



Tropical Journal of

**Obstetrics &
Gynaecology**

ISSN-Print: 0189-5117
Online: 2543-148X

Official Publication of Society of
Obstetrics & Gynaecology of Nigeria

■ Original Article

Pattern of Pre-Malignant Cervical Lesions among Women Attending HIV Clinic in a Tertiary Hospital in North East Nigeria

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ABSTRACT

Background: Almost all cervical cancers are preceded by premalignant lesions which may take up to 25 years to progress to invasive cancer. The prevalence of premalignant cervical lesions has been shown to be higher in HIV-Positive women than in HIV-Negative women, with more severe lesions being commoner in HIV-Positive women. This study offers the opportunity to assess the magnitude of the problem of premalignant cervical lesions among HIV-Positive women in FTH Gombe and to determine the types of lesions common among them. **Objective:** To determine the pattern of premalignant cervical lesions among HIV-Positive non-pregnant women at FTH Gombe.

Methodology: The study is a cross-sectional descriptive study conducted on HIV-positive women in FTH Gombe. Three hundred and sixty-three HIV-positive non-pregnant women were screened for premalignant cervical lesions using liquid-based cytology method and the results were analysed.

Results: Out of 363 patients screened, 21 specimens were inadequate for reporting and therefore excluded from analysis. Of the 342 results analysed, 57 had abnormal cytology, giving a prevalence of 16.67% for abnormal cytology. The predominant cytological abnormality was LSIL which accounted for 75.44% while atypical squamous cells (ASCUS/ASC-H) and HSIL made up 15.79% and 8.77% respectively. There was no invasive or glandular lesion. Three hundred and forty-one (99.71%) patients were on HAART, with a mean duration of 7.22 years. **Conclusion:** The prevalence of premalignant cervical lesions in this study was low, and high-grade lesions were uncommon. The high rate and prolonged use of HAART by the patients suggest its possible contribution to the low prevalence.

Keywords: Cervical cancer screening, premalignant cervical lesions, HIV-positive, Non-pregnant women.

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Introduction

Cervical cancer is the second most common cancer in women worldwide and the majority of these occur in developing countries.¹ Almost all cervical cancers are preceded by premalignant lesions which may take up to 25 years to progress to invasive cancer.² This prolonged stage of pre-cancer makes it possible to detect and treat before malignant transformation occurs. Therefore, identification of the premalignant stage through cervical cancer screening is the key to reducing the incidence and mortality of cervical cancer.

The human immunodeficiency virus (HIV) infection has been shown to be a risk factor for premalignant and malignant conditions of the cervix.³ The prevalence of premalignant cervical lesions is higher in HIV-Positive women than in HIV-Negative women, the incidence being about five times higher among the former.^{3,4} Factors that affect the incidence and prevalence of premalignant cervical lesions in HIV-positive women include CD4 lymphocyte count, HIV viral load, high-risk HPV (HR-HPV) and use of antiretroviral therapy (ART).^{3,5} Cellular immunity is impaired in HIV-infected patients due to depletion of CD4 lymphocytes.⁶ The impaired cell-mediated immunity due to HIV infection results in the body's inability to clear high-risk HPV (HR-HPV), thereby leading to persistence of the virus and eventual transformation to premalignant and, ultimately, malignant lesions.⁷ HIV infected women not on ART are twice more likely to have a precancerous lesion than those on ART.⁸ This is likely due to the effect of ART on the CD4 count. However, persistent HPV infection and premalignant changes have also been observed in the presence of normal CD4 count.⁹ This is supported by the findings of Strickler et al¹⁰ which suggest that apart from CD4 T lymphocytes, other immunologic factors such as a high regulatory T-cells (Tregs) and low plasmacytoid dendritic cells (pDC) are each associated with increased risk of oncogenic HPV infection and persistence among HIV-Positive women.

The Women's Interagency HIV Study (WIHS) found that although HIV-positive women were at

high risk for abnormal cytology, high-grade changes were uncommon.¹¹ Only 5.9% of seropositives in the above study ever developed high-grade lesions and the proportion of high-grade findings did not increase over time. Studies in France, Zambia, Cameroon and Nigeria have shown the prevalence of HSIL among HIV-Positive women to be 7.5%,¹² 32.6%,¹³ 3.3%¹⁴ and 3.3%.¹⁵

Gombe state has an estimated population of 3.3 million people and an HIV seroprevalence of 1.2%.¹⁶ The burden of premalignant cervical lesions among HIV-positive women in Gombe, who have a higher risk for the disease, is not known. The study offers the opportunity to assess the magnitude of the problem of premalignant cervical lesions among this group of patients and to know the need for screening and treatment programmes specific to their needs.

Methodology

This study was a cross-sectional study conducted at the Federal Teaching Hospital (FTH), Gombe, North-East Nigeria. The hospital provides comprehensive HIV care and support services, and has facilities for cervical cancer screening and treatment of premalignant lesions.

Three hundred and sixty-three (363) non-pregnant women were recruited, by convenient sampling, from the HIV clinic where information about the study was provided to them and written consent was obtained. Using a pretested questionnaire, the following information were obtained: age in years, parity, tribe, occupation, marital status, history of previous Pap smear, use of HAART, duration on HAART and cytology result.

Liquid-based cytology was used for the cytological evaluation and the specimens were taken by the lead investigator and trained research assistants. After consenting to the study, patients were advised to come for specimen collection when they were not menstruating and to avoid douching, intercourse and use of vaginal medications or tampons 48 hours prior to specimen collection. The patient, after counselling, was placed in dorsal position with the knees flexed and thighs abducted. A Grave's speculum was inserted into the vagina to

expose the cervix. The broom device (Cervex-Brush, Rovers Medical Devices, Netherlands.) was inserted with the tip entering the endocervical canal and the outer bristles pressed against the cervix, the broom was then rotated in one direction for five complete rotations. The broom end was then snapped off the handle and dropped into a plastic bottle containing a preservative solution (Liquid-PREPLGM International, Inc, Melbourne, FL, USA) and sent to the laboratory. Specimen preparation was done by an experienced laboratory scientist and the final analysis and review of slides were done by two histopathologists. The outcome measures were (1) the prevalence of premalignant lesions and (2) the proportion of different types of abnormal lesions.

Data were managed and analysed using SPSS version 24 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). Statistical significance was set at a p-value less than 0.05.

Results

Out of 363 patients screened for premalignant cervical lesions, 21 samples were inadequate for reporting and were excluded from analysis. The remaining 342 results were analysed and reported. The ages of the patients ranged from 22 to 80 years with a mean age of 39.54 ± 9.48 years. The mean ages of the patients without intraepithelial lesions (39.18 ± 9.21) and with intraepithelial lesions (41.33 ± 10.61) were not significantly different ($p=0.118$). The modal parity was one, and the multipara (para 2 - 4) made up the largest group with 37.13% (Table 1). Most of the women were from the Tangale ethnic group (38.01%), followed

by the Hausa/Fulanis with 21.64%. One hundred and fifty-six (45.61%) of the study participants were married, forming the largest group according to marital status and this was followed by the widowed (29.24%). More than half of the patients were Christians (56.43%) and the rest were Muslims. Over one-third (35.09%) of the patients were unemployed and almost 40% of the patients had a tertiary level of education (table 1).

Of the 342 results reported, 285 (83.33%) were negative for intraepithelial lesions while the remaining 57 had abnormal cytology. Therefore, the prevalence of abnormal cytology is 16.67%.

There was no association between the socio-demographic characteristics such as age with the presence of premalignant lesions (Table 2).

The abnormal lesions identified included atypical squamous cells of undetermined significance (ASCUS), atypical squamous cells-cannot exclude high-grade lesion (ASC-H), LSIL and HSIL. The proportions of the different cytological abnormalities are shown in table 3. There was no invasive or glandular lesion.

Only 16 (4.68%) of the patients have had a previous Pap smear out of which 15 were normal and 1 was abnormal. The only one with a previous abnormal result was among the five patients with HSIL in this study. All 15 patients who had an earlier normal cytology result remained normal. Only one (0.3%) out of the study participants was not yet on HAART. The mean duration of HAART use was 7.22 years. There was no statistically significant association between the duration on HAART and the severity of cervical lesions ($p=1.000$) (Table 4).

Table 1: Sociodemographic characteristics of HIV-Positive non-pregnant women at FTHG

Characteristics	Frequency No (%)
Age groups	
21-30	75(21.9)
31-40	133(38.9)
41-50	91(26.6)
>50	43(12.6)
Parity	
0	53(15.5)
1	64(18.7)
2-4	127(37.1)
≥5	98(28.7)
Educational level	
None	66(19.3)
Primary	62(18.1)
Secondary	81(23.7)
Tertiary	133(38.9)
Occupation	
Unemployed	120(35.1)
Unskilled	57(16.7)
Skilled	93(27.2)
Professional	72(21.1)
Marital status	
Single	47(13.7)
Married	156(45.6)
Separated/Divorced	39(11.4)
Widowed	100(29.2)
Ethnicity	
Tangale	130(38.0)
Hausa/Fulani	74(21.6)
Others	138(40.4)

Table 2: Association between the sociodemographic characteristics and presence of premalignant lesions

Characteristics	Premalignant Lesion		P-Value
	Positive	Negative	
Age			
21-30	11	64	0.197
31-40	19	114	
41-50	15	76	
>50	12	31	
Total	57	285	
Marital status			
Married	20	136	0.446
Single	10	37	
Divorced/Separated	7	32	
Widowed	20	80	
Total	57	285	
Educational Level			
No Formal Education	12	54	0.286
Primary	15	47	
Secondary	12	69	
Tertiary	18	115	
Total	57	285	

Table 3: Pattern of premalignant cervical lesions in the patients

Characteristics	Frequency	Percentage
ASCUS/ASC-H	9	15.79
LSIL	43	75.44
HSIL	5	8.77
Total	57	100

Table 4: Association between the duration on HAART and severity of premalignant lesions

Characteristics	Low-grade Lesions No. (%)	High-grade Lesions No. (%)	TOTAL	χ^2 *	P.Value
≥2 years	11 (91.7)	1 (8.3)	12	-0.248	1.000
>2 years	40 (90.9)	4 (9.1)	44		
TOTAL	51	5 (8.93)	56		

* Fischer's exact test

Discussion

The prevalence of premalignant cervical lesions in this study (16.7%) is higher than 12.6% reported among HIV-positive patients in Enugu, Southeast Nigeria.¹⁵ However, the prevalence is significantly lower than 29.0% reported by Agaba et al¹⁷ in Jos and 31.3% by Chama and colleagues³ in Maiduguri, both in Nigeria. The prevalence is also lower than 20.4% reported among gynaecological clinic attendees in the same facility (FTHG).¹⁸ The lower prevalence of premalignant cervical lesions in this study, compared to other studies which also used cytology for screening, could possibly be explained by the large proportion (99.7%) of the study participants who are on HAART. The effect of antiretroviral drugs on reducing viral load, increasing CD4 count and, by extension, regression of premalignant cervical lesions has been well documented.^{19,20} The study by Chama et al included newly diagnosed HIV-positive patients with low CD4 count while this study recruited patients already enrolled in the HIV clinic. Although CD4 count was not measured in the index study, the long duration on HAART (mean 7.2 years) may have had a positive impact on their immune status.

Only five patients in this study had high-grade lesions. This agrees with the findings of Massad et al²¹ that even though HIV-positive women have a higher risk of developing premalignant cervical lesions, high-grade lesions are not common. In contrast, Bateman et al²² found that almost half (45%) of HIV-positive women in their study had high-grade lesions or higher. The findings of 1.5% for HSIL and 12.6% for LSIL are lower than 2.4% and 16.8% respectively found by Manga et al¹⁸ in the same facility. Interestingly, while the earlier study by Manga et al found 3 cases (1.4%) of malignant changes, there was none in this study. The evidence from this study seems to suggest a higher prevalence of both low- and high-grade lesions in the general population when compared to HIV-positive women in Gombe. Sampling variations could have been responsible for these divergent findings in the same population and the observations may not be significant if tested statistically. The study by Chama et al³ in the same

geographical region involved both HIV- positive and HIV-negative women, and there were significantly more premalignant lesions among the HIV-positive group. Dim and colleagues¹⁵ also found a higher prevalence of both low and high-grade lesions in HIV seropositive patients compared to HIV-negative controls. However, the latter two studies were case control in design and as such have a higher strength of evidence. Further studies involving both HIV-positive and HIV-negative women are needed to validate these observations in Gombe.

The association between the duration on HAART and severity of premalignant lesions was not statistically significant. This is probably because a clear majority of the patients (85.8%) have been on HAART for greater than 2 years and only 5 (1.5%) had high-grade lesions. Well-designed studies are needed to ascertain possible cut-off duration at which, after adjusting for other factors, the use of HAART protects against the incidence of SILs. Since HIV-positive women have been established to have a higher predisposition to precancerous lesions and HAART use is associated with regression of lesions, the role of HAART as a primary or secondary preventive intervention for premalignant cervical lesions in HIV-positive women needs to be examined.

The low (4.7%) previous uptake of cervical cancer screening in this study is consistent with findings from other Nigerian studies.^{23,24} The commonest reason identified by Ezechi et al²⁴ for women's refusal to take a Pap smear is cost. This could partly explain why the acceptance of Pap smear is high in studies such as this, where the test is free of charge, but routine uptake remains abysmally low. The low utilisation of cervical cancer screening services could also be attributed to lack of awareness about the services. Awareness about cervical cancer and its prevention remains low in Nigeria.^{25,26} Of the 16 patients who had been screened previously, the 15 patients who had previous normal results remained normal on rescreening. The only patient with a prior abnormal result had HSIL in this study. However, the specific abnormality in the previous test was

not known, therefore, it was not possible to ascertain if the lesion has been persistent or a result of progression. This also brings to the fore, the need for treatment and/or follow-up in patients with premalignant lesions because while regression is common, persistence and progression of lesions are possible outcomes.

The limitations of the study include the non-inclusion of the patient's CD4 count which would reflect their immune status and the lack of control group for comparison.

Conclusion

The prevalence of premalignant cervical lesions in

HIV-positive women in FTH Gombe is low when compared to other Nigerian studies and is also lower than in the general population in Gombe. The pattern of premalignant lesions showed that high-grade lesions were not common among HIV-positive women in Gombe. The high rate and prolonged duration of HAART use by the patients suggest its possible contribution to the low prevalence. The proportion of the patients who had a previous Pap smear was very low. We recommend that cervical cancer screening be included at programmatic level for HIV positive women at the FTHG.

References

1. Denny L, Anorlu R. Cervical Cancer in Africa. *Cancer Epidemiol Biomarkers Prev.* 2012; 21 (9):14349.
2. Vink MA, Bogaards JA, Kemenade FJ Van, Melker HE De, Meijer CJLM, Berkhof J. Clinical Progression of High-Grade Cervical Intraepithelial Neoplasia?: Estimating the Time to Preclinical Cervical Cancer From Doubly Censored National Registry Data. *Am J Epidemiol.* 2013;178(7):11619.
3. Chama CM, Nggada H, Gashau W. Cervical dysplasia in HIV infected women in Maiduguri , Nigeria. *J Obstet Gynaecol* 253, 286-288., 2005; 25(3):2868.
4. Kafuruki L, Rambau PF, Massinde A, Masalu N. Prevalence and predictors of Cervical Intraepithelial Neoplasia among HIV infected women at Bugando Medical Centre, Mwanza-Tanzania. *Infect Agent Cancer.* 2013;8(1):54.
5. Singh DK, Anastos K, Hoover DR, Burk RD, Shi Q, Ngendahayo L, et al. Human Papillomavirus Infection and Cervical Cytology in HIV-Infected and HIV-Uninfected Rwandan Women. *J Infect Dis.* 2009;199:185161.
6. Louie KS, Sanjose S De, Mayaud P. Epidemiology and prevention of human papilloma virus and cervical cancer in sub-Saharan Africa? A comprehensive review. *Trop Med Int Heal.* 2009;14(10): 1287302.
7. Ezechi OC, Ostergren PO, Nwaokorie FO, Ujah IAO, Odberg Pettersson K. The burden, distribution and risk factors for cervical oncogenic human papilloma virus infection in HIV positive Nigerian women. *Virology.* 2014;11(1):5.
8. Memiah P, Mbuthia W, Kiiru G, Agbor S, Odhiambo F, Ojoo S, et al. Prevalence and risk factors associated with precancerous cervical cancer lesions among HIV-infected women in resource-limited settings. *AIDS Res Treat [Internet].* 2012;2012:Article-953743. Available from: <http://www.hindawi.com/journals/art/2012/953743/>
9. Bogaert L Van. The impact of human immunodeficiency virus infection on cervical preinvasive and invasive neoplasia in South Africa. *Ecancer medicalscience.* 2013;7:334.
10. Strickler. Howard D., Martinson J, Desai S, Xie X, Burk RD, Anastos K, et al. The Relation of Plasmacytoid Dendritic Cells (pDCs) and Regulatory T-Cells (Tregs) with HPV Persistence in HIV-Infected and HIV-Uninfected Women. *Viral Immunol.* 2014;27(1):205.
11. Cardillo M, Hagan R, Abadi J, Abadi MA. Intraepithelial Lesions in Women Infected with the Human Immunodeficiency Virus. *Cancer Cytopathol.* 2001;93(2):1114.
12. Six C, Heard I, Bergeron C, Orth G, Poveda J, Zagury P, et al. Comparative prevalence , incidence and short-term prognosis of cervical squamous intraepithelial lesions amongst HIV-positive and HIV-negative women. *AIDS.* 1998;12(9):104756.
13. Parham G, Sahasrabudhe, VV Mwanahamuntu M, Shepard B, Hicks M, Stringer E, Al. E. Prevalence and predictors of squamous intraepithelial lesions of the cervix in HIV-infected women in Lusaka,

- Zambia. *Gynecol Oncol*. 2006;103(3):10711022.
14. Atashili J, Miller WC, Smith JS, Ndumbe PM, Ikomey GM, Eron J, et al. Age trends in the prevalence of cervical squamous intraepithelial lesions among HIV-positive women in Cameroon: a cross-sectional study. *Biomedcentral Res Notes* [Internet]. 2012;5(1):590. Available from: BMC Research Notes
 15. Dim C, Ezegwui H, Ikeme A, Nwagha U, Onyedum C. Prevalence of cervical squamous intraepithelial lesions among HIV-positive women in Enugu, South-eastern Nigeria. *J Obstet Gynaecology*. 2011;31:25962.
 16. (NACA) NA for the C of A. REVISED NATIONAL HIV AND AIDS STRATEGIC FRAMEWORK 2019-2021: FUTURE DIRECTIONS FOR HIV/AIDS RESPONSE IN NIGERIA [Internet]. Abuja; 2019. Available from: <https://naca.gov.ng/wp-content/uploads/2019/03/NATIONAL-HIV-AND-AIDS-STRATEGIC-FRAMEWORK-1.pdf>
 17. Agaba PA, Thacher TD, Ekwempu CC, Idoko JA. Cervical dysplasia in Nigerian women infected with HIV. *Int J Gynecol Obstet*. 2009;107:99102.
 18. Manga M, Fowotade A, Abdullahi Y, El-Nafaty A, Adamu S, Bojude A, et al. Comparative Analysis of Cervical Human Papillomavirus DNA Testing and Cytological Findings among Women Presenting for "Pap" Smear in a Tertiary Health Centre in Northern Nigeria. *Int J Trop Dis Heal*. 2016;13(2):18.
 19. Denslow SA, Rositch AF, Firnhaber C, Ting J, Smith JS. Incidence and progression of cervical lesions in women with HIV?: a systematic global review. *Int J STD AIDS*. 2014;25(3):16377.
 20. Mbulaiteye SM, Bhatia K, Adebamowo C, Sasco AJ. HIV and cancer in Africa: Mutual collaboration between HIV and cancer programs may provide timely research and public health data. Vol. 6, *Infectious Agents and Cancer*. 2011. p. 16.
 21. Massad LS, Ahdieh L, Benning L, Minkoff H, Greenblatt RM, Watts H, et al. Evolution of cervical abnormalities among women with HIV-1: evidence from surveillance cytology in the women's interagency HIV study. *J Acquir Immune Defic Syndr*. 2001;27(5):43242.
 22. Bateman AC, Katundu K, Mwanahamuntu MH, Kapambwe S, Sahasrabudde V V, Hicks ML, et al. The burden of cervical pre-cancer and cancer in HIV positive women in Zambia: a modeling study. *BMC Cancer*. 2015;15:541.
 23. Ononogbu U, Almuftaba M, Modibbo F, Lawal I, Offiong R, Olaniyan O, et al. Cervical cancer risk factors among HIV-infected Nigerian women. *BMC Public Health*. 2013;13:582.
 24. Ezechi OC, Gab-Okafor C V, Ostergren PO, Odberg Pettersson K. Willingness and acceptability of cervical cancer screening among HIV positive Nigerian women. *BMC Public Health*. 2013;13:46.
 25. Hyacinth HI, Adekeye OA, Ibeh JN, Osoba T. Cervical Cancer and Pap Smear Awareness and Utilization of Pap Smear Test among Federal Civil Servants in North Central Nigeria. *PLoS One*. 2012;7(10):18.
 26. Ndikom CM, Ofi BA. Awareness, perception and factors affecting utilization of cervical cancer screening services among women in Ibadan, Nigeria: a qualitative study. *Reprod Health*. 2012;9:11.