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HUMAN PAPILLOMAVIRUS AND ABNORMAL CERVICAL LESIONS AMONG HIV-INFECTED WOMEN IN HIV-DISCORDANT COUPLES FROM KENYA

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Abstract

Objectives: HIV infection increases the risk of high-grade cervical neoplasia and invasive cervical carcinoma. The study addresses the limited data describing human papillomavirus (HPV) infection and cervical neoplasia among HIV-infected women in HIV-discordant relationships in sub-Saharan Africa, which is needed to inform screening strategies.

Methods: A cross-sectional study of HIV-infected women with HIV-uninfected partners was conducted to determine the distribution of type-specific HPV infection and cervical cytology. This study was nested in a prospective cohort recruited between September 2007 and December 2009 in Nairobi, Kenya. Cervical cells for HPV DNA testing and conventional cervical cytology were collected. HPV types were detected and genotyped by Roche Linear Array PCR assay.

Results: Among 283 women, overall HPV prevalence was 62% and 132 (47%) had ≥1 high-risk (HR)-HPV genotype. Of 268 women with cervical cytology results, 18 (7%) had high-grade

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Author contribution statement:

B.L.G., A.F.R., C.F., R.B., R.Y.C., J.N.K., and J.S.S. conceived and planned the study. R.B. and R.Y.C. conducted study recruitment and collected specimens. A.F.R., J.A.C., R.B., R.Y.C., and J.S.S. contributed to sample preparation and conducted assays. B.L.G., A.F.R., and J.A.C. planned and carried out the analyses. B.L.G. wrote the manuscript with support from A.F.R., J.A.C., and J.S.S.. All authors provided critical feedback, helped shape the research, analysis and manuscript, and approved the final version to be published.

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cervical lesions or more severe by cytology, of whom 16 (89%) were HR-HPV-positive compared to 82 (41%) of 199 women with normal cytology (p<0.001). Most common HR-HPV types in women with a high-grade lesion or more severe by cytology were HPV-52 (44%), HPV-31 (22%), HPV-35 (22%), HPV-51 (22%), and HPV-58 (22%). HR-HPV genotypes HPV-16 or HPV-18 were found in 17% of women with high-grade lesions or more severe. HR-HPV screening applied in this population would detect 89% of those with a high grade lesion or more severe while 44% of women with normal or low-grade cytology would screen positive.

Conclusion: HR-HPV prevalence was high in this population of HIV-infected women with an uninfected partner. Choice of screening for all HR genotypes versus a subset of HR genotypes in these HIV-infected women will strongly affect the performance of an HPV screening strategy relative to cytological screening. Regional and subpopulation differences in HPV genotype distributions could affect screening test performance.

Keywords

Human papillomavirus; HPV; Kenya; women; cervical cytology; cervical cancer; HIV; HIV-discordant couples

Introduction

Human papillomavirus (HPV) infection is the most common sexually transmitted infection in women worldwide [1]. More than 80% of sexually active adults will be infected with HPV during their lifetime, and most HPV infections present subclinically and are cleared spontaneously [1]. Fourteen HPV types that infect the genital mucosa are classified as high-risk (HR) types: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 [2]. HR-HPV types are the primary cause of invasive cervical cancer (ICC) and are detected in up to 99.7% of ICC cases [3].

Women with HIV are at increased risk of progressing from HPV infection to high-grade cervical precancerous lesions [4], and have an accelerated course from these high-grade lesions to carcinoma [5,6]. ICC is the most common cancer in East African women [7] and is one of the criteria for HIV/AIDS World Health Organization (WHO) clinical stage 4 classification [8].

In Kenya, coverage of cervical cancer screening are low, with only 8% of women age 25–45 reporting ever having been screened [9]. Elevated risk of cervical abnormalities and subsequent progression to cervical cancer among HIV-infected women make them an important target for intervention. However, data are limited on HPV and cervical pre-cancer in HIV-infected women [10,11].

In this study, we sought to determine prevalence and correlates of HPV infection and cytological cervical abnormalities, describe the distribution of HPV genotypes among HIV-infected women in HIV-discordant relationships in Nairobi, Kenya, and inform the design of screening and treatment programs

METHODS

Study Design and Data Collection

We conducted a cross-sectional study of HIV-infected women aged 18–50 years, nested within a prospective study of HIV-discordant couples in Nairobi, Kenya from September 2007 to December 2009, as previously described [12]. Couples were recruited from ≥50 voluntary counseling and testing sites around Nairobi. Heterosexual HIV-discordant couples were eligible if they reported having sex ≥3 times in the 3 months prior to screening, were not pregnant, and planned to remain together for the duration of the study. At enrollment, HIV-infected participants did not have a history of clinical AIDS (WHO stage IV) and were not currently on antiretroviral therapy (ART). Couples were ineligible if the HIV-uninfected partner reported sexual relationships outside the primary partnership. At enrollment, interviews were conducted separately to collect individual socio-demographic and sexual history data from females and their male partners. Written informed consent was obtained and ethical approval was granted by the Institutional Review Board at University (IRB) of Washington (#30243) and the Ethics and Research Committee (ERC) at Kenyatta National Hospital (P25/2/2007).

Participants were tested for HIV-1 by two rapid tests conducted in parallel using the Determine HIV-1/2 rapid test (Abbott Laboratories, Tokyo, Japan; now marketed by Inverness Medical as Alere Determine) and the Bioline HIV 1/2 rapid test (Standard Diagnostics Inc., Suwon, South Korea) and were eligible only if they had concordant rapid test results at screening. Blood was drawn to quantify CD4 T-cell counts (BD FACSCaliber, Becton-Dickinson, Franklin Lakes, New Jersey) and plasma HIV RNA viral load (Gen-Probe transcription-mediated amplification assay) [13].

Cervical Cytology and HPV Detection

Study physicians and clinical officers performed pelvic examinations to collect exfoliated cervical cells using endocervical brushes for diagnosis of cervical abnormalities by conventional cervical cytology. An expert cytologist in the University of Nairobi Pathology Laboratory read the cytology slides. All abnormal cytology and 10% of randomly-sampled normal cytology slides were blindly double-read by an independent cytologist for quality assurance. Cervical cytology was categorized according to the 2001 Bethesda system [14]. Women were classified as having normal cytology if they did not have cervical intraepithelial lesions. Low-grade cervical abnormalities included atypical squamous cells of undetermined significance (ASC-US) and low-grade squamous intraepithelial lesions (LSIL). High-grade cervical abnormalities or more severe included atypical squamous cells cannot exclude a high-grade squamous intraepithelial lesion (ASC-H) and high-grade squamous intraepithelial lesions (HSIL), and women with squamous cell carcinoma (SCC). Kenyan guidelines were available for visual inspection with acetic acid (VIA) / visual Inspection with Lugol’s Iodine (VILI) screening only, but not for conventional cervical cytology screening. We followed the standard of care at Kenyatta National Hospital, whereby women with ASC-US or LSIL were recalled for a repeat cervical cytology screening after 6 month and women with ASC-H and HSIL were scheduled for a colposcopy and management at Kenyatta National Hospital [12].

During the genital exam, cervicovaginal secretions were collected by rotating a cotton swab 360° in the cervical os and rotating another swab across the vaginal wall. Both swabs were placed in the same tube containing 5 ml sterile phosphate buffered saline and immediately transported to the laboratory on ice. An aliquot was used for HPV DNA detection using Linear Array assay (Roche Molecular Systems, Pleasanton, California), according to manufacturer's instructions [15]. The HPV Linear Array assay utilizes the PGMY09/11 primer system for high-efficiency amplification of 37 HPV genotypes [16]. HR-HPV for this analysis included genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 [2]. HR-HPV infections were defined as infection with any of the HR-HPV genotypes, with or without a low-risk HPV (LR-HPV) infection. LR-HPV positivity was defined as infection with only LR-HPV genotypes (genotypes 6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, 87, and 89).

Data Analyses

Descriptive analysis of HPV genotype distribution were conducted by cytological status of HIV-infected women. We calculated HPV prevalence ratios (PRs) and 95% confidence intervals (CIs) for potential female and male partner risk factors for HPV infection and for abnormal cervical cytology. We chose to calculate PRs as opposed to odds ratios (ORs) because the prevalence of the outcomes was not rare, making the interpretation of the ORs more difficult. P-values were based on exact χ^2 tests. We investigated demographic (age, education, employment status, and marital status), biological (CD4 T-cell count, plasma viral load, herpes simplex virus [HSV] serology, parity, and male partner circumcision) and behavioral factors (number of sexual acts in last month, practicing dry sex, unprotected sex, and partner's previous sexually transmitted infections [STIs]) as risk factors for HPV infection. CD4 T-cell counts were categorized as <200, 200–349, 350–499, or ≥500 cells/μL based on historical thresholds for ART initiation. ASC-US and LSIL were analyzed as low-grade cervical abnormalities; and ASC-H, HSIL, and SCC as high-grade abnormalities or more severe. Stata 14.0 was used for data analysis (StataCorp, College Station, Texas).

RESULTS

Study Participants

Of 305 HIV-infected women enrolled in the study, 283 had a valid HPV test, and of these, 268 had available cytology results. Median age of women was 28 years (range 18–50), median age of sexual debut was 17 years of age, and median number of lifetime sex partners was 3 (Table 1). A relatively small proportion of women were using hormonal contraception (20%). Median CD4 T-cell count was 455 cells/μL (interquartile range [IQR]: 299–639) and 90 (32%) women had a CD4 T-cell count <350 cells/μL.

Cervical HPV Infection

Among the 283 HIV-infected women, any-HPV was detected in 176 (62%) women, among whom 116 (66%) had ≥2 concurrent HPV infections, with a median of 2 infections (IQR: 1–4). HR-HPV genotypes were identified in 132 (47%) women overall, of which 101 (77%) occurred in combination with ≥1 other HPV genotype and 76 (58%) included ≥2 concurrent HR-HPV infections. Compared to women without HPV detected or with only LR-HPV, the

presence of a HR-HPV genotype was associated with self-reported unprotected sex in the past month (PR=1.65; [95%CI: 1.31 to 2.09]; p<0.001), higher HIV-1 plasma viral load (PR=1.32 per $\log_{10}$ RNA copies/mL; [95%CI: 1.12 to 1.56]; p=0.001), and lower CD4 T-cell counts (<500 cells/μL) (PR=1.59; [95%CI: 1.20 to 2.10]; p<0.001) (Table 1).

HPV Infection in Relation to Cervical Cytology

Of the 268 women with available cervical cytology results, 199 (74%) had normal cytology, 51 (19%) had a low-grade lesion (ASCUS or LSIL), 16 (6%) had a high-grade lesion (ASC-H or HSIL), and 2 (0.8%) had SCC. We found no sociodemographic or behavioral factors significantly associated with either low- or high-grade lesions (Supplemental Table 1). For subsequent analyses, women with SCC were grouped with those with high-grade cervical lesions.

Among women with normal cervical cytology, 118 (59%) had an HPV infection identified, of whom 82 (69%) were infected with ≥1 HR-HPV genotype and 36 (31%) where infected only with LR-HPV. The most common HPV genotype among women with normal cytology was HPV-52, which was found in 16% of women, followed by HPV-53 (12%) and HPV-68 (8%) (Table 2). By comparison, among 51 women with low-grade lesions, 35 (69%) had an HPV infection, of whom 28 (80%) had HR-HPV genotypes and 7 (20%) had only LR-HPV genotypes. The most common HPV genotypes in women with low grade lesions were HPV-52 (29%), HPV-35 (20%), HPV-18 (14%), HPV-51 (14%), and HPV-66 (14%), all of which are HR-HPV genotypes. Among 18 women with high-grade lesions or SCC, 16 (89%) had an HPV infection identified, all of whom had a HR-HPV genotype. The most common HPV genotypes were HR types HPV-52 (44%), HPV-31 (22%), HPV-35 (22%), HPV-51 (22%), HPV-58 (22%), and LR types HPV-73 (28%) and HPV-55 (17%). Compared to women with normal cytology, HR-HPV genotypes 31, 35, 51, 52, and 58 were significantly more prevalent among women with high-grade lesions or SCC.

Single-type HR-HPV infections (with or without another LR genotype detected) were found in 7 (39%) women with high-grade lesions or SCC, among whom HPV-51 was found in 2 (33%) women and HPV-16, HPV-18, HPV-31, HPV-39, and HPV-58 were found in 1 (17%) woman each. Compared to women with normal cytology, there was a marginally significant 1.98-fold higher prevalence (95%CI: 1.04 to 3.78; p=0.07) of a single HR-HPV genotype and a significant 2.31-fold higher prevalence (95%CI: 1.36 to 3.94; p=0.02) of multiple HR-HPV genotypes among HIV-infected women with high-grade lesions.

HR-HPV genotypes HPV-16 and/or HPV-18 were found in 17% of women with high-grade lesions or SCC. In comparison, HPV-16 was found in 7% of women with normal cervical cytology and 4% of those with low-grade lesions and HPV-18 was found in 5% of women with normal cervical cytology and 14% of those with low-grade lesions. Neither type alone (p=0.99 for HPV-16 and p=0.26 for HPV-18) or in combination (p=0.44) were statistically associated with high-grade lesions or SCC.

We compared the screening performance of HPV detection versus cervical cytology to determine possible implications of screening by HPV testing in this population. A screening strategy based on detection of any HR-HPV infection would have resulted in 47% of women

screening positive (Table 3). Of those women with high grade lesion or SCC by cervical cytology, 89% would have been HR-HPV positive and 11% would have had a negative HR-HPV test. An alternative screening strategy based on detection of only HR-HPV genotypes 16, 18, 31, or 45 would have resulted in 19% of women screening positive. In this scenario, 44% of high grade lesions or more severe would have been HPV 16, 18, 31, or 45 positive, and screening for this subset of HR-HPV genotypes would have missed 56% of the women with high grade cytology or SCC.

DISCUSSION

In 268 HIV-seropositive Kenyan women with discordant HIV-negative male partners, we observed a high prevalence of HPV (62%), HR-HPV genotypes (47%) and high-grade cervical cytology (6%). The most common HR-HPV infections among those with high-grade lesions or more severe were genotypes 52, 31, 35, 51, and 58. In a population of HIV-infected women under similar conditions to this study, screening for HR-HPV would detect 89% of high-grade or SCC cases and would result in positive tests in 44% of women with normal or low-grade cervical cytology. This information should be combined with cost data and mathematical models to design HPV screening, evaluation, and treatment programs that target HIV-infected women to reduce the burden of disease from cervical cancer.

We found HPV (any genotype) in 59% of women with normal cytology, 69% of women with low-grade lesions, and 94% in women with high-grade lesions, estimates generally consistent with previous findings from HIV-infected women from sub-Saharan Africa [17,18]. Our observed HPV prevalence of 59% among women with normal cervical cytology was considerably higher than a global meta-analysis estimate of 36% among HIV-infected women with no cytological abnormalities, but was in line with meta-analysis estimates among HIV-infected women with normal cervical cytology from sub-Saharan Africa (57%) and South America (57%) [17,18]. Our findings are also consistent with another Kenyan study that found that 61% of HIV-seropositive women with normal cytology had an HPV infection of any type and 53% of HIV-seropositive women overall were infected with an HR-HPV genotype [19]. This study was limited to women not currently on ART; given that ART is associated with lower prevalence and persistence of HR-HPV infection and lower risk of high-grade lesions, these findings may not be generalizable to women on ART.

We found that 47% of HIV-infected women from HIV-discordant couples were infected with at least one HR-HPV genotype. Among all HIV-infected women, the most common HR-HPV genotype was HPV-52 (20%) followed by HPV-51 (9%) and HPV-35 (8%), and the most common LR-HPV genotype was HPV-53 (11%). The genotype distribution in our study is more consistent with other studies among HIV-seropositive women from sub-Saharan Africa than with those from other regions [20,21]. In a meta-analysis examining HPV genotype distributions among HIV-infected women with normal cervical cytology in sub-Saharan Africa, HPV-16 and HPV-58 were the most prevalent HR-HPV genotypes, while HPV-53 was also the most prevalent non-HR genotype, and HPV-52 was among the top 4 most common HR-genotypes [18]. Other Kenyan studies found HPV-52 was the most common HPV type among family planning clinic attendees [20] and among female sex workers [21]. Similar to other findings from Western Kenya, compared to

women with normal cytology, those with high-grade lesions or more severe had a 2-fold higher prevalence of a single HR-HPV genotype and 2.3-fold higher prevalence of multiple HR-HPV genotypes [21,22]. While the cross-sectional nature of this study prevents causal conclusions, these observations provide some support for the hypothesis that, at least among HIV-infected women, multiple HR-HPV infections have a cumulative effect on the risk of cervical abnormalities, or may represent an immune marker associated with an increased risk of cervical cancer.

Globally, HPV-16 and HPV-18 are the most common HPV genotypes detected in women with ICC, with meta-analyses estimates that 67–70% of cervical carcinomas globally are attributable to these two HPV genotypes [23,24]. This pattern is similar in Africa, where meta-analysis estimates indicate HPV16/18 are detected in ~73% of women with ICC, regardless of HIV status [25]. Likewise, a previous study from Nairobi found HPV-16/18 in 65% of HIV-seropositive and 60% of seronegative women with ICC [26]. Due to the absence of ICC cases in this study, we were unable to evaluate the contribution of HPV-16/18 specifically to ICC, but found that HPV-16 and HPV-18 were uncommon in women with high-grade lesions who did not have ICC, with each found in only 6% of women with high-grade lesions. This was even lower than a previous Kenyan study that found HPV-16 in 36% of women and HPV-18 in 4% of women attending a family planning clinic who had an HSIL cytological finding [20]. It is unclear whether the lower prevalence of HPV-16 among women with high-grade lesions, and to a lesser degree HPV-18, is due to our relatively small sample size of high-grade or more severe cases (n=18), random chance, regional difference, the influence of HIV infection, or dynamics related to being in an HIV-discordant relationship.

Based on our findings, HPV screening for all HR-HPV genotypes would identify 89% of high-grade lesions/SCC detected by cytology, but would also be positive for 44% of HIV-infected women with normal cytology/low-grade lesions who would have required no or less intensive follow-up based on cytology screening. Screening for all HR-HPV genotypes would be more sensitive than cytological screening, yet would likely result in identification of a large number of women who would not have been identified by cervical cytology. Conversely, screening for a smaller subset of genotypes (e.g., genotypes 16, 18, 31, and 45) appears to fail to identify a relatively large proportion of women who would have been identified with high-grade lesions by cytology. An important limitation in the interpretation these findings is that we did not have histological confirmation of the cytology results. Given the relatively low sensitivity of cytology to detect high-grade lesions, it is possible that HR-HPV screening may identify true cases of cervical lesions that were not detected by cytology.

The success of an HR-HPV screening program will require an accurate, rapid, inexpensive, and highly acceptable testing modality. We conducted a previous study of women's knowledge of HPV and Pap smears in this population and found 82% of women were amenable to self-collection for HPV testing and only 5% reported concerns with self-sampling [27]. Another study in Kenya demonstrated that self-collection is just as efficacious as physician-collected samples for detection of high-grade cervical precancer (CIN2+) [28]. A recent meta-analysis found that self-collection had a lower sensitivity than

clinician samples to detect CIN2+ (77% vs 93%), but that sensitivity was 96% for both sampling methods when polymerase chain reactions were used [29]. Self-collection for HR-HPV could be used to triage women for confirmation with other screening methods [30], and any reduction in sensitivity with self-testing would likely be offset but the increased coverage. With only an estimated 8% of Kenyan women aged 25–45 having ever been screened [9], better screening programs need to be created to reach women who are most in need, including high-risk women who are living with HIV.

This study benefited from a relatively large sample of HIV-infected women with detailed sociodemographic, sexual behavior, and physical exam data collected for both HIV-infected women and their uninfected male partner. Despite this, interpretation of these results is limited to ART-naive HIV-infected women in an HIV-discordant relationship, and our findings may not be generalizable to other HIV-seropositive women, including those on ART. We chose to use prevalence ratios to measure the strength of associations between factors of interest and the presence of HPV infections and abnormal cytology because these prevalence ratios can be directly interpreted as the relative prevalence of the 'outcome' when the outcome is common (e.g., detection of HPV) or rare (e.g, high grade lesions). As unadjusted cross-sectional measures of associations, these findings cannot be interpreted as causal relationships. Despite the sample size and relatively high rate of high-grade lesions, the absolute number of high-grade abnormal cytology cases (n=16) and SCC (n=2) was small. Moreover, our outcome assessment was based on conventional cytology without histological confirmation of high-grade lesions because only a subset of women with a HSIL cytology finding returned for colposcopy in a timely manner; however, cytological results are relevant as they are used in clinical practice for screening and referral to colposcopy.

In summary, we found a high burden of HPV infection among HIV-infected women living in Kenya that was strongly associated with the development of high-grade cervical lesions. The distribution of some HR-HPV types among HIV-infected Kenya women with high-grade lesions differs from other geographic regions and elsewhere in Africa, in particular, an enriched prevalence of HPV-31, 35, and 58, prompting a need for investigation of their contribution to cervical cancer and their relevance to screening in this population. Self-testing or future point-of-care testing optimized to the region-specific HPV genotypic distribution should be considered to reduce the high burden of cervical cancer in Africa.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Messages:

- Nearly half of HIV-infected Kenyan women in discordant relationships were infected with a high risk (HR) HPV genotype.
- Screening for HR-HPV genotypes would identify a large majority of women who have a high-grade cervical lesion or more sever cytology.
- HR-HPV screening would also yield positive results for a large number of women with normal or low-grade cervical cytology, necessitating a well-designed secondary screening process.

Table 1.

Sociodemographic characteristics and prevalence of high-risk human papillomavirus among 283 HIV-infected women in HIV-discordant relationships in Nairobi, Kenya.[a]

Characteristics	Overall Sample n (%) or median (IQR)	HR-HPV Infection prevalence n (%)	PR (95% CI)
All women	283	132 (46.6)	
Age group (years)			
<25	83 (29.3)	44 (53.0)	1 (ref)
25–29	79 (27.9)	36 (45.6)	0.86 (0.63, 1.18)
30–34	62 (21.9)	26 (41.9)	0.79 (0.55, 1.13)
35–39	39 (13.8)	17 (43.6)	0.82 (0.55, 1.24)
40–44	13 (4.6)	6 (46.2)	0.87 (0.47, 1.62)
≥45	7 (2.5)	3 (42.9)	0.81 (0.34, 1.95)
Education			
Less than primary education	68 (24.0)	27 (39.7)	1 (ref)
Primary education or higher	215 (76.0)	105 (48.8)	1.23 (0.89, 1.70)
Marital status			
Married	271 (95.8)	123 (45.4)	1 (ref)
Unmarried	12 (4.2)	9 (75.0)	1.65 (1.16, 2.35)
Earn an income			
No	205 (72.4)	98 (47.8)	1 (ref)
Yes	78 (27.6)	34 (43.6)	0.91 (0.68, 1.22)
HSV-2			
Seronegative	99 (35.5)	44 (44.4)	1 (ref)
Seropositive	180 (64.5)	86 (47.8)	1.08 (0.82, 1.41)
Age at first sexual intercourse			
<16	58 (20.5)	31 (53.5)	1 (ref)
16–18	136 (48.1)	61 (44.9)	0.84 (0.62, 1.14)
≥19	89 (31.5)	40 (44.9)	0.84 (0.60, 1.17)
Lifetime sex partners			
1	14 (5.0)	5 (35.7)	1 (ref)
2	74 (26.2)	32 (43.2)	1.21 (0.57, 2.56)
≥3	195 (68.9)	95 (48.7)	1.36 (0.67, 2.80)
Lifetime STI			
No	201 (72.0)	94 (46.8)	1 (ref)
Yes	78 (28.0)	37 (47.4)	1.01 (0.77, 1.34)
Parous			
No	17 (6.0)	9 (52.9)	1 (ref)
Yes	266(94.0)	123 (46.2)	0.87 (0.55, 1.39)
Unprotected sex in last month [b]			
No	212 (74.9)	85 (40.1)	1 (ref)

	Overall Sample	HR-HPV Infection prevalence	
Characteristics	**n (%) or median (IQR)**	**n (%)**	**PR (95% CI)**
Yes	71 (25.1)	47 (66.2)	**1.65 (1.31, 2.09)**
Sex acts in past month	6 (3–9)		
<4	101 (35.7)	46 (45.5)	1 (ref)
4–5	44 (15.6)	23 (52.3)	1.15 (0.81, 1.63)
6–8	65 (23.0)	27 (41.5)	0.91 (0.64, 1.31)
≥9	73 (25.8)	36 (49.3)	1.08 (0.79, 1.48)
Current hormonal contraception use [c]			
No	227 (80.5)	109 (48.0)	1 (ref)
Yes	55 (19.5)	23 (41.8)	0.87 (0.62, 1.22)
Practice dry sex			
No	137 (48.4)	63 (46.0)	1 (ref)
Yes	146 (51.6)	69 (47.3)	1.03 (0.80, 1.32)
Vaginal washing			
No	196 (69.5)	90 (45.9)	1 (ref)
Yes	86 (30.5)	41 (47.7)	1.04 (0.79, 1.36)
Partner's circumcision status			
Circumcised	235 (83.3)	112 (47.7)	1 (ref)
Uncircumcised	47 (16.7)	20 (42.6)	0.89 (0.62, 1.28)
HIV Plasma RNA (Log_{10} copies/mL)	4.6 (3.7–5.2)	–	**1.32 (1.12, 1.56)** [d]
CD4 count (cells/μl)			
≥500	120 (42.6)	42 (35.0)	1 (ref)
350–499	72 (25.5)	40 (55.6)	**1.59 (1.15, 2.19)**
200–349	67 (23.8)	35 (52.2)	**1.49 (1.07, 2.09)**
<200	23 (8.2)	15 (65.2)	**1.86 (1.27, 2.74)**

Abbreviations: HR-HPV = high-risk human papillomavirus genotype; IQR = interquartile range; CI = confidence interval; HSV-2 = herpes simplex virus type-2; STI = sexually transmitted infection; HIV = human immunodeficiency virus; PR = prevalence ratio.

[a] Numbers may not add to total because of missing data

[b] With study partner.

[c] Self-reported oral, injectable, or implantable contraceptive.

[d] PR is per log_{10} HIV RNA copies/mL

Table 2.

Prevalence of human papillomavirus infections among HIV-infected women, stratified by cervical cytology results.

HPV Type	Normal Cytology (N=199) [a]		Low-grade Cervical Lesion (N=51) [a]			High-grade Cervical Lesion or more severe (N=18) [a]			Overall (N=283)	
	n	(%)	n	(%)	PR (95% CI) versus normal cytology	n	(%)	PR (95% CI) versus normal cytology	s/m	(%)
Negative	81	(40.7)	16	(31.4)	–	2	(11.1)	–	107	(37.8)
Positive	118	(59.3)	35	(68.6)	1.16 (0.93, 1.44)	16	(88.9)	**1.50 (1.23, 1.83)**	60/116	(62.2)
Multiple infections	73	(36.7)	26	(51.0)	**1.39 (1.00, 1.92)**	12	(66.7)	**1.82 (1.25, 2.64)**	116	(41.0)
Any high-risk	82	(41.2)	28	(54.9)	1.33 (0.99, 1.80)	16	(88.9)	**2.16 (1.85, 2.80)**	31/101	(46.6)
Low-risk only	36	(18.1)	7	(13.7)	0.99 (0.50, 1.94)	0	(0)	NA	29/15	(15.6)
High-risk										
16/18	22	(11.1)	8	(15.7)	1.42 (0.67, 3.00)	3	(16.7)	1.51 (0.50, 4.55)	9/26	(12.4)
16	13	(6.5)	2	(3.9)	0.60 (0.14, 2.58)	1	(5.6)	0.85 (0.12, 6.13)	5/12	(6.0)
18	10	(5.0)	7	(13.7)	**2.73 (1.09, 6.82)**	2	(11.1)	2.21 (0.52, 9.32)	4/16	(7.1)
31	4	(2.0)	3	(5.9)	2.93 (0.68, 12.66)	4	(22.2)	**11.06 (3.02, 40.54)**	2/9	(3.9)
33	4	(2.0)	5	(9.8)	**4.88 (1.36, 17.51)**	1	(5.6)	2.76 (0.33, 23.43)	1/10	(3.9)
35	10	(5.0)	10	(19.6)	**3.90 (1.72, 8.87)**	4	(22.2)	**4.42 (1.54, 12.69)**	0/24	(8.5)
39	6	(3.0)	3	(5.9)	1.95 (0.51, 7.54)	2	(11.1)	3.68 (0.80, 16.95)	1/10	(3.9)
45	9	(4.5)	1	(2.0)	0.43 (0.06, 3.34)	1	(5.6)	1.23 (0.16, 9.16)	1/11	(4.2)
51	14	(7.0)	7	(13.7)	1.95 (0.83, 4.58)	4	(22.2)	**3.16 (1.16, 8.60)**	3/23	(9.2)
52	32	(16.1)	15	(29.4)	**1.83 (1.08, 3.11)**	8	(44.4)	**2.76 (1.51, 5.07)**	4/54	(20.5)
56	11	(5.5)	4	(7.8)	1.42 (0.47, 4.27)	2	(11.1)	2.01 (0.48, 8.38)	0/17	(6.0)
58	9	(4.5)	2	(3.9)	0.87 (0.19, 3.89)	4	(22.2)	**4.91 (1.68, 14.39)**	1/15	(5.7)
59	11	(5.5)	3	(5.9)	1.06 (0.31, 3.67)	2	(11.1)	2.01 (0.48, 8.38)	4/12	(6.7)
66	11	(5.5)	7	(13.7)	**2.48 (1.01, 6.08)**	2	(11.1)	2.01 (0.48, 8.38)	1/20	(7.4)
68	16	(8.0)	2	(3.9)	0.49 (0.12, 2.05)	1	(5.6)	0.69 (0.10, 4.91)	4/16	(7.1)
Infection level										
Single LR-HPV	24	(12.1)	4	(7.8)	0.65 (0.23, 1.79)	0	(0)	–	29	(10.3)
Multiple LR-HPV only	12	(6.0)	3	(5.9)	0.98 (0.29, 3.33)	0	(0)	–	15	(5.3)
Single HR-HPV	39	(19.6)	6	(11.8)	0.60 (0.27, 1.34)	7	(38.9)	**1.98 (1.04, 3.78)**	56	(19.8)
Multiple HR-HPV	43	(21.6)	22	(43.1)	**2.00 (1.32, 3.01)**	9	(50.0)	**2.31 (1.36, 3.94)**	76	(26.9)

Abbreviations: HPV = human papillomavirus genotype; HR-HPV = high-risk HPV; LR-HPV = low-risk HPV; s/m = single/multiple.

[a]Excluding 15 women without available cervical cytology results. Includes 2 women with squamous cell carcinoma.

Table 3.

Performance of HPV screening strategies for detection of cytological endpoints among 268 female sexual workers.

		Cytology		
		High Grade/SCC N=18	**Normal/Low Grade N=250**	**Total N=268**
		n (column %)		
Any HR-HPV	Positive	16 (89%)	110 (44%)	126 (47%)
	Negative	2 (11%)	140 (56%)	142 (53%)
HPV 16 or 18	Positive	3 (17%)	30 (12%)	33 (12%)
	Negative	15 (83%)	220 (88%)	235 (88%)
HPV 16, 18, 31, or 45	Positive	8 (44%)	43 (17%)	51 (19%)
	Negative	10 (56%)	207 (83%)	217 (81%)