Cervical Cytopathology Pattern Among HIV Seropositive And HIV Seronegative Women In Zaria

B U Sulaiman, K A Omolara, S O Sunday, S S Mohammed

Citation

B U Sulaiman, K A Omolara, S O Sunday, S S Mohammed. *Cervical Cytopathology Pattern Among HIV Seropositive And HIV Seronegative Women In Zaria*. The Internet Journal of Gynecology and Obstetrics. 2014 Volume 18 Number 1.

Abstract

Background: Cervical cancer is the second commonest cancer in women worldwide. HIV is suggested to be a co-factor in the association between Human Papilloma Virus HPV and CIN.

Objective: To determine the pattern of cervical cytology changes in HIV+ women and characterize the sociodemographic factors that confound the changes seen.

Study Design: Cross Sectional Comparative Study

Setting: Gynecology Clinic of ABUTH Zaria, Nigeria.

Methodology: Following informed consents, 272 HIV positive (HIV+) and 275 HIV negative (HIV-) women were administered questionnaires and Papanicolaou smears were taken.

Results: The average age of the respondents was 32.6 +_ 6.8years range (15-49years). Mean parity for HIV+ was 3.28 and 3.36 for HIV- women, while 70.8% of HIV+ women were married comparable with 72.7% in HIV- women. Twenty-nine percent of HIV+ women had positive smears for cervical intraepithelial neoplasias (CIN) compared with 16.4% in those that were HIV-. This was statistically significant (OR-2.05, p-0.001). The high grade lesions (CINII, CINIII) tended to be higher in the HIV+ women (11.4%) than the HIV- women (0.7%).

Conclusion: HIV+ women in Zaria, Northern Nigeria are at higher risk of severe cervical dysplasia compared with their counterparts who are HIV-. It is recommended that greater effort should be made to make an integrated reproductive health care service a reality within the HIV clinics.

INTRODUCTION

Cervical cancer is an important reproductive public health problem. It is the second commonest cancer in women worldwide with over 450,000 new cases and 300,000 deaths annually. Over 80% of these deaths occur in the developing countries where it is said to be the commonest cancer in women [1-3]. In sub-Saharan Africa, about 190,000 deaths occur each year from cancer of the cervix [4,5]. The incidence and mortality in England and Wales is approximately 9.3 and 3.7/100,000 women [2]. In the United States of America, the age-adjusted incidence rate of 8.1 per 100,000 with a mortality rate of 2.6 per 100,000 [6,7-9] was reported. However in Nigeria, the incidence rate of approximately 24.1 per 100,000 was reported from the Ibadan cancer registry [7].

Cancer of the cervix is a slowly developing tumour that takes about eight to ten years to develop from the precancer stage, thus it is a suitable disease for screening [1,7] . There are various methods used in assessing changes in the cervical cells with the commonest being the Papanicolaou smear. Others include; Visual Inspection with Acetic acid (VIA), Visual Inspection with Lugol's Iodine (VILI) which are very useful in low resource settings. The "thin-prep pap" which is a modification of the conventional Pap smear though expensive produces better quality smears and results. HPV DNA testing is also used to improve the efficiency of screening.

Cancer of the cervix has close to 100% cure rate if detected early at the pre-invasive stage through cytological screening [8]. The high risk Human Papilloma Virus (HPV) especially types "16,18,31,45" are central to the development of cervical cancer and its precursors. Primary prevention is

aimed at reducing Human Papilloma Virus infection and following years of research, the bivalent CervarixR vaccine and the quadrivalent GardasilR vaccines have been developed and have proven to be efficacious in preventing infection with HPV [3]. These are administered to girls and women between the ages of 9 to 26 years in three doses within 6 months [9]. Secondary prevention using cervical cytology, VIA or VILI has to continue for the other high risk strains, 31, 35, 45 and for older unvaccinated women in the populace.

The association between Human Papilloma Virus and Human Immunodeficiency Virus (HIV) is an important one. The prevalence of both viruses in a population is strongly related to sexual behaviour pattern [10-12]. Nonetheless, data from Africa, America and Europe till date are conflicting on whether or not there is increased risk of cervical cancer in HIV positive women [13,14].

More than one third of the 8 million persons infected with the HIV virus worldwide are women [14] Over 25.8 million adults and children are living with HIV/AIDS in sub-Saharan Africa and 13.5 million are women [14]. The first case of AIDS in Nigeria was reported in 1986 and since then, the HIV prevalence has been increasing from 1.8% in 1991 to 5.8% in 2001[15]. However, the report of 2008 national HIV Sentinel Survey reported a reduced prevalence of 4.6% [16]. The first HIV sero-positive patient was detected at the Ahmadu Bello University Teaching Hospital Zaria in 1987 and increasing numbers have since emerged [16].

The 1993 Centre for Disease Control revised classification for HIV added moderate or severe cervical dysplasia as a "category B" AIDS defining condition and invasive cervical cancer as an AIDS or "category C" defining condition [10].

HIV-seropositive women were shown in separate studies to be at an increased risk of developing squamous intraepithelial lesions and invasive cancer of the cervix, vagina, vulva, anus and perianal regions [12,17]. HIV is suggested to be a co-factor in the association between HPV and cervical intraepithelial neoplasia (CIN) and this effect seems to vary with level of immune function [10,14,17]. Studies have also shown that standard modalities of screening and treatment as applicable to the general 'at risk' population on these cervical conditions may suffice for HIV/AIDS positive women [10,11]. In a study from Senegal both HIV I and HIV II were found to be associated with Squamous Intraepithelial lesions [17]. In women with HIV, untreated CIN I is likely to persist and the likelihood is higher than that in HIV seronegative women [18].

Currently, the use of highly active antiretroviral (ARV) agents has prolonged the life expectancy and improved the quality of life of people living with HIV; the increasing population of these women may then be faced with another dilemma of cancer of the cervix which is better prevented than managed.

The justification for this study is to know if a relationship exists between CIN and HIV in this center since studies done in other centers in North East and North Central Nigeria found a strong association between HIV positivity and cervical dysplasia in women. There was also the association between levels of immune suppression with severity of dysplasia.

The aim of this study is to assess the pattern of cervical cytopathology among HIV positive women attending clinics in ABUTH Zaria.

OBJECTIVES

To determine:

1. The prevalence of abnormal cervical smears among HIV positive women in Zaria
2. The association between abnormal cervical smears and HIV
3. The socio-demographic factors associated with abnormal cervical smears in HIV positive women.
4. The pattern of Cervical Intraepithelial Neoplasia (CIN) changes present.

METHODS

This was a cross-sectional case-control study to investigate cervical smear patterns among HIV positive and HIV negative women conducted in the virology clinic and the gynaecology clinics of ABUTH Shika. HIV positive women aged 15-49 years attending these clinics were enrolled after giving informed consents. A control group consisting of HIV negative women matched for age was recruited from the reproductive health clinics following pre-test HIV counseling, a negative HIV screening test and a post-test counseling.

The sample size was determined using the formula:

Where

z = standard normal deviate for a normal distribution and is taken as 99% confidence interval = 1.96 from the z table.

p= proportion or prevalence, is taken as 0.23 . 18

q= 1 – p

d = degree of precision which is taken as 0.05 (precision limit = 0.05)

Unbalanced Eqn Unbalanced Eqn

$$= \frac{3.84x0.177}{0.0025} = 272$$

272 was the minimum sample size that could be used.

The respondents were administered questionnaires to collect information on their sociodemographic characteristics, obstetric history, contraceptive, sexual history and history of smoking. Their papanicolaou smears were then taken; with the patient in the dorsal position, the vulva was parted with the left hand and a bivalve speculum inserted into the vaginal cavity exposing the cervix. The ectocervix was cleansed using a sterile swab and the wooden Ayre's spatula inserted into the cervix and rotated 360 degrees to abrade the surface slightly and to pick up cells from the squamocolumnar area of the cervical os. The specimen was smeared on the slide and put in a container of 95% alcohol for fixation. This was then analyzed in the histopathology department of the hospital. The slides were then reported by a consultant pathologist. Patients who had abnormal smears were referred to the Gynaecology clinic for further management. The papanicolaou smears were collected over a period of one year.

The information obtained was coded and recorded on data sheets designed for the study and analyzed using SPSS statistical soft ware version 15. Test of significance were based on p< 0.05 using the appropriate tests.

RESULTS

The mean age of the respondents was 32.6 ±6.8years (range 15-49 years). The mean parity in the HIV positive women was 3.28 ± 1.90 this was not significantly different from that for HIV negative women with 3.36 ±1.62 (p= 0.598). In the unmarried HIV positive women, 27.3% had positive smears; There was no statistical significance difference in the occupational status of the HIV positive and the HIV negative women where 28.0% and 23.6% were civil servants.(p=o.385) The greater majority in both groups were house wives; 33.6% and 34.5% respectively. The HIV positive women had a lower level of education (25.6%) than those that were HIV negative 17.8% though it was not statistically significant.(p= 0.057) . The mean number of sexual partners (1.66± 1.074 and 1.65 ± 0.968 CI: 157-188) respectively in the HIV positive and the HIV negative respectively was not significantly different.

The prevalence of positive smears in HIV positive women was 28.7% and was significantly higher than 16.4% found in HIV negative women (p=0.001, OR=2.05).

Table 2 showed HIV status relates to the severity of cervical changes with the HIV status. The high grade lesions (CIN II, CIN III) tended to be higher in the HIV +ve women (11.4%) than HIV –ve (0%) women. There were 20 (7.4%) HIV positive women with CIN II and 11(4.0%) with CIN III, constituting high grade lesions. None of the HIV negative women had high grade lesion. Three women were diagnosed with carcinoma in situ among the HIV positive women.

The comparison of sociodemographic factors and sexual variables in relation to the presence or absence of positive smear is shown in table 3. There was no statistical significant difference between those with positive smears and those with negative smears in terms of parity, marital status, the age at coitarche and educational level. There was however a significant difference in the age ranges and having a positive smear. (p=0.001). The women with a CD4 count of less than 300 had a higher number of positive smears (29.3% n=39) than those with a CD4 count of 500 and above (24.7% n= 19). All women denied history of smoking.

DISCUSSION

The women in the study were from various tribes; constituting mostly those from the southern part of Kaduna 44.6% and the Hausa/ Fulani having 36.7%. One hundred and fourteen HIV positive women had post secondary education out of the total of 272 and not surprising 120 of them were married bearing in mind the commonest mode of transmission of the virus in our environment. This is similar to the finding from Jos by Tanko et al [19]. There were more divorced and widowed women in the HIV positive group and they also had more sexual patners, this is similar to the Jos study [19].

The prevalence of squamous intraepithelial lesions (SILs) in

this study was significantly higher in HIV positive than in HIV negative women 28.7% and 16.4% respectively. This is in keeping with reports from both the developed and the developing countries. A study from Baltimore, the United States 13% of HIV positive women had abnormal cervical cytology compared with 2% of HIV negative women[20]. Another study from Thailand by Hluangdansakul and others showed a prevalence of 10.5% in HIV positive women [21]. African researchers have also demonstrated high prevalence in their results. The highest prevalence so far reported was from Zambia with a figure of 76% [22]. Tanko et al from Jos reported a prevalence of 21% in the HIV positive group and 6% in the HIV negative group[19], but it is higher than the report from Lagos with a prevalence of 10.9% in the HIV positive group and 4.3% in the HIV negative women [23]. Saidu from Ilorin reported higher prevalence (23.8% compared to 11.3%) in HIV positive women when compared with HIV negative women, this is similar to Chamah in Maiduguri and [18,24].Other factors such as age, parity, marital status, educational level, number of sexual partners were found to be confounding factors in development of SILs in HIV women in different studies [17,22,25,26].

In this study, only age was found to be statistically significant in smear positive and smear negative HIV positive women. This is similar to a report by Audu from Maiduguri [27], although they also noted associations with parity. HIV infection was the strongest association in the development of SILs among all the variables in this study. It has been reported that women on highly active anti retroviral agents (HAART) have an added advantage of potential regression of HPV infection and subsequent induction of regression of SILs [28,29,30]. In this study, despite the fact that the majority of HIV positive women were on HAART they still had a higher prevalence than the HIV negative women . The regression or progression rate of the cervical changes noticed could be studied further in another prospective study.

CONCLUSION

Several studies have demonstrated the high association between HIV infection in women and squamous intraepithelial changes. The finding from this study is in tandem with other studies carried out in different centers across the country. In view of the on-going HIV pandemic especially in sub-Saharan Africa, more women would be at risk of developing pre- invasive and invasive cancer of the cervix. As progress continues with management of HIV positive women with antiretroviral, immunosupportive therapy and in preventing and treating opportunistic infections, the life span of these women is expected to increase. The clinical significance of more severe infection with HPV may overtime be manifested in higher rates of cervical dysplasia and carcinoma in the population of HIV-infected women. There is therefore need to intensify efforts to prevent HPV infection and precancer and cancer of cervix.

RECOMMENDATIONS

Based on the findings in this study of the high risk of developing high grade SIL by HIV positive women, it is recommended that cervical smear should be more frequent with intervals between smears shorter; such as every six months in these women.

Cervical cancer prevention services in HIV affected women should be integrated with the Anti Retroviral Therapy programmes; this will afford the opportunity to reduce the burden of HIV infection and cervical cancer in resource poor settings where both diseases are prevalent.

Table 1

Prevalence Of Squamous Intraepithelial Lesions In Hiv+ And Hiv- Women.

Cytological result	HIV POSITIVE (+)		HIV NEGATIVE (-)		TOTAL	
	N	%	N	%	N	%
Negative smear	194	71.3	230	83.6	424	77.5
Positive smear	78	28.7	45	16.4	123	22.5
TOTAL	272	100	275	100	547	100

Chi- square=11.9 df=1 p=0.001

Table 2

Relationship Between CIN And HIV Status

Cytology result	HIV positive		HIV negative		Total	
	N	%	N	%	N	%
CIN I	47	17.3%	45	16.4%	92	16.8%
CIN II	20	7.4%	0	0	20	3.7%
CIN III	11	4.0%	0	0	11	2.0%
Others	194	71.3%	230	83.6%	424	77.5%
Total	272	100	275	100	547	100%

Chi-square= 42.83 df = 3 p= 0.000

Table 3

Comparison Of Baseline Characteristics Of Hiv+ Women Based On Cytopathologic Diagnosis

	SMEAR -		SMEAR +		TOTAL		P VALUE
	N	%	N	%	N	%	
Age							0.001
15-24	16	94.1	1	5.9	17	100	
25-34	104	77	31	23	135	100	
35-44	53	68.8	24	31.2	77	100	
≥45	21	48.8	22	51.2	43	100	
Marital Status							
Married	85	70.8	35	29.2	120	100	0.836
Unmarried	109	72.7	41	27.3	150	100	
Parity							
<5	158	75.9	50	24.0	208	100	0.047
≥5	38	59.4	26	40.6	64	100	
No of Sexual partners:							
Single	121	69.5	53	30.5	174	100	0.117
Multiple (including polygamy)	74	75.5	24	24.5	98	100	
Age at coitarche							
<15	26	65	14	35	40	100	0.434
15-30	166	72.2	64	27.8	230	100	
≥30	2	100	0	0	2	100	
Educational level							0.211
≤Primary	47	65.3	25	34.7	72	100	
>Primary	147	73.5	53	26.5	200	100	
CD4 Count							0.568
<300	94	70.7	39	29.3	133	100	
300-499	42	67.2	20	32.8	62	100	
≥500	58	75.3	19	24.7	77	100	

References

1. Thomas J. Olukunle O, Iyare I. Current concepts in cervical carcinogenesis and new perspectives in prevention. Arch. Ibadan Med 2002; 3(1): 36 – 39.
2. Rowlands P.K. Barros-Lopes A. Invasive carcinoma of the cervix. Curr. Obstet Gynaecol 2001; 11:172 – 177.
3. Waggoner S.E. Cervical cancer. Lancet 2003; 361: 2217 – 25.
4. Rostad B, Schei B. da Costa F. Risk factors for cervical cancer in Mozambican women. Int. J. Gynecol obstet. 2003; 80: 63-65.
5. Roberts A.A. Ayankogbe O.O Osisanya T.F Bamgbala A.O Ajekigbe A.T Olatunji B.S et all. Knowledge of cervical cancer Risk factors among refugee women in Oru camp. Nig Med Pract. 2004; 46 (4): 67 – 70.
6. Rafindadi AH, Ifenne I, Shittu S.O., Bako A.U. Olasinde T.A. A study of some aetiological factors in 41 cases of cancer of the cervix uterine in Zaria Nig. Qt Hosp. Med. Journ. 1999; 9(27): 87 – 89.
7. King C.S. Carcinoma of the cervix and cervical cytology – short epidemiological review Cent. Afr. J. Med. 1992; 38 (5): 198 – 202.
8. Okeke T.A. Okafor U. Akpala C.O. Epidemiological studies of a cervical cancer screening programme population Sahel Medical Journal.1999; 2(17):30 - 33.
9. U.S. Panel Endorses, cervical cancer vaccine for girls June 29 2006. available at http//www.n/mmhgov/medlineplus/news/fullstory35502htm/ .
10. Olaniyan O.B. Denny L. Abnomal cytology in HIV-positive women referred for colposcopy. An Analysis of cytology-colposcopy-Histology correlation. Trop J Obstet Gynaecol 2005; 22(2): 129 – 132.
11. Adachi A. Fleming I. Burk R.D. Ho Gy, Klein R.S. Women with Human Immunodeficiency Virus infection and abnormal Papinocolaou Smears. A prospective study of colposcopy and clinical outcome. Obstet Gynecol 1993; 81:372 – 7.
12. Sun XW. Kuhn L. Ellerbrock T.V. Chiason M.A. Bush T.J. Wright T.C. Human Papillomavious infection in women infected with the Human Immunodeficiency Virus. N Eng. J Med 1997; 337 – 9.
13. Adewuyi S.A, Shittu S.O, Rafindadi A.H. Cervical cancer in HIV Seropositive Patients. West African Journal of Radiology. 2007;14(1):31-37.
14. Mandelblatt J.S. Kanetky P. Eggert L. Gold K. Is HIV Infection a cofactor for cervical Squamous Cell Neoplasia? Cancer Epidermiol Biomarkers Prev 1999; 8: 97 – 106.
15. Johnson J.C. Burnett A.F. Willet G.D. Young M.A. Doniger J. High Frequency of latent and clinical Human papilloma virus cervical infections in Immuno compromised Human Immunodeficiency Virus infected women Obstet Gynecol 1992; 79: 321 –7.
16. Habib A.G. Keshinro I.B. Gebi U.I. Olatunde B.O. Onyemelukwe G.C. Kangave D. Clinical Presentation of HIV infection in Northen Nigeria and its Relationship to CD4 + T-Cell counts Nig. Med. Pract. 1998; 35(1/2): 3 –8.
17. Langley C.L,Benga-De E, Critchlow C.W, Ndoye I. Mbengue-Ly, Kuypers J et all. HIV-1,HIV-2,human papiloma virus infection and cervical neoplasia in high risk African women. AIDS 1996; 10(4): 413-7
18. Saidu R, Abdul I.S, Jimoh AAG, Olatinwo A.W, Obiagha I.O,S Salame A.K. Association of squamous intraepithelial lesions in HIV in Ilorin. Trop J Obstet Gynaecol, supplement I 2006; 23(1):s10. .
19. Tanko N.M, Echejo G.O, Manasseh A.N, Mandong B.M, Banwat E.B, Daru P.H Cervical dysplasia in HIV Seropositive Women in Nigeria Highland Medical Research J 2006;4(2): 21-26.
20. Ahdieh L, Munoz A, Vlahov D. Cervical neoplasia and repeated positivity of Human papilomavirus infection in human immuno deffeciency virus sero positive and sero negative women, Am J Epidermiol.2000;151:1148-1157.
21. Hluangdansakul W. Phinchantra P. Bowonwatanuwong C. Prevalence of SIL and SCCA in Human Immunodeffeciency Virus-seropositive women at Anonymous clinic in Chonburi Hospital. J Med Assoc Thai. 2006;89(3): 289-93.
22. Chirenje Z.M. HIV and cancer of the cervix. Best practice and Research, clinical obstet and Gynaecol 2005; 19(2): 269-276.
23. Anorlu R.I Igwilo C.I Akanmu A.S Banjo A.A Odunukwe N.N
Okany C.C et all Prevalence of abnormal cervical smears among
patients with HIV in Lagos Nigeria. West Afr J med 2007;26(2): 143-7
24. Chama C.M, Nggada H, Gashau W. Cervical neoplasia in HIV infected women in Maiduguri Nigeria. J Obstet Gynaecol 2005;25(3): 286-288.
25. Miotti P.G, Dallabetta G.A, Daniel R.W. cervical abnormalities,Human papiloma virus, and Human

immunodeficiency virus infections in women in Malawi. J infect Dis 1996; 173: 14-17.
26. La Ruche G. You B, Mensah-Ado I. Human papilomavirus infections: relation with cervical dysplasia-neoplasia in African women. Int J Cancer 1998; 76:480-6.
27. Audu B.M, Elnafaty A.U, Pindiga H.U. Prevalence of Abnormal Cervical Smears from Sporadic Screening in a Gynaecological clinic. Nigerian Medical Practioner 2007; 51(6): 114-118.
28. Minkoff H. Ahdieh L, Massad S, Anastos K,Watts H,Melnick S. et all. The effect of highly active antiretroviral therapy on cervical cytologic changes associated with oncogenic HPV among HIV-infected women. AIDS 2001; 15: 2157-2164.
29. Heard I. Schmitz V. Costagliola D. Orth G. Kazatchkine M D. Early regression of cervical lesions in HIV-seropositive women receiving highly active antiretroviral therapy. AIDS 1998;12:1459-1464.
30. Massad L.S, Evans C.T, Minkoff H, Watts D.H, Stricler H.D, Darragh T et all. Natural history of Grade 1 cervical intraepithelial neoplasia in women with Human Immunodefficiency Virus. Am J Obstet Gynecol 2004;104(5): 1077-1085.

Author Information

Bawa Umma Sulaiman
Department of Obstetrics and Gynecology, Ahmadu Bello University Teaching Hospital
Shika-Zaria, Nigeria
drusbawa@yahoo.co.uk

Kolawole Abimbola Omolara
Department of Obstetrics and Gynecology, Ahmadu Bello University Teaching Hospital
Shika-Zaria, Nigeria
kolabimbo@yahoo.com

Shittu Oladapo Sunday
Department of Obstetrics and Gynecology, Ahmadu Bello University Teaching Hospital
Shika-Zaria, Nigeria
oladaposhittu@yahoo.com

Shehu Sani Mohammed
Department of Pathology, Ahmadu Bello University Teaching Hospital
Shika-Zaria, Nigeria
msshehu2@yahoo.com