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Original Research

The immunological and virological correlates of Cervical Precancerous Lesions among HIV-Infected Women on ART in Faith Alive Hospital, Jos, Nigeria.

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Abstract

Background: Immuno-suppression in women living with HIV (WLHIV) increases the persistence of high-risk human papillomavirus (HPV) and reduces the ability to clear cervical precancerous lesions; as such, WLHIV are more predisposed to cervical cancer. Widespread use of antiretroviral therapy (ART) among WLHIV enhances immune reconstitution, controlling HIV replication and reversing the weakened immune system. This impedes HPV persistence and the development of precancerous lesions. The immune status of WLHIV is related to their CD4 count and viral load. These factors are impacted by the duration of effective ART. This study aimedto determine the association between cervical precancerous lesions with viral load, CD4 count, and duration on ART among WLHIV.

Methodology: A retrospective study on 1113 WLHIV aged 16 -55 years screened for cervical cancer using visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) within a 16-month period in Faith Alive Hospital, Jos, Nigeria. Sociodemographic characteristics of study participants, CD4 count, viral load, duration on ART, and screening results were documented. The data were analysed using IBM-SPSS 26, and logistic regression was performed to determine factors associated with pre-cancerous lesions.

Results: The prevalence of cervical precancerous lesions was 9.1%, the prevalence of suspected cancer was 1.6% and the mean age of clients with pre-cancerous lesions was 41.32±9.89 years. Unsuppressed baseline viral load (≥1000 copies/ml) and <6 months of exposure to ART were found to be strongly associated with cervical precancerous lesions.

Conclusion: This study demonstrated a higher burden of cervical precancerous lesions in viral unsuppressed women on ART initiation and in women with <6 months of exposure to antiretroviral therapy. Early commencement and prolonged use of ART on WLHIV to ensure early and sustained viral suppression to reduce the risk of cervical cancer is recommended.

Keywords: Faith Alive; WLHIV; VIA; Immunological and Virological Correlates.

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Introduction

Among several risk factors that have been identified for cervical cancer, undeniably the most important is infection with the high-risk Human Papillomavirus (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 be subsequently cleared by the immune system. However, in some individuals, infection may become persistent and chronic, leading to the formation of cervical precancerous lesions and cervical cancer if untreated.[2] Immune suppression, as in HIV infection, increases the risk of persistent HPV infection and reduces the ability of the immune system to clear precancerous lesions, and as such, WLHIV are at increased risk of developing cervical cancer.[3-5]High-risk HPV persistence and the development of cervical precancerous lesions with subsequent progression to invasive cancer are impeded using ART. [6-8]

The immune status of WLHIV is directly related to their CD4 count and viral load; these two factors can also be impacted by the duration on effective ART.[7,8] Low CD4 counts (<500cells/mm^3) and high viral loads (≥1000 copies/ml) indicate immune suppression and poor response to ART medications for women on prior ART.[7,9] Besides the established risk factors for cervical precancerous lesions such as parity, early coitarche, multiple sexual consorts, cigarette smoking, prolonged use of oestrogen based modern contraceptive methods, and persistent HPV infection; unsuppressed HIV viral load, low CD4 count and duration on ART treatment could also be predisposing factors for cervical precancerous lesions and cervical cancer among WLHIV.[7,10] There are diverse literature reports on the association of cervical precancerous lesions with low CD4 count, unsuppressed viral load, and duration on ART.[11-13] CD4-lymphocytes are important for immune surveillance, maintenance, and suppression of tumour promotion, which suggests that high CD4 count may prevent cervical neoplastic lesions by preventing persistence of high-risk HPV in WLHIV.[12,13] Antiretroviral therapy impairs the proliferation of HIV, thereby suppressing the HIV viral load.[12-15] This study therefore aimed to determine the association between cervical precancerous lesions and viral load, CD4 count, and duration on ART among WLHIV.

Materials and Methods

Study Setting

Data were obtained from Faith Alive Hospital, Jos, Plateau State, Nigeria, a faith-based Non-Governmental Organization that operates free antiretroviral therapy (ART) and free cervical cancer screening, and treatment with thermal ablation for eligible women. Lesions were eligible for same-day treatment if dense aceto-white changes close to or abutting the squamo-columnar junction (SCJ) in the transformation zone, occupying less than 75% of the cervix, not extending into the cervical canal, and were not suspicious of cancer. Women who had treatment of cervical precancerous lesions by thermal ablation were followed up for 2-6 weeks. Those suspicious of cancer were not eligible and were referred to Jos University Teaching Hospital for colposcopy and biopsy to confirm cervical cancer. Those confirmed with invasive cancer had radiotherapy, and an extended hysterectomy plus chemotherapy for women who could not afford the former. Thermal ablation therapy was performed by experienced nurses (case finders) who were trained in screening and treatment of cervical precancerous lesions.

Data Collection

A retrospective data review of sexually active WLHIV on ART who met the criteria for visual inspection with acetic acid for cervical cancer screening, aged 16–55 years at Faith Alive Foundation Hospital, Jos, Nigeria, between September 2020 and December 2021 (16-month period). 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 screening results were extracted from care cards, service registers of cervical cancer unit and their corresponding CD4 counts (baseline and current CD4 counts), viral loads (baseline and current viral loads) and duration on ART of the study participants were obtained from site electronic management record system.

Data Analysis

The analysis involved all WLHIV screened within the period under review. Screening results were categorised as normal, precancerous lesions, and suspected cancer. Retrieved data from the site's electronic management record system: 87.5% for CD4 count, 92.0% for viral load, and 93.4% for duration on ART. The association between cervical precancerous lesions, CD4 count (baseline and current), viral load (baseline and current), and duration on ART was assessed by logistic regression. Data was analysed using IBM-SPSS 26.

Ethical consent

The Faith Alive Hospital Ethical Committee approved the study protocol, and consent waiver was obtained as all data were retrospectively collected and anonymized for analysis.

Results

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

Demographic characteristics	Frequency(n=1113)	Percentage
Age classification (Years)		
16-25	29	2.7
26-35	254	22.8
36-45	452	40.6
46-55	274	24.6
>55	104	9.3
Marital status		
Married	713	64.2
Single	247	22.2
Widowed	101	9.1
Others	52	4.7
Level of education		
Non-formal	26	2.3
Primary	328	29.5
Secondary	492	44.2
Tertiary	267	24.0
Parity		
Nullipara	157	14.1
1-2 para	381	34.2
≥3 para	575	51.7

Multiple sexual partners		
0-1(Single)	343	30.8
≥ 2 (Multiple)	770	69.2
Coitarche		
<18	485	43.6
≥18	628	56.4
STI		
Yes	606	54.4
No	507	45.6

One thousand, one hundred and thirteen (1113) WLHIV on ART had cervical cancer screening by VIA/VILI within the period under review. The mean age of the clients was 40.1 ± 10.3 years. Most of the clients were inthe age band 36-45 years (40.6%), married (64.1%), had a secondary level of education (44.2%), parity ≥3 (51.7%), had multiple sexual partners (69.2%), and had an STI (54.4%). About half of the clients had coitarche <18 years (Table 1)

Table 2: Distribution of CD4 count, Viral load, and duration on ART among WLHIV

CD4/Viral load status	Frequency	Percentage
Baseline CD4(n=974)		
<200	224	23.0
≥200	750	77.0
Current CD4(n=974)		
<200	145	14.9
≥200	829	85.1
Baseline Viral load (n=1024)		
<1000	942	92.0
≥1000	82	8.0
Current Viral load (n=1024)		
<1000	996	97.3
≥1000	28	2.7
Duration of ART (months) n=1040		
1-6	332	31.9
7-12	433	41.6
>12	275	26.4

Out of the 974 clients that had reported CD4 measurements on the database, 224 (23.0%) had baseline CD4 count <200 cell/ml and 145 (14.9%) had current CD4 count < 200 cells/ml. Baseline and current viral load suppression among study participants were 92.0% (942/1024) and 97.3% (996/1024) respectively. About three-quarters of the clients had documented evidence of being on antiretroviral drugs within the last 12 months to this assessment (Table 2)

Table 3: Prevalence of cervical pre-cancerous lesions and suspected cancer

Precancerous Lesions/suspected cancer	Frequency	Percentage
Positive	101	9.1
Negative	994	89.3
Suspected Cancer	18	1.6
Total	1113	100.0

101(9.1%) of the clients had cervical precancerous lesions, 18(1.6%) had cervical lesions suspicious of cancer (Table 3).

Table 4: Association between VIA result, CD4, viral load, and duration on ART among WLHIV

CD4/Viral load status	VIA results		χ^2	p-value
	Positive	Negative		
Baseline CD4(n=974)				
<200 cells/mm^3	23(10.4)	199(89.6)	0.706	0.401
≥200 cells/mm^3	63(8.5)	676(91.5)		
Current CD4(n=974)				
<200	18(12.6)	125(87.4)	2.729	0.099
≥200	68(8.3)	750(91.7)		
Baseline Viral load (n=1024)				
<1000	79(8.5)	852(91.5)	7.167	**0.007***

≥1000	14(17.5)	66(82.5)		
Current Viral load (n=1024)				
<1000	90(9.1)	894(90.9)	0.121	0.727
≥1000	3(11.1)	24(88.9)		
Duration of ARV (n=1040)				
1-6	40(12.3)	286(87.7)	6.570	**0.037***
6-12	38(8.9)	389(91.1)		
>12	17(6.2)	256(93.8)		

*Significant at p-value≤0.0.5

Baseline viral load ≥1000 copies/ml and ART duration less than six (6) months were associated with cervical precancerous lesion (Table 4).

Table 5: Socio-demographic factors associated with cervical precancerous lesions.

Variables	Occurrence of precancerous lesion		χ^2	p-value
	Positive	Negative		
Age classification (Years)				
16-25	2(6.9)	27(93.1)	7.288	0.121
26-35	29(11.7)	218(88.3)		
36-45	43(9.7)	402(90.3)		
46-55	15(5.5)	256(94.5)		
>55	12(11.7)	91(88.3)		
Marital status				
Married	63(9.0)	637(91.0)	0.546	0.909
Single	23(9.5)	219(90.5)		

Widowed	11(10.9)	90(89.1)		
Others	4(7.7)	48(92.3)		
Level of education				
Non-formal	3(11.5)	23(88.5)	1.405	0.704
Primary	34(10.6)	288(89.4)		
Secondary	40(8.2)	445(91.8)		
Tertiary	24(9.2)	238(90.8)		
Parity				
Nulliparous	14(9.0)	141(91.0)	1.284	0.526
Para 1-2	49(8.4)	533(91.6)		
Para ≥3	38(10.6)	320(89.4)		
Multiple sexual partner				
1	23(6.8)	313(93.2)	3.275	0.070
≥2	78(10.3)	681(87.1)		
Coitarche				
<18	47(9.9)	430(90.1)	0.400	0.527
≥18	54(8.7)	564(91.3)		
STI				
Yes	66(11.1)	531(88.9)	5.259	**0.022***
No	35(7.0)	463(93.0)		

History of STI was found to be associated with cervical precancerous lesions, *significant at p-value ≤0.05 (Table 5).

Table 6: Logistic regression of factors associated with cervical pre-cancerous lesions

Factors	AOR	95% C. I.		p-value
Age classification (Years)				
16-25	0.464	0.088	2.461	0.367
26-35	0.738	0.307	1.770	0.495
36-45	0.775	0.351	1.710	0.528
46-55	0.465	0.191	1.131	0.091
>55	1			
Multiple sex partner				
≥2	0.557	0.321	0.965	**0.037**
1	1			
STI				
Yes	1.685	1.047	2.711	**0.032**
No	1			
Current CD4				
<200	1.136	0.607	2.128	0.690
≥200	1			
Baseline Viral Load				
<1000	0.420	0.213	0.826	**0.012**
≥1000	1			
Duration of ARV				
1-6	2.012	1.006	4.024	**0.048**
7-12	1.398	0.760	2.570	0.281
>12	1			

Unsuppressed baseline viral load was significantly associated with cervical precancerous lesions among WLHIV; likewise, ART initiation was less than six months. STI and multiple sexual partners were also factors associated with cervical precancerous lesions, AOR: Adjusted Odds Ratio, 95% CI, p-value≤0.05(Table 6)

Discussion

Findings from this study showed that unsuppressed baseline viral load (≥1000 copies/ml) was associated with cervical precancerous lesions (AOR 0.420; 95% CI, 0.213-0.820, p=0.012) likewise being on ART for less than six months period (AOR 2.012; 95%CI,1.006-4.024, P=0.048). Current CD4 count < 200 cells/mm^3 was not found to be associated with cervical precancerous lesions (AOR 1.136;95% CI,0.213-0.826, P=0.690). Other factors associated with cervical precancerous lesions were a history of STIs and multiple sexual partners. The prevalence of cervical precancerous lesions was 9.1% while the prevalence of suspected cancer was 1.6% among WLHIV who had cervical cancer screening by VIA/VILI. The mean age of clients with cervical precancerous lesions was 41.32±9.89 years.

This finding with unsuppressed baseline viral load means that women with suppressed baseline viral load are 68% less likely to develop cervical precancerous lesions, and this was at par with the findings of Zelalem et al in Ethiopia[7], Lewis et al in Malawi [8], and Chambuso et al in Tanzania.[13] However, this is not in keeping with the report by Ezechi et al in South-west Nigeria [6] and Gupta et al in India. [10]

In our study, there was no association between CD4 count <200 cells/ mm^3 (advanced HIV infection) and cervical precancerous lesion, and this is comparable to the finding of Chambuso et al in South Africa.[15] We used absolute CD4 count in our study, which was found by Chambuso et al in South Africa, not to be associated with cervical precancerous lesions, but CD4 percentage. Moreso, most of the clients involved in our study had an absolute CD4 count ≥ 200 cells/mm^3 at the time of commencement of ART. However, other studies found a strong association between absolute CD4 count <200 cells/mm^3 and cervical precancerous lesions. [6,14,15]

We found ART initiation less than six months to be strongly associated with cervical precancerous lesions among WLHIV, while taking ART for a longer period was not. Hence, a longer duration on ART suppresses viral load, thereby reducing the risk of cervical precancerous lesions. This finding was also corroborated by studies done in Southwest Nigeria [6], Malawi [8], and Yunnan.[11]

STI was found to be associated with cervical precancerous lesions among WLHIV, likewise having multiple sexual partners. These findings were also in keeping with findings in other studies. [16-19]

Limitation

The time interval between the current HIV viral load, current CD4 count, and cervical cancer screening was not considered. Viral load, CD4 count, and duration on ART retrieval from the site's electronic management record system were not 100%. Adherence to ART was also not considered.

Conclusion

This study revealed that WLHIV with suppressed baseline viral load are less likely to develop cervical precancerous lesions, and the use of ART for over six months is also less likely to be associated with cervical precancerous lesions. Thus, early commencement and prolonged use of ART among WLHIV will ensure early and sustained viral suppression to reduce the risk of cervical precancerous lesions and eventual cervical cancer. Scale-up in the "screen-and-treat" approach for secondary prevention of cervical cancer until widespread HPV testing to triage clients is feasible.

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Conflicts of Interest: The authors declare no conflicts of interest.

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