www.jmscr.igmpublication.org Impact Factor (SJIF): 6.379

Index Copernicus Value: 71.58

ISSN (e)-2347-176x ISSN (p) 2455-0450

crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i6.28



# Abnormal Cervical Epithelial Cytology in HIV-Seropositive Women and Correlation with CD4 Counts and Viral Load in Uyo, Akwa Ibom State, Nigeria

#### Authors

#### Onwuka Chidi Okorie (MBBS, FMC Path, FWACP)<sup>1</sup>, Dr Ojeh Samuel Ohidueme (FWACS)<sup>2</sup> Adekunbiola A.F. Banjo (MBBS, FMC Path, MSc Clinical Cytology, FIAC)<sup>3</sup>

Department of Histopathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State Nigeria Department of Obstetrics and Gynecology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State Nigeria

Department of Anatomic and Molecular Pathology, Lagos University Teaching Hospital, Idi-Araba, Lagos Nigeria

Corresponding Author

#### Onwuka Chidi Okorie (MBBS, FMCPath, FWACP)

Department of Histopathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State Nigeria +234 (0) 8035473424, Email: *dronwuka@yahoo.com* 

#### Abstract

**Background:** In regions where HIV prevalence is high and HPV vaccine coverage is low, the interactions between HPV and HIV infections is expected to increase the incidence of cervical neoplastic lesions. This is the case in Uyo, Akwa Ibom State.

**Objective:** This case-control, cross-sectional study was carried out to determine the prevalence of cervical epithelial abnormalities in HIV-seropositive women in Uyo and correlating it with their CD4 count and HIV viral load.

**Methodology:** Two hundred and thirty one (231) consenting HIV positive women were recruited and screened for cervical cancer and its precursor lesions using conventional Pap smear between February 2013 and April 2014. Pap smears were classified according to the 2001 Bethesda classification. HIV testing was done by two rapid tests (Determine and Unigold), CD4 count was measured by flow cytometry, while the HIV viral load was determined by semi-automated conventional PCR within two weeks of Pap smear screening.

**Result:** The samples 226 HPW were suitable for statistical analysis. The study participants were aged between 18-60 years with a mean age of 35.63±8.44. Majority of the study participants were between the ages of 25 years and 36 years. The mean CD4 count and the mean HIV viral load were 311.08±299.1 cells/mm³ (range 6-1779) and 354449.51±1257979.9/microliter (range <400-9,623,070) respectively. The prevalence of abnormal cervical cytology was 10.6%. There is no significant correlation between the type of cytologic abnormality with the CD4 count and viral load, but HPW with a higher viral load had the lowest mean CD4 count and the worst cytologic abnormality. Women on longer duration of HAART treatment also had a higher mean CD4 count and better cytologic result. 10.9% of the HPW with a negative cytology report had inflammatory smears.

Conclusion: There is a positive association between HIV/AIDS and cervical neoplasia. When the Viral load was grouped into those below 400 vs 401-10,000 vs >10,000 and the CD4 count grouped into those below 200 vs 200-499 vs above 500, a significant correlation was observed between the immune status and cytological abnormality. However, without grouping the CD4 counts and HIV viral loads, there is no significant correlation. We recommend therefore that, cervical cancer screening should be included in the protocol for the routine care of women living with HIV/AIDS in this region regardless of their CD4 counts and HIV viral loads.

**Keywords:** Cervix, Cytology, HIV, CD4 count and Viral load.

#### Introduction

HIV and HPV co-infections pose a great challenge to the health of women in regions where HIV prevalence is high and HPV vaccine coverage is low. Akwa Ibom state, in South-South region of Nigeria has one of the highest prevalence rates of HIV infection among the states of the federation, with a prevalence of  $10.9\%^2$ , and there is no established HPV vaccination programme.

Cervical cancer, an AIDS defining condition, is the third most common cancer in women worldwide, with an age adjusted incidence rate of 28.5 per 100,000 women.<sup>3</sup> Worldwide, about 500,000 new cases of cervical cancer are recorded each year but more than 85% of all cervical cancer related deaths occur in developing countries, where it is the second most common cause of cancer related deaths in women and an important cause of cancer mortality in young women.<sup>4</sup>

HPV is the preeminent aetiological agent of cervical cancer while immunosuppression from HIV infection is a risk factor. <sup>5</sup>The natural history and behavior of HPV is adversely altered in HIV infection. <sup>5,6</sup>

HIV infection causes Acquired Immunodeficiency Syndrome (AIDS), a disease characterized by profound immunosuppression that leads to opportunistic infections, secondary neoplasms including cervical cancer, and neurological manifestations. HIV virus specifically depletes the CD4+ immune cells of the body. Higher HIV viral loads, measured as HIV RNA, are associated with lower CD4 counts. However, in patients treated with highly active antiretroviral therapy (HAART), clinical improvement is often greater than the decrease in plasma viraemia, making it generally accepted that HIV viral load as well as blood CD4+ T-cell count should be considered in monitoring the immune status of the patients.

There are over 100 subtypes of HPV in humans, of which about 23 infect the anogenital region.<sup>8</sup> Based on disease association, these anogenital subtypes are classified into high risk and low risk types.<sup>8</sup>Types 16 and 18 are the major high risk types and are mostly associated with invasive

carcinomas of the uterine cervix and its precursor lesions while types 6 and11 are the main low risk types and are mostly associated with genital warts. Studies have demonstrated an increased prevalence of cervical infection with high risk oncogenic HPV subtypes in females living with HIV/AIDS than in the general population. Immunosuppression from HIV infection increases the incidence and severity of HPV infection with more likelihood of persistence and progression from cervical dysplasia to invasive cancer 10-12.

HPV infects the basal cells of the cervix and the oncogenic potential of the major high risk HPV subtypes (16 and 18) is related to their E6 and E7 proteins which facilitate P53 degradation, displace Retinoblastoma protein (Rb) into the nucleus to stimulate DNA synthesis, and causes centromere instability and over expression of cyclin E and P16.<sup>7</sup>

Invasive cervical cancer is essentially preventable through organized screening programs because it develops from well-defined precursor lesions which can be detected through cervical cytology. <sup>13</sup> Unfortunately in most developing countries like Nigeria, only about 5% of the women have ever been screened in the past five years compared to 85% in developed countries. <sup>14</sup>

The use of Highly Active Anti-Retroviral therapy (HAART) in the management of patients living with HIV/AIDS is expected to improve life expectancy by decreasing the morbidity and mortality from opportunistic infections but has not been shown to slow down the progression from precursor lesion to invasive cancer of the cervix. 10,12 This is anticipated to increase the burden of cervical cancer in resource poor settings where access to Pap smear based screening programs and colposcopy is limited. 15 This situation strengthens the need to include regular screening for cervical cancer as part of the protocol for the management of women living with HIV/AIDS. This is important so that the benefits of anti-retroviral therapy will not be offset by an increased risk of cervical cancer.

To the best of our knowledge, no study has been done in this region of Nigeria with such a high record of HIV prevalence to determine the prevalence of abnormal cervical epithelial cytology in women living with HIV/AIDS. There is therefore a need to conduct such a study. This study also correlated the cytologic findings with the patient's immune status as measured by the CD4 count and/or HIV viral load.

#### **Materials and Methods**

This cross-sectional hospital based study was carried out between February, 2013 and April, 2014 in University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria.

A total of 231 consenting, ever-married, or sexually active adult females attending the HIV clinic and receiving HAART treatment were recruited. The targeted recruitment was based on age, family and social history. Exclusion criteria included Patients below 18 years, newly diagnosed patients who are yet to commence HAART, patients on oral contraceptives or immunosuppressive drugs, patients managed for cervical cancer or other forms of gynaecological malignancies, and pregnant women.

The study was approved by University of Uyo teaching hospital, Uyo institutional health ethical research committee and all consenting subjects signed a written informed consent. In line with the ethical statement of this study, individual results were communicated to the participants and appropriate counseling and referral was made were necessary. Those whose Pap test result showed a High grade lesion or worse were recalled for biopsy confirmation before referral. This was done in collaboration with Physicians in the HIV and Gynaecology clinics of the hospital. A questionnaire was applied to elicit information on every woman's background and relevant risk factors including socio-economic and marital status, menstrual and obstetric history and use of Oral contraceptive pills. All the women were screened for cervical cancer by conventional Papanicolaou (Pap) smear method while observing standard precautions and protocols. The 2001 Bethesda System (TBS) of reporting cervical and vaginal cytology was used as the basis for cytology classification.

The CD4 counts and viral load estimations were done in the PEPFAR laboratory.

The Blood for CD4 counts and HIV-1 RNA viral load determination was collected by a staff of the PEPFAR laboratory on the day of the Pap smear or within two weeks of the Pap smear while observing standard precaution and protocols. The CD4 counts were performed by the Flow cytometry method while the viral load estimation was done using semi-automated conventional PCR method.

The data and result collated were analyzed using Microsoft Excel 2007 and SPSS version 17 and the result presented as tables and charts. Statistical comparison was done using chi-square and Fischer exact with the level of significance set at P less or equal to 0.05. The findings of this study were compared with those of previous studies.

#### **Results**

The study participants were aged between 18-60 years with a mean age of 35.63±8.44 years. Table 1 summarizes the socio-demographic variables of the study participants.

The Pap smear result shows that out of the 231 HPW, 202 (89.3%) were negative for Squamous Intraepithelial Lesions (NILM) while the rest were sub-classified as ASCUS (6 cases, 2.7%), LGSIL (13cases, 5.6 %), HGSIL (5 cases, 2.2%). Five of the HPW (2.2%) had an inadequate smear due to scant cellularity and excessive mucus obscuring the squamous epithelial cells while 22 (10.9%) of the HPW with NILM had inflammatory smear (This represents 9.7% of the total HPW). There was no case of cervical cancer. This result makes the prevalence of cervical epithelial abnormality in this study to be 10.7% and shows that there is a significant relationship between HIV status and abnormal Pap test result (p < 0.05), [see table 3].

The age distribution of the Pap smear results in this study shows that the age groups with the worst abnormal cervical epithelial cytology according were age groups 25-31 and 39-45 years [see table 4]. The age specific prevalence rate was highest among women that are 46 years and above (16.7%) [see table 5].

Table 6 summarizes the relationship between the duration on HAART treatment (DOT), mean CD4 count and results of Pap test. The mean CD4 count in this study was 311.08±299.1cells/mm<sup>3</sup> (range 6-1779) while the mean duration of treatment was 39.40±38.7 months (range 1-140). The result show that the longer the duration on HAART treatment, the greater the level of mean CD4 count showing that there is an improvement in CD4 count with HAART treatment. Also, women with the longest duration of treatment also have the highest percentage of normal and abnormal cervical epithelial cytology. suggest that improved CD4 count in HPW on HAART may prevent establishment of new HPV associated cervical lesion but does not lead to the regression of established cervical lesions.

Table 7 summarizes the relationship between CD4 count and Pap smear results of the 65 women that had their HIV-1 viral load estimated. The mean HIV viral load in this study was 354,  $449.51\pm1,257,979.9$  microliter (Range <400 - 9,623,070). The result showed that women with viral load of less than 400 also have the highest mean CD4 counts.

Table 8 below summarises the distribution of Pap test result according to CD4 category in HPW. The result shows that there is no statistically significant relationship between the CD4 cell category and the type of Pap smear result seen in HPW (p value >0.05).

In this study, there was poor correlation between the duration on HAART, mean CD4 cell count and mean HIV-1 viral load in the HPW. While the CD4 cell count was improving with HAART, some women still have a high viral load despite the initiation of HAART. On bivariate correlation, the Viral Load does not show a significant negative correlation with the CD4 count (r = -0.034; p > 0.05).

**Table 1:** Socio-demographic and Clinical characteristics

Characteristics	HIV positive (n=226)
Age	Number (%)
18-24	14 (6.2)
25-31	61 (27.0)
32-38	62 (27.4)
39-45	53 (23.5)
≥46	36 (15.9)
Age at Menarche	
≤ 14	152 (67.3)
≥ 15	74 (32.7)
Age at first intercourse	
≤ 18	154 (68.1)
≥ 19	72 (31.9)
Life time No. Of sexual partners	
1_3	97 (42.9)
$\geq 4$	129 (57.1)
Parity	
0-2	157 (69.5)
3_5	51 (22.6)
$\geq 6$	18(8.0)
Oral contraceptive use	
yes	24 (10.6)
No	202 (89.4)
Alcohol use	
Yes	74 (32.7)
No	152 (67.3)
Smoking	
Yes	2 (0.9)
No	224 (99.1)

**Table 2:** Important socio-demographic factors of the HPW

	<u> </u>		
Characteristics	Total No	Mean ±SD	
Age	226	$35.63 \pm 8.44$	
CD4	226	$311.08 \pm 299.1$	
Viral load	65	$354449.51 \pm 1257979.9$	
DOT	226	$1.31 \pm 0.9$	

Key: CxCa is Cervical cancer, DOT is Duration on HAART treatment

**Table 3:** Distribution of Pap result

Pap Test Result	Number (%)	
NILM	202 (89.3)	
ASC-US	6 (2.7)	
LGSIL	13 (5.8)	
HGSIL	5 (2.2)	
SQCC	0 (0)	
TOTAL	226 (100)	

KEY:NILM (NEGATIVE FOR SQUAMOUS INTRAEPITHELIAL LESION/MALIGNANCY), ASCUS(ATYPICAL SQUAMOUS CELLS OF UNCERTAIN SIGNIFICANCE), LGSIL(LOW GRADE SUAMOUS INTRAEPITHELIAL LESION), HGSIL(HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION), SQCC(SQUAMOUS CELL CARCINOMA). HPW(HIV POSITIVE WOMEN), HNW (HIV NEGATIVE WOMEN). FIVE SMEARS OF HPW WERE INADEQUATE.

**Table 4:** Age distribution of Pap test result

	PAP Smear Result in Number and (%)					
AGE Group	NILM-I	NILM	ASCUS	LGSIL	HGSIL	SQCC
18 - 24	1 (4.5)	11 (6.1)	2 (33.3)	0 (0)	0 (0)	0 (0)
25 - 31	4 (18.2)	52 (28.9)	1 (16.7)	2 (15.4)	2 (40.0)	0 (0)
32 -38	2 (9.1)	51 (28.3)	1 (16.7)	6 (46.2)	1 (20.0)	0 (0)
39 - 45	8 (36.4)	39 (21.7)	0 (0)	1 (7.7)	2 (40.0)	0 (0)
≥46	7 (31.8)	27 (15.0)	2 (33.3)	4 (30.8)	0 (0)	0 (0)
Total	22 (100.0)	186 (100.)	6(100)	13 (100.0)	5 (100.0)	0 (0)

KEYS: NILM [NEGATIVE FOR SQUAMOUS INTRAEPITHELIAL LESION/MALIGNANCY], NILM-I [NILM WITH INFLAMMATORY SMEAR], LGSIL [LOW GRADE SQUAMOUS INTRAEPITHELIAL LESION], HGSIL [HIGH GRADE SUAMOUS INTRAEPITHELIAL LESION], SQCC [INVASIVE SUAMOUS CELL CERVICAL CANCER].

**Table 5:** Age specific prevalence rate

Age Gro	oup No. Screene	d No. Positiv	ve Age Specific Prevalence (%)
18-24	14	2	14.3
25-31	61	5	8.2
32-38	62	8	12.9
39-45	53	3	5.7
≥46	36	6	16.7
Total	226	24	

Table 6: Relationship between Duration on HAART treatment, Mean CD4 cell count and Pap test result

DOT	MEAN CD4	NILM-I	NILM	ASCUS	LGSIL	HGSIL	TOTAL
(MONTHS)	± SD	NO. (%)	NO. (%)	N0. (%)	NO.(%)	NO.(%)	NO.(%)
1-6	242.67±217.10	9 (4.0)	60(26.5)	3(1.35)	5(2.2)	1(0.4)	78(34.5)
7-12	268.88±193.18	3(1.3)	11(4.9)	0(0)	2(0.9)	0(0)	16(7.1)
13-18	236.44±219.68	1(0.4)	7(3.1)	0(0)	1(0.5)	0(0)	9(4.0)
≥19	$358.25\pm349.94$	9(4.0)	102(45.1)	3(1.35)	5(2.2)	4(1.8)	123(54.4)
TOTAL	307.35±298.68	22(9.7)	180(79.6)	6(2.7)	13(5.8)	5(2.2)	226(100)

KEY: DOT(DURATION ON HAART TREATMENT),NILM(NEGATIVE FOR SQUAMOUS INTRAEPITHELIAL LESION/MALIGNANCY),NILM-I(NILM WITH INFLAMMATORY SMEAR), ASCUS(ATYPICAL SQUAMOUS CELLS OF UNCERTAIN SIGNIFICANCE), LGSIL(LOW GRADE SUAMOUS INTRAEPITHELIAL LESION), HGSIL(HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION). FIVE SMEARS OF HPW WERE INADEQUATE.

Table 7: The relationship between Mean CD4 count, HIV Viral load and Pap test result in HPW

$\mathbf{VL}$	HPW	MEAN CD4 ± SD	NILM-I NO. (%)	NILM NO. (%)	ASCUS NO. (%)	LGSIL NO. (%)	HGSIL NO. (%)	TOTAL NO. (%)
< 400	27	301.89±260.1	2 (3.1)	21 (32.3)	0 (0)	2 (3.1)	2 (3.1)	27 (41.6)
401-10,000	7	138.29±90.1	0 (0)	7 (10.8)	0 (0)	0 (0)	0 (0)	7 (10.8)
>10,000	31	$78.71 \pm 74.6$	6 (9.2)	23 (35.4)	1 (1.5)	1 (1.5)	0 (0)	31 (47.6)
TOTAL	65	177.83±205.6	8 (12.3)	51 (78.5)	1 (1.5)	3 (4.6)	2 (3.1)	65 100)

KEY: VL(HIV-1 RNA VIRAL LOAD),NILM(NEGATIVE FOR SQUAMOUS INTRAEPITHELIAL LESION/MALIGNANCY),NILM-I(NILM WITH INFLAMMATORY SMEAR), ASCUS(ATYPICAL SQUAMOUS CELLS OF UNCERTAIN SIGNIFICANCE), LGSIL(LOW GRADE SUAMOUS INTRAEPITHELIAL LESION), HGSIL(HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION).

**Table 8:** The relationship between CD4 count category and Pap test result in HPW

PAP TEST	<200 NO.(%)	200- 500 NO. (%)	>500 NO. (%)	Total NO.(%)	Chi-square	P-value
NILM-I	13 (12.7)	7 (9.7)	2 (3.8)	22 (9.7)	10.77	0.08
NILM	80 (78.4)	55 (76.4)	45 (86.5)	180(79.6)		
ASCUS	1 (1.0)	4 (5.6)	1 (1.9)	6 (2.7)		
LGSIL	5 (5.0)	5 (6.9)	3 (5.8)	13 (5.8)		
HGSIL	3 (2.9)	1 (1.4)	1 (1.9)	5 (2.2)		
Total	102 (100)	72 (100)	52 (100)	226 (100)		

Table 9: Relationship between DOT, Mean CD4 and Mean VL.

DOT (MONTHS)	MEAN CD4 ±SD	MEAN VL ±SD	NO. OF HPW	WITH VL
1-6	245.47±217.1	1126.71±1922.7	7	
7–12	268.88±193.18	2,412,450.75±4,807,094.57	4	
13-18	246.40±209.49	208,701.00±182,679.55	3	
≥19	365.10±350.87	250,106.37±518,754.10	51	
TOTAL			65	

KEY: DOT [DURATION ON HAART], VL[VIRAL LOAD]

#### Discussion

The study participants were aged between 18 and 60 years with a mean age of 35.63±8.44. The mean age, age range, and other sociodermographic variables are similar to those noted in related studies. 16-22

The result of Pap smear cytology showed that 24 out of the 226 women had abnormal cervical epithelial cytology (prevalence of 10.6 %). The prevalence of cervical dysplasia in women living with HIV/AIDS varies with several studies in different environment ranging from 10.2%<sup>23</sup> to 34%.<sup>24</sup>Studies in the general population have reported lower prevalence, ranging from 4.8% to 14% <sup>17,25-27</sup>

Several interactions between HPV and HIV exist to explain why HIV-infected women have a higher prevalence of abnormal cervical epithelial cytology. These includes: reduced local cervical cellular mediated immunity from generalized

immunosuppression causing persistence of HPV infection, direct viral-viral interaction which may enhance transcription of HPV oncoproteins, and increased immune escape pathways.<sup>28</sup> The lower frequency of abnormal cervical cytology seen in the HIV population in this study may be because most of the participants have been on HAART treatment with improved CD4 count level as reflected by a higher mean CD4 counts with longer duration of treatment. This fact is supported by studies that have shown that HAART has a positive impact on the natural history of HPV-related diseases in HPW.<sup>29-31</sup> Treatment with HAART leads to reconstitution of the immune system leading to decreased incidence of HPV infections. Whatever the figure obtained, these studies have shown that women living with HIV/AIDS have a higher prevalence of abnormal cervical epithelial cytology and therefore buttresses the need to include regular cervical

cancer screening as part of the protocol for the management of HIV patients in this region.

The epithelial abnormality seen in this study includes ASCUS (6 cases, 2.65%), LGSIL (13 cases, 5.75%) and HGSIL (6 cases, 2.2%). No case of ICC or glandular cell abnormality was detected. About one-tenth of the patients had (9.7%).inflammatory smear Inflammatory conditions of the cervix are risk factors for both HIV infection and HPV associated cervical disease. Some HPW may care less about using safe sex practices because of their HIV status which may explain the higher prevalence of inflammatory smears observed in this and other studies. There is also the problem of lowered local cervical immunity that may also explain the persistence of cervical infections despite antibiotic treatment. HIV-induced inflammatory responses may interfere with a woman's ability to mount an effective immune response to HPV and other microbial infections.<sup>32</sup>

The mean CD4 count recorded in the HPW in this study was 311.08±299.10 cells/mm<sup>3</sup> (range 6-1779) while the mean duration on HAART treatment was 39.40±38.7 months (range 1-140). The high mean CD4 count in this study may be attributable to the long duration of treatment for most of the patients used in this study and is higher than the median CD4 counts reported in earlier studies. There is a positive correlation between the duration of HAART use and CD4 count level as observed in this study (see table 9). HAART helps in reconstituting the immune system which reflects in buildup of CD4 cell count.

The report of this study shows that there is no statistically significant relationship between the CD4 count category and the type of Pap smear result reported in the HPW (P>0.05). HPW with CD4 count <200 had the highest frequency of NILM, LGSIL, HGSIL and inflammatory smears (see table 8). HPW with high CD4 count also have abnormal Pap test result. Despite the lack of statistically significant relationship between CD4 count category and the distribution of Pap test

result in HPW, this finding shows that women with CD4 count <200 have the worst cytologic abnormality. This is supported by similar reports by Chama et al<sup>16</sup>, Agaba et al<sup>18</sup>, and Davis et al<sup>33</sup>. Other researchers have reported no relationship between CD4 count and CIN but that nadir CD4 is associated with CIN recurrence. 30,34 Another study has reported that the use of HAART improves CD4 count and leads to the clearance of HPV but not to regression in neoplasia. 35 This study concluded that HAART helps in the reconstitution of the immune system with decrease in opportunistic infection but does not halt the progression of CIN in HPW making it necessary that this group of women be monitored with regular routine Pap smear. The study by Firnhaber et al in South Africa using 601 HPW on HAART who were followed over a five year period reported that HAART use was associated with a robust reduction in the rate of incidence and progression of cervical lesions.<sup>36</sup>The higher mean CD4 count associated with the longer duration on HAART treatment may explain the lower frequency of cervical lesions observed in HPW in this study.

The mean HIV-1 RNA viral load recorded was  $354,449.51\pm1,257979.9$  copies/ml (range <400-9,623,070) while the mean CD4 count recorded was 311.08±299.10 cells/mm<sup>3</sup> (range 6-1779). HIV-1 RNA viral load values of 400 copies/ml and below were regarded undetectable as 400 is the limit of detection for the assay method used. This study shows that the correlation between CD4 count and viral load is not perfect (table 8 and 9). These supports earlier findings that CD4 does not always correlate with HIV load making it necessary for patients living with HIV/AIDS to be monitored using CD4 count and viral load.7 Apart from viral replication, other factors may contribute to the fall in CD4 positive cells in HIV infection<sup>7</sup>.

Despite the absence of general significant correlation between the type of cytologic abnormality with the CD4 count and viral load, when the Viral load was grouped into those below

400 vs 401-10,000 vs >10,000 and the CD4 count grouped into those below 200 vs 200-499 vs above 500, a significant correlation was observed. This indicates a positive association between HIV/AIDS and cervical neoplasia. This agrees with the study that has reported the regression of CIN with improvement in CD4 count in HPW on HAART.<sup>30</sup> Interestingly in this present study, no case of cervical cancer was reported in the HIV patient. It follows that apart from HIV; other factors are important in the progression from squamous intraepithelial lesion to cervical cancer and supports the recommendation that every woman should have a regular Pap smear screening regardless of HIV status. The frequency of the Pap smear test is determined by age and the presence of other risk factors.<sup>37</sup>

The pathogenesis of cervical cancer is multifactorial with several studies showing that young age at first intercourse, multiple sexual partners, high parity, cigarette smoking, race, and low socio-economic status are important risk factors. In this study, factors noted to be associated with cervical neoplasia in HIV patients include CD4 count below 200 and high HIV Viral load. This agrees with the findings in most of the studies cited above. 16,18,33

The following conclusions can be made from this study in Uyo: There is a positive correlation between CD4 count and duration of HAART treatment with the abnormal cervical smear. HPW with longer duration on HAART had a higher mean CD4 count and better cytologic result. HPW with CD4 cell count of <200 had the worst cytologic result. These findings show that immunosuppression is a risk factor in the pathogenesis of cervical cancer. Also, there was a poor correlation between HIV viral load and the CD4 count. HIV viral load does not appear to be an independent risk factor for abnormal cervical smear in HIV-infected women in this study.

We recommend that all HPW should have a regular Gynaecologic examination including cervical cancer screening in line with the WHO guideline.

#### References

- 1. CDC. 1993 Revised Classification System for HIV Infection and expanded Surveillance case definition for AIDS among adolescents and adults. MMWR [Online] 1992; 41 [No. RR-17].[Accessed 19<sup>th</sup> September 2012].
- Federal Republic of Nigeria, Global AIDS response progress report 2012. [Online]. Available from:www.unaids.org/es/dataanalysis/moni toringcountryprogress/progress reports/2012 countries/file,68516. [Accessed 19th September 2012].
- 3. IARC. Globocan. Human papillomavirus and cervical cancer summary report. 2007; 5-8.
- 4. Harshad S, Khunying K, Marya P, Elaine C, Amy K, Enriquito L et al. Cervical cancer screening using VIA: operational experiences from Ghana and Thailand. Reprod. Health Mat. 2008; 16(32): 67-77. Doi: 10.1016/S0968-8080(08)32401-X.
- 5. Strickler HD, Burk RD, Fazzani M, Nastos K, Minkoff H, Massad LS. Natural History and possible reactivation of HPV in Human Immunodeficiency Virus- positive women. J Natl Cancer Inst 2005, 97: 577-586.
- 6. Parkin DM, Bray F: chapter 2: The burden of HPV related cancers. Vaccine 2006, 24(3): S11-25.
- 7. Abbas AK. Chapter 6: Diseases of Immunity. In: Kumar V, Abbas A, Faustus N, Aster JC (eds). Robbins and Cotran Pathologic Basis of Disease. 8<sup>th</sup> Edition. philadelphia: Elsevier B.V.2010; pp. 245-258.
- 8. Bonnez W, Reichman RC. Chapter 144: Papillomaviruses. In: Gerald LM, John EB, Rapheal D (eds). Mandell, Douglas and Bennett's Principles and Practice of Infectious disease. 7<sup>th</sup> Edition. Philadelphia: Churchill Livingstone; 2010. p1123-1124.

- 9. Nweke IG, Banjo AAF, Abdulkareem FB, and Nwadike VU. Prevalence of Human Papilloma Virus DNA in HIV Positive Women in Lagos University Teaching Hospital (LUTH) Lagos, Nigeria. Br Microb Res J [Online] 2013; 3(3): 400-413. Available from: www.sciencedomain.org [accessed 6<sup>th</sup> July, 2014].
- 10. Moodley JR, Constant D, Hoffman M, Salimo A, Allan B, Rybicki E et al. Human papillomavirus prevalence, viral load and pre-cancerous lesions of the cervix in women initiating highly active antiretroviral therapy in South Africa: a cross-sectional study. BMC Cancer. 2009;9: 275.
- 11. Adjorlolo-Johnson G, Unger E R, Boni-Ouattara E, Touré-Coulibaly K, Maurice C, Vermon SD et al. Assessing the relationship between HIV infection and cervical cancer in Côte d'Ivoire: A case-control study. BMC Infectious Diseases. 2010;10: 242.
- 12. Mogtomo MLK, Malieugoue LCG, Djiepgang C, Wankam M, Moune A, and Ngane AN. Incidence of cervical disease associated to HPV in human immunodeficiency infected women under highly active antiretroviral therapy. Infect agents and cancer. 2009; 4(1): 9.
- 13. WHO Cervical Cancer Summary report update, September 15:2010.
- 14. Duraisamy K, Jaganathan KS, and Bose JC. Methods of detecting cervical cancer. Adv Biol Res 2011; 5(4):226-232.
- 15. Schiffman M, Castle P, Jeronimo J, Rodriguez A, and Wacholder S. Human Papillomavirus and Cervical cancer. Lancet 2007; 370: 890-907.
- Chama CM, Nggada H, and Gashau W.
   Cervical dysplasia in HIV infected women in Maiduguri, Nigeria. J Obstet Gynaecol.2005; 25(3): 286-288.
- 17. Omole-Ohonsi A. Risk factors for cervical Dysplasia in Amino Kano Teaching

- Hospital. Ibom Medical Journal. 2013; 6(1): 29-36.
- 18. Agaba PA, Thacher TD, Ekwempu CC, and Idoko JA. Cervical dysplasia in Nigerian women infected with HIV. Int J Gynaecol Obstet. 2009; 107(2): 99-102.
- 19. Swende TZ, Ngwan SD, Swende LT. Prevalence and risk factors for cervical squamous intraepithelial lesions among women infected with HIV-1 in Markurdi, Nigeria. International Journal of women's Health 2012;4:55-60.
- 20. Anorlu RI, Igwilo CI, Akanmu AS, Banjo AAF, Odunukwe NN, Okanny CC et al. Prevalence of abnormal cervical smears among patients with HIV in Lagos, Nigeria. West Afr J Med. 2007; 26(2): 143-147.
- 21. Meniah P, Mbuthia W, Kiiru G, Agbor S, Odhiambo F, Ojoo S et al. Prevalence and Risk factors associated with precancerous cervical lesions among HIV-infected women in resource-limited settings. AIDS Res Treat [Online]. 2012; 2012: 7 pages. Available from: http://dx.doi.org/10.1155/2012/953743. [accessed 10th January, 2014].
- 22. Teixeira NCP, Araujo ACL, Correa CM, Lodi CTC, Lima MIM, Carvalho NO et al. Prevalence and risk factors for cervical intraepithelial neoplasia among HIV-infected women. Braz J Infect Dis 2012; 16(2):164-169. Available at http://dx:doi.org/10.1016/S1413-8670(12)70299-4. [accessed 20/3/13]
- 23. Sadan O, Schejter E, Ginath S, Bachar R, Boaz M, Menczer J et al. Premalignant lesions of the uterine cervix in enlarge cohort of Isreali Jewish women. Arch Gynaecol Obstet. 2004; 269 (3): 188-191. Available at: Doi:10.1007/s00404-002-0371-y. [accessed 5/5/14]
- 24. Omar T, Scwartz S, Hanrahan C, Modisenyane T, Tshabangu N, Golub J et al. Progression and regression of premalignant cervical lesions in HIV-

- Infected women from Soweto: a prospective Cohort. AIDS. 2011; 25(1): 87-94. Available at: Doi:10.1097/QAD.obo13e32834ofd99. [accessed 5/5/14].
- 25. Oguntayo OA and Samaila MOA.
  Prevalence of cervical intraepithelial neoplasia in Zaria. Ann Afr Med. 2010; 9
  (3): 194-195. Doi:10.4103/1596-3519.68351.
- 26. Swende TZ, Jogo AA and Ageda BR. Prevalence of cervical intraepithelial neoplasia among seronegative women in Markurdi, Nigeria. Trop J Obstet Gynaecol 2010; 27(suppl 1) S19.
- 27. Ahmed S, Avidimine S, Abu T, Oguntayo A and Sabitu K. Cervical dysplastic changes in women of reproductive age in Zaria, Northern Nigeria. Trop J Obstet Gynaecol 2010; 27(suppl 1): S19.
- 28. Schiffman M, Castle P, Jeronimo J, Rodriquez A, Wacholder S. Human Papillomavirus and cervical cancer. Lancet 2007;370:890-907.
- 29. Minkoff H, Zhong Y, Burk R, Palefsky J, Xue X, Watts D et al. Influence of adherent and effective antiretroviral therapy use on human papillomavirus infection and squamous intraepithelial lesions in human immunodeficiency virus-positive women. Obstet Gynecol 2010; 201(5): 681-90.
- 30. Adler H, Kakinami L, Modisenyane T, Tshbangu N, Mohapi L, DeBruyn G et al. Increased regression and decreased Incidence of human papillomavirus-related cervical lesions among HIV-infected women on HAART. AIDS 2012; 26(13): 1645-52.
- 31. Heard I, Tassie JM, Kazatchkine MD and Orth G. Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV seropositive women. AIDS. 2002; 16(13): 1799-1802.

- 32. De Vuyst H, Lillo F, Broutet N, Smith JS. HIV, HPV, and Cervical Neoplasia and Cancer in the era of HAART. Eur J Cancer Prev 2008; 17: 545-554.
- 33. Davis AT, Chakraborty H, Flowers L, Mosunjac MB. Cervical dysplasia in the women infected with Human Immunodeficiency Virus (HIV): A correlation with HIV viral load and CD4 count. Gynaecol Oncol 2001; 80 (3):350-354. Available at http:// dx.doi.org/10.1006/gyno.2000.6104.
- 34. Lehtovirta P, Paavonen J, Heikinheimo O. Risk factors, Diagnosis and prognosis of cervical intraepithelial neoplasia among HIV-infected women. Int J STD AIDS. 2008; 19(1):37-41.
- 35. Paramsothy P, Jamieson D, Heilig C, Schuman P, Klein R, Shah K et al. The effect of HAART on HPV clearance and cervical cytology. Obstet Gynecol 2009; 113(1): 26-31.
- 36. Firnbaher C, Westreich D, Schulze D, Williams S, Siminya M, Michelow P et al. Highly active antiretroviral therapy and cervical dysplasia in HIV-positive women in South Africa. JIAS [Online] 2012; 15: 17383. Available from: http://dx.doi.org/10.7448/IAS.15.2.17382. [accessed 12/3/14].
- 37. American Cancer Society. Guidelines for the Prevention and Early Detection of Cervical Cancer. published online March 14, 2012 in *CA:A Cancer Journal for Clinicians*.
- 38. Castellsague X, Munoz N. Cofactors in HPV carcinogenesis of parity, oral contraceptive, and tobacco smoking. J Natl Cancer Inst Monogra 2003: 20-28.