CERVICAL DYSPLASIA IN HIV SEROPOSITIVE WOMEN IN NIGERIA

Tanko N.M *, Echejo G.O *, Manasseh A.N*, Mandong B.M *, Banwat E.B ** Daru P.H ***

*Departments of pathology, ** Medical Microbiology and *** Obstetrics and gynaecology, Jos University Teaching Hospital, Jos.

Correspondence address to: Dr Matthew N. Tanko,
Department of pathology, Jos University Teaching Hospital PMB 2076, Jos Plateau State.
E-mail: comexet@yahoo.co.uk
Running title: **HIV infection and cervical dysplasia; Tanko** *et al.*

Abstract

Objective: To identify social, behavioural and epidemiologic predictors of cervical dysplasia in HIV- infected women in central Nigeria.

Design: A cross sectional study.

Setting: Jos University Teaching Hospital (JUTH), Nigeria.

Patients: Cases were HIV- positive heterosexually active women diagnosed between January and April 2005 in JUTH. Controls were HIV- negative heterosexually active women recruited from HIV testing sites. Family and social history and cervical smears were obtained from the subjects.

Results: Univariate analysis of 178 HIV-positive and 116 HIV- negative women showed that HIV-positive cases were more likely to be unemployed (OR= 7.31, RR= 1.83, P< 0.0001), divorced (OR= 3.69, P< 0.006, RR= 1.60), widowed (OR= 5.63, RR= 1.77, P< 0.0001), housewives (OR= 2.19, RR= 1.83, P< 0.03), singles (OR= 3.19, RR= 1.57, P < 0.0001), have had STDs (OR= 3.30, RR= 1.66, P< 0.0001) and more lifetime sexual partners (OR= 2.05, RR= 1.53, P< 0.0001). Inflammatory smears were more associated with HIV-positive cases (OR= 2.71, P< 0.0001). High grade dysplasia was more likely to be present in HIV-infected women (OR= 10.71, RR= 1.95, P< 0.003). The prevalence of cervical dysplasia was found to be 21% and 6% in HIV cases and controls respectively.

Conclusion: We conclude that the prevalence of cervical dysplasia is two times higher in HIV- infected women than HIV- negative women in Jos. Socioeconomic factors such as poverty and social insecurity are risk factors for HIV infection as well are predictors of cervical dysplasia.

Keywords: HIV infection, cervix, dysplasia, Nigeria

INTRODUCTION

The human immunodeficiency virus epidemic in Nigeria is increasingly affecting heterosexual men and women. In HIV infected women, cervical cancer presents one of the most serious challenges in the oncologic care of immunosuppressed patients. Recent data indicate that heterosexual transmission surpasses any other route of HIV infection and that the prevalence of HIV infection ranges from 4.4% to 6.4% in Nigeria.[1]

Studies from the western world conducted in 1994 and 2001 have reported an increase in the incidence of cervical squamous intraepithelial lesion (dysplasia) among HIV- infected women and that cervical dysplasia in this group of women is of higher histological grade than their HIV-negative counterparts. Moreover, more extensive involvement of the female lower genital tract with human papilloma virus (HPV) changes have been reported in these studies.[2,3,4]

Few epidemiologic studies in Africa have investigated risk factors for HIV transmission and even fewer have investigated the

relationship between HIV infection and cervical dysplasia.[5,6,7] To the authors' best knowledge, there is scarce data on the correlation between HIV infection and cervical dysplasia in central Nigeria. While the development of most cancers in the immunosuppressed patients can be attributed to immune deficiency, the relationship between squamous cell neoplasia of the cervix in HIV infection is quite unique because of common sexual behavioural risk factors.

We conducted a case-control study to evaluate the epidemiologic, behavioural, socioeconomic differences and prevalence of cervical dysplasia among HIV positive (cases) and HIV- negative (controls) women in Jos Central Nigeria.

PATIENTS AND METHODS
Sampling
We recruited study participants from the Jos University Teaching Hospital (JUTH) which is the centre accounting for most of the HIV diagnosis in central Nigeria. Cases and controls were women residing in this geographic region of Nigeria. All the cases were 178 consecutive women receiving a diagnosis of HIV infection from January to April 2005. These cases were recruited from the sexually transmitted disease (STD) clinic, gynaecology clinic and the AIDS Prevention Initiative in Nigeria (APIN) laboratory all of which are located within JUTH. All cases were reactive by double ELISA and confirmed by Western Blot. Controls were 116 consecutive HIV- negative women who were recruited from the gynaecology clinic, family planning clinic and sexually transmitted disease clinic within the same study period. Cases with risk factors for HIV infection other than sexual contact were excluded from the study. All the 294 study participants gave informed consent and the study was approved by the Ethical Committee of the Jos University Teaching Hospital.

Data collection
Trained interviewers using standardized questionnaires collected information about the personal data and sexual history of the participants for the 4 months period. The questionnaire captured the age, occupation, marital status, sexually transmitted disease history, number of lifetime sexual partners and cytological diagnosis of their cervical smears. All the women underwent standardized interviews to document risk for HIV infection and cervical dysplasia. Clinical and gynaecological examination were performed on both cases and controls during which cervical smears were obtained using the Cusco's speculum and Ayre's spatula from both the ecto- and endocervix. Smears were made on two points on glass slides and then fixed immediately in 95% (v/v) alcohol in coupling jars. They were then delivered to the cytopathology laboratory for staining and microscopic examination. All the slides were stained with the Papanicolau reagent and read using the light microscope by a single cytopathologist with experience in the Bethesda system of classification. The smears were reported as normal, inflammatory, Atypical squamous cells of undetermined significance (ASC-US), Low grade squamous intraepithelial lesion (LSIL) or high grade squamous intraepithelial lesion (HSIL).

Data analysis
All data were analyzed using the EPI Info 2002 (version 6) computer software program. Dichotomous variables were analyzed using the Chi-square test. Odds ratios and relative risks were calculated for strength of association. Associations with $P = 0.05$ in univariate analysis were considered significant.

RESULTS
Within the study period, 379 consecutive women received a diagnosis of HIV infection. Of these 379 consecutive HIV positive women recruited into the study, 6 (1.6%) had a history of risk for HIV transmission other than sexual contact and were excluded from the study. One hundred and seventy-eight (47%) agreed to participate in the study. The remaining 195 subjects (51.4%) refused to give consent and therefore did not participate in the study. The social, behavioural and demographic

characteristics of the cases and controls are summarized in Table 1.

The mean age of cases was 33.1 ± 6.8 yrs and that of the control population was 38.6 ± 8.1 yrs. The HIV-positive cases were observed to be younger in age than the control subjects but this diffenence was not statistically significant (OR= 0.83, RR= 0.91, P > 0.05). The prevalence of inflammatory smear in HIV-positive cases was 27% compared to 12% in the control subjects. The combined prevalence of both low grade squamous intraepithelial lesion (LSIL) and high grade squamous intraepithelial lesion (HSIL) in HIV-positive cases was 21% compared to 6% in the control group.

Relating the occupation of both cases and controls to their HIV status in the univariate analysis (Table 1), HIV- positive cases were significantly more likely than control subjects to be unemployed (OR= 7.31, RR = 1.83, P <

0.0001). The analysis of their marital status showed that cases tended to be housewives (OR= 2.19, RR = 1.83, P< 0.03,) or divorced (OR= 3.69, RR= 1.60, P< 0.006), or widowed (OR= 5.63, RR= 1.77, P< 0.0001), or singles (OR= 3.19, RR= 1.57, P< 0.0001,).

Also HIV-positive cases were likely to have a history of STD (OR= 3.30, RR= 1.66, P<0.0001,). Similarly, HIV-positive cases were found to have more number of lifetime male sexual partners than controls (OR= 2.05, P< 0.0001). In the analysis of the cytological diagnosis, two associations were statistically significant. First, HIV-positive cases had more inflammatory smears than controls (OR= 2.71, P< 0.0001, RR= 1.53). Second, cases tended to have more of high grade dysplasia (HSIL) than control subjects (OR= 10.72, RR= 1.95, P< 0.0001). The cytological diagnosis in both HIV-positive cases and control subjects is summarized in Figure 1.

Table 1: Distribution of social, behavioural and demographic characteristics

of HIV positive and HIV negative women

Variable	HIV positive (n = 178) (%)	HIV negative (n = 116) (%)	P-value (<)	O.R	R.R
Means of age	33.1 ß	38. 6 ß	0.83	0.83	0.91
Occupation					
Business	5 (2)	8 (3)	0.50	0.66	0.80
C/S	17 (6)	21 (7)	0.61	0.80	0.89
H/W	27 (9)	13 (4)	**0.03**	2.19	1.39
Student	14 (5)	9 (3)	0.39	1.58	1.23
Teaching	13 (4)	13 (4)	1.00	1.00	1.00
Trading	24 (8)	15 (5)	0.18	1.65	1.25
Health worker	15 (5)	6 (2)	0.75	2.58	1.45
Unemployed	33 (11)	5 (2)	**0.001**	7.31	1.83
Others	30 (10)	26 (9)	0.67	1.17	1.08
Marital status					
Divorced	21 (7)	6 (2)	**0.006**	3.69	1.60
Married	73 (25)	87 (30)	0.220	0.79	0.88
Widowed	40 (14)	8 (3)	**0.001**	5.63	1.77
Single	43 (15)	15 (5)	**0.001**	3.19	1.57

History of STD					
No history of STD	81 (28)	77 (26)	0.78	1.07	1.03
History of STD	97 (33)	39 (13)	**0.001**	3.30	1.66
NO. of lifetime sexual partners					
1 2	112 (38)	92 (31)	0.100	1.35	1.16
3 4	52 (18)	24 (8)	**0.001**	2.42	1.45
5 & above	14 (5)	0 (0)	**0.001**		2.05

O.R= Odd ratio
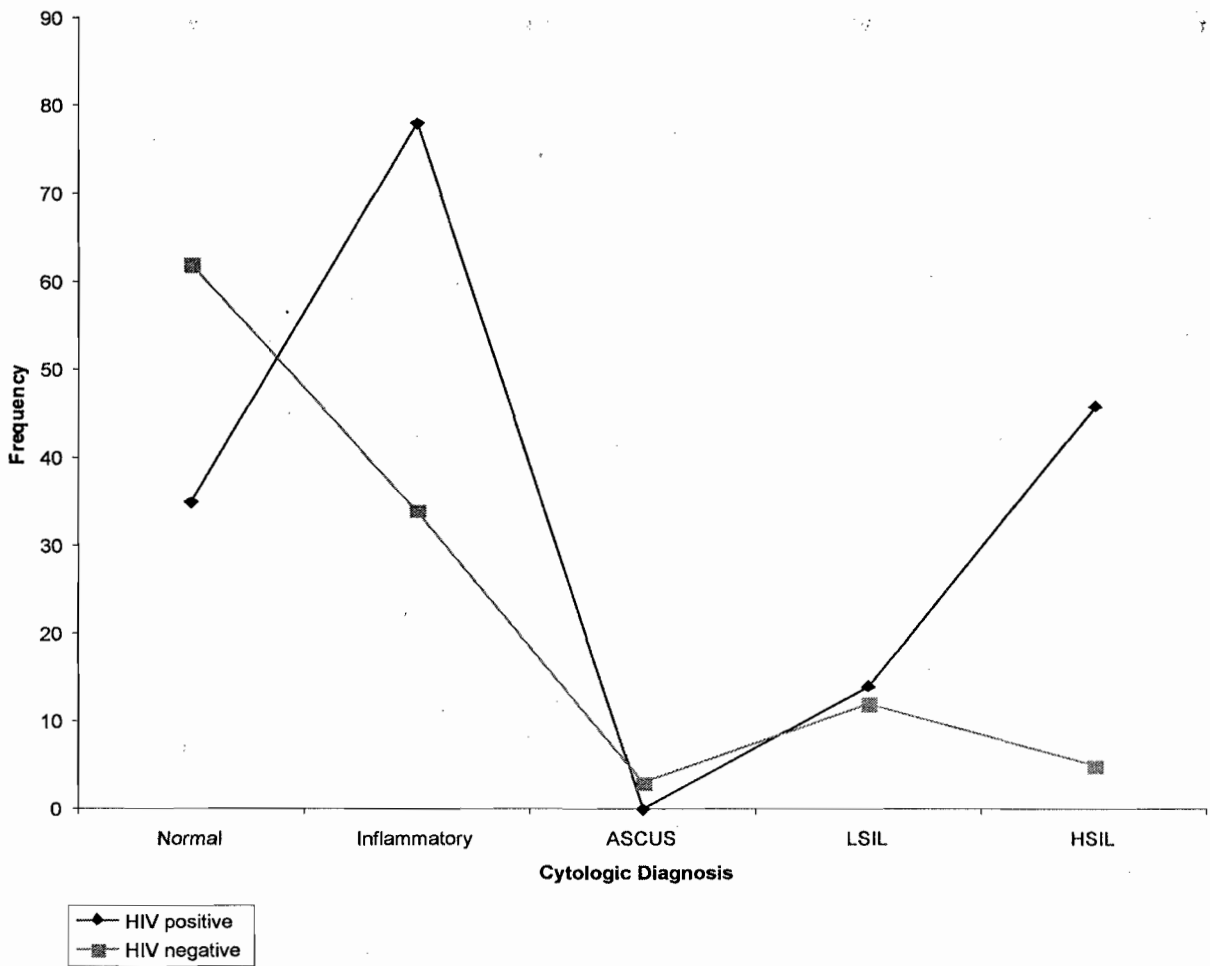**R.R**= Relative Risk

Figure 1: Frequency distribution of cytologic diagnosis of cervical smear in HIV positive and HIV negative women.

ASCUS: Atypical squamous cells of undetermined significance

LSIL: Low grade squamous intraepithelial lesion

HSIL: High grade squamous intraepithelial lesion

DISCUSSION

The prevalence of HIV infection in Nigeria was estimated to be 5.4% in 2003 and 4.4% in 2005.[1] Notably, socioeconomically disadvantaged women are increasingly and disproportionately affected by the HIV/AIDS epidemic in central Nigeria and this mirrors national trends.

We found statistically higher rates of unemployment among HIV-positive cases than control subjects; a finding which reiterates the fact that economic disparities and social dependence are the major risk factors that exposed these women to HIV infection.[8,9] HIV is a disease often linked to poverty and this was reflected in most study participants in the current study. The need to secure essential commodities such as food, shelter and clothing was of higher priority for these women than that of ensuring their health and protecting themselves against HIV infection.

Our data suggest that many of the HIV-positive cases were either divorced, widowed or singles and this again emphasizes exposure due to socioeconomic dependence and desire for social security. Additionally, there was a significantly higher rate of sexually transmitted diseases (STDs) among HIV-positive cases than control subjects and this may suggest that many of these women were victims of multiple male sexual partners. However, our data are limited because we could not establish types of STDs and whether or not these preceded HIV infection or were infact, the result of HIV-related immunosuppression. Be that as it may, some genital infections such as herpes are often acquired at a younger age than HIV.[10]

Similarly, our data suggest that HIV-positive cases tended to have had more multiple lifetime male sexual partners than control subjects. This again suggested that these women needed to sexually serve more men in exchange for money in order to meet up with financial demands placed on them by their peculiar circumstances.

Last, we found significantly higher rate of inflammation among HIV-positive cases than control subjects suggesting exposure to multiple male sexual partners and/or HIV related immunosuppression.

The prevalence of cervical squamous intraepithelial lesion (dysplasia) was 21% among HIV-positive cases and 6% in the control subjects in this study. High- grade dysplasia was found to be approximately two times higher in HIV- positive cases. This finding concurs with that of Chirenje and colleagues in Zimbabwe where HIV- positive women had twice the risk of high-grade dysplasia than their HIV-negative counterparts[6]. Our finding was however lower than that reported by Leroy in Rwanda, where HIV-positive women were found to have four times increased risk of dysplasia than HIV-negative women[11]. Since that study in Rwanda was a large multi-centre study, our relatively small sample size might account for the difference in the risk for cervical dysplasia in HIV-positive women. In a study conducted in Senegal, Faye-Ndao [5] and colleagues found prevalence of cervical dysplasia to be 27% in HIV-positive women, a little higher than the prevalence of 21% we found in our study. Outside Africa, Wright[4] and co-workers found that the prevalence of cervical dysplasia in HIV- positive women residing in New York was 20% compared to 4% in their HIV-negative counterparts. This finding is similar to 21% and 6% found in HIV- positive and HIV- negative women in this present study. In another study from the USA, HIV- positive women and HIV- negative women were followed up for a period of about 30 months. The incidence of dysplasia in HIV-positive and HIV-negative women was found to be 20% and 5% respectively.[12]

Our findings, though comparable to the findings of previous studies both in Africa and abroad, are subject to several limitations. First, we were unable to assess HIV prevalence among the high socioeconomic class in order to substantiate our claims that financial insecurity and social dependence are risk factors for HIV infection. The majority of our study population came from low socioeconomic stratum. Second, we were unable to adequately assess many of the complex sociocultural factors that likely influenced HIV transmission risk in this population. Third, we could neither

demonstrate causality in the associations between HIV and history of STDs nor clarify the suggested relationship between receipt of public assistance and HIV sero-status.

This investigation supports the need for a multidimensional approach to reduce HIV infection and thus the prevalence of cervical dysplasia among women in central Nigeria. It is important to ensure that existing HIV prevention interventions are accessible to the women living in disadvantaged areas of central Nigeria. Also, additional resources and prevention strategies are needed to help address the underlying causes of HIV transmission in our women, such as poverty and lack of social security.

On the basis of our investigation, we believe that improving the long-term economic status of disadvantaged women in central Nigeria will not only benefit the immediate quality of life of these women, but also permit them to place a higher priority on their medical well-being which includes preventing themselves from HIV infection and thus cervical neoplasia.

REFERENCES

1. Federal Ministry of Health National Action Committee on Aids. Situation analysis Report on STD/HIV/AIDS in Nigeria 2003 & 2005.

2. Cardillo M, Hagan R, Abadi J, Abadi MA. CD4 T cell count, viral load and squamous intraepithelial lesions in women infected with the HIV. Cancer 2001; 93:111-114

3. Davis AT, ChakrabortyH, Flowers L, Mosun Jarc MB. Cervical dysplasia in women infected with the HIV: a correlation with HIV viral load and CD4 count. Gynea col Oncol 2001; **80**: 350-354

4. Wright TC, Ellerbrock TV, Chiasson MA, Van Devanter N, Sun XW. Cervical intraepithelial neoplasia in women infected with the HIV: prevalence, risk factors and validity of Pap smears. New York cervical disease study. Obstet Gynaecol 1994; **84**:591-597.

5. Fayo-Ndao MA, Diack-Mbaye A, Woto-Gaye G *et al*. Cervical dysplasia in HIV infection in Senegal. Int Conf Aids July 19-24; 1992

6. Chirenje ZM. Association of cervical squamous intraepithelial lesion and HIV-1 infection among Zimbabwean women in an HIV/STI prevention centre. International Journal of STD and AIDS 2002; **13**: 765-768.

7. La Ruche G. Human Papilloma virus and Human immunodeficiency virus infections: relation with cervical dysplasia-neoplasia in African women. International Journal of Cancer 1998; **76**: 480-486.

8. Rothernberg RB, Wasserheit JN, St Louis ME. The effect of treating sexually transmitted diseases on the transmission of HIV in dually infected persons: a clinic-base estimate. Sex Transm Dis 2001; **27**: 411-416.

9. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect 1999; **75**: 3-17.

10. Freedman E, Mindel A. Epidemiology of herpes and HIV co-infection. J HIV The 2004; **9**:4-8

11. Leroy V. Cervical dysplasia and HIV type 1 infection in African pregnant women: a cross sectional study in Kigali, Rwanda. Sexually Transmitted Infections 1999; **75**: 103-106.

12. Tedd VE, Mary AC, Timothy JB, Xiaows S, Dorothy S, Karen B Wright TC. Incidence of Cervical Squamous Intraepithelial Lesions in HIV-infected women JAMA 2000; **283**: 1031-1037.