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Comparison of findings on cervical cancer screening by visual inspection with acetic acid (VIA) between HIV-positive women on ARTs and HIV-negative women in faith alive hospital Jos, North-Central Nigeria

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Abstract
Background: Cervical cancer is the second most common cancer among women in Nigeria, and the leading cause of cancer-related death in sub-Saharan Africa. HIV-positive women are at heightened risk of developing cervical cancer than HIV-negative women due to immune suppression. In resource constrained settings, visual inspection with acetic acid (VIA) and subsequent treatment of precancerous lesions with thermal ablation remains the practical approach for secondary prevention.
Objective: To compare prevalence of cervical precancerous lesions and suspected cancer between HIV-infected women on ART and HIV-negative women; and to determine the risk factors for precancerous lesions.
Method: A retrospective data review of sexually active HIV-positive women on ART and HIV-negative women aged 16-55 years screened for cervical cancer by VIA at Faith Alive hospital Jos, North-Central Nigeria over a period of 16 months. Precancerous cervical lesions were treated with thermal ablation and monitored for 2-6 weeks after treatment, then yearly. Those with cancer suspicious lesions were referred to Jos University Teaching Hospital for further management. Socio-demographic characteristics of the study participants and the screening results were presented in frequency tables, and logistic regressions performed to determine risk factors for cervical pre-cancerous lesions. Data analysis was performed using IBM-SPSS 26.
Results: 1,113 HIV-positive women on ART and 1,073 HIV-negative women were screened for cervical cancer by VIA. Insignificantly higher prevalence of cervical precancerous lesions (9.1% versus 7.6%, p-value=0.091) and insignificantly lower prevalence of suspected cancer (1.6% versus 2.6%, p-value >0.05) was noted among HIV-positive women on ART compared to HIV-negative women. STI and parity ≥3 were the significant risk factors for cervical precancerous lesions.
Conclusion: We found no significant difference between the prevalence of cervical precancerous lesions and suspected cancer between HIV-positive women on ART and HIV-negative women. STI and parity ≥3 were risk factors for cervical precancerous lesions.

Keywords: Comparison of VIA findings, Screen-and-Treat

Introduction
Among several risk factors that have been identified, undeniably the most important risk factor for cervical cancer is infection with high risk Human Papilloma Virus (HPV) [1-2]. HPV is a common infection of the genital tract and it is believed that most sexually active people will acquire this infection at some point in their lives, which will subsequently be cleared by the immune system. However, in some individuals, infection may become persistent and chronic, leading to formation of precancerous lesions and cancer if untreated [2]. Compared with HIV-negative women, HIV-positive women are more likely to have persistent HPV infection. Although there is widespread use of antiretroviral therapy (ART) among women living with HIV (WLHIV), leading to increased life expectancy and reduced risk of opportunistic infections; this does not appear to lower the risk of HPV infection and

cumulative incidence of cervical cancer among them [3-7]. This increased survival in a moderately immune-compromised state seems to increase the risk of persistent HPV infection and the development of cervical precancerous lesions and cervical cancer [8, 9].

Over the past years, developed countries have established and strengthened cervical cancer prevention programs providing HPV vaccination and periodic screening and treatment of precancerous lesions, thereby reducing its incidence. However, in resource constrained settings, screening programs remain suboptimal with low uptake and as such, incidence of cervical cancer remains disproportionately high in these regions [10-14]. In November 2020 during the 73rd World Health Assembly, WHO launched a global strategy to accelerate the elimination of cervical cancer with some of the key objectives being 70% screening coverage with 90% access to treatment for precancerous and cancerous lesions by 2030 [15]. Although WHO strongly recommends HPV testing as the backbone for screening, however a series of seminal studies have proven the safety, acceptability and effectiveness of screen-and-treat approach for cervical cancer prevention in low-income countries [16, 17]. In this screen-and-treat approach, women are tested through visual inspection of the cervix with acetic acid (VIA), and receive immediate treatment for pre-cancerous lesions using thermal ablation. This approach is a simple and affordable alternative, allowing for nurses, midwives and non-physician healthcare workers to become trained providers, potentially improving access to cervical cancer prevention services [18-21].

In this study, we aimed to compare the prevalence of cervical precancerous lesions and prevalence of suspected cancer between HIV-positive women on ART and HIV-negative women; and to determine the risk factors for cervical precancerous lesions.

Methods

Retrospective data review of sexually active HIV-positive women on ART and HIV-negative women who met criteria for VIA (obvious transformation zone, not extending into endocervical canal), aged 16–55 years screened for cervical cancer using VIA at Faith Alive Foundation Hospital Jos, North-Central Nigeria between September 2020 and December 2021 (16 months period) was carried out. Precancerous lesions were identified as dense aceto-white changes close to or abutting the squamo-columnar junction (SCJ) in the transformation zone, occupying less than 75% of the cervix and not extending into the cervical canal. Confirmed precancerous lesions were treated with thermal ablation at the same time (Screen-and-Treat) and monitored for 2–6 weeks after treatment, then yearly. Women with suspected cancer lesion were referred to Jos University Teaching Hospital for colposcopy and biopsy to confirm cervical cancer. Radiotherapy was offered to those that could afford it while those that could not had extended hysterectomy plus chemotherapy. Clients with negative screening results were counseled to repeat screening annually. Data was extracted from care cards and service registers and analyzed using IBM-SPSS 26. Frequency tables were generated to show the socio-demographic characteristics of the study participants (Age, parity, history of multiple sexual partners, STI, age at first sexual intercourse, marital status and level of education) and the screening results.

Results

Table 1: Socio-demographic Characteristics of Sexually Active Women aged 16 to 55 years.

Demographic variables	HIV status	
	Positive (%)	Negative (%)
Age classification (Years)		
16-25	29(2.6)	80(7.5)
26-35	254(22.8)	286(26.7)
36-45	452(40.6)	351(32.7)
46-55	27(24.6)	222(20.7)
>55	104(9.3)	134(12.5)
Level of education		
Non-formal	26(2.3)	42(3.9)
Primary	328(29.5)	236(22.0)
Secondary	492(44.2)	453(42.2)
Tertiary	267(24.0)	342(31.9)
Marital status		
Married	713(64.1)	622(58.0)
Single	247(22.2)	372(34.7)
Widowed	101(9.1)	44(4.1)
Others	52(4.7)	35(3.3)
Parity		
Nullipara	157(14.1)	226(21.1)
1-2 para	381(34.2)	257(24.0)
≥3 para	575(51.7)	590(54.9)
Sex partner		
0-1(Single)	343(30.8)	364(33.9)
≥ 2 (Multiple)	770(69.2)	709(66.1)
Coitarche		
<18	485(43.6)	398(37.1)
≥18	628(56.4)	675(62.9)
STI		
Yes	606(54.4)	548(51.1)
No	507(45.6)	525(48.9)

1113 HIV-positive women and 1073 HIV-negative women had cervical cancer screening by VIA within the period under review. Mean age of client's 40.06±10.27 years. Majority of the clients were of age band 36-45 years(40.6% Vs 32.7%), had secondary level of education (44.2% Vs 42.2%), were married (64.1% Vs 58.0%), were of parity ≥3 (51.7% Vs 54.9%), had multiple sexual partners (69.2% Vs 66.1%) and STI (54.4% Vs 51.1%) in the past. (Table 1)

Table 2: Prevalence of cervical pre-cancerous lesion and suspected cancer between HIV-positive and HIV-negative women.

VIA	HIV Status		p-value
	Positive (%)	Negative (%)	
Positive	101(9.1)	82(7.6)	0.091
Negative	994(89.3)	961(89.5)	
Suspected cancer	18(1.6)	30(2.8)	
Total	1113(100.0)	1073(100.0)	

101 (9.1%) of HIV-positive women had cervical precancerous lesions, while 82 (7.6%) of HIV-negative women had cervical precancerous lesions. 18 (1.6%) of HIV-positive women had suspicion of cervical cancer while 30(2.8%) of HIV-negative clients had suspicion of cancer. (Table 2**)**

Table 3: Association between independent variables and suspected cancer

Variables	Suspected Cancer		p-value
	HIV-positive (n=18)	HIV-negative (n=30)	
Age classification (Years)			
16-25	0 (0.0)	1 (100.0)	0.777
26-35	7 (50.0)	7 (50.0)	
36-45	7 (33.3)	14 (66.7)	
46-55	3 (33.3)	6 (66.7)	
>55	1 (33.3)	2 (66.7)	
Marital status			
Married	13 (36.1)	23 (63.9)	0.731
Single	5 (41.7)	7 (58.3)	
Level of education			
Non-formal	0 (0.0)	1 (100.0)	0.071
Primary	6 (75.0)	2 (25.0)	
Secondary	7 (25.9)	20 (74.1)	
Tertiary	5 (41.7)	7 (58.3)	
Parity			
Nullipara	2 (66.7)	1 (33.3)	0.379
1-2 para	3 (25.0)	9 (75.0)	
≥3 para	13 (39.4)	20 (60.6)	
Sexual partners			
0-1(Single)	7 (41.2)	10 (58.8)	0.697
≥ 2 (Multiple)	11 (35.5)	20 (64.5)	
Coitarche			
<18	8 (53.3)	7 (46.7)	0.127
≥18	10 (30.3)	23 (69.7)	
Infection			
Yes	9 (40.9)	13 (59.1)	0.654
No	9 (34.6)	17 (65.4)	

HIV-positive women had bimodal age distribution for suspected cancer while HIV-negative women had a modal age distribution. No association between independent variables and development of suspected cervical. (Table 3**)**

Table 4: Association between independent variables and occurrence of cervical precancerous lesions

Demographic variables	HIV- Positive			HIV- Negative		
	VIA positive	VIA negative	P-value	VIA positive	VIA negative	P-value
Age classification (Years)						
16-25	2(6.9)	27(93.1)	**0.121***	9(11.4)	70(88.6)	0.277
26-35	29(11.7)	218(88.3)		25(9.0)	254(91.0)	
36-45	43(9.7)	402(90.3)		29(8.6)	308(91.4)	
46-55	15(5.5)	256(94.5)		13(6.0)	203(94.0)	
>55	12(.7)	91(88.3)		6(4.5)	126(95.5)	
Level of education						
Non-formal	3(11.5)	23(88.5)	0.704	2(4.9)	39(95.1)	0.905
Primary	34(10.6)	288(89.4)		18(7.7)	216(92.3)	
Secondary	40(8.2)	445(91.8)		35(8.1)	398(91.9)	
Tertiary	24(9.2)	238(90.8)		27(8.1)	308(91.9)	
Marital status						
Married	63(9.0)	637(81.0)	0.909	45(7.5)	554(92.5)	0.847
Single	23(9.5)	219(90.5)		29(7.9)	336(92.1)	
Widowed	11(10.9)	90(81.1)		4(9.1)	40(90.9)	
Others	4(7.7)	48(92.3)		4(11.4)	31(88.6)	
Parity						
Nullipara	14(9.0)	141(91.0)	0.898	18(8.0)	207(92.0)	0.099*
1-2 para	33(8.7)	345(91.3)		27(10.9)	221(89.1)	
≥3 para	54(9.6)	508(90.4)		37(6.5)	533(93.5)	
Sex partner						
0-1(Single)	23(6.8)	313(93.2)	0.070*	28(7.9)	326(92.1)	0.967
≥ 2 (Multiple)	78(10.3)	681(89.7)		54(7.8)	635(92.2)	
Coitarche						
<18	47(9.9)	430(90.1)	0.527	31(7.9)	360(92.1)	0.951
≥18	54(8.7)	564(91.3)		51(7.8)	601(92.2)	
STI						
Yes	66(11.1)	531(88.9)	**0.022***	50(9.3)	126(95.5)	0.068*
No	35(7.0)	463(93.0)		32(6.3)	476(93.7)	

STI: sexually transmitted infection, *significant at p-value of 0.25. Risk factors associated with cervical precancerous lesions: age 36-45 years, parity ≥3, multiple sexual partners and STI. (Table 4)

Table 5: Multiple logistic regression of factors associated with cervical pre-cancerous lesion

Variables	AOR	95% Confidence Interval for AOR		p-value
		Lower Bound	Upper Bound	
For HIV- positives				
Age classification (Years)				
16-25	0.469	0.098	2.246	0.343
26-35	0.891	0.432	1.838	0.754
36-45	0.730	0.367	1.451	0.369
46-55	0.410	0.184	0.915	0.029
>55	1			
Sex partner				
0-1(Single)	0.622	0.381	1.014	0.057
.≥ 2 (Multiple)	1			
STI				
Yes	1.634	1.061	2.518	0.026*
No	1			
For HIV- negatives				
Parity				
Nullipara	1.255	0.698	2.256	0.449
1-2 para	1.777	1.055	2.993	0.031*
≥3 para	1			
STI				
Yes	1.548	0.974	2.458	0.064
No	1			

AOR: Adjusted Odds Ratio, CI: confidence interval, * significant p-value< 0.05. STI and parity ≥3 have 1.6 fold and 1.7 fold risk association for cervical precancerous lesions respectively. (Table 5)

Discussion

This study showed prevalence of cervical precancerous lesions of 9.1% and 7.6% for HIV-positive women on anti-retroviral therapy (ART) and HIV-negative women respectively; and prevalence of suspected cancer of 1.6% for HIV-positive women and 2.6% for HIV-negative women. STI and parity ≥3 were significant predictors of cervical precancerous lesions, and the mean age of clients with precancerous lesion by VIA was 41.32±9.89.

The prevalence of precancerous cervical lesions among HIV-positive women was higher than that of HIV-negative women though with insignificant association (9.1% Vs 7.6%, p-value=0.091). This is comparable to the findings of Kiros *et al* in North-West Ethiopia (9.3% Vs 8.6%, p-value =0.859) [22] and Trejo *et al* in Lusaka Zambia (25.4% Vs 23.9%, p-value >0.05) [23]; however, not at par with the findings of Jolly *et al* in Swaziland(22.9% Vs 5.7%, p-value <0.01) [19] and Korn *et al* in Namibia(17.0% Vs 15.0%, p-value=0.02) [18]. The comparable prevalence of cervical precancerous lesions between HIV-positive women and HIV-negative women in our study may be due to the fact that majority of the clients had been long on ART and had achieved viral suppression with immunological response to clear HPV unlike in the study of Jolly *et al*. [19] and Korn *et al*. [18] where most of clients were ART naïve.

There was no significant difference between the prevalence of suspected cancer among HIV-positive women and HIV-negative women in this study (1.6% Vs 2.6%, p-value >0.05). This is at par with the findings of Korn *et al* (16% Vs 11%, p-value >0.05) [18] and Ramadhani *et al* in Morogoro region of Tanzania (11% Vs 8%, p-value=0.3551) [24]. However, unlike other studies we found insignificantly higher prevalence of suspected cancer among HIV-negative women. There was a bi-modal age classification for suspected cancer among HIV-positive women 7 (38.9%) for age 26-35years and age 36-45years; and modal age classification for HIV-negative women 14(46.7%) for age 36-45 years; this suggests that cervical cancer may occur at a lower age among HIV-positive women than HIV-negative women [25]. The bi-modal age classification in this study was in keeping with the bimodal age distribution of the cervical cancer with first peak at ages 43 years and a relative rebound at 61 years considering 5-15 years shift from precancerous state to full blown cervical cancer [25]. Suspected cervical cancer clients were referred to Jos University Teaching Hospital for examination under anesthesia (EUA), clinical staging and biopsy, with subsequent radiotherapy, or extended hysterectomy with chemotherapy for those who could not afford radiotherapy.

Multiple sex partners, age 36-45 years, sexually transmitted infection (STI) and parity ≥3 were factors found to be associated with cervical precancerous lesions and these are at par with findings in other studies [18-22]. After subjecting these factors to multiple logistic regression STI and parity ≥3 were found to be significant predictors of cervical precancerous lesions (AOR 1.634, 95% CI: 1.061-2.518, p-Value 0.026 and AOR 1.78, 95% CI: 1.055-2.993 p-value 0.031 respectively). STIs including Chlamydia trachomatis, Herpes simplex and Genital wart amplifies the risk of precancerous lesion by causing inflammation which resultantly enables HPV tenacity [4].

Prevalence of precancerous cervical lesions across age bands among HIV-positive women versus HIV-negative women in our study was as follows: 2% Vs 11% for 15-25years, 28.7% Vs 30.7% for 26-35 years, 42.6% Vs 35.4% for 36-45 years, 14.9% Vs 15.9% for 46-55 years, and 11.9% Vs 7.3% for ≥55 years. The peak prevalence was found to be at the band 36-45 years and this is in keeping with the findings in other studies [18, 22, 26].

Limitation: Cervical cancer screening by VIA is subject to observer bias and thus making the quality control difficult.

There was no secondary triage procedures like HPV testing, Papanicolaou (PAP) smear and colposcopy prior to the "screen-and-treat" in our facility due to low resource constrains. The low specificity associated with VIA may also leads to overtreatment. Besides, duration on ART, viral load and CD4 counts of HIV-positive women were not incorporated into the study.

Conclusion

This study has been able to reveal insignificantly higher prevalence of precancerous cervical lesions and insignificantly lower prevalence of suspected cancer in HIV-infected women on ART compared with HIV-negative women, with bimodal age distribution of suspected cervical cancer among the former. STI and parity ≥3 were significantly associated risk factors for precancerous cervical lesions. We therefore recommend a scale up in the "screen-and-treat" approach for secondary prevention of cervical cancer until a widespread HPV testing to triage client is feasible.

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Author's Contribution

Not available

Conflict of Interest

Not available

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