable was measured by odds ratio with 95% confidence interval. The qualitative data was also thematically analyzed.

Data Quality Assurance and Control Method
Pre test was conducted before the actual field work to see its clarity and consistency. After the data were collected the questionnaires were checked for completeness, coded and entered into SPSS software package for cleaning and analysis. Mean and standard deviation determined for continuous variables, and categorical variables were summarized by frequency distributions and percentage. Crude and adjusted odds ratio were used to control the possible confounding variables.

Ethical Considerations
The study protocol was reviewed and approved by Institutional review board. Permission to undertake the study was obtained from every relevant authority. In addition, verbal consent was obtained from the study participant and data was kept confidentially.

RESULTS
Socio-demographic characteristics
A total of 435 study subjects were interviewed in the study. The mean age of the respondents were 35.9±4.5 SD years and 233(53.6%) of the mothers were in the age range of 30-39 years. Out of the total mothers 350 (80.5%) were orthodox Christians in religion and the majority 423(97.2%) of respondents be in the right place to Tegaru by ethnicity.

Majority of the respondents number (85.1%) were urban dwellers while 175 (40.1%) of them had no formal education. Regarding to the marital status of the respondents, More than half 224 (56.1%) of them were married. Among the respondents 138(31%) of the mothers were housewives **(Table 1).**

Table 1: Socio-demographic characteristic of respondents in Mekelle City, Northern Ethiopia, 2015 (N = 435)

Characteristics Age (in years)	Frequency	Percentage	Mean(SD)
20-29	54	12.4	35.6(4.2)
30-39	233	53.6	
≥40	148	34	

Marital status		
Single	24	5.5
Married	224	56.1
Divorced	98	22.5
Widowed	69	15.9
Religion		
Orthodox	350	80.5
Muslim	73	16.8
Others*	12	2.7

Occupational status		
farmer	48	11
Housewife	138	31.7
Gov employee	155	35.6
Others**	94	21.6

Educational status		
No formal education	175	40.1
Grade 1-8	129	29.7
Grade 9-12	82	18.9
Above 12	49	11.3

Residence		
Urban	370	85.1
Rural	65	14.9

 * Catholic, protestant and 7th day Adventist.
** Student, daily laborer and trade

Reproductive health characteristics
The mean ages of first sexual intercourse, and first marriage of the study participant's were16.77+2.7, and 16.18+3.81years respectively. Three hundred and five (71.3%) of the participants had their first sexual intercourse before the age of 18 years. Two hundred and twenty three (51.3%) of the participants had their first birth before the age of 18 years. Mean age at first birth was16.77+8.24 years.

In this study 360 (82.80%) study participants had more than one life time sexual partners. Near to one-third (30.1%) of the participants had history of abortion. One hundred forty seven (33.8%) were using contraceptive during the study period among these 84(19.3) used Injectable contraceptive. One hundred eight nine (43.4%) of the study participants used condom during sexual intercourse. Nearly one-fourth(23%) of the study participants had ever history of sexually transmitted disease (STD) and 47 (11.3%) of them had ever history of ulcerative genital lesion (Table 2).

Table-2. Reproductive health characteristics of study participants Mekelle, Ethiopia.
(N = 435)

Characteristics	Frequency	Percentage	Mean(SD)
Age at first sexual intercourse			
<18	305	70.1	16.7(2.7)
≥18	130	29.9	
Age at first marriage			
<18	267	61.4	16.18(3.87)
≥18	168	38.6	
Age at first birth			
<18	223	51.3	16.77(8.24)
≥18	212	48.7	
Life time number of sexual partners			
1	75	17.2	3.9(3.5)
≥2	360	82.8	
History of abortion			
Yes	131	30.1	
No	304	69.9	

Family history of cervical cancer		
Yes	6	1.4
No	429	98.6
Current contraceptive use		
Yes	147	33.8
No	288	66.2
Use of condom during sexual intercourse		
Yes	189	43.4
No	246	56.6
Ever history of STD		
Yes	100	23
No	335	77
Ever history of ulcerative genital lesion		
Yes	49	11.3
No	386	88.7

Immunological and behavioral characteristics
Regarding to CD4 count, two hundred fifty three(58.3%) had base line CD4 count before HAART less than 200copies/ mm3.The mean base line CD4 count before HAART was 212+133.6 copies/mm3.Nearly all the study participants (96.6%) were currently on highly active antiretroviral treatment (HAART). Most women,

91.9%, had current CD4 counts 200 and above. The mean current CD4 count of the participants while initiating HAART was 479+203.9 copies/mm3.

Only 11(2.5%) of the study participants had ever history of cigarette smoking and 6 (1.4%) of them had family history of cervical cancer (Table 3)

Table 3: Immunological and behavioral characteristics of the study participants, in three screening centers, Northwest Ethiopia. 2016.
(n=435)

Characteristics	Frequency	Percentage	Mean(SD)
Base line CD4 count before HAART			
<200	253	58.2	212.(133.6)
≥200	182	41.8	
Recent CD4 count after HAART			
<200	34	8.1	479(203.9)
≥200	386	91.9	
Current use of HAART			
Yes	420	96.6	
No	15	3.4	
ART clinic follow up duration			
1-6 months	416	95.6	
7-12months	19	4.4	
Ever history of smoking			
Yes	11	2.5	
No	424	97.5	
Family history of cervical cancer			
Yes	6	1.4	
No	429	98.6	

Magnitude of precancerous cervical cancer lesion (PCCL) among HIV-infected women
Out of 435screened HIV- infected women, 88 (16.41%)(95% CI = 13%, 29%) were found to be positive for PCCL.

Factors associated with precancerous cervical cancer lesion among HIV-infected women
After controlling the effect of other confounding variables life time history of STD, life time number of sexual partners, age at first birth and base line CD4 count

before HAART to be significantly associated with precancerous cervical cancer lesion.

This study initiate that those mothers whose age at first birth less than 18 years were 3.36 times more likely to develop precancerous cervical cancer lesion than those whose age at first birth more than 18 years [AOR=3.36, 95%CI: 1.79,6.32].

Those HIV infected women who had more than one lifetime sexual partner were 2.91 times more likely to develop precancerous cervical cancer lesion than those

having one life time sexual partners [AOR=2.91, 95%CI:1.13,7.52]. Those women whoever had history of STD were about 4.04times more likely to have precancerous cervical cancer lesion than those without history of STD [AOR=4.04, 95%CI: 2.19, 7.44].In this study those women whose base line CD4 count were less than 200 cells/mm3 were 7.51 times more likely to have precancerous cervical cancer lesions than those patients with a base line CD4 count above 200cells/mm3 before HAART [AOR=7.51, 95%CI3.58,15.68] (Table 4).

Table-4. Logistic regression analysis of factors associated with PCCL in Mekelle. Ethiopia. (n=435)

Characteristic	PCCL		COR(95%CI)	AOR(95%CI)	P-value
	Yes	No			
Age					
20-29	8	48	1.00	1.00	0.32
30-39	65	271	1.44(0.65,3.19)	1.51(0.52,4.39)	
≥40	15	28	3.21(1.21,8.53)	2.97(0.71,10)	
Occupational status					
Farmer	15	33	1.00	1.00	0.06
House wife	30	108	0.61(0.29,1.27)	0.40(0.16,1.02)	
Govt. employee	32	123	0.57(0.29,1.18)	0.44(0.17,1.11)	
Others*	11	83	0.29(0.12,0.70)	0.19(0.06,0.64)	
Educational status					
In-formal education	34	141	0.60(0.29,1.24)	0.82(0.26,2.59)	
Grade 1-8	31	98	0.79(0.38,1.66)	0.97(0.32,2.92)	0.10
Grade 9-12	9	73	0.31(0.12,0.78)	0.33(0.10,1.09)	
Above 12	14	35	1.00	1.00	
Resident					
Urban	70	300	0.609(0.33,1.11)	1.57(0.57,4.44)	0.38
Rural	18	47	1.00	1.00	
Age at first sexual intercourse					
<18	76	229	3.26(0.99, 2.52)	1.05(0.50,2.19)	0.90
≥18	12	118	1.00	1.00	
Age at first birth					
<18	64	159	3.15(1.89-5.27)	**3.36(1.79,5.01)**	<0.001
≥18	24	188	1.00	1.00	
Number of sexual partner					
1	6	69	1.00	1.00	<0.001
≥2	82	278	3.39(1.42,8.09)	**2.91 (1.13,7.52)**	
History of Abortion					
Yes	34	97	1.62(0.99,2.65)	0.86(0.41,1.73)	0.68
No	54	250	1.00	1.00	
Ever history of STD					
Yes	39	61	3.73(2.26,6.17)	**4.04(2.19, 7.44)**	<0.001
No	49	286	1.00	1.00	
Base line CD4 count before HAART					
<200	77	176	6.80(3.50,13.24)	**7.51(3.58,15.68)**	<0.001
≥200	11	171	1.00	1.00	

DISCUSSION
This study revealed the magnitude of precancerous cervical lesion among HIV infected women in Mekelle was found to be 16.41%.This finding is lower than to a study conducted in Ukraine (21%), India (27.7%), Southern Ethiopia (22.1%) and Kenya (26.4%)[6,7,8,9,]. This finding was higher than the study conducted in west Nigeria (14.3%). The Possible reason for this could be the occurrences of precancerous cervical cancer lesion in different regions of Africa could be partly due to differences in the sexual practices and Reproductive health service awareness of the women.

Age at first birth is one of the significant predictors of precancerous cervical cancer lesion in this finding. Those mothers whose age at first birth less than 18 years were 3.36times more likely to develop precancerous cervical cancer lesion than those whose age at first birth more than 18 years[AOR=3.36, 95%CI: 1.79,6.32]. This is the new finding or evidence that age at first birth less than 18 years might contribute to the risk of cervical precancerous lesion in HIV infected women. Those women who gave birth less than 18 years would be at high exposure to HPV through early sexual intercourse and multiple sexual partners. Another finding of the

present study is that history of multiple sexual partners is also an important predictor of precancerous cervical cancer lesion HIV infected women. Those HIV infected women who had more than one lifetime sexual partner were 2.91 times more likely to develop precancerous cervical cancer lesion than those having one life time sexual partners[AOR=2.91, 95% CI: 1.13,7.52]. The finding is consistent with previous studies conducted in southern Ethiopia and Nigeria,[8,10]. This might be due to those women who had more than one lifetime sexual partner develop precancerous cervical cancer lesion because of as the number of sexual partners increases they become more prone to acquiring the HPV infection, which is the causative agent for precancerous cervical cancer and invasive cervical cancer.

In the present study Participants who were base line CD4 count less than 200cells/mm3 before HAART initiation were 7.51times more likely to have precancerous cervical lesion than those who were base line CD4 count more than 200cells/mm3 before HAART initiation[AOR=7.51, 95%CI 3.58,15.68].This finding is consistent with a study done in Tanzania[11]. The possible explanations might be due to the effect of immune function, HIV induced immune suppression leads to inability to control the HPV expression, hence the persistence of HPV infection and the development of cervical lesions.

CONCLUSIONS
The finding of this study revealed that precancerous cervical lesion among HIV infected women is high in Mekelle city Hospitals. Age at first birth less 18 years, ever history of lifetime STD, having more than one life time sexual partners and base line CD4 count less than 200cell/mm3 before HAART initiation were are significant predictors for precancerous cervical lesion in HIV infected women.

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