

Cervical Lesions among HIV-Positive Women receiving Highly Active Antiretroviral Therapy in Jos, Nigeria

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ABSTRACT

Introduction: Cervical lesions and HIV are significant public health concerns, particularly in sub-Saharan Africa, where women face a disproportionate burden of both conditions. Despite advancements in Highly Active Antiretroviral Therapy (HAART), the relationship between HAART and cervical lesion progression remains unclear, especially in resource-limited settings. **Aim and Objectives:** This study aimed to investigate the prevalence and characteristics of cervical lesions among HIV-positive women on HAART. **Materials and Method:** A cross-sectional design was used, recruiting 351 HIV-positive women from the APIN clinic and 162 HIV-negative women from the gynecological clinic at Jos University Teaching Hospital, Nigeria. Smears were collected, stained using Papanicolaou staining method, and examined for premalignant lesions. **Result:** Our data revealed a 16.1% prevalence of cervical lesions among HIV-positive women on HAART, with no significant difference compared to those not on HAART (6.2%, $p=0.484$). However, women on second and third-line HAART exhibited higher lesion severity (23.1% ASC-US, 7.7% ASC-H) compared to those on first-line therapy (88.2% negative results, $p=0.044$). Behavioral factors, such as multiple sexual partners, were significantly associated with lesion prevalence ($p=0.013$). Awareness of cervical screening was high (93.7%), but utilization did not significantly reduce lesion prevalence.

Conclusion: The findings underscore the complex interplay between HIV, HAART, and cervical lesions, highlighting the need for integrated care models that combine HIV management with regular cervical screening.

KEYWORDS: Cervical lesions, Histopathology, Human Immunodeficiency Virus

BACKGROUND

The well-being of women, particularly those living with Human Immunodeficiency Virus (HIV), is challenged by numerous health conditions^[1]. Worldwide an estimate of 20.1 million women is known to be living with HIV^[2], and the situation is not different in Nigeria, with an estimated 2 million individuals living with the virus^[3]. HIV is a direct threat to the immune system and also carries with it associated health concerns, exposing women to various vulnerable complications. One such is the heightened susceptibility of HIV-positive women to cervical lesions^[4]. The link between HIV infection and the elevated risk of developing cervical lesions among women have been sighted in several studies^[5, 6]. The interplay of HIV and cervical health highlights the need to explore into this intricate relationship, understanding its implications for

comprehensive healthcare. Cervical lesions compromise the reproductive health of women and also serve as potential precursors to more severe conditions, including precancerous and cancerous conditions [7, 8].

Furthermore, there is a great deal of curiosity in how HAART can affect cervical health. It is critical to look into the potential influence of HAART on the onset or development of lesions given the intricate connections that appear to exist between HIV infection and cervical lesions. Research suggests that the immune-suppressive effects of antiretroviral medication might influence the health of the cervical region [9].

Buoyed by rising global optimism about the possibility of reducing cervical cancer globally, the World Health Organization (WHO), with endorsement from over 194 countries, including Nigeria, has recently launched a global initiative to accelerate the elimination of cervical cancer as a public health problem by significant expansion of efforts to increase HPV vaccination to 90% coverage, screening to 70% coverage in mid-adult women, and treatment to 90% of those in need of it [10, 11].

MATERIAL AND METHOD

Study Design

The study was a cross-sectional descriptive study that was conducted two clinics, the cytology section of the Reproductive Health Unit (RHU) of the Aids Preventive Initiative of Nigeria (APIN), for HIV-positive women who were attending the adult HIV clinic and the Obstetrics and Gynaecology clinics for non-HIV infected women in Jos University Teaching Hospital (JUTH), Jos, between April, 2024 to September 2024.

Study Area

The study was carried out at the Reproductive Health Unit (RHU) of the APIN/Harvard PEPFAR HIV Clinic, Jos University Teaching Hospital (JUTH), Nigeria (Appendix A1).

Study Population

The targeted study populations were consenting HIV-positive women recruited in AIDS Prevention in Nigeria (APIN) adult outpatient clinic and those that visited for routine follow-up and drug top-ups.

Inclusion

The followings women were included who consent to participate in the study-

- HIV-positive women aged 18 years and above.
- Non-pregnant women and those who were 6 weeks post-partum.

- HIV-positive women on HAART and not yet on HAART.
- HIV-negative women.

Exclusion

The followings were excluded to participate in the study-

- Women who do not give consent to participate in the study.
- Puerperal (virgin), or menstruating
- Pregnant women.
- Women with previous treatment for cervical premalignant lesions, hysterectomy or invasive cervical malignancy

Sample Size

The Fischer 's formula below will be used to calculate sample size of the participants that will participate in this study [13]

The sample size was determined using the formula, where Z_{α} is 1.96 at a 95% level of confidence, P is 0.12 a prevalence of 12.3%, d is the 0.05 margin of error, and N is the samples.

$$N = \frac{Z_{\alpha}^2 X P (1-P)}{d^2}$$

Where:

- N = sample size
- Z_{α} = normal deviation at the desired confidence interval. In this case it will be taken at 95%, Z value at 95% is 1.96.
- At significant level of 0.05 and 95% confidence level for a descriptive study, $Z_{\alpha} = 1.96$
- $P = 12.3\%$ prevalence of cervical lesions in HIV positive women [14].
- $= (12/100=0.12)$
- $d = \text{degree of precision } 5\% \text{ for this study} = (5/100=0.05)$

$$\begin{aligned} \blacksquare N &= \frac{Z_{\alpha}^2 X P (1-P)}{d^2} = \\ \blacksquare N &= \frac{(1.96)^2 \times 0.12 \times (1-0.12)}{0.05^2} \\ \blacksquare N &= \frac{3.8 \times 0.12 \times 0.88}{0.0025} \\ \blacksquare N &= \frac{0.41}{0.0025} = 162 \end{aligned}$$

A total of 5 different groups will be used in this study,

Post- HAART which consists of 3 sub-groups

- first-line regimen group

- second-line regimen group
- third-line regimen group

Pre- HAART (naïve) which serve as

- Comparison group

HIV-Negative, which will serve as

- Negative control

The sample size was determined using Fischer's formula, yielding 162 participants per group (Total 810). To account for an anticipated attrition rate of 20%, the sample size per group was increased to 200, resulting in a total target population of 1,000 (5 groups × 200).

Ethical Clearance

A letter of introduction with reference number UJ/EC/APIN/FHST/MLS/09, was obtained from the Department of Medical Laboratory Science Faculty of Health Sciences and Technology, College of Health Science, University of Jos. The protocol for this study was approved by the Jos University Teaching Hospital Health Research Ethics Committee with reference number REF/JUTH/DCS/REC/127/XXXI/2664. Permission was obtained from the Harvard School of Public Health for both the identification and enrollment of HIV-infected women in JUTH APIN clinic and the use of secondary data and other relevant information needed for this study.

Data Collection

Cytology specimen

The smears were allowed to fix in the fixative (95% ethanol) for at least 30min, the fixed slides were then rinsed in 2 changes of water for 2min each, slides were stained in Harris haematoxylin for about 4 min and rinsed in 2 changes of water for 2 min. The smear was decolorized with 0.1% acid alcohol briefly and processed using standard techniques as described^[15, 16].

Data Analysis

Data obtained were entered into Microsoft Excel worksheet and exported to SPSS software. The data were analyzed by descriptive statistics such as frequencies and percentages using the Statistical Package for Social Science (SPSS) version 26. The association between cervical lesions and HAART was assessed using statistical methods like chi-square tests, and Fisher's exact the prevalence and severity of cervical lesions among HIV-women on HAART and HAART-naïve HIV- positive women was determined, statistically significant was tested at 5% level of significant (95% C.I) when p-value<0.05.

RESULTS

A total number of 351 HIV positive-women were recruited from the out-patients APIN clinic and 162 HIV-negative women from the gynecological clinic all within Jos University Teaching Hospital, Jos. The participants were separated into five groups: Post-HAART group (which consists of first-line regimen group, second-line regimen group, and third-line regimen group), Pre-HAART or naïve group, which serves as the comparison control group (HIV-positive but not on HAART), and HIV-negative group which serves as the negative control. A structural questionnaire was administered to all respondents. The majority of participants on HAART were middle-aged. Specifically, 36 participants (7.0%) were aged 30 years and below, 95 (18.5%) were between 31 and 40 years, 203 (39.6%) were between 41 and 50 years, and 133 (25.9%) were between 51 and 60 years. Regarding marital status, 46 participants (9.0%) were single, 18 (3.5%) were separated, and 12 (2.3%) were divorced. In terms of educational attainment, 20 participants (4.0%) had no formal education, 104 (20.8%) attained only primary education, 158 (31.5%) had completed secondary education, while 219 (43.7%) had attained tertiary-level education. The highest prevalence of cervical lesions was found in the age group 41-50 years (39.6%) across all groups. Participants were predominantly married (60.0%) and had a secondary or tertiary level of education (75.2% combined). Occupational-wise, business constituted the largest group (38.6%), followed by civil servants (32.2%) [Table. 1].

Women who had previously undergone cervical screening demonstrated a marginally higher prevalence of cervical lesions (18.3%) compared to those who had never been screened (12.0%); however, this difference also did not reach statistical significance ($p = 0.130$) [Table. 2].

Notably, women with multiple life partners had a lower prevalence of cervical lesions (11.9%) than those with a single spouse (22.0%), with a statistically significant association ($p = 0.013$). The use of contraceptives, alcohol intake and smoking did not significantly affect the prevalence of cervical lesion in this study ($p > 0.05$) [Table. 3].

HIV-infected women on HAART had a prevalence of 16.12% of cervical lesion when compared with those HIV-infected that are HAART naïve (6.22%) [Table. 4].

Participants on the first line of HAART had the highest proportion of negative results (88.2%) and low prevalence of cervical lesions (11.8%). Whereas, the third-line therapy groups had a lower proportion of negative results (61.5%) and a higher prevalence of lesions, especially ASC-US (23.1%) and LSIL and HSIL had 7.7% each [Table. 5].

Demographics	Groups			
	On HAART n(%)	Comparison group n(%)	Negative control n(%)	Total n(%)
Age groups (yrs)				
≤30	15(4.5)	3(18.8)	18(11.1)	36(7.0)
31-40	52(15.5)	10(62.5)	33(20.4)	95(18.5)
41-50	148(44.2)	2(12.5)	53(32.7)	203(39.6)
51-60	92(27.5)	1(6.3)	40(24.7)	133(25.9)
61-70	28(8.4)	0(0.0)	18(11.1)	46(9.0)
Marital status				
Married	164(49.0)	8(50.0)	136(84.0)	308(60.0)
Single	24(7.2)	6(37.5)	16(9.9)	46(9.0)
Widowed	120(35.8)	1(6.3)	8(4.9)	129(25.1)
Divorced/Separated	27(8.1)	1(6.3)	2(1.2)	30(5.8)
Level of education				
Non-formal	20(6.0)	0(0.0)	0(0.0)	20(4.0)
Primary	86(26.0)	1(7.1)	17(10.9)	104(20.8)
Secondary	116(35.0)	5(35.7)	37(23.7)	158(31.5)
Tertiary	109(32.9)	8(57.1)	102(65.4)	219(43.7)
Occupation				
Civil servant	89(26.6)	4(25.0)	72(44.4)	165(32.2)
Business	241 (71.9)	8(50.0)	70(43.2)	334(65.1)
Student	5(1.5)	4(25.0)	5(3.1)	14(2.7)

Table 1: Demographic characteristics of participants

Variables (n=335)	Cervical lesions		χ^2	p-value
	Positive n(%)	Negative n(%)		
Awareness of cervical screening				
Yes	52(16.6)	262(83.4)	0.721	0.396
No	2(9.5)	19(90.5)		
Screened				
Yes	40(18.3)	178(81.7)	2.292	0.130
No	14(12.0)	103(88.0)		

Table 2: Awareness and Distribution of cervical lesions

Significant value P < 0.05

Risk factors	Cervical lesions		χ^2	p-value
	Positive n(%)	Negative n(%)		
Contraceptive use				
Yes	29(14.3)	174(85.7)	1.281	0.258
No	25(18.9)	107(81.1)		
No of life partners				
Single	31(22.0)	110(78.0)	6.197	0.013
Multi life partners	23(11.9)	171(88.1)		
Alcohol intake				
Yes	11(12.1)	80(87.9)	1.502	0.220
No	43(17.6)	201(82.4)		
Ever smoked cigarette				
Yes	2(33.3)	4(66.7)	1.339	0.247
No	52(15.8)	277(84.2)		
Type of marriage				
Monogamous	42(16.7)	209(83.3)	0.004	0.949
Polygamous	10(16.4)	51(83.6)		

Table 3: Behavioral risk factors and Prevalence of cervical lesions

Significant value P < 0.05

Cervical lesions	Group		χ^2 p-value
	Post-HAART (%)	Pre-HAART (%)	
Positive	54(16.1)	1(6.2)	- 0.484 ^f
Negative	281(83.9)	15(93.8)	

Table 4: Prevalence of cervical lesions in HIV positive women

^fFisher's exact test→ used When one or more cells in a 2x2 contingency table has an expected frequency of <5. Significant value P< 0.05

Stages of cervical lesions	Lines of therapy			χ^2	p-value
	First line n(%)	Second line n(%)	Third line n(%)		
Negative	142(88.2)	131(81.4)	8(61.5)	15.875	0.044
ASC-US	12(7.4)	15(9.3)	3(23.1)		
LSIL	3(1.9)	7(4.3)	1(7.7)		
HSIL	4(2.5)	8(5.0)	1(7.7)		

Table 5: Association between stages of cervical lesions and HAART's therapy

Significant value P< 0.05

Key.

ASC-US - Atypical squamous cells of -undetermined significance

LSIL - low-grade squamous intraepithelial lesion

HSIL - high-grade squamous intraepithelial lesion

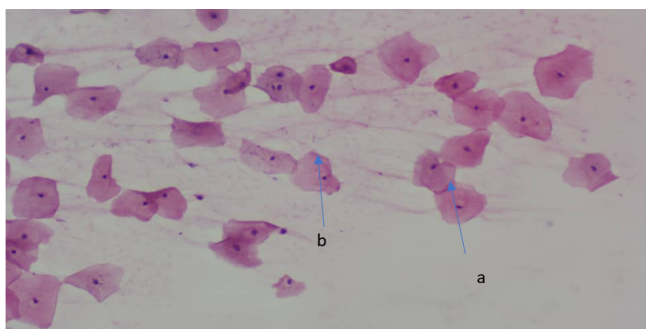


Fig. 1: Cervical smear showing Negative for Intraepithelial Lesion, with pink-stained cytoplasm having well define boards, abundant cytoplasm & low nuclear/cytoplasmic ratio. (a), condensed pyknotic nucleoli, centrally located (b) (Pap Smear; Mag x 40)

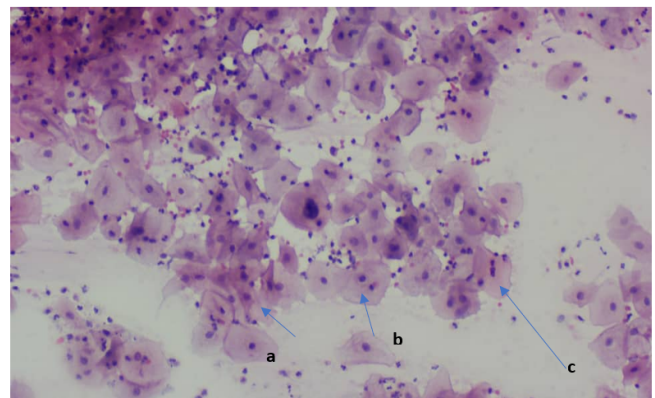


Fig. 2: x40 (Papanicolaou stain) cervical smear showing Atypical Squamous Cells of Undetermined Significance (ASC-US), with hyperchromatic crowded groups of small parabasal cells (a), with slightly enlarged darker nuclei with nucleoli with irregular contours (b & c). (Pap Smear; Mag x 40)

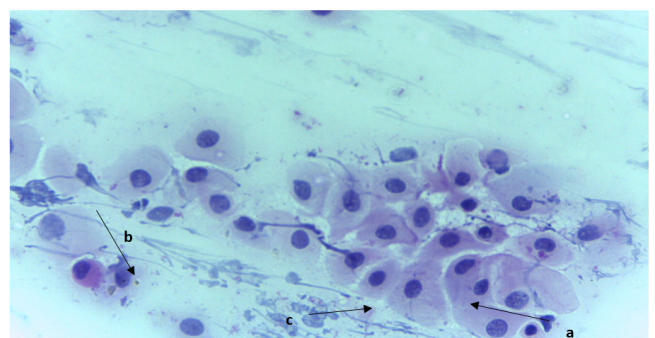


Fig. 3: x40 (Papanicolaou stain) cervical smear showing Low-grade Squamous Intraepithelial Lesion (LSIL), with nuclear being enlarged, coarse but evenly distributed chromatin pattern, hyperchromasia and irregular nuclear contour (a), there is an abundant delicate cytoplasm (b) with presence of koilocytes (c) (Pap Smear; Mag x 40)

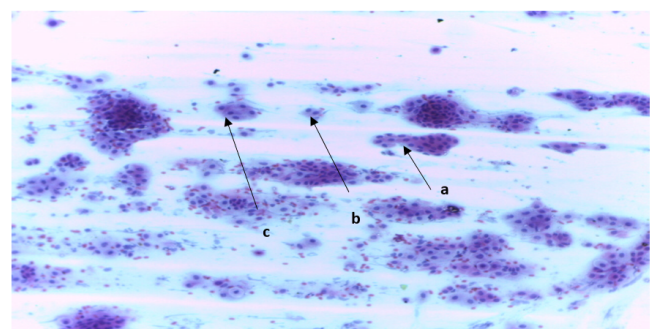


Fig. 4: x40 (Papanicolaou stain) High-grade Squamous Intraepithelial Lesion (HSIL). Cervical smear showing nuclear with hyperchromatic crowded group of cells without distinct cells border (a). very high nuclear cytoplasmic ratio (b & c)

DISCUSSION

Cervical lesions especially Cervical cancer is a leading cause of cancer-related mortality among women globally, with human papillomavirus (HPV) infection playing a pivotal role in its pathogenesis^[15, 17]. HIV-positive women are disproportionately affected due to immune suppression, which accelerates HPV persistence and progression to cervical lesions^[18]. The advent of Highly Active Antiretroviral Therapy (HAART) has significantly improved the prognosis of HIV infection; however, its role in mitigating cervical lesions remains an area of ongoing research^[19, 20].

The present study also observed that the majority of participants across all groups fall within the 41-50 years age group (39.6%). Among those on HAART, 44.2% are aged 41-50 years, followed by those aged 51-60 years (27.5%), suggesting that middle-aged women form the bulk of our population. These findings align with previous reports^[21] in Lagos, and in Benin City^[22], and recent research in Nigeria, which observed that the peak prevalence of HIV infection occurs among individuals aged 30-50 years^[23]. These studies reported a high prevalence of cervical lesions^[24-26] among middle-aged women. Similar observation was reported^[27], a higher prevalence of cervical lesion among women aged 40-49 years in Cameroon. In Abuja, Ononogbu^[28] observed the risk for cervical premalignant and cancer to be associated with age ≤ 40 years. Married participants make up to 60% of the population which emerged as a significant demographic factor, reflecting previous reports^[29, 30] which suggested that marital status influences health-seeking behavior. While widowed individuals are significantly represented at 25.1%, particularly in the HAART group (35.8%), this is consistent with studies that associate spousal loss with HIV-related mortality and increased risk of HIV acquisition among widowed women^[31].

Our data further showed that 83.4% of women who were aware of cervical cancer screening did not have cervical lesions, compared to 90.5% among those unaware of cervical cancer screening ($p = 0.396$). Although, this showed that awareness alone is not significantly associated with cervical lesion prevalence in this study, which is consistent with previous reports^[32, 33]. Interestingly, a comparison of the prevalence of cervical lesions among HIV-positive women and HIV-negative women, revealed a significantly higher prevalence among HIV-negative women (29.6%, $p = 0.001$). This contrasts with studies from Ethiopia and Kenya, where cervical lesion prevalence was higher in HIV-positive women^[34].

And so many other studies in Nigeria^[35-37]. The lower prevalence in this study may be due to HAART's protective effect in reducing HPV persistence and cervical lesion progression^[38] or disparities in cervical screening practices among HIV-negative populations^[39]. However, ongoing screening is necessary, as HIV remains a major risk factor for persistent HPV infection^[26, 40, 41]. Nonetheless, this study has some limitations, and the results should be interpreted with care. We conceived recruitment challenges. There was difficulty enrolling participants due to strict eligibility criteria, lack of interest, and limited access to the target population. We also speculate some reporting bias in the questionnaires administered to the participants. Furthermore, participants withdrawing from the study, leading to a reduced sample size.

CONCLUSION

The findings of this study provide valuable insights into the prevalence of cervical lesions among HIV-positive women, and associated risk factors on cervical health in the study area. While awareness and previous screening did not show significant protective effects, the persistence of cervical lesions underscores gaps in preventive practices. This study highlights the importance of strengthening cervical cancer screening programs, promoting adherence to HAART, and integrating HPV vaccination and lifestyle interventions to reduce the burden of cervical lesions among HIV-positive women.

DISCLOSURE

Acknowledgement: The protocol for this study was approved by the Jos University Teaching Hospital, Health Research Ethics Committee with reference number REF/JUTH/DCS/REC/127/XXXI/2664. Consent was obtained from the Harvard School of Public Health for both the identification and enrollment of HIV-infected women in JUTH APIN clinic and the use of secondary data and other relevant information in the study.

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Conflict of Interest: None.

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