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Assessment of Risk Predisposition to Human Papilloma Virus through Cervical Infections Screening of Women Attending an Outpatient Health Facility In Nairobi, Kenya

Agnes Omire[1], Nancy Budambula[1], Washingtone Ochieng[2,5], Caroline Baliach[2], Danvas Kerosi[1], Hillary Langat[1], Minda Okemwa[3], Leah Kirumbi[2], Rashid Aman[4,5], Bernhardts Ogutu[2,4] and Raphael Lwembe[2,5]

1. Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000-00200, Nairobi, Kenya
2. Kenya Medical Research Institute, P.O. Box 54840-00100, Nairobi, Kenya
3. University of Nairobi, P.O. Box 30197-00100, Nairobi, Kenya
4. Centre for Research in Therapeutic Sciences, P.O. Box 59857-00200, Nairobi, Kenya
5. African Centre for Clinical Trials, P.O. Box 2288-00202, Nairobi, Kenya

Email of the corresponding author: rlwembe@yahoo.com

Abstract

There is limited data on comparative disposition to cervical cancer among HPV infected women in Kenya. We aimed to determine the distribution of HPV infection, cervical abnormalities and infections commonly reported on cervical pap smears among both HIV positive and HIV negative women attending a reproductive health clinic at the largest national hospital in Kenya. A total of 187 women aged 18 to 50 years attending the reproductive clinic at Kenyatta National Referral Hospital in Nairobi were recruited into the study. All consenting subjects were screened for HIV by serology and their cervical smears taken and immediately fixed on slides for Papanicolaou (Pap) staining. A second endocervical swab was collected in the same sitting for HPV DNA extraction and PCR amplification of the HPV LI region. Of the 187 women studied, 27 (14.4 %) were positive for HIV and 90 (48.1%) had one or more infection associated with bacterial vaginosis, candidiasis, cervicitis or inflammation of the cervix of unknown cause. Eight (4.3%) women had abnormal cervix, 3/8 being of high grade squamous intraepithelial lesions (HSIL), 1/8 of low grade squamous intraepithelial lesions (LSIL), 1/8 had adenocarcinoma while the remaining 3 had atypical squamous cells of undetermined significance (ASC-US). The remaining 89/187 (47.6%) women had normal smears with no infection. Of the 89 women with normal smears, 82 (92.1%) were HIV negative. A total of 66 (35.3%) women were positive for HPV L1 DNA by PCR and included 30 of the 89 women with normal cytology. Of the 27 HIV positive women, 14 (51.9%) were also positive for HPV LI DNA. 52 of the 160 (32.5%) HIV negative women were positive for HPV L1 DNA. We report more cases of cervical intraepithelial lesions among HIV positive than HIV negative women. Similarly, the other infections commonly found on Pap smear tests were higher among HIV negative than HIV positive women. HPV prevalence among these clinic-attending women was higher in those with normal cytology, indicating an increased underlying risk of cervical cancer in a setting where routine diagnostic screening is limited or non-existent.

Key words: cervical cancer, HIV, HPV, cervical cytology

1. Introduction

Cervical cancer is among the most common cancers affecting reproductive women all over the world (Ononogbu *et al*. 2013) with East Africa being one of the high risk regions with most cases (GLOBOCAN 2012). Infection with Human Papillomavirus (HPV) is required but is insufficient for cervical cancer (Munoz 2000). Other risk factors include smoking, HIV co-infection, high parity and co-infection with other sexually transmitted diseases. Infection and persistence of HPV in the cervix leads to changes in the epithelial cells of the cervix which cause warts, lesions, and cancer (Doorbar 2006). HPV has onco-proteins E6 and E7 that destroy p53 and pRB tumour suppressor proteins (Zheng & Baker 2006). Cancer usually occurs in people who are infected and do not clear the infection for a long period of time (Doorbar 2006).

Cervical Pap smear is a way to differentiate and detect abnormal from normal cervical cells. The current guidelines recommend that women be screened every 3 years (Kenya national guidelines for cancer management 2013). A cervical Pap smear test looks at the squamous epithelial and endocervical cells for any abnormality in the cervix. Majority of cervical cancers occur at the squamous/columnar junction (Doorbar 2006), the reason why specimen for pap smear are collected at this region. During routine Pap smear, other infections of the genital tract such as candidiasis, bacterial vaginosis, and herpes can also be identified.

Pap smear results are reported according to the Bethesda System which classifies them as as negative (negative for intraepithelial lesion or malignancy), atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells - cannot exclude high grade squamous intraepithelial lesion (ASC-H), low grade squamous intraepithelial lesions (LSILs), high grade squamous intraepithelial lesions (HSILs), endocervical carcinoma in situ (AIS), and abnormal glandular cells including atypical glandular cells of undetermined significance (AGC-US). ASC-US means that there are changes in cells that may lead to cancer but are of uncertain significance. LSILs or HSILs denotes that cancerous changes are likely to

occur and the risk of developing cervical cancer is greater with HSIL. When cell changes are seen at the upper part of the cervix or in the endocervix, it is denoted as AGC-US. The Bethesda System also classifies Pap smear reporting to include microorganisms encountered during routine Pap smear such as *Trichomonas vaginalis*, fungal organisms morphologically consistent with *Candida sp.,* bacteria morphologically consistent with *Actinomyces sp.*, cellular changes consistent with Herpes simplex virus, bacterial vaginosis/shift in vaginal flora, and presence of inflammation, red blood cells or repair cells. It also includes atrophy and glandular cells status after hysterectomy (International Agency for Research on Cancer, 2014).

Due to immunosuppression, HIV positive women tend to have persistent HPV infections, more cytological abnormalities and increased risk to other infections especially sexually transmitted infections (Isaakidis *et al*., 2013). In healthy women HPV infection is rarely persistent and is often cleared or is asymptomatic in the cervix (Doorbar 2006). However if it does not clear, it develops to cervical cancer, a process which might take up to 15 to 20 years (Finhaber and Michelow 2009). However in immunocompromised individuals, it can take only 5 to 10 years. Interactions of HPV and HIV pose a huge health concern especially in a poor resource country like Kenya with high HIV cases especially in women according to the Kenya Aids Indicator Survey (KAIS 2012). Women in poor resource settings are at a greater risk of death from cervical cancer than those in the developed world because of poor access to screening and prompt treatment (Finhaber and Michelow, 2009). The prevalence of cervical abnormalities in women is up to 5 times in HIV positive women than those who are negative for HIV (Memiah et al). Studies in developing countries indicate an increase in cancer rates (Franco et al., 2001). According to Yamada *et al*., 2008, the incidence of cervical lesions and cancer is quite high in women in Nairobi. It is therefore important to know the prevalence of cervical abnormalities not only for HIV negative women but also among HIV positive women for efficient monitoring of precancerous lesions. This is also important for surveillance purposes in order to know whether the screening efforts are adequate.

2. Methods

This study was conducted at a reproductive Health clinic at a National hospital in Kenya. Ethical clearance was obtained from the National Ethical Review Board, (Kenya Medical Research institute and the Kenyatta National Hospital (KNH) Ethical Review Committees). The reproductive health clinic offers family planning services, cervical cancer screening, well baby clinic, fistula care and colposcopy to women. KNH is a national referral hospital with patients from all counties in Kenya. Participants between the ages of 18 and 50 years, who consented to participate and be tested for HIV serologically, were recruited. A sample size of 187 was calculated as representative of the participants. Individuals were approached at the clinic's waiting bay. Those willing to participate were invited and explained further about the study and informed consent obtained.

HIV diagnosis was done using rapid diagnostic testing algorithmn as per the Kenya national guidelines (National AIDS and STI Control Programme, 2008). Determine^{TM} rapid test was used as the first rapid test for screening. All cases reactive to the first test were screened again using the second rapid test UniGold^{TM}. In case of indeterminate results, 3ml of blood was collected for an ELISA test to confirm the HIV status. Both pre and post HIV counselling was done. Participants were then asked to fill a questionnaire designed to elicit demographic data such as age, marital status, family planning methods, level of education, awareness on HPV and cancer.

Cervical Pap smears were made from every cervical swab collected from every woman who consented in the study. The subjects were asked to lie on their back in a lithotomy position and then visual inspection of the external genitalia done by an expert. Speculum examination was done and the cervical os was visually inspected. Cervical swabs were collected by inserting a cytology brush into the endocervical canal making sure ectocervical and endocervical cells were taken by rotating the brush one full turn and removing gently. The cells were then spread evenly on a glass slide and fixed immediately. A second endocervical swab was taken in the same sitting. The brush was then rinsed immediately in cytology solution vial by rotating the brush in the solution at least 10 times and then swirling the brush to release the material into the vial. The tightly closed vials were transported to the Kenya Medical Research Institute for storage and DNA analysis.

Fixed smears were stained to enable visualization of the cell nucleus and cytoplasm. The Pap stain is a polychrome stain made up of one nucleus stain, haematoxylin and two cytoplasmic stains, Orange G and Eosin. The nuclei are stained blue, dark violet to black. The Orang G stain is for mature and keratinized cells. The target structures are stained orange in different intensities. Changes in the size of the nucleus, presence of koilocytosis or changes in the nuclear to cytoplasm ratio were sought after the staining. An independent pathologist and cytotechnologist were involved in the study for quality control. Pap smear results were classified in accordance with the Bethesda System. Presence of other microorganisms during microscopic examination of the stained slides was also noted as either shift in vaginal flora suggestive of bacterial vaginosis, cervicitis, and fungal organisms consistent with Candida, Leptothrix or inflammation of unknown cause.

HPV DNA was detected by nested PCR using HPV consensus primers that target a 450 base pair region in the L1 open reading frame of HPV in the primary reaction and GP5+/GP6+ primers in the nested reaction (Michelle et al. 2011). In the primary PCR, 5µl of the extracted DNA was amplified in a reaction mix containing 1X PCR buffer2.0 mM $MgCl_2$, 500nM forward primer MY09, 500nM reverse primer MY11 and 100µM of each dNTPs and 0.13 units of Taq polymerase enzyme. After an initial denaturation at 95°C for 10 minutes, the reaction was cycled 30 times at 95°C for 30 seconds, 48°C for 30 seconds and 72°C for seconds. The final extension was at 72°C for 10 minutes.
In the nested PCR, 5µl of the primary PCR, 2.0mM $MgCl_2$, 500nM of GP5+, 500nM of GP6+ and 400µM of dNTPs and 0.13 units of Taq polymerase enzyme was used. The cycling conditions were as follows; an initial denaturation at 94°C for 4 minutes, then 94°C for 30 seconds, annealing at 43°C for 30 seconds and extension at 72°C for 30 seconds. The final extension was at 72°C for 10 minutes. After the nested PCR, a 5µl aliquot of the PCR product was mixed with 1µl of 6X loading dye and loaded onto a 2% agarose gel for electrophoresis. Presence of the expected 150 bp amplicon was considered positive for HPV DNA in the sample collected. Statistical analysis was done using SPSS Version 18.0. Chi square was used to compare groups and the level of significance set as less than 0.005 ($p<0.005$).

3. RESULTS

Baseline patient information:

A total of 187 women were enrolled in the study. Participants were between the ages of 18 and 50 years with a median age of 36 years. Majority of the participants (114/187 or 61%) were aged between 25 and 39 years while 64 (34.2%) were over 40 years. Only 9 (4.8%) were aged below 25 years. (Table 1). A total of 100 (53.5%) had had a previous pap smear test and 3 (1.6%) had undergone a visual inspection with acetic acid (VIA). Overall, 86 (46%) had reported normal cytology. By marital status, 149/187 women were actively married, 5/187 were either divorced or widowed (table 1). Majority of the women who participated in the study had had some formal education with only one woman (0.5%) having no formal education. Fifteen (8%) women had no children, 29(15.5%) had one child, 68 (36.4%) had two children and 75(40.1%) had three or more children. Questionnaires were administered to extract women's knowledge of cancer. 167(89.3%) women had heard about cervical cancer, 46(24.6%) had some knowledge of HPV and 45 (24.1%) knew about the risks associated with cervical cancer.

HIV-1 infection status by various socio-demographic indicators.

All recruited patients were first screened for HIV-1 as described in methods. Twenty seven of 187 patients (14.4%) were positive for HIV-1. Of the 27 HIV-1 positive patients, 15 (55.6%) were aged above 40 years, 11 (40.7%) were between 25 and 39 years while 1 (3.7 %) was below 25 years. HIV-1 infections by marital status were as follows: 14 of 149, (9.4%) married, 8 of 33 (24.2%) unmarried and 5/5 (100%) divorced/widowed women were positive for HIV. The differences among these marital status groups was statistically significant ($p<0.001$). When HIV infection was assessed by level of education or age, women who had attained at least secondary education, had the lowest Infection rates ($p=0.035$). Similarly, women aged above 25 years (p 0.041), and that those with reported genital tract inflammation (p value 0.015) had the highest rates of HIV-1 infection. These data are detailed on Table 3.

Cytology screening and Pap smear

Cytology screening was done for all patients to identify their risk predisposition to HPV. Out of 187 patients, 8 (4.3%) had abnormal cytology results, while 179/187 (95.7%) (Table 2) were negative for any cervical intraepithelial lesions or malignancy. Out of the 8 women with abnormal cytology, 3 (37.5%) had high grade squamous intraepithelial lesions; 1 (12.5%) had low grade squamous intraepithelial lesions, 1(12.5%) was positive for adenocarcinoma while 3 (37.5%) had atypical squamous cells of undermined significance (ASCUS). A total of 75% (6/8) of women with abnormal cervical cytology were HIV positive. Abnormal cervical cytology was observed in 22.2 % (6/27) and 1.3% (2/160) of the HIV positive and HIV negative women respectively. All participants aged 25 years and below had normal cytology results while 4/64 (6.3%) women aged above the age of 40 years had abnormal cytology results. There was a statistically significant association between cervical abnormalities and marital status and also between HIV infection and abnormal cytology, with higher abnormality reported among single and married women than widowed or divorced women (P value 0.047) and among HIV-1 positive than HIV-1 negative women (p value 0.000). There was no association between cervical abnormalities and level of education, number of children or family planning method. Detailed analysis of cytology data with respect to age and other variables is captured on table 2. HIV positive women between 25 and 39 (P value 0.019) years and those above 40 (p Value 0.000) years were at a greater risk of having cervical abnormalities.

When patients were next assessed for other infections, 90 (48.1%) had cervical inflammation of various causes. Sixteen of these (17 %) were due to bacterial vaginosis, 2 (2.2 %) due to candidiasis, 10 (11.1%) due to cervicitis, 1 had leptothrix and 61 (67.7%) had inflammation of unknown cause. Among the 90 women with inflammation, 14 (15.6%) were HIV positive

while 76 (84.4%) were HIV negative. By comparison, only 89/187 (47.6%) women studied had normal smears with no infection or cervical abnormalities. Eighty two of these (92.1%) women with normal cytology were HIV negative as shown on Figure 1. Surprisingly, no HIV positive woman in this study was shown to have candidiasis or leptothrix infection (Figure 1).

Distribution of HPV infection among various categories or risk groups of women

A total of 66 out of 187 (35.3%) women were positive for HPV DNA by PCR. Among these 66, 52 (78.8%) were HIV negative while 14 (21.2%) were HIV positive (Figure 1b). The HPV positive rate was seen to be higher in women aged below 25 years with 6/9 (66.7%) being positive for HPV. Of the 89 women with normal cytology, 30 (33.7%) were positive for HPV LI. HPV DNA was not detected in 2/8 (25%) of the women with abnormal cytology. Another 30 of 90 (33.3%) women with cervical inflammation were positive for HPV. Among the 16 women with bacterial vaginosis 5(31.3%) were HPV positive. Additionally, HPV was detected in 4/10 (40%) women with cervicitis and in 20/61 (32.8%) women with inflammation of unknown cause had HPV. Only 2/14 (14.3%) women with both detectable HPV DNA and HIV infections had normal cytology, with the rest showing abnormal cytology.

When HPV infection was assessed by marital status and age, single and married women had the highest rates of infection (p value 0.003). In addition women younger than 25 years were shown to have more HPV infection (value 0.043). There was no association between HPV infection and level of education (p value 0.508), Awareness of HPV and cancer (P value 0.427), family planning (P value 0.063) and the number of children (P value 0.153). These data are in Table 4. The differences among HIV and HPV status groups were statistically significant among women aged 40 years and above (P value 0.044).

4. Discussion

HIV prevalence in women between the ages of 15 to 64 years is 6.9 % (National AIDS and STI control programme, 2013). Our data however indicates a prevalence of 14.4% (27/187). This high prevalence in our study might be partly due to the clinic being in a referral hospital and most HIV positive women are prone to more cervical abnormalities and infection compared to HIV negative women (Finhaber and Michelow 2009, Yamada *et al.* 2008) prompting them to access such services as cervical screening, voluntary counseling and testing for HIV and also to access family planning services. HIV positive rate was seen in women above 25 years (p 0.041), and those with genital inflammation or infection (p value 0.015). HIV positive rate was seen to be increasing with increasing age (Table 3). The level of education was shown to be a significant factor in HIV infection (p=0.035) with women with little or no education having high infection rate. Yamada et al. 2008, found level of education to be a non-significant factor in HIV infection. All of the widowed/divorced women were HIV positive. This trend is similar to the one reported in National AIDS and STI control programme, 2013 with women who were reported to be widowed having a higher HIV prevalence (20.3%) than the single or married.

Health education is among the most effective ways of preventing and fighting sexually transmitted diseases but this information is lacking in the general population (Scarneciu *et al.*, 2014). From our data, it is quite clear that women do not understand cervical cancer and its causes. They are not aware of the role of the HPV infection in progression to cancer and majority have never heard of this virus (75.4%). Da Ros and Schmitt 2008 report that limited screening and poor disease reporting is as a result of people not having enough information about the transmission of sexually transmitted diseases or ignore the precautions required for safe sex. Clearly awareness on HPV and its transmission routes as well as education on the risk factors for cervical lesions or cancer is needed. If women are aware of this virus, they will be in a position to make the initiatives to go for regular pap tests because they know they are at risk especially if they are sexually active, are HIV positive and/or have multiple partners.

Of all the women sampled in this study, 4.3% had abnormal cytology results, while 179/189 (95.7%) of these women were negative for cervical intraepithelial lesions or malignancy. Abnormal cytology was observed in 22.2 % (6/27) and 1.3% (2/160) in HIV positive and HIV negative women respectively compared to 47% and 14 % respectively reported by Yamada et al. 2008. All participants aged 25 years and below had normal smears. There were higher cytological abnormalities in single and married women than widowed or divorced women (P value 0.047). Higher rate of abnormal cytology (p value 0.000) were seen in HIV positive women with a total of 75% (6/8) of women with cervical abnormal cytology being HIV positive.. Our results strongly indicate that HIV infection indeed does have some effect on cervical abnormalities or lesions. This is also in line with other studies that show HIV to be a risk factor for cervical abnormalities and cancer (Yamada et al. 2008, Finhaber and Michelow 2009.

In this study, 48.1% (90/187) had infection as either bacterial vaginosis (8.6%), cervicitis (5.3%), candidiasis (1.1%) leptothrix (0.5%) and unknown inflammation (32.6%). In a study by Oliver 2013 among women with abnormal visual inspection tests, 4.7% of the women sampled had infection with 2.2 % (5) having bacterial vaginosis and 1.7% (4) having candida. No studies to our knowledge in Kenya have been done to compare other cytological findings routinely found on Pap smear tests among HIV positive and negative women. We expect that HIV positive women would be prone to more infections

compared to the HIV negative women. Our results however are contradictory to this with statistically higher prevalence of infection being seen in HIV negative women (Figure 1). No HIV positive woman had candidiasis which is a common fungal infection. This could be attributed to some of the HIV positive women being on antibiotics like Septrin since the primary goal of antiretroviral therapy is to restore immunity.

We report a higher HPV prevalence of (35.5%) in both HIV positive and HIV negative women in this study. This is lower than the previous studies done in Kenya. A study by Yamada and her coworkers in 2008, revealed an HPV prevalence of 27% in women generally. A study by Muchiri et al. 2012 in Tigoni Kenya revealed a prevalence of 32.7%. This clearly indicates that HPV is very prevalent in Kenya and the prevalence is shown to be increasing, however more studies need to be done to prove this. The prevalence of HPV was 32.5% and 51.9% in HIV negative women and HIV positive women respectively. In Yamada et al. 2008, the prevalence of HPV in HIV negative women and HIV positive women was 17% and 49% respectively. The prevalence of HPV seems to be increasing and particularly for the HIV negative women.

The prevalence of HPV in women with normal cytology was 33.7%. which is slightly higher than what Muchiri et al 2012 reported (20.7%). The prevalence of coinfection of HPV and HIV in this study was 51.9% (14/27). This is lower than the one reported by Muchiri et al 2012 of 67.5%. There was significant statistical association between HPV infection, marital status and age (p value <0.05).

5. Conclusion

Our results indicate a resurgence of cervical infections and HPV prevalence coupled by lack of public awareness hence effective education programmes, screening and prompt treatment of early stages of cancer is advocated for. There were also higher cases of HPV in women with normal cytology, efforts to include HPV testing during routine pap smear is warranted.

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Table 1: baseline patient information

	Had Pap smear before			Know or heard of cervical cancer	
	YES	NO	Visual Inspection	YES	NO
Age (years)					
<25	1(0.5)	7(3.7)	1(0.5)	8(4.3)	1(0.5)
25-39	57(30.5)	57(30.5)	0(0.0)	101(54.0)	13(7.0)
>40	42(22.5)	20(10.7)	2(1.1)	58(31.0)	6(3.2))
Marital status					
Single	15(8.0)	17(9.1)	1(0.5)	31(16.6)	2(1.1)
Married	81(43.3)	66(35.3)	2(1.1)	131(70.1)	18(9.6)
Divorced/widowed	4(2.1)	11(0.5)	0(0.0)	5(2.7)	0(0.0)
Family planning					
Hormonal	23(12.3)	23(12.3))	0(0.0)	38(20.3)	8(4.3)
Non-Hormonal	77(41.2)	61(32.6)	3(1.6)	129(69.0)	12(6.4)
Total	100(53.5)	84(44.9)	3(1.6)	167(89.3)	20(10.7)

Table 2: Association of cervical abnormalities with various socio-demographic variables

	Number (%) with		
	Negative for intraepithelial lesions and malignancy	Abnormal cytology	P value
Age (years)			
<25	9(100)	0(0.0)	0.556
25-39	110(96.5)	4(3.5)	
>40	60(93.8))	4(6.3)	
Marital status			
Single	29(87.9)	4(12.1)	0.047*
Married	145(97.3)	4(2.7)	
Divorced/widowed	5(100)	0(0.00)	
Know causes of cervical cancer			
Yes	41(91.1)	4(8.9)	0.079
No	138(97.2)	4(2.8)	
HIV Status			
Positive	21(77.8)	6(22.2)	0.000*
Negative	158(88.3)	2(1.3)	
Family Planning			
Hormonal	45(97.8)	1(2.2)	0.417
Non hormonal	134(95)	7(5)	
Total	179(95.7)	8(4.3%)	

***P value is significant**

Table 3: HIV infection by various socio-demographic indicators

	Positive	Negative	P value
Age			
<25	1(11.1)	8(88.9)	0.041*
25-39	11(9.6)	103(90.4)	
Over 40	15(23.4)	49(76.6)	
Marital status			
Single	8(24.2)	25(75.8)	0.000*
Married	14(9.4)	135(90.6)	
Divorced or widowed	5(100)	0(0.0)	
Level of education			
None	1(100)	0(0.0)	0.035*
Primary	9(18.8)	39(81.2)	
Secondary	13(15.1)	73(84.9)	
Tertiary	4(7.7)	48(92.3)	
Number of live children			
None	3(20.0)	12(80.0)	0.926
One	4(13.8)	25(86.2)	
Two	9(13.2)	59(86.8)	
Three or more	11(14.7)	64(85.3)	
Inflammation/infection of the cervix			
No inflammation	7(7.9)	82(92.1)	0.015*
Inflammation	20(20.4)	78(79.6)	
Total	27(14.4)	160(85.6)	

***P value is significant**

Table 4: Distribution of HPV infection by various categories.

	Number	HPV DNA Positive	HPV DNA Negative	P value
Age				
<25	9(4.8)	6(66.7)	3(33.3)	0.043*
25-39	114(61)	43(37.7)	71(62.3)	
Over 40	64(34.2)	17(26.6)	47(73.4)	
Marital status				
Single	33(17.6)	20(60.6)	13(39.4)	0.003*
Married	149(79.7)	44(29.5)	105(70.5)	
Divorced/widowed	5(2.7)	2(40.0)	3(60.0)	
Done pap smear previously				
Yes	100(53.5)	31(31.0)	69(69.0)	0.261
No	84(44.9)	33(39.3)	51(60.7)	
Visual inspection with acetic acid	3(1.6)	2(66.7)	1(33.3)	
Family planning				
Hormonal	46(24.6)	11(23.9)	35(76.1)	0.063
Non hormonal	141(75.4)	55(39.0)	86(61.0)	
Cytology results				
Normal	89(47.6)	30(33.7)	59(60.3)	0.056
Abnormal	8(4.3)	6(75.0)	2(25.0)	
Inflammation	90(48.1)	30(33.3)	60(66.7)	
Total	187	66(35.7)	121(64.7)	

***P value is significant**

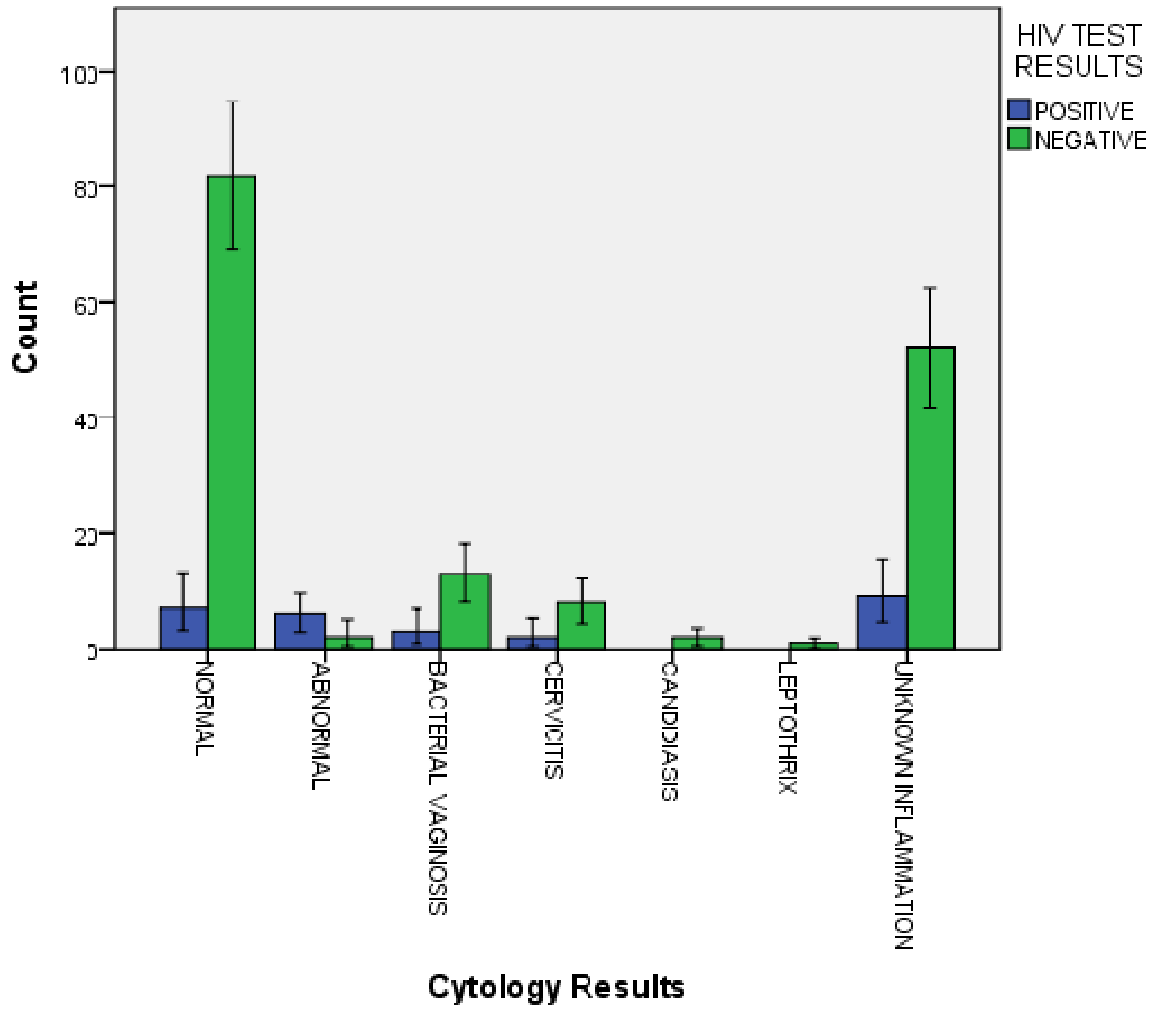

Figure 1a: Prevalence of Cervical abnormalities with HIV status.
Error bars: 95% CI. Abnormal results include Atypical Squamous Cells of Undetermined Significance (ASCUS), Low grade Squamous Intraepithelial Lesions (LSIL), High Grade Squamous Intraepithelial Lesions (HSIL) and adenocarcinoma. Normal cytology results indicate those with no inflammation nor abnormal cytology results.

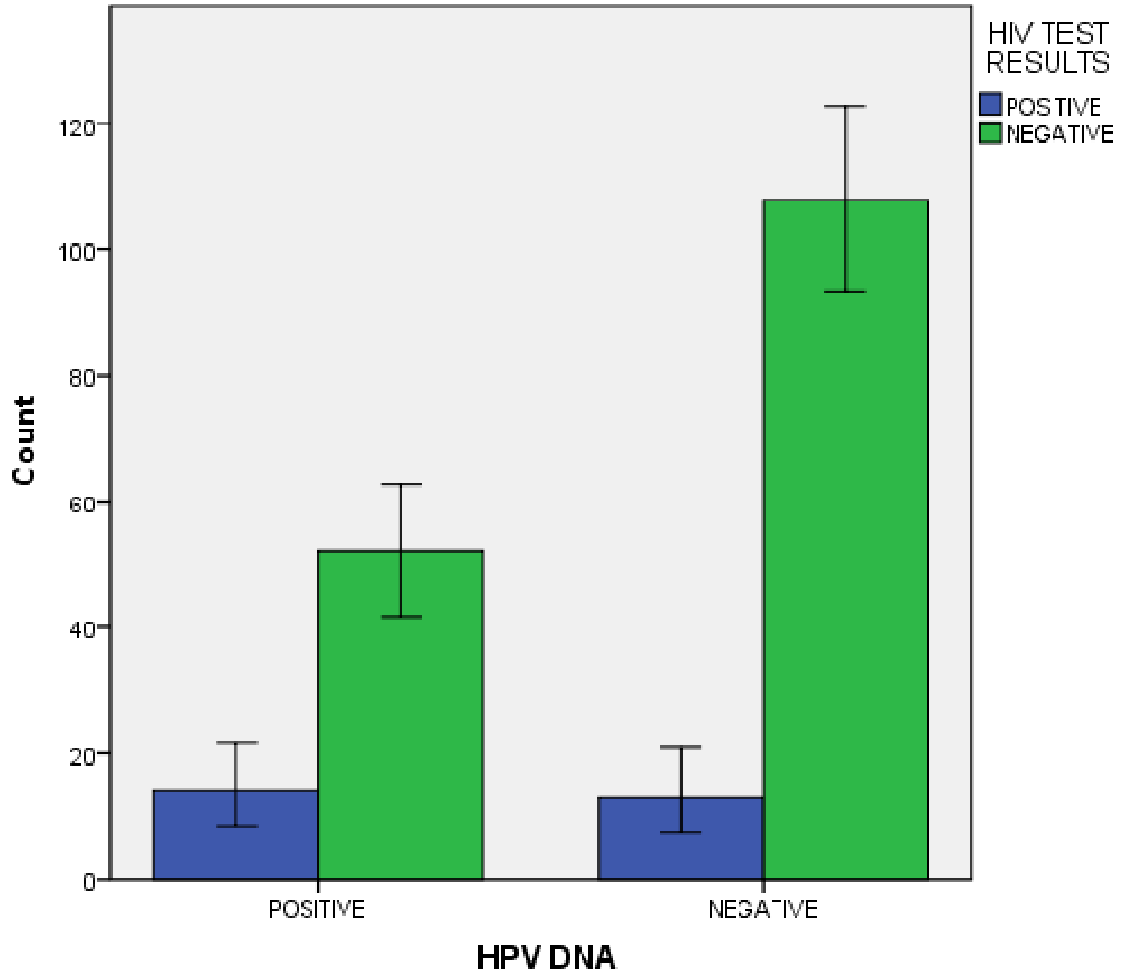

Figure 1b: Association of HIV and HPV infections
Error bars: 95% CI.