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Prevalence and Correlates of Genital Warts in Kenyan Female Sex Workers

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Abstract

Background—Our goal in the present study was to investigate the prevalence and correlates of genital warts in a population of female sex workers in Mombasa, Kenya. Because of the high prevalence of HIV-1 in this population, we were particularly interested in the association between HIV-1 infection and genital warts.

Methods—We conducted a cross-sectional study of the prevalence and correlates of genital warts among high-risk women in Mombasa, Kenya. Between 2001 and 2007, 1182 women were enrolled, of whom 613 (51.4%) were HIV-1-seropositive. Chi square tests and logistic regression were used to examine the associations between genital warts and potential correlates.

Results—Genital warts were identified on clinical examination in 27 (2.3%) women. Women who were HIV-1-seropositive were nearly 8 times as likely to have genital warts compared to HIV-1-seronegative women (OR 7.69, 95% CI 2.30–25.6).

Conclusion—Understanding the prevalence and correlates of genital warts will help to determine whether coverage for the wart-inducing subtypes 6 and 11 in an HPV vaccine is an important consideration in resource-limited countries.

Keywords

genital warts; human immunodeficiency virus; human papilloma virus; Africa

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Conflicts of Interest:
All authors claim no conflict of interest.

Introduction

Sub-Saharan Africa has a high prevalence of both human immunodeficiency virus type 1 (HIV-1) and human papillomavirus (HPV).[1, 2] In this context, it is important to note that HIV-1 infection may facilitate transmission and acquisition of HPV,[3,4] as well as the development of clinically evident genital warts in those co-infected with both viruses.[5, 6] Of 140 identified subtypes of HPV, subtypes 16 and 18 cause approximately 70% of cervical cancer, while subtypes 6 and 11 are responsible for approximately 90% of genital warts.[7] Few studies have characterized the prevalence and correlates of genital warts in sub-Saharan Africa, but prevalence is believed to be high in all parts of the world.[8]

Currently, two vaccines are available for HPV prevention. One is bivalent and protects against subtypes 16 and 18 (Cervarix®, GlaxoSmithKline). The other is quadrivalent and protects against infection with subtypes 6, 11, 16, and 18 (Gardasil®, Merck). Both are over 95% effective in preventing cervical cancer, and the quadrivalent vaccine is equally effective in preventing genital warts.[9,10]

Both vaccines have been licensed in parts of sub-Saharan Africa, and pilot projects assessing HPV vaccine acceptability and feasibility have been conducted in the region.[11] At present, only Rwanda has a national policy for HPV vaccination,[12] but other resource-limited countries may find it easier to finance HPV vaccination in the near future. In November 2011, Merck offered a price of $5 per dose for their quadrivalent vaccine to the GAVI Alliance. Discussions are underway with GlaxoSmithKline about reduced pricing options for the bivalent vaccine.[13] With the availability of HPV vaccines that differ mainly in their ability to prevent genital warts, knowledge of the prevalence and correlates of genital warts in sub-Saharan Africa will be useful in program planning. A substantial prevalence of genital warts would suggest that populations in these areas might benefit from vaccination including coverage for the genital wart-associated HPV subtypes.

Our objective was to investigate the prevalence and correlates of genital warts in a population of female sex workers in Mombasa, Kenya. Because of the high prevalence of HIV-1 in this population, we were particularly interested in the association between HIV-1 infection and genital warts.

Materials and Methods

This cross-sectional analysis utilized data from enrollment visits of an open cohort study at a municipal communicable disease clinic in Mombasa, Kenya. Cohort procedures have been published in detail.[14] Briefly, subjects were interviewed for demographic, medical and sexual histories. HIV-1-seropositive and HIV-1-seronegative women were enrolled, regardless of the presence or absence of reported symptoms. A physical examination including a speculum-assisted pelvic examination was performed by an experienced research clinician, and included documenting the presence of genital warts specifically on the vulva, vagina, or cervix. Prior to collecting data independently, research clinicians were mentored in the diagnosis of genital pathology by trained STD clinicians, and a pictorial atlas of STDs was posted in the examination room to aid diagnosis. Patients with lesions that were clinically concerning for cancer or were too large to treat with cryotherapy or podophyllin were referred for surgical consultation. Laboratory screening for HIV-1 and other genital tract infections was performed. This study was approved by the human subjects research committees of Kenyatta National Hospital and the University of Washington. Written informed consent was obtained from all participants.

There were 1252 participants enrolled between March 2001 and December 2007. We excluded 70 (5.6%) women with missing or inconclusive HIV-1 status or genital wart data.

Thus, our analyses included 1182 women. HIV-1 serostatus was determined by enzyme-linked immunosorbent assay (ELISA; Detect HIV1/2, BioChem Immunosystems, Montreal, Canada or PT-HIV 1,2-96, Pishtaz Teb Diagnostics, Tehran, Iran). Positive samples were confirmed using a second ELISA (Recombigen, Cambridge Biotech, Worcester, MA, USA or Vironostika HIV-1 Uniform 11AG/AB, bioMerieux, Marcy l'Etoile, France). A vaginal saline wet mount was examined for the presence of yeast on microscopy. Bacterial vaginosis (BV) was diagnosed by Nugent's criteria.[15]

Analyses were performed using SPSS (version 17.0, IBM) and R (version 2.13, ISBN 3-900051-07-0). The 95% confidence interval (CI) for prevalence of genital warts was estimated by bootstrap sampling. Associations between presence of genital warts and enrollment characteristics were evaluated by univariate Mantel-Haenszel odds ratio estimates with corresponding Chi-square tests. Variables associated with genital warts in univariate analysis ($P < 0.1$) were included in a multivariate logistic regression model. In the multivariate model, age was dichotomized as <=30 or >30, based on the median age of the subjects in the cohort.

The association between CD4 count <200 and presence of genital warts for the subset of HIV-1 positive women was also assessed by Mantel-Haenszel odds ratio estimates, a Chi-square test, and multivariate logistic regression. Potential confounding factors associated with genital warts among HIV-1 positive women in univariate analysis ($P < 0.1$) were included in the multivariate model.

Results

Of the 1182 women enrolled between March 2001 and December 2007, 613 (51.4%) were HIV-1-seropositive. Genital warts were identified in 27 (2.3%; 95% CI: 1.4–3.1%) women. Of these, 20 had vulvar lesions (74%), 13 (48%) had vaginal lesions, and 3 (11%) had cervical lesions. These percentages add up to >100%, as some women had genital warts in multiple locations. The anatomical locations of genital warts did not differ significantly by HIV status (data not shown). Baseline characteristics of the women are presented in Table 1.

Genital warts were observed in 24 (3.9%) HIV-1-seropositive women versus three (0.5%) seronegative women (odds ratio [OR] 7.69, 95% CI 2.30–25.6) (Table 2). There was a higher prevalence of genital warts in women with vaginal yeast compared to those without (OR 2.92, 95% CI 0.95–5.51), although this association was not statistically significant. Results were similar in a multivariate model that included both HIV-1-serostatus and the presence of vaginal yeast.

Among the 518 HIV-1-seropositive women with available CD4 counts, the risk of genital warts was significantly greater among the 104 (20%) women with CD4 <200 compared to those with CD4 ≥200 (OR 2.92, 95% CI 1.08–7.85). The association between CD4 count and the presence of genital warts was similar in an analysis that adjusted for age (OR 3.13, 95% CI 1.14–8.57).

Discussion

The prevalence of genital warts in this population of high-risk women was 2.3%. Women who were HIV-1-seropositive were nearly 8 times as likely to have genital warts compared to those who were HIV-1-seronegative. Among those who were HIV-1-seropositive, genital warts were more common when CD4 counts were <200 cells/μL.

Our results showing a modest prevalence of genital warts among female sex workers in Kenya parallel those across a range of settings in sub-Saharan Africa.[3,4, 16–20] In addition,

our findings are similar to those of studies showing that genital warts are more common with HIV and with progressive immunosuppression.[16–20] This finding may be a result of HIV-1 infection prolonging the duration and increasing the recurrence rate of HPV infection,[5, 21] and suggests that the quadrivalent vaccine could be particularly important as a public health consideration in populations with high HIV-1 infection prevalence. Specifically, where the older girls and young women who would be vaccinated have a high lifetime risk of both HIV and HPV infections, vaccination prior to coitarche using a vaccine that prevents infection with the genital wart associated HPV subtypes could substantially reduce the population-level prevalence of genital warts.

We found a modest association between genital warts and the presence of yeast, which was of borderline statistical significance after adjusting for HIV-1-serostatus. These findings could be explained on the basis of genital warts providing an environment that facilitates local colonization with yeast. In light of the multiple statistical comparisons presented, it should also be noted that this association could have occurred by chance.

One of the strengths of this study was a large sample size. Additionally, our ability to recruit from a population of high-risk women who were invited to the clinic for routine HIV-1 and STI screening may have reduced bias. Female sex workers in this community attended the clinic even when they were asymptomatic. This study design may have reduced the risk for bias towards an over-estimate of the population prevalence of genital warts compared to studies in cohorts presenting primarily because of symptoms, such as STI clinic attendees.

These findings should be interpreted in the context of a number of limitations. The point prevalence of genital warts was modest, so we had limited power to explore correlates. Data on participant complaints regarding genital lesions, the number and morphology of genital warts, anal or perineal warts, or the presence of giant warts (Buschke-Lowenstein tumors), were not collected. While patients with clinically concerning lesions and those too large for treatment with cryotherapy or podophyllin were referred for surgical consultation, we do not have data about their surgical pathology, and did not systematically collect information about post-operative outcomes. No HPV testing was performed. The population in this study included only high-risk women based on self-reported transactional sex. Their HIV-1 prevalence is much higher than that of Kenya generally,[22] and they could also have had a higher risk of HPV. On the other hand, some women with large or numerous genital warts might have been unable to work as sex workers, so would not have presented to our clinic. Finally, cross-sectional design limits any determination of whether HIV-1 infection or HPV was the original infection or whether one increased susceptibility to the other.

These results are timely, given current discussions around selection of HPV vaccines for use in different settings. The cost of the different vaccines will also be an important factor. If there is no difference in cost, then the quadrivalent vaccine would seem to have a clear advantage. However, if the cost of the bivalent vaccine is lower, then the medical and psychosocial costs of genital warts must be weighed against the added cost of the quadrivalent vaccine. Cost effectiveness studies modeling the expected quality-adjusted life-years saved by the quadrivalent versus bivalent vaccine could be beneficial. Whether protection against genital warts influences acceptability and uptake of vaccination in different populations may also be important to consider.

In conclusion, our results demonstrate a modest point prevalence of genital warts in this population of high-risk women, suggesting that their lifetime risk of genital warts may be substantial, consistent with other studies of lifetime prevalence of genital warts in various parts of the world.[23,24] Understanding the prevalence and correlates of genital warts in

different populations will be useful for determining the importance and cost-effectiveness of using a quadrivalent versus bivalent HPV vaccine.

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TABLE 1

Baseline Characteristics of 1182 Female Participants

Characteristic	n (%)
Age >30 years at enrollment	640 (54.1%)
Education ≥8 years	427 (36.1%)
Ever married	738 (62.4%)
Works in a bar *	883 (74.7%)
Ever smoked	145 (12.3%)
Age at first sex <15 years	102 (8.6%)
Unprotected sex (past week)	487 (41.2%)
Yeast present on vaginal wet mount	160 (13.5%)
Bacterial vaginosis by Nugent's criteria	420 (35.5%)
HIV-1 seropositive	613 (51.9%)
Genital warts present on exam	27 (2.3%)

* Women who did not report work in a bar included those who worked in nightclubs (n=127), from home (n=32), or reported an "other" work location (n=140).

TABLE 2

Bivariate and Multivariate Association with Genital Warts (N=1182)

Characteristic	OR (95% CI)	*P*	aOR (95% CI)	*P*
Age >30 years at enrollment	0.78 (0.36–1.68)	0.5	-	-
Education ≥8 years	0.50 (0.19–1.24)	0.1	-	-
Ever married	1.02 (0.46–2.25)	1.0	-	-
Works in bar *	0.97 (0.41–2.31)	0.9	-	-
Ever smoked	2.09 (0.83–5.27)	0.1	-	-
Age at first sex <15 years	2.50 (0.34–18.6)	0.4	-	-
Unprotected sex (past week)	1.14 (0.53–2.47)	0.7	-	-
Yeast present on vaginal wet mount	2.92 (0.95–5.51)	0.06	2.47 (1.01–5.99)	0.05
BV by Nugent's criteria	1.25 (0.58–2.72)	0.6	-	-
HIV-1-seropositive	7.69 (2.30–25.6)	0.001	7.89 (2.36–26.39)	0.001

* Women who did not report work in a bar included those who worked in nightclubs (n=127), from home (n=32), or reported an "other" work location (n=140).

BV, Bacterial vaginosis; CI, confidence interval; OR, Odds ratio; aOR, adjusted Odds Ratio