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Research Article

The Impact of Human Immunodeficiency Virus and Human Papillomavirus Co-Infection on HPV Genotype Distribution and Cervical Lesion Grade in a Semi-Urban Population in Tigoni, Kenya

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Background: Cervical cancer, a common cause of death among women, is attributable to human papilloma virus (HPV). Human immunodeficiency virus (HIV) infection can potentially alter the incidence of cervical cancer. Prophylactic HPV vaccines are a major advance against cervical cancer. Epidemiological research on HPV and cervical cancer is therefore justified.

Objective: To determine the impact of HIV and HPV co-infection on the HPV genotype distribution and cervical lesion grade in Tigoni, Kenya.

Methodology: This was a cross-sectional study. Women aged 25 to 60 years were invited for cervical cancer and HIV screening. HPV typing was done by PCR on residual cervical samples after cytology reporting.

Results: Of 438 samples, 140 (31.96%) were positive for at least one type of HPV. The most frequent HPV types were 16, 56, 53, 35, and 39. When co-infection with HIV was examined, 37 (32.5%) were HPV-/HIV+, 63 (19.4%) were HPV+/HIV-, 77 (67.5%) were HPV+/HPV+ ($p<0.0001$). High risk (HR)-types were the more frequent across all positive samples; HR-HPV+/HIV+ were 43 (37.7%), ($p<0.0001$).

Conclusion: HIV infection was a significant risk factor in HPV infection with 65.5% of cases being both HPV and HIV infected. Over 77% of those individuals who had a CIN III or greater were HPV positive. HR-HPV types were found across all diagnostic categories in the cases that had a cervical tissue biopsy with HPV type 16 being the most dominant type, particularly in high grade lesions.

Key words: HIV, HPV genotype, cervical lesions

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1. Introduction

Cervical cancer is an important global public health problem and a common cause of death among women, and it is attributable to human papillomavirus (HPV) (Walboomers et al, 1999; Parkin et al, 2008). In a large series of invasive cervical cancer from around the world, HPV-DNA was detected in 99.7% of the tumors, leading to the conclusion that HPV was a necessary cause of cervical cancer (Bosch et al, 1995; Walboomers et al, 1999; Bosch et al, 2007). The identification of HPV's role in cervical cancer has led to important advances in primary prevention through vaccination and diagnosis through HPV detection (Stanley et al, 2008; Bosch et al, 2008). However, tangible reduction in the incidence of cervical cancer and the impact on global public health will probably take decades. As HPV types are divergent, efficacy of current vaccines is type-restricted, and therefore development of the next generation of HPV vaccines will require inclusion of relevant antigens from several HPV types (Lowy, 2008). Geographical profiling of HPV type distribution will be important in making vaccines more relevant for target populations.

Most women will be infected with HPV sometime in their lifetime. Results from large meta-analyses studies indicate that at any given point in time, 10.4% (95% confidence interval (CI) 10.2-10.7) of women worldwide are positive for cervical HPV DNA (Bosch et al, 2008). The prevalence of HPV is higher in less developed regions (13.4%; 95% CI: 13.1-13.7) than in the more developed regions (8.4%; 95% CI: 8.3-8.6) (Bosch et al, 2008). The same studies indicate that African women at 22.1% (95% CI: 20.9-23.4) and East African women in particular, have the highest HPV prevalence rates (31.6%; 95% CI: 29.5-33.8) (Bosch et al, 2008). HPV type 16 is the most common in all continents, with an estimated point prevalence of 2.6% (95% CI: 2.5-2.8) worldwide, and HPV type 18 the second most frequently detected type (Clifford et al, 2005). Regional differences are thought to be related to geographical and immunogenetic factors, such as defects in cellular immunity through chronic cervical inflammation, malnutrition and more recently, HIV infection; Type 16 though appears to be less influenced by immune impairment than other types (Clifford et al, 2005).

Although many women get infected with HPV, most do not develop cervical cancer. Several co-factors are postulated to influence the disease process. The potential co-factors include exogenous factors such as tobacco smoking, hormonal contraceptives, and co-infections with other sexually transmitted infections (Munoz et al, 2006). In addition, viral co-factors, such specific HPV types, viral load, and viral integration, as well as host co-factors such as endogenous hormones, genetic factors, and factors related to the immune response may variably influence the course of HPV infection (Munoz et al, 2006).

Women with HIV infection have been shown to be more likely not only to have a concurrent HPV infection but also to have an increased risk for a high grade cervical squamous intraepithelial lesion (La Ruche et al, 1998; Temmerman et al, 1999; Womack et al, 2000; Baay et al, 2004; Hawes et al, 2006; Didelot-Rousseau et al, 2006; Ngándwe et al, 2007). HPV is the commonest sexually transmitted infection, with more than 75% of sexually active adults acquiring one or more genotypes in their lifetime (Bosch et al, 2008). However, by age 30 years, most women clear the infection due to an effective cell-mediated immune response, and only a small number thereafter are diagnosed with a HPV-associated lesion (Schiffman, 1992). It is thought that it is through its effect on CD4+ cells and regulation of immune responses to a variety of antigens that HIV attenuates the systemic response to HPV (Palefsky, 2006).

The prevalence of HIV among adult Kenyan women was 13% in 2003 with trends reported to have decreased to 5.1% by 2006 (KDHS, 2003). The high prevalence of HIV may increase the incidence of cervical pre-cancer and potentially, of cervical cancer. Gichangi et al (2002), however, demonstrated that a two to three-fold increase in HIV prevalence did not translate to a proportionate increment in incidence of cervical cancer. They hypothesized that HIV-infected women die from HIV-related opportunistic infections before they develop invasive cervical cancer. The mean survival time for women with HIV in 2008 was reported to be 5 years (Yamada et al, 2008) while typically more than 10 years elapse before the development of cervical cancer after HPV infection. Yamada et al (2008) also advanced the possibility that sub-clinical cervical cancer may be missed in many women dying prematurely from AIDS-related opportunistic infections.

This study was carried out to establish whether the co-infection of HIV and HPV has an influence on HPV genotype distribution and on the prevalence and grade of cervical neoplasia.

2. Methodology

2.1 Study population

In a population-based study in Tigoni, Kenya, women aged 25 to 60 years eligible for cervical cancer screening were screened for cervical cancer and HIV infection. Inclusion criteria included age between 25 and 60 years, sexually active but not pregnant, and should not have had a hysterectomy or ablation of the cervix. Exclusion criteria were prior conization or other treatment for cervical neoplasia, mental incompetence, and not giving consent to participate.

The prevalence of cervical neoplasia in some studies had shown to be about 10% in HIV negative women and more than 29% in HIV positive women (ter Muelun, 1992). It was expected then that more than 500 women would have abnormal smears in this population and these would be enrolled for the subsequent studies for the description of prevalence and types of HPV in HIV positive and negative women. Out of these it was conservatively expected that about 60% (Rozeendal et al, 2000), would have low grade lesions and these would be enrolled for colposcopy and biopsy in the evaluation of CIN in HIV positive and HIV negative patients.

Assumptions at recruitment:

1. That Tigoni District Hospital, being a district public hospital, would provide most of the health care

services that the local communities would need, and was accessible to all age groups, all genders and all religions.

2. That there was no exclusion on the basis of socio-economic status in service provision by the Tigoni District Hospital.

3. That the study did not specifically select those who were immune-compromised by HIV infection.

4. That there was no exclusion of those screened from social networks or women's groups (an important vehicle for recruitment for the study).

Most women in this peri-rural community belonged to a church or women's group. In previous community mobilization activities for health events such as health field days, the University of Nairobi's Centre for Health and Behaviour Studies had used the women leaders of these groups to get the word out and to send invitations. We used the same social networks for recruitment and for re-calling those women who needed follow-up and did not return for their appointment.

2.2 Investigations

Informed consent was obtained from the women and a pre-tested questionnaire administered to collect socio-demographic, gynecological history and lifestyle information. A gynecological examination was performed and a liquid-based cervical sample collected. The cervical cytology was reported using the Bethesda system 2001 (Solomon et al, 2002). A total of 629 out of 4,500 women had an abnormal pap smear [Atypical squamous cells of undetermined significance (ASCUS)]. Over 72% of those with abnormal smear had colposcopy and biopsy and their residual liquid-based pap smears were further processed for HPV typing. A tracer was also engaged to trace women who had abnormal cytology and needed colposcopy or were HIV positive and did not return for their appointments.

HPV typing was done on the residual sample by polymerase chain reaction (PCR) as described by Depuydt et al (2006). Amplification of β-globin DNA was performed as a positive control for the presence of amplifiable DNA in the specimens. Testing was done at Labo RIATOL, Antwerp, Belgium. All samples were subjected to 19 different quantitative PCRs. Oligonucleotide primers and probes for PCR detection and quantification of HPV 16 E7, 31 E6, 33 L1, 35 E4, 39 E7, 51 E6, 52 L1, 58 L1, 58 E6 and 67 L1 were selected. The viral load of HPV type 16 E7, 18 E7, 31 E6, 33 L1, 33 E6, 35 E4, 39 E7, 45 E7, 51 E6, 52 L1, 52 E7, 53 E6, 56 E7, 58 L1, 58 E6, 59 E7, 66 E6 and 68 E7 was determined using a *Taq*Man-based real-time PCR analysis. All positive smears and tissue biopsy slides were sent to University of Ghent for a second reading as a quality control measure. For analysis, the HPV types were classified according to oncogenic risk. High risk types included 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59; Probable high risk (or intermediate risk): 26, 53, 66, 68, 73, 82; and low risk types: 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and CP6108 (Munoz et al, 2006).

Blood was obtained for HIV testing at the same time at which the pap smears were taken. HIV testing was performed using enzyme-linked immunosorbent assay (ELISA) and all positives confirmed by a second ELISA. Blood was drawn for CD4 counts on the return appointment if the woman was HIV positive. All those who had an abnormal smear were referred for colposcopy and biopsy. The biopsy results for those who returned for that appointment are included in the analysis.

2.3 Statistical Analysis

Data was entered into SPSS version 11.5 and analyzed. Continuous variables were summarized as means and standard deviations, and categorical variables were summarized into frequencies and percentages. Data analysis was descriptive and categorical for cervical neoplasia and HPV/HIV co-infection, as well as categorical for HPV types in cervical neoplasia for both HIV positive and negative women. Odds ratios were calculated for HPV and HIV infection in women with cervical neoplasia. Levels of significance were set at 0.05.

2.4 Ethical Considerations

Ethical approval to carry out this study was granted by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UON Study approval No: **P144/12/2003**).

Pap smears and blood samples were obtained after written, informed consent. The participants received all their pap smear and HIV results after post-test counseling, but were informed that the results of HPV typing would not be availed to them since, at the time, they had no clinical utility.

3. Results

The demographic characteristics of the women with HPV results are shown in **Table 1**. Out of 629 samples for which HPV typing was done, 438 had a HPV result of which 32.7% were positive. The positive rate was highest in the youngest age group (25-29 years) at 28.6%, dipped marginally to 26.4% in the next age group and then increased, also marginally to 27.1% in the age group 35-39. Thereafter, it decreased with age, although there was a small peak in the 50-54 years. Factors such as age, contraceptive use and HIV status were significant in HPV infection ($p<0.05$), while being currently post-partum or menopausal, age at first intercourse, number of sexual partners either lifetime or recent and parity were not (**Table 2**, Supporting Information).

HPV genotyping results were initially grouped according to HPV risk group and cytologic diagnostic category as shown in **Table 3** (Supporting Information). Of the total 324 pap smears reported as normal cytology, 67 (20.7%) were HPV positive, 14.2% were High Risk (HR)-HPV positive, the remainder, 6.5% were Intermediate HPV-type positive, and 79.3% were negative HPV. The HR-HPV types were dominant in all diagnostic categories but HR-HPV and intermediate HPV types had similar positive rates in LSIL categories. LR-HPV types were uncommon in this group. When

presence of any HPV was analyzed according to cervical biopsy result, 75.6% (31) of those who had a normal biopsy result were negative, and 34% (12) of those reported as having a Cervical intraepithelial neoplasm grade III (CIN III) or greater were positive (**Table 4**, Supporting Information). The association between the HPV status and the diagnostic categories was significant (p<0.0001).

Table 1: Unadjusted analysis for HPV infection

Variable	Total (n=438)	HPV Status		O.R (95% C.I)	p-value
		Positive (n=140) (%)	Negative (n=298) (%)		
Age in years					
25-29	108	40 (28.6)	68 (22.8)	1	
30-34	96	37 (26.4)	59 (19.8)	1.07 (0.58-1.96)	0.939
35-39	103	38 (27.1)	65 (21.8)	0.99 (0.55-1.81)	0.904
40-44	62	14 (10.0)	48 (16.1)	0.50 (0.23-1.07)	0.075
45-49	37	3 (2.1)	34 (11.4)	0.15 (0.03-0.56)	0.001
50-54	20	5 (3.6)	15 (5.0)	0.57 (0.17-1.84)	0.435
55+	12	3 (2.1)	9 (3.0)	0.57 (0.11-2.48)	0.534
Gynecologic status					
Menopause	39	8 (5.7)	31 (10.4)	0.52 (0.21-1.23)	0.108
History of contraceptive use	**n= 419**	**n=136**	**n=283**		
None	183	76	107	2.08 (1.35-3.22)	<0.001
Current contraceptive					
IUD	37	6	31	0.52 (0.18-1.40)	0.232
Hormonal (Oral)	51	20	31	2.34 (1.14-4.77)	0.018
DMPA	56	19	37	1.74 (0.86-3.51)	0.134
Other	92	15	77	0.43 (0.21-0.86)	0.016
HIV test					
Positive	114	77	37	8.62 (5.20-14.34)	<0.001
Parity					
Median range		3(0-9)	3(0-9)		0.301

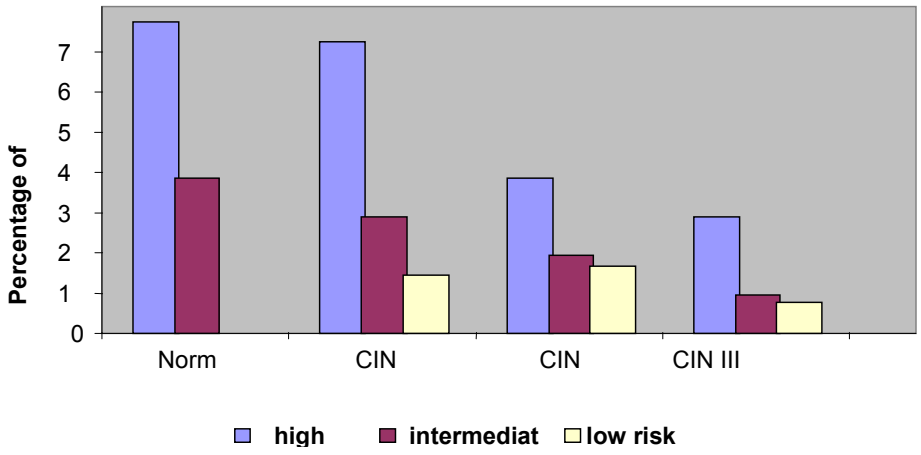
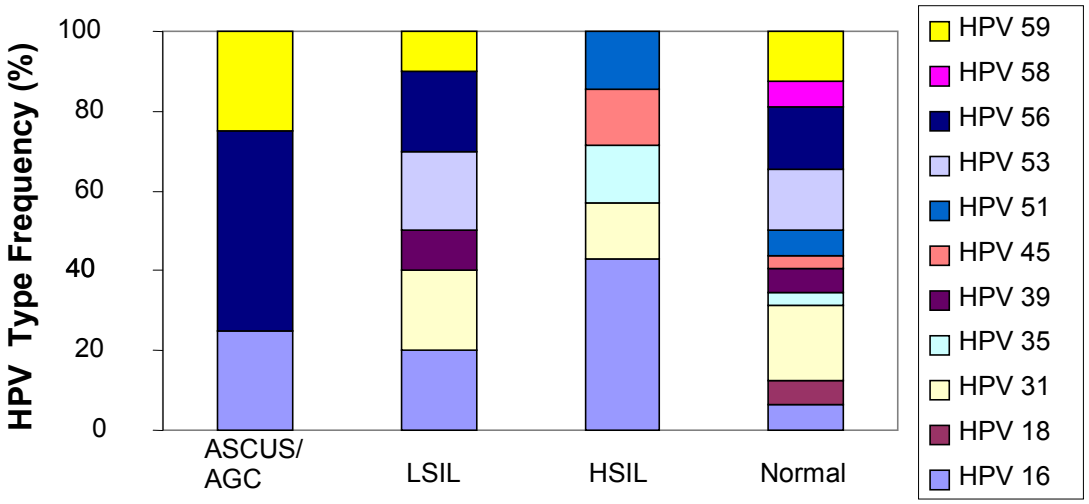


Figure 1: Distribution of HPV risk type and cervical lesion

Table 6: HPV prevalence and risk status by HIV status among women in Tigoni (n=438)

HPV	HIV STATUS			P-value
	Population (n=438)	Sero-negative (n=324)	Sero-positive (n=114)	
Status				
- negative	298(68.0)	261(80.6)	37(32.5)	
- positive	140(32.0)	63(19.4)	77(67.5)	<0.0001
Risk Status				
- High	91(20.8)	48(14.8)	43(37.7)	
- Intermediate	44(10.0)	14(4.3)	30(26.3)	
- Low	5(1.1)	1(0.3)	4(3.5)	<0.0001
HPV Types (HPV present n=140)				
HPV 16	27(6.2)	11(3.4)	16(14.0)	0.629
HPV 18	8(1.8)	3(0.9)	5(4.4)	0.661
HPV 31	17(3.9)	8(2.5)	9(7.9)	0.856
HPV 33	13(3.0)	3(0.9)	10(8.8)	0.095
HPV 35	18(4.1)	6(1.9)	12(10.5)	0.287
HPV 39	22(5.0)	7(2.2)	15(13.2)	0.176
HPV 45	14(3.2)	3(0.9)	11(9.6)	0.062
HPV 51	13(3.0)	6(1.9)	7(6.1)	0.930
HPV **53***	27(6.2)	7(2.2)	20(17.5)	0.027
HPV 56	25(5.7)	8(2.5)	17(14.9)	0.149
HPV 59	11(2.5)	7(2.2)	4(3.5)	0.196
HPV **66***	14(10.0)	4(6.3)	10(13.0)	0.193
HPV **68***	10(7.1)	3(4.8)	7(9.1)	0.322

***** *Intermediate risk (IR)-HPV types*



ASCUS/AGUS – Atypical squamous cells of undetermined significance/Atypical glandular cells, LSIL – Low grade squamous intra-epithelial lesions, HSIL – High grade squamous intra-epithelial lesions

Figure 2: HPV type frequency and cervical neoplasia grade

The results of HPV oncogenic risk categories and the cervical biopsy results are presented in **Table 5** (Supporting Information). HR-HPV types were found in all biopsy diagnostic categories in the 76 cases that had a tissue biopsy, and were the dominant types in this group. Intermediate risk and LR-HPV types were much lower.

The individual HPV types and their distribution by HIV status is shown in **Table 6** and **Figure 1**. A total of 77 (67.5%) were HIV+/HPV+; 261 (80.6%) were HIV-/HPV-; 63 (19.4%) were HIV-/HPV+; and 37 (32.5%) were HIV+/HPV-. The association between HPV and HIV was significant. The HPV type distribution however, did not seem to be influenced by the HIV status ($p>0.05$) (**Table 6**) in the 140 cases that were positive for HPV. When compared with HIV as a risk factor for HPV infection, 37 (32.5%) were HPV-/HIV+, 63 (19.4%) were HPV+/HIV-, 77 (67.5%) were HPV+/HPV+ ($p<0.0001$); HR-HPV+/HIV+ were 43 (37.7%), IR-HPV+/HIV+ 30 (26.3%), and LR-HPV+/HIV+ 4 (3.5%), ($p<0.0001$). High risk (HR)-types were the more frequent across all positive samples. Type 16 was the most frequent type in both normal and abnormal cytology samples, although it had the highest frequency in high-grade cervical lesions. The 5 most frequent HPV types were 16, 56, 53, 35, 39 with 15%, 10.5%, 9.3%, 7.9%, and 7.9% respectively. Type 18 had an overall frequency of 1.3%.

The ten most frequent HPV types in normal, squamous intra-epithelial lesions and ASCUS/AGC are represented graphically in **Figure 2**. Pap smears reported as normal had the broadest spectrum of HPV types, of which 31 was the most frequent, followed by 53 and 56; in LSILs, HPV types 16, 31, 53 and 56 had similar frequencies, and 59 and 39 were about half frequent; in HSIL, HPV type 16 was the most frequent, followed by similar frequencies for types 31, 35, 45 and 51. Three types were found in the few cases of ASCUS/AGC, type 56 being the most frequent, and followed by 16 and 59. There was no type 18 or the related type 45 found in ASCUS/AGC, which was only found in normal pap smears.

When HPV type 16 was analyzed for cervical grade of disease, the frequency increased with the severity of cervical lesion (**Figure 3**). It was also present in normal smears.

The CD4 lymphocyte counts for those who were HIV positive are shown in **Table 7** (Supporting Information) and the distribution across clinical utility categories in women with abnormal cytology in **Figure 4.** The rates of HPV infection and abnormal cytology increased as CD4+ cell counts decreased as did the number of HPV types, especially the HR and LR types involved in the infection. HIV negative women were included as controls.

4. Discussion

The results of this study show a high prevalence of HPV infection in cervical samples at a given point in time of 32.7% in a population of women with a high HIV prevalence of 14.2%. The age-adjusted global figure of HPV DNA in women with normal cytology in large meta-analysis studies was 10.5% and 31.6% for Eastern Africa (Bosch et al, 2006) in which PCR-based assays were used for HPV DNA detection in cervical cells. Prevalence of HPV in women with cervical lesions is generally reported in the range of 50-85% (Bosch et al, 2006). In our study population, the HPV prevalence in samples with abnormal cytology was 52%, and 80% in those who had biopsy confirmed CIN III or greater. The prevalence of HPV is high in young women in this study as expected, where prevalence mirrors incidence, declining with age, as women clear the infection. There was a small increase in the age group 50-54 years. A similar trend has been previously documented by Bosch et al (2006) who raised several possibilities for the second increase: new HPV infections acquired by middle-age women due to changes in sexual behaviour, reactivation of latent infection following immune senescence, and/or a cohort effect translating high exposure throughout their lifetime in elderly populations. Follow-up and behavioral studies have reported a high rate of new sexual partners among the 40 years and older in developed countries (Munoz et al, 2004; Wellings et al, 2006) and the difference of close to ten years in the age groups between Europe and the United States for the second peak was thought to be suggestive of a behavioral factor rather than a biological factor linked to menopause or immune senescence (Bosch et al, 2006). Bosch et al (2006) also raised the concept of latency of HPV infection as best demonstrated in recurrent respiratory papillomatosis (RRP) in which LR-HPV types 6/11 keep recurring from apparently normal tissue in the absence of obvious external infection.

Sexual history by age at first intercourse, number of lifetime and recent sexual partners did not seem to influence the prevalence of HPV infection in this study group. Majority of women reported having had only one lifetime sexual partner, consistent with other large studies that examined population distributions in Kenya and some developing countries by age and sex and number of sexual partners in the past year from 15 to 45 years (Wellings et al, 2006). Contraceptive use was significant factor for HPV infection in this study group ($p<0.001$), and even though the numbers are small, this finding is consistent with findings in an IARC monograph classifying hormonal contraceptives as carcinogenic to the cervix and increased risk for women who tested positive for high risk HPV-DNA and for CIN 3/carcinoma *in situ* (Smith et al, 2007). The hypothesized mechanism through which hormonal contraceptives may act as a cofactor for cervical neoplasia is that estrogens and progestagens enhance HPV gene-expression in the cervix through progesterone-receptor mechanisms and hormone-response elements in the viral genome (Bosch et al, 2006).

HR-HPV types, and in particular HPV type 16, were the most frequent across all diagnostic categories. The prevalence in HSIL was lower than the reported 85% in cross-sectional studies of the natural history of cervical cancer supportive of the contribution of HPV in HSIL (thought to represent the true morphological precursor of invasive cervical cancer) (Clifford et al, 2005). There is substantial variability however, in attributable risk of HPV in the various studies of the meta-analysis between CIN 2 and CIN 3; this is thought to be probably due to variations in the quality of specimens tested and the HPV DNA assays used (Clifford et al, 2005).

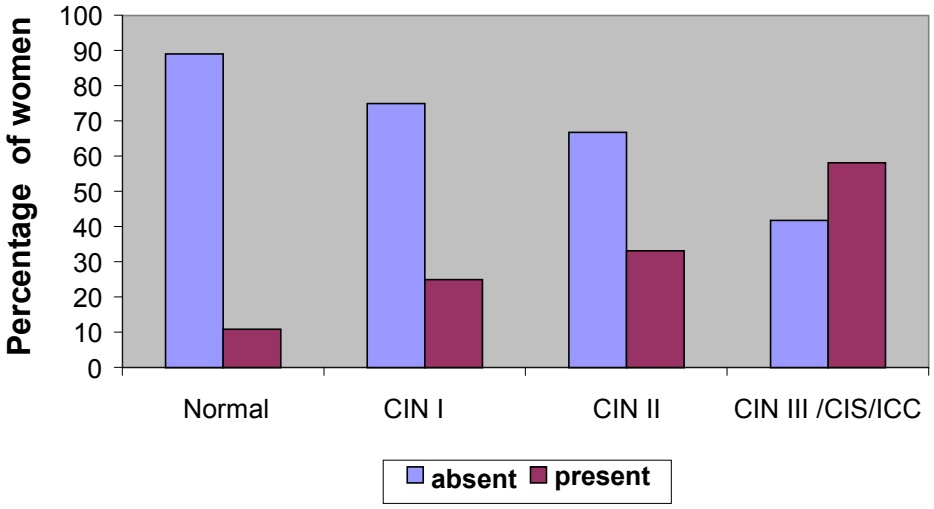


Figure 3: Distribution of HPV 16 by cervical lesion grade

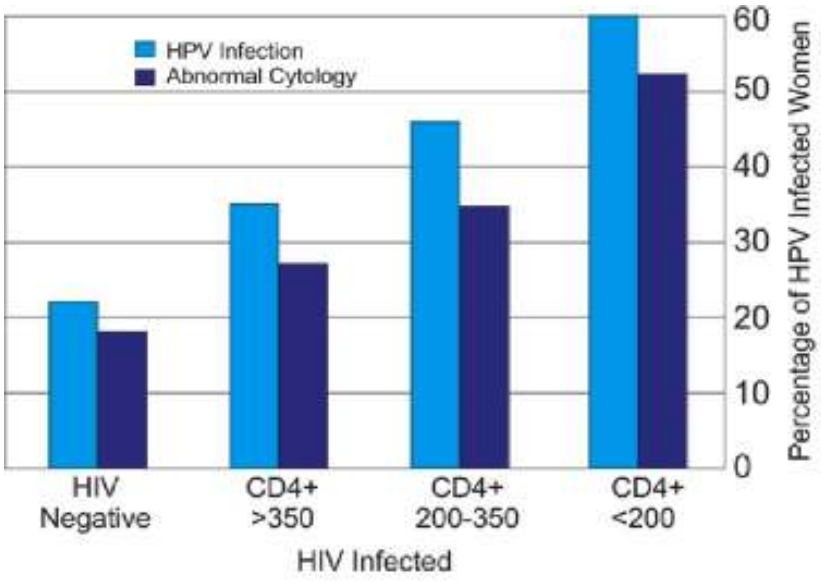


Figure 4: Comparison of HPV infection and abnormal cytology in HIV sero-negative and HIV-seropositive women versus CD4+ counts (cells/µl)

The most frequent HPV types in this study in women with normal cytology in descending order were: HPV-31, -56, -53, -59, -16, -18, -39, -51, -58, -45, and -35, in LSIL in descending order were HPV-16, -31, -51, -56, -59, and -39; in HSIL were HPV-16, -51, -45, -35, and -31; and in ASCUS/AGC HPV-56, -16 and -59. In comparison a comprehensive meta-analysis of 53 studies published up to 2006 in women with and without cervical lesions showed the following HPV types in order of decreasing prevalence: in women without cervical abnormality: HPV-16, -42, -58, -31, -18, -56, -81, -35, -33, -45, and -52; in LSIL: HPV-16, -31, -51, -53, -56, -52, -18, -66, and -58 and for HSIL: HPV-16, -31, - 58, -18, -33, -52, -35, -51, -56, -45, -39, -66, and 6 [Smith et al 2007]; with women in Africa being less likely to be infected with HPV 16 than other HR-HPV and LR-HPV types than their counterparts in Europe, although more likely to be infected with other HR-HPV and LR-HPV types [Clifford et al 2005].

No meta-analysis on HPV type-specific prevalence among women with ASCUS currently exists, probably because the diagnosis of ASCUS, unlike that of LSIL, is less well standardized given the wide variability in intra- and inter-observer definition, and HPV positivity varies greatly in published studies (Clifford et al, 2006). There were close similarities in the most frequent types, except for the low frequency of HPV type 18 and 45 in cases with abnormal cervical cytology in our series. In a study in Thika, Kenya, Ngugi et al (2011) found similar HPV type distribution with highest frequency of HPV type 16, and type 18 being less common than internationally reported. The intermediate types were also less frequent in our population than is reported in meta-analysis studies.

The results indicated an increase in HPV and abnormal cervical lesions as CD4+ cells decreased, as has been reported elsewhere (Yamada et al, 2008); the prevalence of oral, anal and cervical HPV infection in HIV positive compared to HIV negative individuals increases with progressively lower CD4+ cell counts, as does the incidence of high-grade intraepithelial lesions (Palefsky, 2006).

5. Conclusion

HPV infection rate was high in this population with a high HIV prevalence. Age, contraceptive use, and HIV infection were significant factors in HPV infection with 65.5% of cases being both HPV and HIV infected. Over 77% of those individuals who had a CIN III or greater were HPV positive. HR-HPV types were found across all diagnostic categories in the cases that had a cervical tissue biopsy with HPV type 16 being the most dominant type, particularly in high grade lesions. Types 18 and 45, some of the more frequently reported elsewhere in women with cervical lesions, were absent in the abnormal cases. The rates of HPV infection and abnormal cytology increased as CD4+ cell counts decreased, as did the number of HPV types involved in the infection. HPV type distribution in this population has implications for HPV-DNA based diagnostics and future vaccine developments for the region.

Conflict of Interest declaration

The authors declare no conflict of interest

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Supporting Information

The Impact of Human Immunodeficiency Virus and Human Papillomavirus Co-Infection on HPV Genotype Distribution and Cervical Lesion Grade in a Semi-Urban Population in Tigoni, Kenya

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Table 2: HPV infection status, cervical biopsy results and sexual history

	HPV Status			
Variable	**Positive**	**Negative**	**O.R (95% C.I)**	**p-value**
Age at first intercourse				
<18	23	42	1.16 (0.58-2.31)	0.783
18+	36	76	1	
Number of lifetime sexual partners				
1	15	51	1	
2+	44	67	2.23 (1.06-4.73)	0.032
Number of recent sexual partners				
1	48	101	1	
2+	5	7	1.50 (0.39-5.64)	0.532
Biopsy Results				
Normal	9	31	1	
CIN I	8	6	4.59 (1.07-20.66)	0.023
CIN II	6	1	20.7 (1.95-521.1)	0.003NS
CIN III/CIS/ISC	12	3	13.8 (2.71-80.09)	0.003NS
	HIV Status			
Variable	**Positive**	**Negative**	**O.R (95% C.I)**	**p-value**
Risk Status				
High	43	48	0.22 (0.01-2.27)	0.199
Intermediate	30	14	0.54 (0.02-6.06)	1.000
Low	4	1	1	

NS – not significant; CIN – cervical intraepithelial neoplasia; CIS – carcinoma in situ; ISC – invasive squamous carcinoma

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Table 3: Distribution of HPV risk group and cytologic diagnostic category (n=443)

HPV	Cytology			
	Normal n (%)	**ASCUS/AGC n (%)**	**LSIL n (%)**	**HSIL/AIS/Squamous cell carcinoma n (%)**
Positive				
HR –HPV	46 (14.2)	10 (25.0)	15 (34.1)	20 (57.1)
IR-HPV	21 (6.5)	3 (7.5)	15 (34.1)	5 (14.3)
LR-HPV	0 (.0)	1 (2.5)	2 (4.5)	2 (5.7)
Sub-total positive	67 (20.7)	14 (35)	32 (72.7)	27 (77.1)
Negative	257 (79.3)	26 (65.0)	12 (27.3)	8 (22.9)
Total	324 (73.1)	40 (9.0)	44 (9.9)	35 (7.9)

ASCUS – atypical squamous cells of undetermined significance; AGC – atypical glandular cells; AIS – adenocarcinoma in situ; LSIL – Low grade squamous intraepithelial lesion; HSIL – High grade squamous intraepithelial lesion; HR – High risk; IR – intermediate risk; LR – low risk

Table 4: Un-adjusted analysis for HPV infection by cervical biopsy result (n=76)

Characteristic	HPV STATUS		P-value
	Negative (n=41/76)	**Positive (n=35/76)**	
Cervical biopsy Results			
- Normal	31 (75.6)	9 (25.7)	
- CIN I	6 (14.6)	8 (22.9)	<0.0001
- CIN II	1 (2.4)	6 (17.1)	
- CIN III /CIS/ISC	3 (7.3)	12 (34.3)	

The percentages were calculated down the column

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Table 5: Comparison of oncogenic HPV types with cervical lesion grade (n=76)

HPV	Population (n=76)(%)	Cervical lesion grade			
		Normal (n=40)(%)	CIN I (n=14)(%)	CIN II (n=7)(%)	CIN III /CIS/ISC (n=15)(%)
Status					
- negative	41 (53.9)	31 (77.5)	6 (42.9)	1 (14.3)	3 (20.0)
- positive	35 (46.1)	9 (22.5)	8 (57.1)	6 (85.7)	12 (80.0)
Risk Status					
- High	22 (62.9)	6 (66.7)	5 (62.5)	3 (50.0)	8 (66.7)
- Intermediate	10 (28.6)	3 (33.3)	2 (25.0)	2 (33.3)	3 (25.0)
- Low	3 (8.6)	0 (.0)	1 (12.5)	1(16.7)	1 (8.3)
Types					
HPV 16	12 (34.3)	1 (11.1)	2 (25.0)	2 (33.3)	7 (58.3)
HPV 18	1 (2.9)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)
HPV 31	2 (5.7)	1 (11.1)	0 (0.0)	1 (16.7)	0 (0.0)
HPV 33	1 (2.9)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)
HPV 35	6 (17.1)	0 (0.0)	4 (50.0)	1 (16.7)	1 (14.3)
HPV 39	6 (17.1)	1 (11.1)	0 (0.0)	3 (50.0)	2 (28.6)
HPV 45	3 (8.6)	0 (0.0)	2 (25.0)	0 (0.0)	1 (14.3)
HPV 51	3 (8.6)	1 (11.1)	1 (12.5)	0 (0.0)	1 (14.3)
HPV **53**	7 (20.0)	2 (22.2)	2 (25.0)	1 (16.7)	2 (28.6)
HPV 56	8 (22.9)	3 (33.3)	4 (50.0)	0 (0.0)	1 (14.3)
HPV 59	2 (5.7)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)
HPV **66**	3 (8.6)	0 (0.0)	1 (12.5)	2 (33.3)	0 (0.0)
HPV **68**	3 (8.6)	1 (11.1)	0 (0.0)	0 (0.0)	2 (28.6)

*Intermediate risk-HPV (IR-HPV) types are in **bold***

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Table 7: HPV prevalence and risk status in HIV positive women stratified by CD4 levels

HPV Prevalence	Population	CD4 levels		
		<200	200-350	>350
	70 (73.7%)	**32 (78.0%)**	**18 (85.7%)**	**20 (60.6%)**
Risk Status				
- High	42 (44.2%)	18 (43.9%)	14 (66.7%)	10 (30.3%)
- Intermediate	23 (24.2%)	10 (24.4%)	3 (14.3%)	10 (30.3%)
- Low	5 (5.3%)	4 (9.8%)	1 (4.8%)	0 (0.0%)
HPV Types				
HPV 16	16 (16.8%)	9 (22.0%)	4 (19.0%)	3 (9.1%)
HPV 18	4 (4.2%)	3 (7.3%)	1 (4.8%)	0 (0.0%)
HPV 31	8 (8.4%)	5 (12.2%)	3 (14.3%)	0 (0.0%)
HPV 33	8 (8.4%)	6 (14.6%)	0 (0.0%)	2 (6.1%)
HPV 35	13 (13.7%)	10 (24.4%)	0 (0.0%)	3 (9.1%)
HPV 39	14 (14.7%)	6 (14.6%)	2 (9.5%)	6 (18.2%)
HPV 45	10 (10.5%)	7 (17.1%)	3 (14.3%)	0 (0.0%)
HPV 51	7 (7.4%)	5 (12.2%)	2 (9.5%)	0 (0.0%)
HPV **53***	15 (15.8%)	7 (17.1%)	2 (9.5%)	6 (18.2%)
HPV 56	18 (18.9%)	10 (24.4%)	5 (23.8%)	3 (9.1%)
HPV 59	4 (4.2%)	3 (7.3%)	0 (0.0%)	1 (3.0%)
HPV **66***	8 (8.4%)	6 (14.6%)	1 (4.8%)	1 (3.0%)
HPV **68***	6 (6.3%)	3 (7.3%)	0 (0.0%)	3 (9.1%)

***** *Intermediate risk (IR)-HPV types*

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