

Progression and Regression of Pre-malignant Cervical Lesions in HIV-infected Women from Soweto: A Prospective Cohort

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Background

Cervical neoplasia is a leading cause of cancer death in sub-Saharan Africa. The association between HIV and cervical cancer is well documented; pre-malignant disease is more frequent, of a higher grade, and more likely to persist and progress in HIV-infected women. The natural history of squamous intraepithelial lesions (SILs) and the impact of ART is poorly reported in high HIV prevalence settings. This data will help inform screening intervals, ART commencement and the potential benefits of HPV vaccination

Objective

To report the incidence, progression and regression of pre-malignant lesions in HIV-infected women.

Methods

Women in pre-ART care and women receiving ART are offered annual cervical smears as part of a larger package of HIV primary care in Soweto, South Africa. Care includes: co-trimoxazole preventive treatment, symptom screening and investigation of TB, symptom screening and treatment of STI's, treatment of HIV-related illnesses and ongoing immune monitoring with initiation of ART at CD4 counts of <200 or WHO stage 3 or 4. Cervical smears are reported by an accredited laboratory using the Bethesda System. Women with high-grade lesions or worse are referred for colposcopy and assessment for possible loop excision of the transformation zone. For this study, we included any woman who had at least one smear in the prevalence calculation and any women with at least two smears to assess incidence, progression and regression. Analysis of progression included smears at least 5.5 months apart, and of regression at least 11 months apart.

Results

2,533 women are in the Wellness program, 76.8% (n=1,951) had at least one determinantal cervical smear and 30.0% (n=763) had more than one smear greater than 5.5 months apart.

Baseline Characteristics of women who had at least one smear vs. those who did not			
	No smear	At least one smear	P value
Median Age at entry into cohort	32.3	32.6	0.70
Median CD4 count	245	328	0.00*
Median BMI	24.8	25.2	0.19
Ever had STI at baseline	50.7%	53.4%	0.25
% who always use condom with regular partner	56.6%	59.5%	0.20
% who always use condom with casual partner	5.9%	4.9%	0.32
Ever Smoked	22.0%	14.2%	0.00*

Prevalence of pre-malignant lesions of the cervix in HIV-infected women at their first smear		
	N	Prevalence (95% CI)
Normal	1,155	59.2 (57.0-61.3)
ASCUS	72	3.7 (2.9-4.5)
LSIL	367	18.8 (17.1-20.5)
ASC-H	21	1.1 (0.6-1.5)
High grade	334	17.1 (15.4-18.8)
Invasive cancer	0	0

Acknowledgements

The women who participated in the study. A grant from PEPFAR through USAID funds care and treatment people in this cohort. A Fogarty ATRIP grant for research training in HIV/AIDS related malignancies provided analytical training. The primary care nurses and other research staff at PHRU who collect the data. Our collaborators at Chris Hani Baragwanath Hospital who we refer patients for colposcopy and LLETZ.

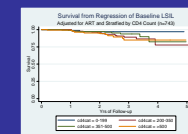
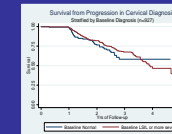
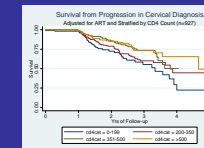
		Progression/Regression at subsequent smear (per 100py)				Overall incidence of SIL
		Normal	ASCUS	L-SIL	ASC-H/HSIL	
Smear at entry to cohort	Normal	-----	1.1 (0.7-1.9)	9.1 (7.6-11.0)	2.8 (2.0-3.9)	0
	LSIL	17.5 (13.1-23.2)	-----	---	14.4 (10.6-19.6)	0
						11.7 (9.9-13.8)

Predictors of Progression			
Based on 161 cases of progression	Progression Rates (per 100 PY) n=927	Univariate Hazard Ratio (95% CI) n=927	Multivariate Hazard Ratio (95% CI) n=927
Overall	11.4 (9.7-13.3)	NA	NA
CD4 count <200	17.9 (12.9-24.8)	2.19 (1.33-3.59)	2.27 (1.38-3.72)
200-350	12.6 (9.8-16.2)	1.47 (0.94-2.29)	1.55 (0.99-2.43)
351-500	8.8 (6.3-12.3)	1.05 (0.64-1.74)	1.10 (0.66-1.81)
>500	8.5 (5.9-12.4)	Ref.	Ref.
ART YES	10.7 (9.7-13.6)	0.78 (0.51-1.21)	0.87 (0.56-1.36)
ART NO	11.5 (9.7-13.6)	Ref.	Ref.
Age For every increase 5 yrs	-----	0.83 (0.74-0.94)	0.83 (0.74-0.94)
Smoking Yes	12.7 (8.6-18.8)	1.11 (0.73-1.71)	1.11 (0.72-1.71)
No	11.1 (9.4-13.2)	Ref.	Ref.

In another model with age as a categorical variable, women under 35 years were at increased risk for LSIL.

Change from Baseline LSIL (n=191)	N	%
Regression	47	24.60%
Progression	38	19.90%
Remained LSIL at 2 nd Visit (>1 yr later)	106	55.50%

Proportion with Incident HSIL after Normal, ASCUS or LSIL at Baseline (n=682)
83 (12.2%)
Proportion with Incident LSIL, or worse after Normal at baseline (n=544)
157 (28.9%)



Conclusions

HIV-infected women have high rates of prevalent and incident HSIL and LSIL with low risk of regression of LSIL. CD4 count <200 and younger age is associated with progression. ART did not appear to confer protection against progression. Earlier initiation of screening, shorter screening intervals in women with CD4 counts <200, and more proactive management of LSIL should be tested. Our results add urgency to improving access to an affordable, effective HPV vaccine.