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Int J STD AIDS. Author manuscript; available in PMC 2015 April 01.

Published in final edited form as:
Int J STD AIDS. 2014 April ; 25(5): 315–324. doi:10.1177/0956462413504554.

Individual and Partner Risk Factors Associated with Abnormal Cervical Cytology among Women in HIV-discordant Relationships

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Abstract

Individual and sexual partner characteristics may increase risk of abnormal cervical cytology among women in HIV-discordant relationships. Papanicolaou smears were obtained in a prospective cohort of Kenyan HIV-discordant couples. Of 441 women, 283 (64%) were HIV-infected and 158 (36%) were HIV-uninfected with HIV-infected partners. Overall, 79 (18%) had low-grade and 25 (6%) high-grade cervical abnormalities. Lack of male circumcision, male HSV-2 seropositivity and lower couple socioeconomic status were associated with cervical abnormalities ($p<0.05$). HIV-uninfected women with HIV-infected male sex partners (CD4>350 cells/μL) had the lowest prevalence of high-grade cervical lesions. HIV-infected women (CD4>350 cells/μL) and HIV-uninfected women with HIV-infected partners (CD4≤350 cells/μL) were at similar intermediate risk ($P>0.05$), and HIV-infected women (CD4≤350 cells/μL) had significantly higher risk of high-grade cervical abnormalities ($p=0.05$). Women in HIV-discordant relationships have high rates of cervical lesions and this may be influenced by couple-level factors, including HIV status and CD4 count of the infected partner.

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Human Subjects: Written informed consent was obtained from all study participants, and human experimentation guidelines of the US Department of Health and Human Services were followed. The study was approved by the institutional review board of the University of Washington and the Ethical and Scientific Review Committee of Kenyatta National Hospital, Nairobi, Kenya.

Conflict of interest: The authors report no conflicts of interest.

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Keywords

Cancer; cervical; cytology; discordant couples; HIV

INTRODUCTION

Cervical cancer is the second most common cancer among women worldwide, and the majority of cases occur in developing countries where routine cytologic screening and treatment are less common (1). Studies have shown that HIV infection and lower CD4+ T-cell counts are associated with an increased risk of human papillomavirus (HPV), the primary cause of invasive cervical cancer (2, 3), in both men and women (4–8). Furthermore, HIV infection and low CD4+ T-cell counts are associated with an increased risk of cervical intraepithelial neoplasia (CIN) and cervical cancer in women (9–14). While many studies have examined these associations among HIV-infected men and women, few studies have investigated factors associated with cervical lesions among HIV-discordant couples, where one partner is HIV infected and the other HIV uninfected (15).

There are an estimated 800,000 to 1 million women living with HIV-1 in Kenya (16) and there are high rates of HIV discordance among couples in East and Southern Africa, with one study finding that up to one-third of couples tested in the community were HIV discordant (17). A study done in South Africa found that HIV-discordant couples were more likely to share multiple HPV types compared to HIV-concordant negative couples, where both partners are uninfected, including HPV types 16 and 18 associated with malignancy (18). It is not known whether the male partner's HIV infection and immunosuppression alters his HIV-uninfected female partner's risk of developing cervical cancer. To begin to better understand this relationship, we determined the association between high-grade cervical lesion and male and female HIV infection status, immunosuppression, and individual and partnership-level characteristics among HIV-1 discordant couples in Nairobi, Kenya.

MATERIALS AND METHODS

Study design and participant enrollment

This was a cross-sectional study of HIV-1 discordant couples enrolled in a prospective cohort study from 2007–2009 at Kenyatta National Hospital in Nairobi, Kenya. Couples were recruited from ≥50 voluntary counseling and testing (VCT) sites in greater Nairobi, as previously described (19). VCT is widespread in Kenya and couples VCT has been promoted to increase the number of people aware of their status and to promote disclosure within couples. Participants were followed quarterly for up to two years. The present study focused on cervical samples collected at study baseline, although follow-up cytology was conducted per the study protocol at one year intervals and in response to abnormal cytological findings for clinical management.

Heterosexual HIV-1 discordant couples, in which each partner considered the other their primary sex partner, were eligible for the study if they planned to maintain their relationship for 24 months, had vaginal intercourse with their current partner ≥3 times in the three months prior to enrollment, and if the HIV-infected partner had not been previously diagnosed with acquired immune deficiency syndrome (AIDS). Potential participants were excluded if the female partner was pregnant at enrollment or if the HIV-infected partner had ever used antiretroviral therapy (ART) prior to enrollment. Informed consent was obtained following protocols approved by all collaborating institutions and couples were provided condoms and risk reduction counseling at all visits.

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Data collection

Interviews were conducted separately to collect individual sociodemographic and sexual history data from females and their male partners. Couple-level characteristics were formed by combining the male and female partner's individual-level characteristics. Categories for combined female and male age were generated using the median ages for each respective gender as the cutoff. Blood was drawn to determine HIV status using HIV-1 ELISA (Vironostika®, bioMerieux), and to quantify CD4+ T-cell counts among the HIV-1 infected partner (BD FACSCaliber™, Becton-Dickinson). Categories for CD4 T-cell count were generated using a CD4 cutoff of 350 cells per μL, based on the World Health Organization's recommendations for starting antiretroviral treatment at the time of the study (20).

Cervical cytology

A genital exam was performed by study clinicians to collect exfoliated cervical cells using endocervical brushes for diagnosis of cervical abnormalities by conventional cytology. Cytology slides were read by an expert cytologist at the University of Nairobi's Pathology laboratory. All abnormal cytology slides and 10% of normal slides (randomly sampled) were blindly double-read by an independent cytologist for quality assurance.

Cervical cytology was categorized according to the 2001 Bethesda system (21). Women who were negative for intraepithelial lesions were classified as normal cervical status. Low-grade cervical abnormalities included atypical squamous cells of undetermined significance (ASC-US) and low-grade squamous intraepithelial lesions (LSIL); high-grade abnormalities included atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion (ASC-H), high-grade squamous intraepithelial lesions (HSIL), and squamous cell carcinoma (SCC). Since Kenyan guidelines are available for VIA/VILI screening but not for Pap smear screening, we followed the standard of care at Kenyatta National Hospital, whereby women with ASC-US or LSIL were recalled for a repeat Pap smear and women with ASC-H and HSIL were scheduled for a colposcopy and management at Kenyatta National Hospital.

Data analysis

Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for potential female, male, and combined partnership-level risk factors for abnormal cervical cytology. Separate models were used to assess the risk of low-grade and high grade cervical abnormalities, with women with normal cervical cytology used as the reference group for each set of comparisons. Based on knowledge of the biology of HPV and cervical cytology and for consistency with previously published findings, all analyses were adjusted for the age of the female partner. Stata 10.1 was used for data analysis (StataCorp, College Station, Texas) and differences were considered statistically significant if $P<0.05$.

RESULTS

Study participants

Of the 469 couples who were enrolled, 441 couples had cytology readings available for analysis. Median age of women was 29 years and the median age of the male partners was 35 years (Tables 1 and 2). Fewer women had reported less than primary education (24%) and an individual income (30%) and most women reported never using hormonal contraception (80%) and never smoking (93%) (Table 1). Fewer men reported less than primary education (15%), almost half of the men had a history of smoking (42%), and most men were circumcised (79%) and reported an income (85%) (Table 2). Among the 441 discordant couples, the female partner was HIV-1 infected in 283 (64%) couples. Median CD4 T-cell count among HIV-1-infected females was 448 cells per μL (IQR 298–639) and

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median CD4 T-cell count among HIV-1-infected males was 355 cells per μL (IQR 236–513).

Cervical cytology and couple HIV status

The majority of the Pap smears were normal (76%) (Table 3). The 104 (24%) abnormal cytology readings included 38 (9%) cases of ASC-US, 41 (9%) cases of LSIL, 9 (2%) cases of ASC-H, 14 (3%) cases of HSIL, and 2 (<1%) cases of SCC. There was no difference in the prevalence of cervical abnormalities among HIV-1-infected (26%) compared to uninfected women (20%; p=0.35). There was a higher prevalence of high-grade lesions and cervical cancer among HIV-1-infected women compared to HIV-1-uninfected women, which was not significant (7% vs. 4%; p=0.17).

Individual-level risk factors for cervical abnormalities

Women currently using hormonal contraceptives had a higher odds of low-grade abnormalities (OR=2.0; 95% CI: 1.2, 3.6; p=0.01) compared to women not on hormonal contraceptives (Table 4). In addition, informal housing, as reported by female participants, was associated with a higher odds of both low-grade (OR=2.0; 95% CI: 1.2, 3.4; p=0.01) and high-grade (OR=2.7; 95% CI: 1.1, 6.7; p=0.03) abnormalities compared to women in formal residences. Increasing age at sexual debut was associated with a lower odds of high-grade abnormalities (OR=0.8; 95% CI: 0.7, 1.0; p=0.02). There was no difference in the odds of low-grade (OR=1.2; 95% CI: 0.7, 2.1; p=0.42) or high-grade (OR=2.0; 95% CI: 0.8, 5.1; p=0.17) cervical abnormalities among HIV-infected compared to HIV-uninfected women. The median log HIV viral load among women with normal cytology was 5 (IQR, 4–5), among women with low-grade abnormalities was 5 (IQR, 3–5), and among women with high-grade abnormalities was 5 (IQR 4–5). The median CD4 T-cell count (cells/μL) among women with normal cytology was 457 (IQR, 306–681), among women with low-grade abnormalities was 424 (IQR, 292–597), and among women with high-grade abnormalities was 384 (IQR, 254–557). HIV viral load and CD4 T-cell count were not associated with abnormal cytology. There were also no significant differences in the odds of low- or high-grade cervical abnormalities by age, monthly income, history of Pap screening, lifetime number of sex partners, HSV-2, and any unprotected sex in the month before enrollment.

Among male participants, HSV-2 seropositivity was associated with 90% higher odds (OR=1.9; 95% CI: 1.2, 3.2; p=0.01) of low-grade abnormalities in their female partner and an income of greater than 8,000 Kenyan Shillings was associated with an 8-fold increase in the odds (OR=8.4; 95% CI: 2.0, 36.3; p<0.01) of high-grade abnormalities in their female partner (Table 5). There were no significant differences in the odds low- or high-grade cervical abnormalities in women by their male partner's age, circumcision status, income, age at sexual debut, lifetime number of sex partners, residence type, any unprotected sex, HIV-1 status, log HIV viral load, and CD4 T-cell count.

Couple-level risk factors for cervical abnormalities

We next investigated the association between cervical cytology and HIV status and CD4 count within partnerships. HIV-1-uninfected women with a HIV-1-infected male sex partner with a CD4 count >350 cells/μL had the lowest prevalence of high-grade cervical lesions at 3% (Table 6). Relative to these women, the odds of high-grade cervical abnormalities, versus normal cytology, was approximately 2-fold greater and was similar for HIV-1-uninfected women with a HIV-1-infected male sex partner with a CD4 ≤350 cells/μL (OR=2.1; 95% CI: 0.4, 12.2; p=0.39) and HIV-infected women with CD4 count >350 cells/μL (OR=2.2; 95% CI: 0.5, 10.2; p=0.33). These point estimates were relatively imprecise and differences were not statistically significant. In comparison, risk of high-grade cervical

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abnormalities was nearly 5-fold higher among HIV-infected women with a CD4 count ≤350 when compared to the lowest risk group (OR=4.7; 95% CI: 1.0, 22.8; p=0.05).

Compared to a combined monthly income of >8,000 Kenyan shillings, a combined monthly income of ≤8,000 Kenyan shillings was associated with a 2.5-fold increase in the odds of high-grade cervical abnormalities versus normal cytology (OR=2.5; 95% CI: 1.0, 6.3; p=0.04) (Table 6). There were no significant differences in the odds of female cervical abnormalities when considering both partners' ages, any unprotected sex in the month before enrollment (reported by either member of the couple), and combined lifetime number of sex partners.

DISCUSSION

This study assessed individual and partnership-level risk factors for abnormal cervical cytology in a cohort of HIV-discordant couples in Nairobi and found high rates of cervical abnormalities consistent with other sub-Saharan African studies. A large proportion of women in the cohort were HIV-infected women (>60%) and a number of studies around the world and in Africa have shown an increased risk of HSIL or worse in the setting of HIV-1 infection (9, 10, 12, 22–24). HIV is likely to have contributed to the number of abnormalities we observed. It is also plausible that being in a regular sexual partnership with an HIV-infected man increases HPV exposure and in this way contributed to our findings. We were not able to demonstrate this definitively in our study, possibly due to the low percentage of unprotected sex and because women in this study had relatively high CD4 counts. Previous studies have shown a stronger association between HIV-1 infection and an increased risk of HSIL for women with a low CD4 count (25). Nonetheless, our findings add to the body of literature describing prevalence of cervical abnormalities in sub-Saharan Africa by providing HIV-discordant couple cohort data. Cervical abnormalities have not been well-studied among women in HIV-discordant relationships despite the fact that HIV discordance is extremely common in sub-Saharan Africa, accounting for approximately 20–30% of couples in areas of high HIV prevalence (17), making this is an important contribution.

In this study we also observed differences in cervical abnormalities among subgroups of HIV-infected and uninfected women. Risk of high-grade cervical abnormalities was approximately 5-fold higher among HIV-infected women with a CD4 count ≤350 when compared to HIV-uninfected women with male HIV-infected partners who were not immunosuppressed. When we evaluated whether HIV status and immune suppression (CD4≤350) in a male partner increased the risk of a high-grade cervical lesion or cervical cancer in their female sex partner, we found that the risk of abnormal cytology was not significantly increased. However, previous studies have found HIV-infected men with low CD4 T-cell counts to be at greater risk for HPV infection than uninfected men (26, 27), making it plausible that HIV-infected, immunosuppressed men are more likely to transmit HPV to female partners. This merits additional evaluation in studies using HPV genotyping or a larger sample size than was available in this study.

Similar to other groups, we found that surrogates for socioeconomic status were associated with detection of cervical HSIL and other high-grade abnormalities. We examined this at both the individual and couple level. Informal housing as reported by the female partner was associated with an increase in low- and high-grade cervical abnormalities. An increase in combined monthly income was significantly associated with lower risk of high-grade lesions and cervical cancer. These results correspond with other studies among populations in developing countries that have found low socioeconomic status to be associated with an increased risk of high-risk HPV infection and cervical cancer (28–38). Among women in

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Malawi, researchers found low socioeconomic status to be associated with cervical cancer, and in Kenya, investigators found that women had difficulty justifying to their partner the costs of getting screened when she was 'feeling healthy' (29, 39). Additionally, a study by the Program for Appropriate Technology in Health (PATH) noted that the lack of male partner support and active opposition by male partners were reasons for why women did not seek cervical screening services or make follow-up visits (40). In the present cohort of women, only 14% had ever had a Pap smear prior to study enrollment, which is higher than the national screening prevalence of 3.2 % in Kenya, and the most commonly cited reason was lack of knowledge (41, 42).

Our study enrolled a large cohort of HIV-1 discordant couples, however, we were limited by the number of women with a high-grade cervical lesion or invasive cervical cancer, diminishing the power to assess associations. While the small number of high-grade cervical lesions (n=25) made it difficult to observe a difference between the 4 groups of women categorized by HIV status and immunosuppression and draw definitive conclusions from our data, our results would support conducting similar evaluations in larger cohorts, including collection of male partner data. A second limitation is that the study outcome of high-grade cervical lesions and invasive cervical cancer was based on cytology and not histology results. Although histologic confirmation is considered to be a more definitive indication of HPV-related cervical abnormalities this methods is no more reproducible than cytologic interpretations (43). Furthermore, Pap smears and cytology results are still used extensively in the clinical arena, including in high HIV prevalence areas with limited resources, making this a relevant outcome even if it does not achieve gold-standard status. Due to relatively few women with abnormal cervical cytology, it was not possible to adjust associations for factors other than age. However, the lack of strong associations between the factors investigate and the presence of abnormal cervical cytology makes it unlikely that appreciable residual confounding was present.

In summary, risk of high-grade cervical abnormalities was high among immunosuppressed HIV-infected women (CD4 ≤350) compared to uninfected women in the lowest risk category, and we observed a pattern of increased risk for low-grade and high-grade cervical abnormalities. Specifically, there was progression from risk for the HIV-uninfected woman coupled with an HIV-infected male sex partner who was less immunosuppressed to the HIV-infected woman with immunosuppression (CD4 count ≤350). These results raise questions about the role of male HIV status in women's risk of HPV acquisition and about whether HPV and cervical screening management recommendations for HIV-infected women should be considered for HIV-uninfected women in HIV-discordant relationships. In areas of where HIV prevalence is high, HIV-discordant couples represent a sizeable proportion of all couples and could be readily reached if their partner is engaged in HIV care. Additional studies using other screening and treatment methods would help to guide practice and inform policies that could benefit this vulnerable group of women.

Acknowledgments

This research was funded by US National Institutes of Health (NIH) grant NIH/NIAID R01 AI068431. B.L.G. was supported by an NIH/FIC postdoctoral fellowship T32 AI07140. R. Y. Choi received support from the International Research Scientist Development Award K01 TW008406. C.F. received support from NIH grants K23 HD41879 and K24 AI087399. B.L.-P. received support from NIH grant K01 TW06080. R.B. was a scholar in the University of Washington (UW) AIDS International Training and Research Program supported by the NIH Fogarty International Center grant D43 TW00007. A.G. was a scholar and fellow and A.R. was a scholar in the Fogarty International Clinical Research Scholars/Fellows funded under NIH Fogarty International Center grant R24 TW007988. This publication was made possible with help from the University of Washington Center for AIDS Research (CFAR), an NIH funded program (P30 AI027757), which is supported by the following NIH Institutes and Centers (NIAID, NCI, NIMH, NIDA, NICHD, NHLBI, NIA). The content is solely the responsibility of the

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Table 1

Female participant characteristics.

	Overall (N=441)		HIV-uninfected (N=158)		HIV-infected (N=283)	
Characteristic	**n (%) or Median (IQR)**					
Age	29	(24–34)	29	(25–35)	28	(24–33)
Age at sexual debut	18	(16–19)	18	(16–20)	17	(16–19)
Less than primary education	108	(24)	44	(28)	64	(23)
Earn a Monthly income	133	(30)	52	(33)	81	(29)
History of smoking[a]	33	(7)	10	(6)	23	(8)
Number of live births[b]	2	(1–3)	2	(1–4)	2	(1–3)
Hormonal contraception	87	(20)	37	(24)	50	(18)
Lifetime number of sex partners	3	(2–4)	3	(2–3)	3	(2–4)
Informal Residence[c]	233	(53)	79	(50)	154	(55)
Any unprotected sex in previous month	70	(16)	22	(14)	48	(17)
CD4 T-cell count[d] **(cells/μL)**	NA	NA	NA	NA	448	(298–639)

Abbreviations: HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; NA, not applicable.

[a] History of smoking: ≥1 cigarette/day for ≥6 consecutive months

[b] Hormonal contraception includes injection, oral and implant-based contraceptive

[c] Informal residence defined as non-permanent housing or slum dwelling

[d] Evaluated among HIV-1 infected female participants (n=283)

Missing data: age at sexual debut (9), number of live births (8), use of hormonal contraception (7), lifetime number of sex partners (7), residence (1), any unprotected sex in the month before enrollment (10), CD4 count (1)

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Table 2

Male participant characteristics.

	Overall (N=441)		HIV-1-uninfected (N=283)		HIV-1-infected (N=158)	
Characteristic	**n (%) or Median (IQR)**					
Age	35	(30–41)	34	(28–39)	36	(32–43)
Age at sexual debut	18	(16–19)	18	(16–20)	17	(15–19)
Less than primary education	64	(15)	41	(14)	23	(15)
Earn a monthly income	375	(85)	240	(85)	135	(85)
History of smoking[a]	187	(42)	111	(39)	76	(48)
Circumcised	345	(79)	233	(83)	112	(71)
Lifetime number of sex partners	5	(3–9)	5	(3–8)	6	(4–10)
Informal residence[b]	224	(51)	145	(51)	79	(50)
Any unprotected sex in previous month	70	(16)	45	(16)	25	(16)
CD4 T-cell count[c] **(cells/μL)**	NA	NA	NA	NA	355	(236–513)

Abbreviations: HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; NA, not applicable.

[a] History of smoking: ≥1 cigarette/day for ≥6 consecutive months

[b] Informal residence defined as non-permanent housing or slum dwelling

[c] Evaluated among HIV-1 infected male participants (n=158)

Missing data: age at sexual debut (3), circumcision (5), lifetime number of sex partners (2), any unprotected sex in the month before enrollment (3), CD4 count (4)

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Table 3

Cytology results among 441 women in HIV-1 discordant couple relationships.

	Overall (N=441)		HIV-1-uninfected (N=158)		HIV-1-infected (N=283)	
	n (%)					
Normal cervical cytology	337	(76)	127	(80)	210	(74)
Low-grade cervical abnormalities						
ASC-US	38	(9)	11	(7)	27	(10)
LSIL	41	(9)	14	(9)	27	(10)
High-grade cervical abnormalities						
ASC-H	9	(2)	4	(3)	5	(2)
HSIL	14	(3)	2	(1)	12	(4)
SCC	2	(0)	0	(0)	2	(1)

Abbreviations: ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesions; ASC-H, atypical squamous cells cannot exclude high-grade squamous intraepithelial lesions; HSIL, high-grade squamous intraepithelial lesions; SCC, squamous cell carcinoma; HIV-1, human immunodeficiency virus type 1.

Int J STD AIDS. Author manuscript; available in PMC 2015 April 01.

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Table 4

Female participant characteristics by cervical cytology.

		Normal cytology (N=337)		Low-grade abnormalities (N=79)				High-grade abnormalities (N=25)			
Characteristic	**N**	**n (%)/Median (IQR)**		**n (%)/Median (IQR)**		**aOR[a]**	**95% CI**	**n (%)/Median (IQR)**		**aOR[b]**	**95% CI**
Age		29	(24–34)	28	(24–32)	1.0	(0.9, 1.0)	27	(25–34)	1.0	(0.9, 1.1)
Monthly income											
>8,000 Ksh	40	30	(75)	9	(23)	1.0	Referent	1	(3)	1.0	Referent
≤8,000 Ksh	401	307	(77)	70	(17)	0.7	(0.3, 1.5)	24	(6)	2.4	(0.3, 19.1)
Hormonal contraception											
No	353	279	(79)	54	(15)	1.0	Referent	20	(6)	1.0	Referent
Yes	87	58	(67)	**24**	**(28)**	**2.0**	**(1.2, 3.6)**	5	(6)	1.2	(0.4, 3.4)
Parity		2	(1–3)	2	(1–3)	1.1	(0.9, 1.4)	2	(2–2)	1.0	(0.7, 1.3)
History of Pap screening											
No	388	293	(76)	71	(18)	1.0	Referent	24	(6)	1.0	Referent
Yes	53	44	(83)	8	(15)	0.9	(0.4, 1.9)	1	(2)	0.3	(0.0, 2.1)
Age at sexual debut		18	(16–20)	18	(16–19)	1.0	(0.9, 1.1)	**17**	**(15–18)**	**0.8**	**(0.7, 1.0)**
Lifetime number of sex partners		3	(2–4)	3	(2–4)	0.9	(0.8, 1.1)	3	(2–4)	0.9	(0.7, 1.1)
HSV-2 seropositivity											
No	150	119	(79)	25	(17)	1.0	Referent	6	(4)	1.0	Referent
Yes	287	215	(75)	53	(18)	1.3	(0.8, 2.2)	19	(7)	1.8	(0.7, 4.6)
Residence type											
Formal	207	173	(84)	27	(13)	1.0	Referent	7	(3)	1.0	Referent
Informal	233	163	(70)	**52**	**(22)**	**2.0**	**(1.2, 3.4)**	**18**	**(8)**	**2.7**	**(1.1, 6.7)**
Unprotected sex in previous month											
None	367	282	(77)	65	(18)	1.0	Referent	20	(5)	1.0	Referent
Any	70	52	(74)	13	(19)	1.0	(0.5, 2.0)	5	(7)	1.4	(0.5, 3.8)
HIV-1 status											
Seronegative	158	127	(80)	25	(16)	1.0	Referent	6	(4)	1.0	Referent
Seropositive	283	210	(74)	54	(19)	1.2	(0.7, 2.1)	19	(7)	2.0	(0.8, 5.1)
Log HIV-1 viral load		5	(4–5)	5	(3–5)	1.0	(0.8, 1.3)	5	(4–5)	1.4	(0.8, 2.2)

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		Normal cytology (N=337)		Low-grade abnormalities (N=79)				High-grade abnormalities (N=25)			
Characteristic	**N**	**n (%)/Median (IQR)**		**n (%)/Median (IQR)**		**aOR[a]**	**95% CI**	**n (%)/Median (IQR)**		**aOR[b]**	**95% CI**
CD4 T-cell count (cells per μL)		457	(306–681)	424	(292–597)	0.9[c]	(0.8, 1.1)	384	(254–557)	0.8[c]	(0.7, 1.1)

Bold typeface indicates significant association ($p<0.05$)

Abbreviations: aOR, adjusted odds ratio; HSV-2, herpes simplex virus type 2; HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; CI, confidence interval.

[a] Low-grade abnormalities (ASCUS and LSIL) versus normal, adjusted for female participant's age

[b] High-grade abnormalities (ASC-H, HSIL, SCC) versus normal, adjusted for female participant's age

[c] per 100 cells per μL

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Int J STD AIDS. Author manuscript; available in PMC 2015 April 01.

Table 5

Male participant characteristics by female partner's cervical cytology result.

		Normal cytology (N=337)		Low-grade abnormalities (N=79)				High-grade abnormalities (N=25)			
Characteristic	**N**	**n (%) or Median (IQR)**		**n (%) or Median (IQR)**		**aOR[a]**	**95% CI**	**n (%) or Median (IQR)**		**aOR[b]**	**95% CI**
Age		35	(30–41)	34	(28–40)	1.0	(1.0, 1.0)	34	(31–43)	1.0	(1.0, 1.1)
Monthly income											
>8,000 Ksh	173	142	(82)	29	(17)	1.0	Referent	2	(1)	1.0	Referent
≤8,000 Ksh	268	195	(73)	50	(19)	1.2	(0.7, 2.0)	**23**	**(9)**	**8.4**	**(2.0, 36.3)**
Male circumcision											
No	93	65	(70)	24	(26)	1.0	Referent	4	(4)	1.0	Referent
Yes	345	270	(78)	55	(16)	0.6	(0.3, 1.1)	20	(6)	1.3	(0.4, 4.0)
Age at sexual debut		18	(16–19)	17	(15–20)	1.0	(0.9, 1.1)	18	(16–20)	1.1	(0.9, 1.2)
Lifetime number of sex partners		5	(3–9)	5	(3–10)	1.0	(1.0, 1.0)	4	(3–7)	1.0	(0.9, 1.0)
HSV-2 seropositivity											
No	222	179	(81)	31	(14)	1.0	Referent	12	(45)	1.0	Referent
Yes	217	156	(72)	**48**	**(22)**	**1.9**	**(1.2, 3.2)**	13	(6)	1.2	(0.5, 2.8)
Residence type											
Formal	217	176	(81)	32	(15)	1.0	Referent	9	(4)	1.0	Referent
Informal	224	161	(72)	47	(21)	1.6	(1.0, 2.6)	16	(7)	1.9	(0.8, 4.5)
Unprotected sex in previous month											
None	369	283	(77)	68	(18)	1.0	Referent	18	(5)	1.0	Referent
Any	70	52	(74)	11	(16)	0.9	(0.4, 1.8)	7	(10)	2.1	(0.8, 5.3)
HIV-1 status											
Seronegative	283	210	(74)	54	(19)	1.0	Referent	19	(7)	1.0	Referent
Seropositive	158	127	(80)	25	(16)	0.8	(0.5, 1.4)	6	(4)	0.5	(0.2, 1.3)
Log HIV-1 viral load		5	(4–5)	5	(4–6)	1.1	(0.8, 1.6)	5	(4–5)	1.2	(0.6, 2.4)
CD4 T-cell count (cells per μL)		358	(220–509)	364	(273–515)	1.0[c]	(0.8, 1.2)	325	(208–567)	1.0[c]	(0.7, 1.5)

Bold typeface indicates significant association ($p<0.05$)

Abbreviations: aOR, adjusted odds ratio; HSV-2, herpes simplex virus type 2; HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; CI, confidence interval.

[a] Low-grade abnormalities (ASCUS and LSIL) versus normal, adjusted for female participant's age

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[b] High-grade abnormalities (ASC-H, HSIL, SCC) versus normal, adjusted for female participant's age

[c] per 100 cells per μL

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Table 6

Partnership characteristics by female partner's cervical cytology result.

		Normal cytology		Low-grade abnormalities				High-grade abnormalities			
Characteristic	**N**	**n**	**(%)**	**n**	**(%)**	**aOR[a]**	**95% CI**	**n**	**(%)**	**aOR[b]**	**95% CI**
HIV-1 infection and CD4 count (cells/μL)											
HIV(−) female, HIV(+) male CD4>350	78	64	(82)	12	(15)	1.0	Referent	2	(3)	1.0	Referent
HIV(−) female, HIV(+) male CD4≤350	76	60	(79)	12	(16)	1.1	(0.5, 2.7)	4	(5)	2.1	(0.4, 12.2)
HIV(+) female CD4>350, HIV(−) male	191	148	(77)	33	(17)	1.1	(0.5, 2.3)	10	(5)	2.2	(0.5, 10.2)
HIV(+) female CD4≤350, HIV(−) male	91	61	(67)	21	(23)	1.9	(0.9, 4.2)	9	(10)	4.7	(1.0, 22.8)
Age											
Female<29, Male<35	163	122	(75)	29	(18)	1.0	Referent	12	(7)	1.0	Referent
Female<29, Male≥35	51	35	(69)	14	(27)	1.7	(0.8, 3.6)	2	(4)	0.6	(0.1, 2.7)
Female≥29, Male<35	52	37	(71)	14	(27)	1.9	(0.8, 4.5)	1	(2)	0.2	(0.0, 1.7)
Female≥29, Male≥35	175	143	(82)	22	(13)	0.8	(0.3, 2.3)	10	(6)	0.4	(0.1, 1.7)
Combined monthly income											
>8,000 Ksh	210	167	(80)	36	(17)	1.0	Referent	7	(3)	1.0	Referent
≤8,000 Ksh	231	170	(74)	43	(19)	1.1	(0.7, 1.9)	**18**	**(8)**	**2.5**	**(1.0, 6.3)**
Any unprotected sex in previous month											
Both partners report no	332	256	(77)	61	(18)	1.0	Referent	15	(5)	1.0	Referent
Either or both partners report yes	109	81	(74)	18	(17)	0.9	(0.5, 1.7)	10	(9)	2.1	(0.9, 4.9)
Combined lifetime number of sex partners											
Median (IQR)		8	(6–13)	9	(6–13)	1.0	(1.0, 1.0)	7	(6–10)	1.0	(0.9, 1.0)

Bold typeface indicates significant association ($p<0.05$)

Abbreviations: aOR, adjusted odds ratio; HSV-2, herpes simplex virus type 2; HIV-1, human immunodeficiency virus type 1; IQR, interquartile range; CI, confidence interval.

[a] Low-grade abnormalities (ASCUS and LSIL) versus normal, adjusted for female participant's age

[b] High-grade abnormalities (ASC-H, HSIL, SCC) versus normal, adjusted for female participant's age

Missing data among couples with normal cervical cytology: combined HIV-1 infection and CD4 T-cell count (4), combined lifetime number of sex partners (6); Missing data among couples with evidence of high-grade cervical lesions or cervical cancer: combined lifetime number of sex partners (2)