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ORIGINAL ARTICLE

DETERMINANT FACTORS OF VISUAL INSPECTION WITH ACETIC ACID (VIA) POSITIVE LESIONS AMONG HIV POSITIVE WOMEN IN MEKELLE HOSPITAL, NORTHERN ETHIOPIA: A CASE CONTROL STUDY

Zekariase Gessesse[1], Zemen Tadesse[1], Mussie Alemayehu[1], Abiy Hiruye[2], Yeneneh Getachew[2], Miliard Derbew[3], Damen Haile Mariam[3], Dereje Mammo[2], Kantelhardt Eva[4], Henock Yebyo[1], Hailay Gebre Michael[1]

ABSTRACT

Background: *Cervical cancer is the second commonest type and third cause of cancer death among women in low -income countries. Women living with HIV/AIDS are at greater risk ofdeveloping cervical cancer. The study aimed to identify the determinant factors forsuspected precancerous cervical lesions among HIV- positive women in Mekelle hospital, Ethiopia.*

Methods: *Anunmatched case-control study was conducted among randomly selected HIV positive women in Mekelle hospital in 2014. In Mekelle Hospital, routine screening for lesions ofthe cervix uteri by visual inspection with acetic acid (VIA) is done in HIV positive women by trained nurses. Suspicious findings are treated by cryotherapy or referred to the Gynaecologist. A number of 116 cases, who had suspicious findinsgs on VIA, and 232 HIV-positive controlswithout suspicious findings on VIA were randomly selectedand enrolled into the study. The determinant factors for precancerous cervical lesion were analyzed using multiple logistic regression and described as adjusted odds ratio (AOR).*

Results: *HIV positive women who had CD4 cells less than 350/mm^3 were two times more likely to have precancerous cervical lesion compared to those with CD4 cells above 350/mm^3. Women with two (AOR=3.6; 95% CI: 1.7, 7.7) and three (AOR=2.5; 95% CI: 1.2, 5.4) sexual partners were four and three times more likely to have precancerous cervical lesion, respectively,as compared to those who had one sexual partner. Age, History of STI and duration of ART had no influence on presence of VIA positive lesions in HIV positive women.*

Conclusion*: CD4 count cells and number of sexual partners were predictors of VIA positivecervical lesion among HIV positive women.*

Key words: *Precancerous cervical lesion, VIA, HIV positive women, determinants, Tigray.*

INTRODUCTION

Cervical cancer is the leading cause of gynecologic-related morbidity and mortality in developing countries (1, 2). An estimated 500,000 new cases and 250,000 deaths occur worldwide annually with vast majority (80%) of them in developing countries (2). Globally the highest incidence rates are in Eastern, Western, and Southern Africa, as well as South-Central Asia and South America (3). Women in developing countries are at greater risk of death from cervical cancer because only few women have access to screening and treatment services (4). Cervical cancer is preventable or curable if patients are identified atearly stage. However, women in developing countries often seek treatment when symptoms occur in the late stage of the disease. This is attributable to low knowledge and generally poor health seeking behavior (4-6).

The causal relation between cervical cancer and human Papillomavirus is well established (7). High parity, tobacco smoking, oral contraceptives may modify the risk in women infected with HPV (1).

[1]Mekelle Hospital, Mekelle, Ethiopia;
[2]Ethiopian Medical Association, Addis Ababa, Ethiopia;
[3]Medical Education Partnership (MEPI), Addis Ababa University, Ethiopia.
[4]Clinic and poly clinic for Gynecology Institute for medical biometry, epidemiology and Informatics, Martin Luther-University of Halle, Ernst-Grube str. 40 06097 Halle Germany

Cervical cancer is always fatal if it is not detected early and treated in time. In particular, women living with HIV/AIDS are at greater risk and are liable to rapid development of precancerous lesion (8-10). Due to the known correlation between severe immunodeficiency and precancerous cervical lesion, all HIV positive women need screening for cervical cancer (11).

In 2012 Cervical cancer was ranked the 2nd most frequent cancer among women and the 2nd most frequent cancer among women between 15 and 44 years of age. There are nearly half a million women over age 15 living with HIV in Ethiopia. Still there are very limited cervical cancer screening campaigns in the country. Awareness creation and education, especially to the high risk groups such as HIV positive women are still lacking (12, 13). For effective prevention and control of cervical cancers among HIV positive women, studies are needed to identify determinant factors in the Ethiopian settings.

MATERIALS AND METHODS

An unmatched case-control study was conducted on HIV positive patients in Mekelle Hospital to identify the determinants for VIA positive lesions. This hospital is the second largest in Northern region of Ethiopia. The hospital serves as referral hospital together with Ayder hospital-its sister hospital-to more than five million people of Tigray andadjacent regions. The hospital has provided HIV treatment and care to about 2,587 HIV positive women(14).

The cases were those with suspicious lesion using Visual Inspection with Acetic Acid (VIA), while the controls were those negative on VIA. In Ethiopia, HIV treatment and care is provided in public hospitals, such as Mekelle hospital, at free of charge. Thus, all women receive HIV-related services in all public hospitals, regardless of their socio-economic differences. The selection of both cases and controls was random. Taking power of 80%, proportion of cases exposed to multiple sexual partner 51.6%, a 1:2 case-to-control ratio and 95% confidence interval sample size was calculated using two population proportion formula. As such, 116 cases and 232 controls were recruited. A structured checklist was used to retrieve data. The checklist comprised of socio-demographic and economic characteristics, reproductive history, healthcare-related factors and possible risk factors associated with suspected pre-cancerous cervical lesion. The checklist was adapted after review of literatures to fit the local context. Further, the instrument was pretested among18 HIV positive women in a different hospital to ensureits applicability for the study. Six health professionals data collectors and 2 supervisors were recruited to ensure the quality of data. They were trained on the methodology and contents of the tools. The training included also session on research ethics and confidentialityparticularly,with regard to HIV status.

The questionnnaire was reviewed for completeness and input errors at the end of each data collection day. Then, data was entered, cleaned and analyzed using SPSS version 20 for windows. Exploratory Data Analysis was done to check for data entry errors, and necessary assumptions before running any analysis. Inconsistent and incomplete values were then double checked against the hard copies of the filled-out checklists.

Characteristics of the HIV positive women were analyzed using descriptive statistics. Multiple logistic regression was used to estimate association between the risk factors and suspected precancerous cervical cancer. Odds ratio (OR) and 95% confidence interval (CI) was used to estimate the effects of the factors among HIV positive population of Tigray region, Northern Ethiopia. A p-value less than 5% was deemed as cut-off point for significant association for all tests.

Ethical clearance was obtained from the Ethical Review Board of Tigray Regional Health Bureau. Since the data were collected from existing paper database, there was no way to consent the HIV positive women for using their data. Ethical approval and permission of the chief executive officer of the hospital was secured to access the data. Yet, the data was kept confidential. In addition, patient-identifying attributes were not reported in the results.

RESULTS

Socio-demographic description of study participants: A total of 348 charts (116:232 case: control) of HIV-positive women were considered for the study. Two-third (67.2%) of the women were older than 30 years. Six-in-ten and seven-in ten of the the cases and controls were older 30 years, respectively. The majority of women were illiterate (46.6% of the cases and 54.7% of the controls). More than two-third of the patients were from urban areas [Table 1].

Table 1:-Socio-demographic description of HIV positive women, Mekelle hospital, northern Ethiopia, 2014

	Cases (n= 116)	**Controls (n=232)**	**Total**
Socio-demographic characteristics	**n(%)**	**n(%)**	**n(%)**
Age (years)			
30 or younger	46(39.7)	68(29.3)	114(32.8)
Older than 30	70(60.3)	164(70.7)	234(67.2)
Educational status			
Illiterate	54(46.6)	127(54.7)	181(52)
Grades 1-8	31(26.7)	51(22)	82(23.6)
Grades 9-12	20(17.2)	36(15.5)	56(16.1)
College or beyond	11(9.5)	18(7.8)	29(8.3)
Marital status			
Married	57(49.1)	83(35.8)	140(40.2)
Single	13(11.2)	30(12.9)	43(12.4)
Widowed	24(20.7)	37(15.9)	61(17.5)
Separated	22(19)	82(35.3)	104(29.9)
Residence			
Urban	80(69)	160(69)	240(69)
Rural	36(31)	72(31)	108(31)

Reproductive history and health care factors: On average, seven-in-every-ten of both cases and controls had their first sexual intercourse before 18 years old. The median ages of sexual debut for both cases and controls were 17 and 18 years, respectively. Only 22.4% of those with suspicious cervical lesion and 19% of the controls were using contraceptives during their last visit to the hospital. Depo-Provera was the most common contraceptive used by both groups. Sixty and seventy percents of the cases and controls had 1-3 children, respectively [Table 2].

Information about WHO HIV staging and CD4-cell counts were obtained from the patient charts. Based on this, 71.6% of the patients with suspicious cervical lesion and 69.8% controls were WHO stage one. Half of the cases and 40% of the controls had CD4 count less than 350cells/mm^3. The exposure to multiple sexual partners of both groups was more or less similar, 43% versus 42.2%, for sucpicious cervical lesions and the controls, respectively.

Similarly, 40% of both cases and controls had history of STIs. History of STI was reported in 11.2% and 12.5% of partners of the cases and controls, respectively. At the time of the study, 50% of the cases and 44% of the controls were on ART for four to six years. The median years of stay with HIV, since they knew their sero-positivity, was five in the suspicious cervical lesions groupand six years in the controls [Table 3].

Predictors of precancerous cervical lesion: Controlling for the effect of other confounders, CD4 cells count, having multiple sexual partners, and marital status were found to be significant predictors forsuspicious cervical lesion. HIV positive women with CD4 count less than 350/mm^3 had a double risk of suspicious cervical lesion compared to those with more CD4 cells (AOR=1.6; 95% CI: 0.97, 2.68). Having two (AOR=3.6; 95% of CI: 1.7, 7.7) and three or more sexual partners (AOR=2.5; 95% of CI: 1.2, 5.4) were at higher risk ofsuspicious cervical lesion. Similarly, the odds of having suspicious cervical lesion was higher among married compared to the separated (AOR=2.3; 95% of CI: 1.28, 4.26) (Table 4).

Table 2:-Reproductive history of HIV positive women, Mekelle hospital, northern Ethiopia, 2014

Characteristics	Cases n(%)	Controls n(%)	Total n(%)
Age at first sexual intercourse			
Younger than 18	80(69)	160(69)	240(69)
18 or older	36(31)	72(31)	108(31)
Contraceptive use			
Yes	26(22.4)	44(19)	70(20.1)
No	90(76.4)	188(81)	278(79.9)
Type of contraceptive use			
Condom	7(27)	6(14)	15(20.8)
Depo provera	16(61)	35(79)	51(70.8)
Pill	3(12)	3(7)	6(8.4)
Parity			
None	14(12.1)	43(18.5)	57(16.4)
One to three	78(67.2)	133(57.3)	211(60.6)
More than three	24(20.7)	56(24.1)	80(23)
Number sexual partners to the women			
One	53(45.7)	110(47.4)	163(46.8)
Two	50(43.1)	107(46.1)	157(45.1)
Three or above	13(11.1)	15(6.5)	28(8)
Number of sexual partners of husband/ partner			
One	56(48.3)	79(34.1)	135(38.8)
Two	49(42.2)	91(39.2)	140(40.2)
Three or above	11(9.5)	62(26.7)	73(21)

Table 3:-Healthcare factors associated with precancerous cervical lesion, Mekelle hospital, Northern Ethiopia, 2014

Characteristics	Case n(%)	Control n(%)	Total n(%)
WHO stage			
First	83(71.6)	162(69.8)	245(70.4)
Second	16(13.8)	31(13.4)	47(13.5)
Third	14(12.1)	22(9.5)	36(10.3)
Fourth	3(2.6)	17(9.3)	20(5.7)
CD4 cell count (cells/mm^3)			
<350	58(50)	90(38.8)	148(42.5)
>=350	58(50)	138(59.5)	196(56.3)
History of STIs of the women			
Yes	46(39.7)	94(40.5)	140(40.2)
No	70(60.3)	138(59.5)	208(59.8)
History of STIs of husband/partner			
Yes	13(11.2)	29(12.5)	42(12)
No	103(88.8)	203(87.5)	306(88)
Duration of ART			
1-3 years	23(19.8)	28(12.1)	51(14.7)
4-6 years	58(50)	102(44)	160(46)
>6 years	35(30.2)	102(44)	137(39.4)
Duration since HIV diagnosis			
1-3 years	24(20.7)	28(12.1)	52(14.9)
4-6 years	59(50.9)	101(43.5)	160(46)
>6 years	33(28.4)	15(6.5)	48(13.8)
Opportunistic infections			
Yes	8(6.9)	8(3.4)	16(4.6)
No	108(93.1)	224(96.6)	332(95.4)
Previous suspicious lesions			
Yes	7(6)	11(4.7)	18(5.2)
No	109(94)	221(95.3)	330(94.8)
Previous abnormal PAP smear			
Yes	3(2.6)	7(3)	10(2.9)
No	113(97.4)	225(97)	338(97.1)
Chronic corticosteroid use			
Yes	5(4.3)	7(3)	12(3.4)
No	111(95.7)	225(97)	336(96.6)

Table 4:-Predictors of precancerous cervical lesion among HIV positive women, Mekelle hospital, northern Ethiopia, 2014

	Suspicious cervical lesion		**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
	Yes n (%)	**No n (%)**		
Characteristics				
Marital status				
Married	57(40.7)	83(59.3)	2.5(1.4,4.5)	2.4(1.28,4.26)*
Single	13(30.2)	30(69.8)	1.6(0.7,3.6)	1.5(0.65,3.476)
Widowed	24(39.3)	37(60.7)	2.4(1.2,4.8)	2.3(1.10,4.7)*
Separated	22(21.2)	82(78.8)		1
age				
Younger than 30 years	46(40.4)	68(59.6)	1.5(0.99,2.52)	1.6(0.97,2.68)
Older than 30	70(29.9)	164(70.1)	1	1
CD4 cell count (cells/mm^3)				
<350	58(39.2)	90(60.9)	1.5(1.2,2.4)	1.6(1.01,2.6)*
>350	58(29)	142(71)	1	1
Number of sexual partners				
One	56(41.5)	79(58.5)	1	1
Two	49(35)	91(65)	3.9(1.9,8.2)	3.6(1.7,7.7)*
Three or above	11(15.1)	62(84.9)	3.0(1.5,6.3)	2.5(1.2,5.4)*

*p<0.05

DISCUSSION

This study revealed that marital status (married), low CD4 cellcount and higher number of sexual partners were predictors of suspicious cervical lesion. Sexual intercourse at early age is associated with precancerouscervical lesion (15). This study pointed out that patients with and without suspicious cervical lesion had early initiation of sexual intercourse than the control.

The median age of first sexual intercourse for patient with and without precancerous cervical lesion was 17 and 18 years, respectively. The finding seem to be similar with that of a study among HIV-positive women in South Ethiopia (16).

A study done among HIV-infected Nigerian women shows that women age beyond 40 years have the lowest risk of screening positivity (RR=0.4) (17). This is also supported by our finding whereby 60.3% of the suspicious cervical lesion occurred in the age group less than 30. A number of other studies reported that the level of CD4 count is associated with suspiciouscervical lesion (17-19). Similarly, our study shows that HIV positive women with CD4 cells count less than 350/mm^3 were more likely to have suspicious cervical lesion compared to those with CD4 cells of 350/mm^3 or beyond. This is explained by the fact that HIV-induced immunosuppressant playing significant role in not effectively clearing HPV and may increase the development of Cervical neoplasia (20).

Studies on the impact of HAART on natural history of cervical squamous intraepithelial lesions (SILs) have produced inconsistent result. However, this study showed thatthere is correlation between length of stay under ART and suspiciouscervical lesions. This is supported by a study from Ethiopia which showed that Cervical precancerous lesions are associated with not being on ART; and another study revealed positive impact of HAART on the natural history of Human Papillomavirus-related cervical disease in HIV-infected women (18, 21).

No association has been found between STIs andsuspicious cervical lesion in our study although the association is demonstrated in other studies. For instance, a study from southern Ethiopia reported that women with STIs were more likely to develop precancerous cervical lesion than without STIs(16). Another study from Nigeria revealed that the presence of other vaginal wall abnormalities were associated with screening positivity (16,17). It has been postulated that *Chlamydia trachomatis* increases risk of invasive cervical cancer (22).

Number of sexual partners is also a positive predictor for precancerous cervical lesion. The increase in number of sexual partners raises the risk of having the diseases. This finding was supported by a study from the southern Ethiopia, which reported that women with one sexual partner in their life-time had lower risk of having cervical lesion and other studies as well (15, 16).

Our study revealed that married women were at higher risk of developing cervical lesion compared to separated. In one hand, this seems plausible since separated women may have lower sexual activity. However, this finding seems conflicting to studies that show association between number of sexual partner andprecancerous cervical lesion; i,e., the separated women may have higher likelihood for multiple sexual partners unlike the married ones. As such, this could not be explained as it stands. Furthermore, there may not be a true association between married women and cervical precancerous lesionsince women were asked solely about their marital status at the time ofstudy period. The study did not ask about prior multiple sexual activity.

The study may have a limitation in that few women had difficulty recalling their prior exposure to multiple sexual partners during the interview. However, since their number was small it may not bias the final estimation of the associations. In addition, efforts were made to help women recall during the interview. The knowledge of women about their husbands number of sexual partners may also be limited.

Conclusions: Suspicious cervical lesion were mainly observed in older women (older than 30), those with history of STIs and who stayed for fewer years under ART. Regarding the predictors, low CD4 count cells, being married compared to separated and increased number of sexual partners were the determinants for having precancerous cervical lesion.

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