

# A pilot study to compare HIV status, cervical and penile pathology among couples attending the urology unit at the University Teaching Hospital Lusaka, Zambia

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## ABSTRACT

**Background:** Cancer of the cervix is the most common malignancy in women of childbearing age in Zambia. It is known to be associated with HIV infection and oncogenic strains of HPV. However, there are few studies of penile lesions as a predictor of malignant and premalignant cervical lesions in female partners.

**Objectives:** The aim of the study was to determine the association between men with penile lesions and premalignant cervical lesions in their female partners.

**Design:** Thirty-seven couples were screened for penile and cervical lesions to determine the association between the two. The male partners had a biopsy and the female partners had a Pap smear.

**Results:** Among 37 female partners, 29 (78.3%) had some type of cervical lesion. Two (5.4%) were undetermined and 6 (16.3%) of the females had normal Pap smears. Among the spouses with diseased cervixes 22 (59.4%) were premalignant and 5 (13.5%) were malignant. The combined prevalence of malignant or premalignant cervical lesions among female partners was 73.0%. The HIV prevalence in the cohort was 88.9% (among those

who agreed to be tested). The prevalence of premalignant or malignant cervical lesions was 75% in HIV positive and HIV negative females, and 66.7% in those who refused HIV testing.

**Conclusion:** This small pilot study suggests a high prevalence of premalignant or malignant lesions in females whose partners have penile lesions. In this cohort, HIV infection was not associated with a higher risk of neoplastic cervical lesions.

## INTRODUCTION

The University Teaching Hospital Lusaka is the main national referral hospital in Zambia. It has an immediate catchment area of 2.5 million and a national catchment area exceeding 10 million. Cancer of the cervix is the leading cancer seen at the University Teaching Hospital; it represents 29% of all cancers seen in the hospital over the last 10 years<sup>1</sup>. Studies of women seen at the hospital show a high incidence of oncogenic HPV strains 16 and 18<sup>2</sup>. There is a high prevalence of STIs of about 8% in the national population<sup>3</sup>. It is likely that the high incidence of STIs and penile lesions are some of the factors responsible for an increasing incidence of cancer of the cervix. There is high national HIV prevalence of 14.3%; there is also a high HIV prevalence of 69% among patients with STIs and of 45% among women with cervical cancer in Zambia<sup>4</sup>.

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## OBJECTIVES

The purpose of the study was to determine the association between men with penile lesions and premalignant cervical lesions in their female partners

The primary objective was to determine the proportion of spouses with precancerous cervical lesions. The secondary objective was to determine the prevalence of HIV among this sub-population.

## METHODS

Patients presenting to the urology clinic from 1<sup>st</sup> January 2006 to 31<sup>st</sup> December 2006 with any pathological penile lesions were recruited into the study. A penile lesion was defined as a macroscopically visible acquired non traumatic lesion on the glans, prepuce or penile shaft. Penile lesions were grouped into 1 of 4 categories based on clinical and histological diagnosis: penile ulcers, penile warts/infections, benign penile lesions and malignant penile lesions. Similarly, cervical lesions were graded based on histopathology findings as CIN (Cervical Intraepithelial Neoplasms) 1 to 3, CIS (Carcinoma in Situ) or invasive cancer of the cervix using the grading system of the Royal College of Pathologists. For inclusion into the study, the index patient had to have a spouse or a regular female partner. A regular female partner was defined as someone with whom the client had regular sexual contact in the last 6 months.

The index patient and his partner were both recruited into the study. Informed consent was obtained from male and female participants. Social demographic information was obtained from the couple and an HIV test was done using the Ministry of Health test guidelines<sup>5</sup>. The male client had a biopsy of the lesion done and the spouse had a Pap smear. Routine Hematoxylin and Eosin (H&E) staining was used in both cases. The specimens were labeled, processed and reported by a single consultant pathologist on the study team. The analysis was done by couple to correlate serostatus with presence of cervical lesions in the female partner. Subtyping of HPV was done through PCR using the standard techniques<sup>2</sup> in a collaborating laboratory in the U.S. Though the yield was low and therefore not included in the study

The odds of acquiring precancerous lesions in this population was calculated as the proportion of spouses with cervical lesions over the total number of spouses in the study. The couples prevalence of HIV was calculated as the total number of HIV-positive couples over the total number of couples in tested. Using Stata software version 11.0, the Pearson correlation coefficient was determined to show relationships between severity of penile lesions and cervical lesions. Linear regression was used to determine significance of association. The study was approved by the University of Zambia Biomedical Research Ethics Committee (UNZA REC).

## RESULTS

There were a total of 37 couples. The age range was 23 to 66 years. The average male age was 36 years, while the average female age was 31 years.

The penile lesions were categorized into 4 groups; penile ulcer, penile warts/infection, benign penile tumors, and malignant penile tumors. The most common penile lesions in the cohort were penile warts (18) (48.7%) followed by cancer of the penis (9) (24.3%).

**Figure 1:** Description of the penile lesions of the male partners

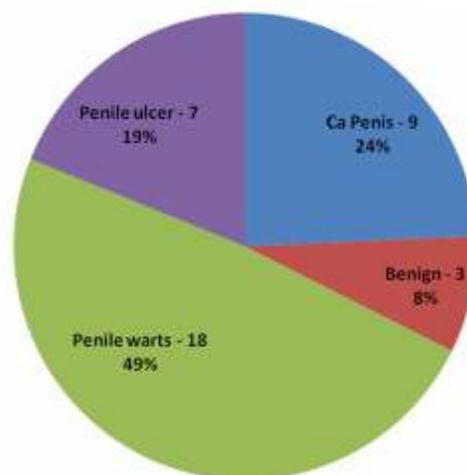
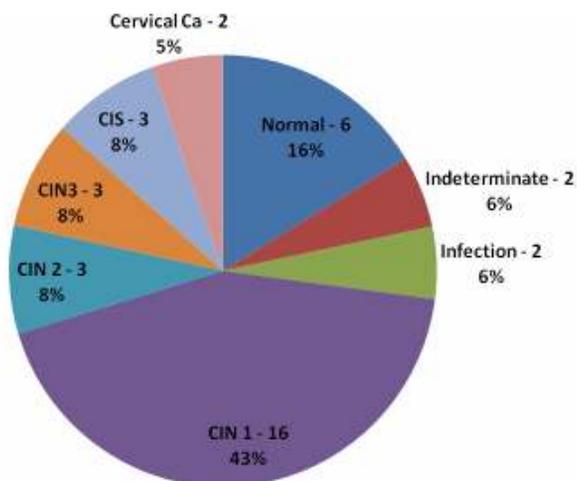


Figure 2 shows the cervical lesions categorized into 8 groups. Five categories signified malignant or premalignant cervical disease (CIN 1-3, CIS, and Ca Cx). The most common cervical lesion was CIN 1 (43.2%). A total of 29 (78.3%) female partners had cervical lesions. Six (16.3%) female partners had

normal Pap smears. Twenty-seven (72.9%) of these female partners had malignant or premalignant cervical diseases. Two (5.4%) had an indeterminate result (loss of materials or failure of processing).

**Figure 2:** Description of cervical lesions



CIN= Cervical intraepithelial neoplasm  
CIS= Carcinoma in situ

Twenty-seven (72.7%) couples agreed to be tested for HIV. Among the couples tested, 23 pairs (85.2%) were HIV-positive. Two (7.4%) were discordant and two (7.4%) were negative. The lesions and the HIV status were examined for each sex separately (Tables 1 and 2). Twenty-five (93%) of 27 men were HIV positive, including 100% of those with cancer of the penis. The HIV prevalence was equal (85.7%) for women with cancer/precancerous lesions (18 of 21) and those with normal, infectious, or indeterminate results (6 of 7). Among the women who were HIV-positive, 18 (75%) had malignant or pre-malignant cervical lesions. Three HIV-negative women had pre-malignant cervical lesions (75%), including 2 with CIN 2 and 1 with CIN 3, but there were no cancers in this group.

**Table 1:** HIV Status and penile lesions

|                         | HIV positive | HIV negative | Not Tested | Total     |
|-------------------------|--------------|--------------|------------|-----------|
| Penile Ulcers/Infection | 6            | 0            | 1          | 7(18.9%)  |
| Penile Warts            | 9            | 2            | 7          | 18(48.6%) |
| Benign penile lesion    | 1            | 0            | 2          | 3( 8.2%)  |
| Cancer of the Penis     | 9            | 0            | 0          | 9(24.3%)  |

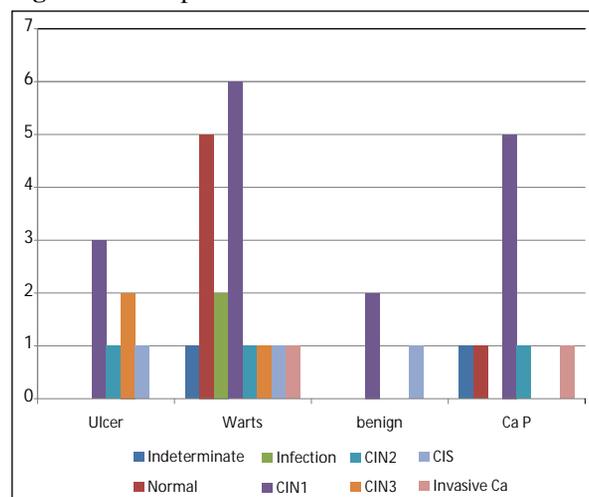
**Table 2:** HIV status and cervical lesions

|                 | HIV positive | HIV negative | Not Tested | Total      |
|-----------------|--------------|--------------|------------|------------|
| Normal          | 4            | 0            | 2          | 6 (16.3%)  |
| Indeterminate   | 1            | 1            | 0          | 2 (5.4%)   |
| Infection       | 1            | 0            | 1          | 2(5.4%)    |
| CIN 1           | 12           | 0            | 4          | 16 (43.2%) |
| CIN 2           | 1            | 2            | 0          | 3(8.1%)    |
| CIN 3           | 2            | 1            | 0          | 3(8.1%)    |
| CIS             | 2            | 0            | 1          | 3(8.1%)    |
| Cervical Cancer | 1            | 0            | 1          | 2 (5.4%)   |

CIN= Cervical intraepithelial neoplasm  
CIS= Carcinoma in situ

Figure 3 shows the distribution of cervical lesions based on the types of the partners' penile lesions. The Pearson correlation coefficient was 0.047, and the test of statistical significance showed this was not significant (p=0.8).

**Figure 3.** Descriptions of Nature of Cervical Lesions



**DISCUSSION**

About 490,000 women are newly diagnosed and 274,000 women die worldwide from invasive cancer of the uterine cervix induced by oncogenic types of human papillomavirus (HPV). In Zambia, cancer of the cervix is the most common cancer, with an incidence of 67.1 per 100,000 per year<sup>1,6</sup>. The risk of male to female transmission has not been well studied. Some studies have looked at the relation between women with cervical lesions and assessed the incidence of HPV-induced lesions in their male partners<sup>7</sup>. The risk to men of penile lesions appear to

be less than the risk to women; this risk is given as 68%<sup>7</sup>. This may be due to the differences in epithelial surfaces in the two sites.

Though the sample is small and the results are preliminary, some interesting discussion points are raised by the study. The results showed a mean age typical for men and women presenting with cervical and penile lesions<sup>3,4,5</sup>. There was a high proportion of cervical lesions in the study cohort of 78.3%. This is higher than the findings demonstrated by other studies which have looked at cervical lesions in women and studied the risk of penile lesions in their male spouses. The study found a high proportion of premalignant and malignant lesions in female partners (72.9%). Studies done in Zambia have shown a high HIV HPV co-infection in antenatal women in at the University Teaching hospital Lusaka<sup>3,7,8</sup>. The HIV infection suppresses cellular immunity, which plays a key role in clearance of HPV infection. HPV infection is common in the general population and even more so in HIV-infected populations<sup>3,7,8</sup>. The intense counseling and the fact that couples were already in a clinic setting with a disease may have motivated them to agree to testing. The study showed 5.4% of the couples were discordant; this is lower than the 20% found in the general population. This may be because the sample was small and consisted of a high risk subpopulation of couples<sup>9</sup>. The HIV prevalence was also high at a rate of 85.2%. This is much higher than the population prevalence of 14.3% and the prevalence among STI clients of 69%<sup>4</sup>. The high prevalence of co-infection with HPV and possible ulcerative lesions could indicate both high risk behavior and potentiation of HIV transmission, though a larger study would be needed to confirm this.

In Zambia, there is a high prevalence of oncogenic strains of HPV compared to elsewhere<sup>2,6,7</sup>. There is a high prevalence of HIV infection and STIs. The level of risk is higher than that anticipated by the researchers and suggests that HPV, ulcerative STI, and HIV increases the risk of premalignant and malignant cervical lesions in female spouses of men with penile lesions. The study analyzed the dose response relationship to determine whether the severity of the penile lesion correlated with the severity of the cervical lesion. It is likely a larger sample is required to show such a relationship.

Male circumcision has been shown to reduce penile lesions and HPV colonization<sup>10</sup>. In view of screening programs for cervical cancer, which have been started in selected centers by the Ministry of Health in Zambia, male circumcision may be recommended to male partners of women with existing cervical lesions as a means of ameliorating this risk.

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