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## Prevalence of Cervical Intraepithelial Lesion in Relation to HIV Status in Uyo Akwa Ibom State, Nigeria

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### **Abstract:**

*Aim: The interaction between HPV and HIV infections is important in the development of cervical cancer especially where HIV prevalence is high and HPV vaccine coverage is low. This study was carried out to determine the prevalence of cervical intraepithelial lesions in relation to HIV status among women in Uyo, Akwa Ibom State.*

*Methodology: A total of 235 HIV negative women (HNW) and 231 HIV positive women (HPW) between the ages of 18-60 years were recruited and screened using conventional Pap smear in the cytology clinic of University of Uyo Teaching Hospital. The results were classified according to the 2001 Bethesda System of classification.*

*Result: Majority of the study participants were between the ages of 25 years and 36 years. 95.1% of the HNW and 89.3% of the HPW were negative for Squamous Intraepithelial Lesions (SILs). The prevalence of abnormal cervical cytology was more than two times higher in the cases than in the controls (10.6% vs 4.9%,  $p < 0.05$ ). The frequency for all categories of SILs was higher in the HPW.*

*Conclusion: This result supports the inclusion of cervical cancer screening in the routine care of women living with HIV/AIDS in this region.*

**Keywords:** Squamous intraepithelial lesion, Cervix, Prevalence.

### **1. Introduction**

In regions of the world where women do not have access to regular gynaecological care and screening, cervical cancer is the second most common cause of cancer related deaths.<sup>1</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 like Nigeria, where it is an important cause of cancer mortality in young women.<sup>2</sup>

HPV is the preeminent aetiological agent of cervical cancer while immunosuppression from HIV infection is a risk factor.<sup>3</sup> The natural history and behaviour of HPV is adversely altered in HIV infection.<sup>3,4</sup> The other risk factors for the development of cervical cancer include multiple sexual partners, early onset of sexual activity, other sexually transmitted diseases (including, *Herpes simplex Virus*, *Chlamydia trachomatis* etc.), early age at first pregnancy, high parity, low socioeconomic class, cigarette smoking, immunosuppression from any other cause, vitamin deficiency, and oral contraceptives use.<sup>5</sup>

In humans, there are over 100 subtypes of Human Papilloma viruses, of which 23 infect the anogenital region.<sup>6</sup> The anogenital subtypes are classified into high risk and low risk types based on their disease association.<sup>6</sup> Types 16 and 18 and the less commonly types 31,45,33,35,39,51,52,56,58,59,66,68 and 70 are termed the high risk types because they have oncogenic potential and are mostly associated with invasive carcinomas of the uterine cervix and its precursor lesions while types 6 and 11 and less commonly types 42,43, and 44 are the low risk types as they are mostly associated with genital warts.<sup>6</sup> Several 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.<sup>7-10</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>11</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>12,13</sup>

Because of the high prevalence of HIV infection in this region,<sup>14</sup> and the positive association between HIV and high risk anogenital HPV infections in the pathogenesis of cervical cancer,<sup>7-10</sup> it is important to determine the prevalence of squamous intraepithelial lesion in this region as a public health measure, considering the importance of early detection and treatment in the prevention of cervical cancer. Review of literature shows that no such study has been done in Uyo. There is therefore a need to conduct such a study. This study aims to determine the prevalence of abnormal cervical epithelial cytology in HIV-positive and HIV-negative women in Uyo.

## 2. Materials and Methods

In this cross-sectional comparative hospital based case-control study, a total of 466 consenting women were recruited and comprises 231 HPW as case-participants and 235 HNW as control-participants. The cases included ever-married or sexually active adult females attending the HIV clinic and receiving HAART treatment while the control subjects included ever-married or sexually active adult females from the general population attending the Gynaecology, General Out-Patient, and Family planning clinics of University of Uyo Teaching Hospital. In both groups of patients, the women were recruited by Doctor-Patient interaction using simple random sampling and the targeted recruitment was based on age, family and social history. Patients who refuse to give consent, patients bleeding per vaginum, patients on oral contraceptives or immunosuppressive drugs, patients being managed for cervical cancer or other forms of gynaecological malignancies, and pregnant women were excluded from the study.

The study was approved by University of Uyo teaching hospital, Uyo institutional health ethical research committee. All consenting subjects signed a written informed consent. 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) while observing standard precautions and protocols. Using the spatula, a smear was made on two pre-labeled frosted clean grease free slides in a thin layer of cells. The smeared slides were immersed promptly in 95% ethyl alcohol fixative contained in a coupling jar and transported to the histopathology laboratory of the hospital where the slides were stained with conventional Pap stain using standard protocols. The 2001 Bethesda System (TBS) of reporting cervical and vaginal cytology was used as the basis for cytology classification. In line with the ethical statement of this study, individual results were communicated to the participants and appropriate counseling and referral was made where necessary.

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 between the two groups 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.

## 3. Results

A total of 466 women were recruited and screened for cervical cancer using conventional Pap smear cytology but only 449 participants comprising 226 HIV-positive women(HPW) and 223 HIV-negative(HNW) were used for statistical analysis. The results for seventeen women comprising five HPW and twelve HNW were excluded due to inadequate Pap smear and incomplete data respectively.

Table 1 summarizes the socio-demographic characteristics of the women in this study. The study participants were aged between 18-60 years with a mean age of  $35.24 \pm 9.26$  years and  $35.63 \pm 8.44$  years in the control- and case- participants respectively. Majority of the study participants were aged between 25-38 years. More than half of the HNW were married (64.1%) and had a secondary or tertiary level of education (75.6%). Only about one-third of the HPW were married (36.7%) but most of them also had a secondary or tertiary level of education (76.1%).

Most of the women in this study attained menarche at or below 14 years (72.6% of the controls and 67.3% of the cases) and also had their sexual debut at or below 18 years (55.2% of the controls and 68.1% of the cases) but most of the HPW (57.1%) have four and above lifetime number of sexual partners unlike the HNW (39.2%).

The range of parity of the women in the control group was 0-9 with a mean of  $2.28 \pm 2.3$  while those of the HIV-positive group were 0-11 and  $2.0 \pm 2.25$  respectively. This shows that majority of the participants have a parity between 0 and 2 (57.8% of controls and 69.5% of cases). Only about one-tenth of the participants in both groups had ever used combined oral contraceptive pills while about one-third of them occasionally take alcohol. Most of the study participants are non-smokers (99.6% of HNW and 99.1% of HPW).

Characteristics	HIV negative (n=223)	HIV positive (n=226)
<b>Age</b>	Number (%)	Number (%)
18-24	15 (6.7)	14 (6.2)
25-31	61 (27.4)	61 (27.0)
32-38	64 (28.7)	62 (27.4)
39-45	49(22.0)	53 (23.5)
≥ 46	34 (15.2)	36 (15.9)
<b>Age at Menarche</b>		
≤ 14	162 (72.6)	152 (67.3)
≥ 15	61(27.4)	74 (32.7)
<b>Age at first intercourse</b>		
≤ 18	123(55.2)	154 (68.1)
≥ 19	100 (44.8)	72 (31.9)
<b>Life time No. Of sexual partners</b>		
1_3	136 (61.0)	97 (42.9)
≥ 4	87 (39.0)	129 (57.1)
<b>Parity</b>		
0-2	129 (57.8)	157 (69.5)
3_5	73 (32.7)	51 (22.6)
≥ 6	21 (9.4)	18(8.0)
<b>Oral contraceptive use</b>		
yes	29 (13.0)	24 (10.6)
No	194 (87.0)	202 (89.4)
<b>Alcohol use</b>		
Yes	96 (43.0)	74 (32.7)
No	127 (57.0)	152 (67.3)
<b>Smoking</b>		
Yes	1 (0.4)	2 (0.9)
No	222 (99.6)	224 (99.1)

Table 1: Socio-demographic and Clinical characteristics

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 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 in the case-participants. Among the HNHW, 212 participants (95.1%) were negative for Squamous Intraepithelial Lesion/Malignancy (NILM) while the rest were classified as ASCUS (4 cases, 1.8%), LGSIL (3 cases, 1.35%), HGSIL (3 cases, 1.35%), and Squamous cell carcinoma (1 case, 0.4%). Twelve (5.7%) of the HNHW with a negative report had inflammatory smear (This represents 5.4% of the total HNHW). This result makes the prevalence of cervical epithelial cell abnormality in this study to be 4.9% in the control-participants and 10.7% in the case-participants and shows that there is a significant relationship between HIV status and abnormal Pap test result ( $p < 0.05$ ), [see table 2].

Pap Test Result	HIV STATUS		chi-square	p value
	HNW No. (%)	HPW No. (%)		
<b>NILM</b>	212 (95.1)	202 (89.3)	12.12	0.03
<b>ASC-US</b>	4 (1.8)	6 (2.7)		
<b>LGSIL</b>	3 (1.3)	13 (5.8)		
<b>HGSIL</b>	3 (1.3)	5 (2.2)		
<b>SQCC</b>	1 (0.4)	0 (0)		
<b>TOTAL</b>	<b>223 (100)</b>	<b>226 (100)</b>		

Table 2: Distribution of Pap result according to HIV status

Key: NILM(Negative for Squamous Intraepithelial Lesion/Malignancy), ASCUS (Atypical Squamous Cells of Uncertain Significance), LGSIL (Low Grade Squamous Intraepithelial Lesion), HGSIL (High Grade Squamous Intraepithelial Lesion), SQCC (Squamous Cell Carcinoma). HPW (HIV Positive Women), HNHW (HIV Negative Women). Five Smears of HPW Were Inadequate.

The age distribution of the Pap smear results in this study shows that the age groups with the worst abnormal cervical epithelial cytology according to HIV status were age groups 25-31 and 39 – 45 years in the cases and 32 – 38 years in the control-participants

[see table 3]. The age specific prevalence rate was highest among women that are 46 years and above in both the control- and case-participants (14.7% and 16.7% respectively) [see table 4].

HIV Status	AGE Group	PAP Smear Result in Number and (%)					
		NILM-I	NILM	ASCUS	LGSIL	HGSIL	SQCC
HNW	18 - 24	0 (0)	15 (7.5)	0 (0)	0 (0)	0 (0)	0 (0)
	25 - 31	3 (25.0)	55 (27.5)	0 (0)	2 (66.7)	1 (33.3)	0(0)
	32 - 38	3 (25.0)	59 (29.5)	1 (25.0)	0 (0)	0 (0)	1 (100)
	39 - 45	5 (41.7)	43 (21.5)	0 (0)	0 (0)	1 (33.3)	0 (0)
	≥46	1 (8.3)	28 (14.0)	3 (75.0)	1 (33.3)	1 (33.3)	0 (0)
	<b>Total</b>	<b>12 (100)</b>	<b>200 (100)</b>	<b>4 (100)</b>	<b>3 (100)</b>	<b>3(100)</b>	<b>1 (100)</b>
HPW	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)
	<b>Total</b>	<b>22 (100.0)</b>	<b>186 (100.)</b>	<b>6(100)</b>	<b>13 (100.0)</b>	<b>5 (100.0)</b>	<b>0 (0)</b>

Table 3: Age distribution of Pap test result according to HIV status

Keys: HNW [HIV Negative Women], HPW [HIV Positive Women], 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].

The age specific prevalence rate was highest among women that are 46 years and above in both the control- and case- participants (14.7% and 16.7% respectively) [see table 4].

	Age Group	No. Screened	No. Positive	Age Specific Prevalence (%)
HNW	18-24	15	0	0
	25-31	61	3	4.9
	32-38	64	2	3.1
	39-45	49	1	2
	≥46	34	5	14.7
	<b>Total</b>	<b>223</b>	<b>11</b>	
HPW	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
	<b>Total</b>	<b>226</b>	<b>24</b>	

Table 4: Age specific prevalence rate according to HIV status

#### 4. Discussion

In this hospital based, age-matched, cross-sectional case-control study, the study participants were aged between 18 and 60 years with a mean age of 35.24±9.26 and 35.63±8.44 in the control- and case-participants respectively. The mean age and age range seen in this study was similar to those noted in related studies.<sup>15,16</sup>

In both groups of study participants, majority of the women had their menarche before the age of 14 years (72.6% of the controls and 67.3% of the cases) but more women in the HIV-positive group had sexual debut before the age of 18 years (68.1% vs 55.2%) and four or more numbers of life time sexual partners (57.1% vs 39.0%). This is important because early age at sexual debut and multiple sexual partners are risk factors for cervical neoplasia.<sup>5</sup> This finding is similar to that reported by Chama et al where the population studied were generally promiscuous with more than 90% of them having multiple sexual partners.<sup>17</sup>

The result of the Pap smear cytology in this study showed that 24 out of the 226 HIV-positive women (HPW) and 11 out of the 223 HIV-negative women(HNW) had abnormal cervical epithelial cytology. The prevalence of abnormal cervical epithelial cytology is therefore about two times higher in HPW compared to the HNW (%10.6 Vs 4.9%; P<0.05; OR 2.3, 95% CI 0.9-5.5). The prevalence of cervical dysplasia in women living with HIV/AIDS varies with several studies in different environment ranging from 10.2%<sup>18</sup> to 34%.<sup>19</sup> Studies in the general population have reported a lower prevalence, ranging from 0.98% in a Jewish population<sup>18</sup> to between 4.8% and 14% in northern regions of Nigeria.<sup>20-22</sup>

The higher prevalence of abnormal cervical epithelial cytology in HPW reported in this study agrees with the reports from many studies done in Nigeria<sup>16,17</sup> and other sub-Saharan African countries.<sup>9,10,23,24</sup> However, the level of prevalence obtained in this study is lower than that seen in most of these studies cited. Geographical differences in the prevalence of HPV infection may explain the

differences in the prevalence of cervical dysplasia seen in women living with HIV/AIDS from different studies. Whatever the level of prevalence obtained, this present study and other studies have shown that women living with HIV/AIDS have a higher prevalence of cervical disease and therefore buttress the need to include regular cervical cancer screening as part of the protocol for the management of HIV patients in this region.

Several interactions between HPV and HIV exist to explain why HIV-infected women have a higher prevalence of cervical dysplasia and these includes : reduced local cervical cellular mediated immunity from generalized immune suppression causing persistence of HPV infection, direct viral-viral interaction which may enhance transcription of HPV oncoproteins, and increased immune escape pathways.<sup>25</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 cellular immunity. 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>26-28</sup> Treatment with HAART leads to reconstitution of the immune system leading to decreased incidence of HPV infections.

Similarly, the lower prevalence of abnormal cervical epithelial cytology reported in the control population of this study when compared to other studies may be due to the fact that majority of them have tertiary education with a better standard of living, are not selected from a diseased population but rather women attending the family planning clinic, gynaecology clinic for cases of infertility, and general out-patient department mostly for the management of hypertension.

The epithelial abnormality seen in the HPW includes ASCUS (6 cases, 2.65%), LSIL (13 cases, 5.75%) and HSIL (6 cases, 2.2%). No case of invasive squamous cell cancer or glandular cell abnormality was detected. In the control group, the abnormal epithelial cytologic pattern comprises ASCUS (4 cases, 1.8%), LSIL (3 cases, 1.35%), HSIL (3 cases, 1.35%) and 1 case of invasive squamous cell cancer (0.4%). The frequency of inflammatory smears was also greater in the HIV group (22 cases, 9.7%) than in the controls (12 cases, 5.4%). This shows that all categories of squamous intraepithelial lesions, especially the high-grade types were higher in the HPW. This finding is supported by similar findings in related studies.<sup>16,29-31</sup>

This study also shows that HPW have a higher prevalence of inflammatory smear (9.7% Vs 5.4%). The study by Koffi et al in Central African Republic also reported a higher prevalence inflammatory smears in HPW.<sup>32</sup> 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. The lowered local cervical immunity in HIV infection 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>33</sup>

## 5. Conclusion

From this study in Uyo, it can be concluded that there is a higher prevalence of cervical epithelial cell abnormality in HPW than in HNW (10.6% Vs 4.9%) and this was statistically significant ( $p < 0.05$ ). Also, all categories of Squamous Intraepithelia Lesions were more frequent in the HPW. We recommend that all women, especially the HPW should have a regular routine cervical cancer screening. Since the age specific prevalence rate was highest among women that are 46 years and above in both the control- and case-participants, 35-45 years can be chosen for targeted screening in resource limited settings.

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## 7. References

- i. Ntekim A. Cervical cancer in sub-Sahara Africa. Rajamanickan R, editor. Topics on cervical cancer with an advocacy for prevention. 1st edition [Internet]. In-Tech, 2012; pp 51-74. [Accessed March 18,2013]: Available from <http://www.intechopen.com/books/topics-on-cervical-cancer-with-an-advocacy-for-prevention/cervical-cancer-in-sub-sahara-africa>.
- ii. 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.
- iii. 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.
- iv. Parkin DM, Bray F: chapter 2: The burden of HPV related cancers. *Vaccine* 2006, 24(3): S11-25.
- v. Castellsague X, Munoz N. Cofactors in HPV carcinogenesis of parity, oral contraceptive, and tobacco smoking. *J Natl Cancer Inst Monogra* 2003: 20-28.
- vi. 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.
- vii. 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](http://www.sciencedomain.org) [accessed 6<sup>th</sup> July, 2014].
- viii. Ezechi OC, Ostergren PO, Nwaokorie FO, Uja IAO, and Pettersson KO. The burden, distribution and risk factors for cervical oncogenic human papilloma virus infection in HIV positive Nigerian women. *Virology Journal* 2014; 11: 5. Available from: <http://www.virologyj.com/content/11/1/5>. [accessed 6th July, 2014].



- ix. 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.
- x. 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.
- xi. WHO Cervical Cancer Summary report update, September 15:2010.
- xii. Program for appropriate Technology in Health. Cervical cancer Prevention. The Reproductive health outlook 2003 summer edition. [Online]. Available from:<http://www.rho.org/asstes/RHO-cxca-10-9-03.pdf>. [accessed 19th September, 2013].
- xiii. Duraisamy K, Jaganathan KS, and Bose JC. Methods of detecting cervical cancer. *Adv Biol Res* 2011; 5(4):226-232.
- xiv. Federal Republic of Nigeria, Global AIDS response progress report 2012. [Online]. Available from:[www.unaids.org/es/dataanalysis/monitoringcountryprogress/progress-reports/2012-countries/file,68516](http://www.unaids.org/es/dataanalysis/monitoringcountryprogress/progress-reports/2012-countries/file,68516). [Accessed 19th September 2012].
- xv. 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.
- xvi. 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.
- xvii. Chama CM, Nggada H, and Gashau W. Cervical dysplasia in HIV infected women in Maiduguri, Nigeria. *J Obstet Gynaecol*.2005; 25(3): 286-288.
- xviii. Sadan O, Schejter E, Ginath S, Bachar R, Boaz M, Menczer J et al. Premalignant lesions of the uterine cervix in enlarge cohort of Israeli Jewish women. *Arch Gynaecol Obstet*. 2004; 269 (3): 188-191. Available at: Doi:10.1007/s00404-002-0371-y. [accessed 5/5/14]
- xix. Omar T, Schwartz 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.0bo13e32834of99. [accessed 5/5/14].
- xx. 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.
- xxi. 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.
- xxii. 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.
- xxiii. Menéndez C, Castellsagué X, Renom M, Sacarlal J, Quintó L, Lloveras B et al. Prevalence and Risk Factors of Sexually Transmitted Infections and Cervical Neoplasia in Women from a Rural Area of Southern Mozambique. *Infect Dis Obstet Gynecol*, 2010. [Online]. Available at doi:10.1155/2010/609315. [Last accessed 19/12/12].
- xxiv. Ng'andwe C, Lowe JJ, Richards PJ, Hause L, Wood C and Angeletti PC. The distribution of sexually-transmitted Human Papillomaviruses in HIV positive and negative patients in Zambia, Africa. *BMC Infect Dis* [Online]. 2007;7, 77. Available from: <http://www.biomedcentral.com/1471-2334/7/77>. [accessed 19th September, 2012].
- xxv. Schiffman M, Castle P, Jeronimo J, Rodriquez A, Wacholder S. Human Papillomavirus and cervical cancer. *Lancet* 2007;370:890-907.
- xxvi. 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.
- xxvii. 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.
- xxviii. 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.
- xxix. 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.
- xxx. Dim CC, Ezegwui HU, Ikeme AC, Nwagha UI and Onyedum CC. Prevalence of cervical squamous intraepithelial lesions among HIV-positive women in Enugu, South-eastern Nigeria. *J Obstet Gynaecol* 2011; 32 (8): 759-762.
- xxxi. Bassey G, Jeremiah I, Ikimalo JI, Fiebai PO, Athanasius BP. Abnormal cervical cytology among HIV-positive women in Nigeria. *Int J Gynaecol Obstet* 2014; 125 (2): 103-6.
- xxxii. Koffi B, Serdouma E, Mbolissa-Nguerekoudou W, Ngadjou-Kouchou-Fondjo M, Pengoussou-Gbatoumba V, Sepou A et al. Cervical dysplasia in women with HIV in areas of high prevalence of infection. *Gynecol Obstet Fertil*. 2010; 38(10): 576-80. Available at: doi: 10.1016/J.gyobfe.2010.08.031.
- xxxiii. 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.