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PREVALENCE OF CERVICAL CYTOLOGY ABNORMALITIES AMONG HIV INFECTED WOMEN AT RWANDA MILITARY HOSPITAL
J. Wanyoike-Gichuhi, MBChB, MMed (Obs / Gyn), P. Kayumba, MBChB, MMed, Department of Obstetrics and Gynaecology College of Health Sciences, University of Nairobi, P. O. Box 19676-00202, Nairobi and W. Khisa, MBChB, MMed (Obs / Gyn) Kenyatta National Hospital, P. O. Box 20723-00202, Nairobi, Kenya.

Request for reprint to: Dr. J. Wanyoike – Gichuhi, Department of Obstetrics and Gynaecology, College of Health Sciences, University of Nairobi, P. O. Box 19676-00200, Nairobi , Kenya.

PREVALENCE OF CERVICAL CYTOLOGY ABNORMALITIES AMONG HIV INFECTED WOMEN AT RWANDA MILITARY HOSPITAL

J. WANYOIKE-GICHUHI, P. KAYUMBA and W. KHISA

ABSTRACT

***Objectives*: To establish the prevalence of cervical cytology abnormalities, determine the correlation between CD4+ cell count and abnormal Pap smear, determine the correlation between WHO-HIV staging and abnormal pap smear among HIV infected women attending HIV clinic at Rwanda Military Hospital.**
***Design*: Cross-sectional descriptive study**
***Setting*: Rwanda Military Hospital Kigali, Rwanda**
***Subjects*: All HIV-positive women, 18-69 years who had been or were sexually active and were attending the HIV-clinic and consented to participate in the study.**
***Results*: Two hundred and ninety three women infected with HIV had cervical smear taken for cytology. Of the 293 women who were recruited for the study, cervical Squamous Intra epithelial Lesion (SIL) were present in 58 (20%). Of those with cervical SIL, 33 (56.89%) women had low-grade SIL, 15(25.86%) had Atypical Squamous Cells of Undetermined Significance (ASCUS), six (10.34%) had high-grade SIL, three (5.17%) had Squamous cell carcinoma (SCC) and one (1.72%) had Atypical Glandular Cells of Undetermined Significance (AGUS). In the current study, use of ARV drugs was not associated with a reduction in the risk of cervical SIL**
***Conclusion*: A high prevalence of cervical SIL was found among HIV-infected women at Rwanda Military Hospital. Increased immune suppression was significantly associated with cervical SIL.**

INTRODUCTION

Cervical cancer is the second most common cancer in women worldwide, and the seventh most common overall (in both sexes combined). In developing countries however, cancer of the uterine cervix is ranked second to cancer of the breast, whereas in developed countries cervical cancer is ranked fifth (1). Worldwide, cervical cancer accounts for almost half a million (529,800) new cases annually of all cancers diagnosed in women. More than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers (2).

The incidence of the cervical cancer incidence in East African countries is (34.5/100,000 women/ year) (2).

Annually, cervical cancer is responsible for 275,100 deaths, about 88% of which occur in developing countries: 53 000 in Africa, 31 700 in Latin America and the Caribbean, and 159 800 in Asia (1, 2). Invasive cancer of the cervix is considered to be a preventable condition, given that it is associated with a long pre-invasive stage, making it amenable to screening and treatment as long as it is detected early and managed effectively (4,5).

Cancer of the cervix has been classified as an acquired immune deficiency syndrome (AIDS) defining cancer by the US Centers for Disease Control and Prevention (6).

As more women contract the virus, the risk of cervical squamous intra-epithelial lesions (SIL) or cervical intra-epithelial neoplasia and ultimately cervical cancer increases (7).

Human papillomavirus (HPV) is known to play an important etiological role in the development of cervical cancer. HPV genotypes that have only rarely

or not been found in invasive cancer of the cervix are defined as low risk types they include HPV 6 and HPV 11. High-risk types, such as HPV (16, 18, 45, 31, 33, 45, 52, 58, 35, and 51) are among most common types found in invasive cervical cancers and are the main factors implicated in cervical carcinogenesis (8).

Factors that contribute to the development or cervical cancer after infection with HPV include immunosupression. Immunosuppression by HIV infection is a strong risk factor for abnormal cytology (SIL). Immunocompromised individuals such as transplant recipients and human immunodeficiency virus-infected individuals are more prone to HPV infections and HPV-associated diseases (9).

In immunocompetent individuals, HPV infections normally clear in six to twenty-four months in 70% of females (10). The natural history of HPV infection is altered in persons infected with the human immunodeficiency virus (HIV) and there is an increased likelihood of persistent HPV infections in this population. This persistent infection increases their risk of having cervical dysplasia and cervical intraepithelial neoplasms (CIN).

Primary prevention of cervical cancer involves prevention of HPV infection. Preventing HPV infection is important in preventing cervical cancer because almost all cervical cancer cases are caused by HPV, a virus transmitted through sexual contact (11). Primary prevention can be achieved through; Behavioural change approaches and the use of biological mechanisms, including HPV vaccination (Gardasil and Cervirex).

Secondary prevention aims at preventing invasive cervical cancer by detecting and treating pre-cancerous lesions of the cervix before they progress to cancer. Cervical cancer is the most effectively controlled by screening through cervical cytology (pap smear) compared to other cancers because pre-cancerous lesions are detected and treated (3).

MATERIALS AND METHODS

The study was done at Rwanda Military Hospital. Rwanda Military Hospital is the largest Hospital located in Kicukiro District of Kigali city. Consent was obtained from all participants and no incentives were given to study the subjects. The sample size was 293. The study population comprised of all HIV-positive women, 18-69 years who had been or were sexually active and were attending the HIV-clinic and consented to participate in the study.

Women on their routine follow up for HIV who met the inclusion criteria and consented to participate in the study were screened for cervical cancer using conventional pap smear. Pregnant and post-natal mothers were excluded from our study.

Study participants from their routine HIV clinic were referred to the study room, the study was explained to them, those who were found to be eligible and were willing to participate in the study were recruited. The data were coded and were analysed using EPI info version 6.

RESULTS

A total of 293 women were enrolled in the study. The mean age of our participants was 36.3 (SD 8.2). Youngest was 19 years and the oldest was 59 years. Majority of the women 127 (43.3%) were aged between 30-39 years. Majority of our study participants 257(87.7%) had sexual debut after 16 years with a mean age at sexual debut of 18.9. Most participants 251(85.7%) in our study had more than one sexual partner and those who had more than four lifetime sexual partners were the majority155 (52.9%). Majority of the patients 225(76.8%) were on follow up for more than four years and 171(58.4%) were on follow up for more than six years.

Table 1
Socio-Demographic Characteristics

Factor	N	% (95% CI)	Mean (SD)
Age			
< 20	1	0.3 (0.0 - 1.0)	
20 - 29	68	23.2 (18.3 - 28.1)	
30 – 39	127	43.3 (37.6 - 49.1)	36.3 (8.2)
40 – 49	78	26.6 (21.5 - 31.7)	
50 - 59	19	6.5 (3.6 - 9.3)	
Total	293		
Age at 1st Sexual Intercourse			
< 16	36	12.3 (8.5 - 16.1)	
16+	257	87.7 (83.9 - 91.4)	18.9 (3.6)
Total	293		
Number of lifetime Sexual Partners.			
1	42	14.3(10.3 - 18.4)	
2-3	96	32.8 (27.4 - 38.2)	4.2 (3.8)
4 +	155	52.9 (47.2 - 58.7)	
Total	293		
Duration since diagnosis of HIV (yrs)			
< 1	5	1.7 (0.2 - 3.2)	
2-3	63	21.5 (16.8 - 26.2)	
4-5	54	18.4 (13.9 - 22.9)	6.9 (4.0)
6+	171	58.4 (52.7 - 64.0)	
Total	293		
Ever Been screened for			
Cancer of the cervix.			
Yes	2	0.7 (0.0 - 1.6)	
No	291	291 (99.3 - 100.0)	-
Total	293		

Only two out of 293 patients had had cervical cancer screening done prior to this research and neither of two knew about her results.

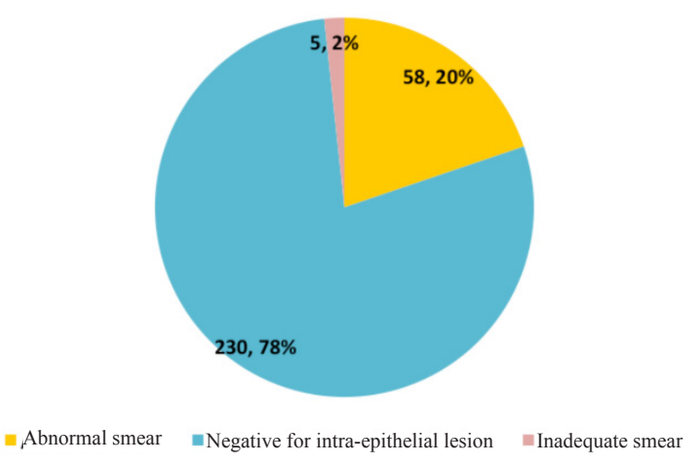
Table 2
Clinical findings

Finding	N	% (95% CI)	Mean (SD)
Initial CD4 Count			
< 200	143	48.8 (42.8 - 54.7)	223 (162)
200 +	150	51.2 (45.3 - 57.2)	
Total	293		
Current CD4 Count			
< 200	21	7.2 (2.7 - 7.9)	497 (209)
200 +	272	92.8 (92.0 - 97.3)	
Total	293		
WHO Staging			
I	217	74.1 (69.0 - 79.1)	
II	31	10.6 (7.0 - 14.1)	
III	37	12.6 (8.8 - 16.5)	-
IV	8	2.7 (0.9 - 4.6)	
Total	293		
On ART			
Yes	284	96.9 %	
No	9	3.1 %	
Total	293		

The mean CD4 count was 223 (SD 162) at the beginning of follow up with 143 (48.8%) patients having CD4 count less than 200/mm^3 and the current mean CD4 count was 497 (SD 209) with only 21 (7.2%) having CD4cell count less than 200/mm^3.

Majority of our patients 217 (74.1%) in this study were in WHO HIV/AIDS class 1 at the time of the study. Most of the patients 284 (96.9%) were on HAART during the time of the study.

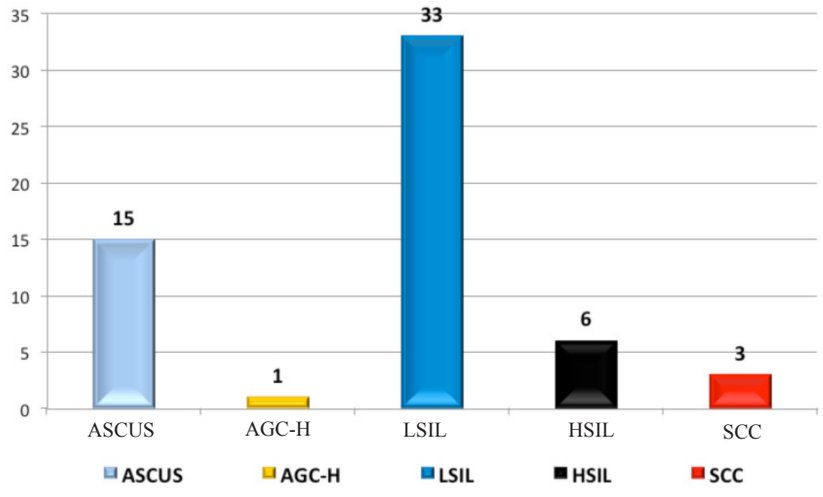
Figure 2
Prevalence of abnormal cytology



A total of 293 women were enrolled in the study. Five were excluded from the analysis due to inadequate smear or missing cervical cells at all.

The prevalence of cervical cytology abnormalities in this research was 58 out of 288 (20%) with LSIL being the most prevalent at 33 out of 288 (11.30%), ASCUS 15 out of 288 (5.13%), HSIL 6 out of 292 (2.05%), SCC was seen in 3 out of 288 (1.02%) and lastly AGC-H was 1 out of 288 (0.34%).

Figure 3
Bethesda classification N=58%



Cervical cytology abnormality

LSIL was the most common lesion seen among the abnormal Pap smears.

Table 3
CD4 cell count and abnormal Pap smear, N = 288, P value = 0.033

	Abnormal Pap smear		Negative for IE lesion		P value	OR(95%CI)
	Freq	%	Freq	%		
Current CD4 count						
<200 cells/mm³	8	13.8	13	5.7		
> 200 cells/mm³	50	86.2	217	94.3	0.033	2.7(1.1-6.8)

Women whose current CD4+ cell count was less than 200 cells/mm³ were 2.7 times more likely to have abnormal pap smear than women whose current CD4+cell count was above 200 cells/mm³ [Odds ratios (OR) = 2.7,95% CI (1.1-6.8)]. P = 0.033

Table 4
WHO-HIV classification and abnormal smear, N=288, P Value = 0.705

		Abnormal cytology		Negative for intraepithelial lesion	
		Freq	%	Freq	%
Who-HIV classification	i.	46	79.3	168	73.0
	II.	6	10.3	24	10.4
	III.	5	8.6	32	13.9
	IV.	1	1.7	6	2.6

The association between WHO-HIV classification and abnormal Pap smear was not found to be statistically significant. P value = 0.705.

Table 5
Other variables

	Results					
	Positive		Negative		p-value	OR (95% CI)
	Freq	%	Freq	%		
Age						
< 30	15	25.9	53	23.0		
30+	43	74.1	177	77.0	0.851	1.2 (0.6 - 2.3)
On ART						
Yes	54	93.1	225	97.8		
No	4	6.9	5	2.2	0.065	0.3 (0.1 - 1.2)
Age at first sexual intercourse						
< 16	7	12.1	29	12.6		
16+	51	87.9	201	87.4	0.912	0.9 (0.4 - 2.3)
No. of Sexual Partner						
1	7	12.1	35	15.2		
1+	51	87.9	195	84.8	0.544	0.8 (0.3 - 1.8)
Duration since diagnosis						
1 - 3	11	19.0	54	23.5		
4+	47	81.0	176	76.5	0.462	0.8 (0.4 - 1.6)

There was no statistically significant association between the variables in the table above (Table 5) and abnormal Pap smear.

DISCUSSION

During the early days of the HIV epidemic, HIV-infected women who had cervical human papillomavirus infection and SIL frequently died of AIDS well before developing invasive cervical cancer (12). However, following the introduction of HAART, the clinical course of HIV has been substantially prolonged, making HIV-infected women a clinically significant group of patients who have an increased risk of acquiring human papillomavirus infection and developing SIL and invasive cervical cancer (13).

According to the World Health Organization (WHO), invasive cervical cancer (ICC) is the second most common cancer in women worldwide and is more frequent in low income countries (14). Recent guidelines recommend that, following two initial normal Pap-smears at a six month interval, all HIV-positive women should undergo annual cervical cytologic examination. In addition, it is recommended that all immunosuppressed women with atypical squamous cells undergo colposcopy (15). This study provides the first comprehensive analysis of the prevalence of cervical cytological abnormalities in this population at Rwanda Military Hospital.

The prevalence of cervical cytology abnormalities in our study was (20%) 58/288, (Figure 1). This is comparable to 21.3%(60/280) as documented in the study done in Thailand by Pimpika Tansupswatdikul, Somkid Piyaman MD *et al* in 2009 which was aimed at establishing prevalence of abnormal cervical cytology from Pap smear in HIV-infected women (16).

The reported prevalence in this study is however higher than the 2.9% and 13.3%, 10.9% reported by Kapiga *et al* (17) among HIV-seropositive pregnant women in Tanzania, Chalermchockcharoenkit *et al* in Thailand and Anorlu in Nigeria (18, 19) among HIV-infected women by postpartum Papanicolaou smear.

However, other researchers have reported higher prevalences in Africa involving HIV-positive women; In Makurdi, Nigeria (57.7%) (12), Tanzanian 28% (20) and South African 31% (21), Kenya (46%) (22).

The prevalence of cervical cytology in the Rwandan general population in not known but the World Health Organization ranks Rwanda among the countries worldwide with the highest cervical

cancer incidence, estimated at 34.5/100,000 (IARC 2008).

CD4 Cell count: Immunosuppression by HIV infection is a strong risk factor for abnormal cytology (SIL). In this study, 48.8% of HIV-positive women had baseline CD4 counts less than 200 cells/mm^3, which is diagnostic of immunologic AIDS. Prolonged CD4 lymphopenia in patients infected with HIV results in defective T-cell proliferation regardless of the current CD4 count or viral load (23). Davis *et al* reported that the strongest predictor of genital dysplasia was a nadir CD4 and CD4 count less than 200 cells/mm^3 (7).

The effect of HAART on the prevalence of SIL has not been significant or it has remained unchanged (24). Similarly in this study, the use of HAART was not associated with a significant reduction in the risk of SIL.

In conclusion, a high prevalence (20%) of cervical cytology abnormality was found among HIV infected women at Rwanda Military Hospital, Rwanda. Decreased CD4 cell counts were associated with abnormal Pap smear. CD4 cell counts less than 200 cells/mm^3 was significantly associated with positivity of the cervical cytology. There was no statistically significant association between WHO stage and abnormal Pap smear.

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