

The Association Between HIV Status and Cervical Neoplasia as Detected in a See-and-Treat Program in Lusaka, Zambia

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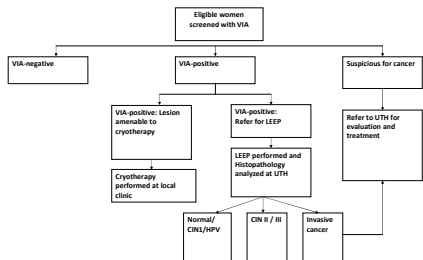
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Background

- Zambia has the second highest incidence and mortality from cervical cancer in Africa and the 6th highest in the world
- Cervical cancer is the most common malignancy diagnosed in Zambian women and their leading cause of cancer-related death
- Previous research has shown that HIV positive women are at higher risk of developing cervical neoplasia than their HIV negative counterparts
- The HIV prevalence in Zambia is 16-25% and two-thirds are women
- The impact of HIV and antiretroviral therapy (ART) on the development and progression of microinvasive and invasive cervical cancer (ICC) is controversial

Setting

- In January 2006, a see and treat cervical cancer prevention program was established in Lusaka, Zambia
- In the see and treat program nurses apply acetic acid to the cervix for 3 minutes and visually inspect for signs of neoplasia
- Nurses offer same day cryotherapy to eligible clients
- Patients with cervical lesions that were complex or suspicious for cervical cancer (ICC) underwent histological evaluation



Analytic Methods

- We determined the statistical association between HIV status and histological diagnoses using the Pearson chi-square test statistic and logistic regression
- We included variables in the multivariate model that met a significance level of less than 0.01 as well as other known factors related to both cervical cancer and HIV
- All statistical analyses were completed in SAS 9.1

Results

- 14,239 women were screened between January 2006 and August 2008
- 922 women underwent histological evaluation
- Of the women who underwent histological evaluation, 748 were tested for HIV
- Of the women tested for HIV, 75% were HIV positive
- Of the HIV positive women, 51% were taking ART at the time of evaluation
- Median CD4 count among HIV infected women:
 - ART naive: 346
 - ART experienced: 349
 - Overall: 348

Pathological Outcomes Stratified by ART History

	ART experienced n=268	ART Naive n=299
Normal, n _i (%)	21 (8%)	21 (7%)
Benign, n _i (%)	38 (14%)	47 (16%)
CIN 1, n _i (%)	79 (29%)	96 (32%)
CIN 2/3, n _i (%)	79 (29%)	80 (27%)
Cervical Cancer, n _i (%)	51 (19%)	55 (18%)
• Microinvasive Cancer, n _i (%)	39 (15%)	42 (14%)
• Invasive Cancer, n _i (%)	12 (5%)	13 (4%)

Pathological Outcomes Stratified by HIV Serostatus

	HIV positive n=567	HIV negative n=181
Normal, n _i (%)	42 (7%)	19 (11%)
Benign, n _i (%)	85 (15%)	33 (18%)
CIN 1, n _i (%)	175 (31%)	53 (29%)
CIN 2/3, n _i (%)	159 (28%)	37 (20%)
Cervical Cancer, n _i (%)	106 (19%)	39 (22%)
• Microinvasive Cancer, n _i (%)	81 (14%)	17 (9%)
• Invasive Cancer, n _i (%)	25 (4%)	22 (12%)

Multivariate Analysis for CIN2/3, Microinvasive, and Invasive Cervical Cancer

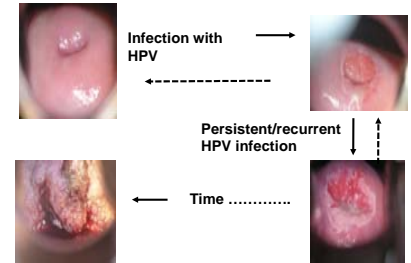
	CIN2/3 n=230	Cervical Cancer n=187	Microinvasive n=116	Invasive n=71
HIV seropositivity	1.90(1.14,3.15)	0.72(0.47,1.09)	1.58(0.80,3.09)	0.31 (0.14, 0.86)
<=3 lifetime sexual partners	0.95(0.65,1.38)	0.84(0.42,1.71)	0.71 (0.43, 1.17)	0.85 (0.42, 1.72)
Age 35-44 years (compared to <=34 years)	0.82(0.54,1.22)	1.59(1.02,2.49)	1.32 (0.79, 2.19)	2.19 (0.99,4.87)
Age >=45 years (compared to <=34 years)	0.82(0.42,1.62)	1.72(0.87,3.42)	0.42 (0.12, 1.44)	5.89 (2.32, 14.97)
Vaginal Itching	1.11(0.76,1.62)	0.91(0.59,1.41)	0.89 (0.54, 1.49)	1.04 (0.50, 2.15)
Never used condoms with regular partner	0.69(0.43,1.12)	0.79(0.45,1.37)	1.16 (0.69, 1.93)	0.78 (0.38, 1.64)
Married, cohabiting husband	1.01(0.69,1.48)	1.21(0.79,1.86)	1.39 (0.84, 2.32)	0.83 (0.41, 1.67)
Income (<=500,000 K)	0.94(0.63,1.38)	1.33(0.86,2.05)	1.60 (0.96, 2.65)	0.88 (0.43, 1.83)

The Sociodemographic and Clinical Variables of Women Tested for HIV

	HIV positive n=567	HIV negative n=181
Age (years) Mean(±SD)	33.46(+7.16)	33.65(+9.44)
Number of lifetime sexual partners Median(range)	3(0-90)	3(1-14)
Married, cohabiting husband, n _i (%)	286(51%)	123(69%)
Never used condoms with regular partner, n _i (%)	220(39%)	109(60%)
Vaginal/Vulval Itching, n _i (%)	224(41%)	56(32%)
Income <=500,000 K, n _i (%)	330(69%)	75(54%)
Age at menarche (years) Mean(±SD)	14.59(+1.76)	14.76(+2.40)
Age at first sex (years) Mean(±SD)	17.44(+2.81)	17.81(+2.90)
Time between age at menarche and age at first sex (years) Mean(±SD)	3.00(+2.62)	3.15(+2.89)
Time sexually active (years) Mean(±SD)	15.87(+7.35)	15.61(+9.44)
Number of pregnancies Median(range)	3(0-13)	3(1-12)
Number of live births Median(range)	3(0-12)	3(0-11)
Educated at primary school and below, n _i (%)	242(45%)	69(42%)

Interpretation

- The relationship between HIV and CIN 2/3 is well-documented and is thought to be due to HIV-induced modulation of the immune response to human papillomavirus (HPV)
- The association between HIV and ICC could possibly be explained by the limited role of the immune system and the more prominent role of genetic alterations in the progression of CIN2/3 to ICC
- Time from HPV infection to the development of invasive cervical cancer may dictate disease progression



Conclusions

- HIV positive women in Zambia are more likely to be diagnosed with cervical intraepithelial neoplasia (CIN2/3), but are less likely to be diagnosed with invasive cervical cancer (ICC)
- Our findings may reflect the possibility that HIV positive women are dying from other AIDS-related illnesses before developing ICC
- Studies have suggested that as women in resource-constrained environments, like Zambia, continue to gain access to antiretroviral therapy and live longer, their risk for developing cervical cancer will increase
- Our study confirms this association between invasive cancer and older age
- This study underscores the importance of routine cervical cancer screening in women receiving HIV care and treatment

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