THE PREVALENCE OF ABNORMAL CERVICAL CYTOLOGY IN HIV POSITIVE MOTHERS AT SIX WEEKS POSTPARTUM AT K.N.H

A dissertation submitted in part fulfillment for the degree of masters of medicine (Obstetrics and gynecology), at the University of Nairobi.

By

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

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DEDICATION

This work is dedicated to my wife Dr. Annette Sang, pediatrics department and our lovely daughters Barbara, Charlene and Deborah.

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Table of Contents *Page No.*

List of Tables

List of Figures

LIST OF ABBREVIATIONS.

AGC	Atypical glandular cells.
ASC-US	Atypical squamous cells of undetermined significance
ASC-H	Atypical squamous cells, cannot exclude high grade lesion.
CIN	Cervical intra-epithelial neoplasia
DNA	Deoxy- ribonucleic acid
ELISA	Enzyme Linked Immunosorbent Assay
ERC	Ethics and Research Committee
HAART	Highly Active Antiretroviral Therapy
HGSIL	High grade squamous intra-epithelial lesion
HIV	Human immuno- deficiency virus
HPV	Human papilloma virus
HSV	Human simplex virus
ICC	Invasive cervical cancer
KNH	Kenyatta National Hospital
KDHS	Kenya demographic health survey.
LGSIL	Low grade squamous intra-epithelial lesion
O.R	Odds Ratio
PCR	Polymerase chain reaction
PMTCT	Prevention of Mother to Child Transmission.
SPSS	Statistical Package for Science Software
VLPS	Virus like particles
WHO	World health organization
VIA	Visual inspection with acetic acid

ABSTRACT

BACKGROUND:

Cancer of the cervix is one of the leading causes of morbidity and mortality among women especially in the developing world where cervical cytology screening is not readily available to the general population. Cervical intraepithelial neoplasia (CIN) precedes invasive disease by many years and is amenable to treatment by either ablation or excision procedures. The prevalence is even higher in HIV positive women and disease progression from CIN to ICC is faster. In a set up like ours where population based screening is low, postnatal clinic especially for the HIV positive mothers provide an opportunity for cervical cytology screening.

OBJECTIVE:

Broad objective

To determine the prevalence of abnormal cervical cytology and VIA findings among HIV positive women at 6 weeks postpartum at KNH.

Specific objective

Among HIV positive mothers at 6 weeks postpartum;

1. Describe cervical cytology findings.
2. Describe vaginal examination findings including VIA.
3. Compare cervical cytology and VIA findings.

Methods

Between 18th April and 17th October 2008, 175 postnatal HIV positive mothers seeking postnatal care services at KNH were interviewed, their cervix examined by VIA and evaluated for abnormal cervical cytology by Pap smear.

Results

Sixty five (37%) of the women enrolled had abnormal cervical cytology,with 95% being squamous cell abnormalities, 9% ASCUS, 7%AGUS, 17% LSIL, 6% HSIL and 3%SCC. Sixty eight (39%) women had positive results by VIA. In 25% of the smears, infections or bacterial vaginosis was reported. There was moderate agreement between VIA and Pap smear.

Conclusion.

Cervical cytology abnormalities and VIA abnormalities are common in HIV positive mothers as determined by both postpartum Pap smear cytology and VIA.

Recommendations.

There is need to strengthen cervical cytology screening including pelvic examinations for infections in HIV positive mothers.

INTRODUCTION AND LITERATURE REVIEW

Disease burden

Globally cervical cancer is the third most common cancer in women after breast cancer and colorectal cancer. Parkin et al estimated that cervical cancer was seventh most frequent cancer, representing 9.8% or 371,200 new cases worldwide.[1] A conservative estimate of the global prevalence (based on the number of patients still alive 5 years after diagnosis) suggests that each year there are 1.4 million cases of clinically recognized cervical cancer. It is also likely that 3-7 million women worldwide may have high grade dysplasia.[2]

In industrialized countries the incidence rates are generally low with age standardized rates less than 14 per 100,000 women compared with 37.4 per 100,000 in East Africa.[1] The International Agency for Research on cancer of the WHO estimates that nearly 80% of cervical cancer cases occur in developing countries and, in many such regions, it is the most common cancer and leading cause of death from cancer among women.[3] Within Africa, the incidence and prevalence estimates vary widely between geographic regions. Five of the seven countries with the highest incidence rates are in Eastern and Southern Africa; while in Northern Africa the incidence is lower.[3]

In Kenya the national incidence of cervical cancer is unknown as there is no population
based cancer registry. It is estimated the incidence is between 37 -47 per 100,000 women
Per year.[2] It is the second commonest malignancy, after breast cancer, as reported in cancer registry in the department of pathology.[4] Kaguta in his review of all Gynecological malignant tumors in the year 1974 to 1981 showed that malignant tumors of the cervix accounted for 75 percent of all gynecological tumors in women as seen in Kenyatta National Hospital.[5]

Cervical intra-epithelial lesions (CIN)

Cervical intraepithelial lesions refer to pre-invasive pathological intermediates of cervical cancer that are slow to progress and can be easily detected and treated. The abnormalities observed on a cytological smear or tissue biopsy of the cervix represent alterations in the degree of differentiation of cervical epithelial cells.

These changes depending upon lesion severity are manifested by nuclear enlargement and granulation, the presence of koilocytes, an increased nucleocytoplasmic ratio, and in high-grade lesions frequent mitosis.

Older definitions used the terms mild, moderate and severe cervical dysplasia to denote the presence of neoplastic cellular atypia from the basal layer to a point short of entire epithelium, while carcinoma in situ (CIS) was used to describe atypical cells spanning the full thickness of the epithelial layer. This nomenclature though still in use has been replaced by the term Cervical Intraepithelial Neoplasia (CIN), which divides the epithelial thickness into thirds to express severity:

- CIN 1 refers to cellular dysplasia confined to the basal third of the epithelium (formally mild dysplasia)
- CIN 11 refers to lesions confined to the basal two thirds of the epithelium (formally moderate dysplasia)
- CIN 111 refers to cellular dysplasia encompassing greater than two thirds of the epithelial thickness; including full thickness lesions (formerly severe dysplasia and CIS).

Today Cytologic smears are classified according to the Bethesda system, introduced in 1988 to improve the clinical relevance of the reporting of cervical cytology smear results. In this system, mild dysplasia/CIN 1 was combined with koilocytic or condylomatous atypia to create low-grade squamous intraepithelial lesion (LSIL or LGSIL). Moderate and severe dysplasia/CIS were merged to form the category of high-grade squamous intraepithelial lesion (HSIL or HGSIL) because of similarities in both the cytologic features and prognosis of these groups. Atypical squamous

cells (ASC) and atypical glandular cells (AGC) express equivocal findings. ASC is further subdivided into atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells, cannot exclude high grade squamous intraepithelial lesion (ASC-H). In addition, a description of specimen adequacy and suitability were added to improve consistency and quality of reporting.

Cervical intra-epithelial lesions (CIN) are typically seen in younger women and many years before a diagnosis of invasive cervical cancer.

The diagnosis of CIN is usually made in women in their twenties, carcinoma in situ in women 25 to 35 years of age, and invasive cancer after the age of 40, typically 8 to 13 years after a diagnosis of CIN III. Ostor in 1993 in a critical review reported progression of more than 12 % of CIN 111 to ICC. The risk for progression to ICC for CIN 1 and CIN 11 were 1 % and 5% respectively. However progression to CIN 111 was 11 % and 12% for CIN 1 and CIN 11 respectively [6]. (See table below)

Natural history of squamous cell intraepithelial lesion

Lesion	Regression	Persistence	Progress to CIN III	Progress to ICC
LGSIL(CIN 1)	57%	32%	11%	1%
LGSIL (CIN II)	43%	35%	22%	5%
HGSIL	32%	56%	-	12%

From Ostor AG. Natural history of CIN.[6]

The prevalence of CIN varies according to the geographic area and socioeconomic characteristics of the population studied, from as low as 1.05 percent in some family planning or gynecology clinics to as high as 13.7 percent in sexually transmitted disease clinics.[7] In Kenya the prevalence of cervical dyspasia nationally is unknown. However data is available for specific subpopulations. Among FP attendees, the most studied group in Kenya, 2-5.1 % have been reported to have cervical

dysplasia.[8, 9, 10] Among a mixture of FP and STD patients in Nairobi Kenya, the incidence of cervical dysplasia was 6,648 per 100,000 (6.6%) in 1997.[8] Fonck et al found a much higher prevalence of cervical dysplasia among women seeking STD treatment in Nairobi (13,077/100,000 or 13.1% women STD clients).[11] Kirima J, in a retrospective study of all cervical smear reports in Kenyatta National Hospital, Nairobi, found the prevalence rate of cervical intraepithelial neoplasias from December 1977 to November 1979 to be 20.4 per thousand (0.02%) among women attending gynecology outpatient clinic.[12]

Risk factors for cervical neoplasia

A consistent and dominant role of sexual activity in the etiology of cervical neoplasia has been demonstrated in numerous studies; moreover, the incidence of squamous cell cancer of the cervix in women who have not had any sexual relationships is almost nonexistent.[13] Sexual risk factors for CIN includes, sexual activity at an early age, history of sexually transmitted infections e.g. Chlamydia, herpes simplex virus, multiple sexual partners, or engaging in sexual activity with promiscuous men.[14]

These data firmly implicate a venereal agent as a major causal factor. This agent has been shown to be infection with the human papilloma virus (HPV).[15,16] In fact, the association between HPV and cervical neoplasia has proven so strong that most other behavioral, sexual and socioeconomic variables are found to be dependent upon HPV infection and do not hold up as independent risk factors.[17,18] Other consistently reported risk factors include; cigarette smoking, multiparty, [19, 20] exogenous or endogenous immunodeficiency, [21, 22] long-term oral contraceptive use, [23-25] and dietary factors [26] such as low carotene or low vitamin c intake[27] and folate deficiency.[28]

Human papilloma virus

HPV infection is endemic among sexually experienced individuals. At least 80 percent of sexually active women have acquired a genital HPV infection by 50 years of age; the point prevalence is much lower at 14-35 percent.[29] Most HPV infections are transient; overall 80 to 90 percent resolve within 2 to 5 years. Transient infections are particularly common in young women. In adolescents, for example, the average length of a newly diagnosed HPV infection is 13 months and most infections have resolved within 24 months.[30] It is unclear whether HPV positive women who become HPV negative actually clear the virus from their bodies or retains the virus in an inactive or low-level state.

HPV is found in 70 to 78 percent of patients with pathologically confirmed CIN 1 and 83 to 89 percent of patients with CIN 11/111.[31,32] The prevalence of HPV DNA in invasive cancer is even higher.

Over 90 percent of squamous cell carcinomas and adenocarcinomas/adenosquamous carcinomas are HPV positive compared to only 16 percent of controls. [30, 32, 33] The two major factors associated with development of cervical cancer are HPV subtype and persistence. There are 70 distinct HPV subtypes; approximately 35 types are specific to anogenital epithelium and have varying potentials to cause malignant change. Low risk subtypes, such as HPV 6 and 11, do not integrate into the host genome and are associated with lesser lower genital tract dysplasias eg LGSIL, mild dysplasia, CIN I and benign condylomas, intermediate- risk subtypes can cause higher -grade dysplasia such as HGSIL that persists, but rarely progresses to the invasive stage. High risk HPV subtypes, such as 16 and 18, are strongly associated with HGSIL and progression to invasive cancer.

Persistent oncogenic HPV infection is a key factor in progression to high-grade cervical lesions [34, 35, 36, 37] and cervical cancer,[38, 39] while clearance of HPV predicts regression of abnormal cervical cytology at an average interval of three months

later.[40] Women with otherwise normal Pap smear who have persistent HPV infection have higher likely hood of developing invasive cervical cancer than women with normal smears and no evidence of HPV infection.[40,41] A prospective longitudinal study showed persistent HPV infection (defined as positive HPV DNA by PCR at two consecutive visits four months apart) with the same oncogenic type was associated with the highest risk of HSIL (relative risk[RR] 10 to 12) or persistent any grade SIL (RR 7 to 19).[36] However, HSIL and persistent SIL did not develop in women who cleared the HPV infection by third follow up visit. The effect of the amount of HPV virus being shed on CIN risk is controversial: most studies show an increased risk of CIN with an increasing viral load, [41] while others do not .[42,43]

Other risk factors

Cigarette smoking is highly associated with cervical neoplasia and is thought to act as a co-carcinogen.[54] Cigarette smoking and HPV infection have synergistic effects on development of CIN11/111.[55] The relative risk of cervical cancer is increased two to four-fold among cigarette smokers compared to nonsmokers [56] and among HPV positive smokers compared to HPV positive nonsmokers.[57] The cumulative exposure to cigarette smoking (as measured by pack-years smocked) is strongly related to the risk of dysplasia and cervical carcinoma in situ.[58]

Breakdown products of cigarette smoke, such as nicotine, cotinine or NNK (4-metylnitrosamino-1-(3-pyridil)-1-butanone) have been found to concentrate in cervical mucous, where they may induce cellular abnormalities in cervical epithelium and decrease local immunity.[59,60] Impaired host immunity may then allow persistence of oncogenic virus.

Herpes simplex virus (HSV) infection may be another carcinogenic. A link between past Chlamydia trachomatis infection and cervical cancer risk has also been reported. Infection with Chlamydia, HSV, or other sexually transmitted diseases may be surrogate marker of exposure to HPV, rather than a causal factor itself. Long-term use of contraceptives has been implicated as a co factor that increases the risk of cervical carcinoma in women who are HPV positive.

HIV infection and cervical neoplasia.

Maiman et al 1998 and cherry and Robinson 1993 reported high HIV seroprevalence in patients referred for colposcopy than in pregnant women in America.[44] In Kenya, Rogo and kavoo 1990 reported HIV seroprevalence of 2-9% among cervical cancer patients.[45] The incidence of CIN is 4 to 5 times higher among HIV infected compared to HIV negative women or adolescents with high-risk sexual behaviors as illustrated in a study by Ellerbrock.[46] The increased risk of CIN appears to be related to increased prevalence of HPV infection in HIV infected women.

The risk of HPV infection and cervical neoplasia increases with increasing degrees of immunosuppression (as measured by CD4 counts and HIV viral load). Ahidieh et al found that HIV infected patients were more likely to be repeatedly HPV positive over six year period than women without HIV infection (79 versus 48 Percent) and that a subsequent positive HPV test was most common in those with CD4 counts less than 200/mcl (93 percent).[47] Maiman et al in 1991 reported that HIV infected women with CIN had lower CD4 counts 221 cells/mm cube vs. 408 cells /mm cube and CD4 to CD8 ratios (0.33 vs. 0.62) than those without CIN.[48]

Lehtovirta et al of Helsinki found prevalence 4, 24, 15, and 5 percent among HIV positive women for ASCUS, AGCUS, LGSIL, and HGSIL respectively.

In this study the cumulative risk of developing SIL among the HIV positive women was 17 percent at 1 year and 48 percent at 5 years and this risk was increased in those less than 31 years.[49] A study in Lusaka by Parham et al. on CIN among HIV positive women found a prevalence of 76 percent.[50] In a study by charlermchockcharoenkit of siriraj the prevalence of CIN was 13.3 percent among HIV positive mothers attending postnatal clinic.[51] That this effect of HIV could be due to immunosuppression is further supported by the observation that women with chronic conditions requiring long-term immunosuppressive therapy are at

increased risk of developing CIN. This association has been described in transplant recipients and women with systemic lupus erythromatosus.[52, 53]

Cervical cytology screening

Women are typically screened for CIN by some type of cytology e.g. conventional papanicolaou smear or liquid based techniques such as thin prep or surepath. Evidence based data show that both liquid based and conventional methods of cervical cytology are acceptable for screening.[61]

Pregnant women in many ANC settings outside Kenya routinely undergo cervical cytology screening at the first prenatal visit. As a result many women discover they have an abnormal cervical cytology smear during pregnancy. In a Japanese study by morimura et al, the effectiveness of cervical cytology in pregnancy was similar to that in mass screened non pregnant women.[63] Sarkas S et al of Nottingham found the incidence of abnormal cytology in pregnancy matched that in general population(6%) though the incidence of unsatisfactory smears was very high(36%).[63] The physiologic changes of pregnancy render the transformation zone easily accessible for satisfactory colposcopy by 20 weeks of gestation in almost all women. This virtually eliminates the need for cervical cone biopsy with its associated risks of bleeding and pregnancy loss, unless micro-invasive disease is suspected.

Even high grade lesions discovered in pregnancy have a high rate of regression in the postpartum period. In one study, 70 percent of women with CIN 111 had regression and none progressed to invasive carcinoma.[64] This underscores the role for conservative ante partum management followed by careful postpartum evaluation.

Colposcopy (without ECC) should be repeated each trimester and colposcopy and cervical cytology should be performed 6 to 12 weeks postpartum.[65] Pap smear at postpartum is also convenient to the patient since she does not have to be booked for

Pap smear in 3-4 months. It may also be the only opportunity for contact with this patient as alluded to earlier.

Colposcopy

Colposcopy is the primary technique for evaluation of abnormal cervical cytology. The colposcope facilitates examination of the cervical, vaginal, vulva and anal epithelium by providing illuminated five to fifteen magnifications of these areas. Abnormal areas of the epithelium turn white following the application of dilute acetic acid. Capillaries may also be identified within the abnormal epithelium. Capillary thickness and the intercapillary distances correlate with the severity of the lesion; high-grade lesions tend to have a courser vessel pattern and larger intercapillary distance. The most severely abnormal areas can be targeted for biopsy to determine a pathologic diagnosis.

Vaccination

Cervical cancer is considered a preventable disease. Prevention can be achieved by screening, early detection and treatment and modifying the risk factors. In populations where frequent screening for cervical cancer precursors is practiced using the Pap test a decrease in the incidence and mortality of cervical cancer has been observed.[66, 67] The ultimate eradication of HPV -induced cervical cancer will likely be achieved through immunization against oncogenic HPV subtypes. The licensed HPV vaccine is a quadrivalent vaccine composed of a mixture of four HPV type specific non-infectious virus like particles (VLPs) prepared from the L1 proteins of HPV 6, 11, 16 and18 combined with an aluminum adjuvant. Clinical trials indicate that the vaccine has a high efficacy in preventing persistent HPV infection, cervical cancer precursor lesions, vaginal and vulvae precursor lesions, vaginal and vulvae cancer lesions and genital warts caused by HPV types 6, 11, 16 or 18 among females who have not already been infected with the respective HPV type.[68]

The vaccine is administered by intramuscular injection, and the recommended schedule is a 3-dose series with the second and third doses administered 2 and 6 months after the first dose. The recommended age for vaccination is 11 -12 years. The vaccine can be administered as early as 9 years. Catch –up vaccination is recommended for females aged 13 -26 years who have not been previously vaccinated.

Vaccination is not a substitute for routine cervical screening and vaccinated females should have cervical cancer screening as recommended.[68] Although there is overwhelming evidence that cervical cancer today is almost totally preventable through screening for premalignant lesions and their treatment this service is unfortunately not readily available to the general population in most developing countries including Kenya.[69, 70]

The approach to cervical cancer prevention must be part of holistic approach contextualized in a basic developmental and human rights framework. That same woman should not become a terminal victim of malnutrition, tuberculosis, AIDS, malaria or physical abuse. Cervical cancer screening and treatment programs in Africa need to be scaled up and integrated with overall reproductive and primary health care programs.

Research questions.

In postpartum HIV positive mothers at 6 weeks postpartum, how common are cervical cell abnormalities and what are the VIA findings? How do the two compare?

STUDY JUSTIFICATION

Cancer of the cervix is one of the leading causes of morbidity and mortality among women in the developing world. It is the commonest female reproductive tract cancer in Kenya.[3]

Cervical dysplasias have been found to be prevalent in HIV infected women.[46] The current prevalence among the HIV positive women in Kenya is unknown.

In Kenya and most of the developing world, population based cervical screening has not been successfully implemented. This service is therefore largely opportunistic. Most pregnant HIV-infected women like other women present for delivery after late antenatal booking or without antenatal care. Postnatal clinics provide an opportunity for cervical screening for dysplasia or cancer in these women.

This study was designed to document the prevalence of abnormal cervical cytology and VIA findings among HIV positive mothers at postpartum.

No similar studies have been carried out in this country.

OBJECTIVES.

Broad objective.

The main objective of the study was to determine the prevalence of abnormal cervical cytology and VIA findings in HIV positive mothers at 6 weeks postpartum in Kenyatta National Hospital.

Specific objectives.

Among HIV positive mothers at 6 weeks postpartum;

1) Describe cervical cytology findings.
2) Describe vaginal examination findings including VIA.
3) Compare cervical cytology and VIA findings.

METHODOLOGY

Study Design

Hospital based descriptive cross-sectional study.

Study site

The study was carried out at the Kenyatta National Hospital, Clinic 18. This is Kenya's largest referral hospital, located in the capital city Nairobi.The hospital attends to referral patients and also acts as a primary hospital serving many inhabitants of Nairobi. It is one of the only two public institutions providing tertiary delivery services in the city.

Antenatal, postnatal and other specialized clinics e.g. colposcopy services are provided at clinic 18. The prevention of mother to child transmission is an integral part of these services.

Study Population

The study population comprised HIV positive mothers seeking postnatal care services at KNH.

Study Period

The study was conducted between April and October 2008.

Inclusion Criteria

Mothers at 6 weeks postpartum with confirmed HIV positive status and willing to consent.

Exclusion Criteria

Mothers with confirmed cancer of the cervix, vaginal bleeding or unwilling to give consent.

Sample size estimation

The sample size was determined by the use of the following formulae (Fishers formulae) to achieve an adequate sample to accurately estimate the prevalence of abnormal cytology in the study population.

$$n = \frac{Z^2_{\alpha/2} * P(1-P)}{D^2}$$

Where n = required sample size

P = prevalence of abnormal cervical cytology in HIV+ mothers at six weeks postpartum (13%), based on the estimated prevalence from a similar study in Thailand.[51] This is the only study in a developing country performed in a similar setting.

D = Precision with which to measure prevalence, set at plus or minus 5%.

The $Z_{\alpha/2}$ is the cut off points along the x-axis of the standard normal probability distribution that represents probability matching the 95% confidence interval (1.96). Substituting the above in the formulae we get;

$n \approx 173.8$

$= 174$ patients

Sampling Procedures

Eligible women attending the postnatal clinic during the study period were consecutively recruited till the desired sample size was achieved.

Study Procedures

Clinical procedures.

As part of the implementation of prevention of mother to child transmission (PMTCT) programme HIV positive mothers who deliver at the Kenyatta National Hospital labour ward are given appointments for follow up at the postnatal clinic two weeks after delivery and followed to six months postpartum. Some of the mothers followed up in this clinic are referrals or transfer in from other facilities in Nairobi.

The HIV positive postpartum mothers were approached at clinic 18 and informed of what the study entailed its usefulness and the possible adverse effects of procedure. Those who met the eligibility criteria and gave consent were recruited to the study. The questionnaire on the social demographic characteristics, the obstetrics and gynecologic history, HIV disease, the CD4 count status and use of ARVS was administered. The principal investigator did a physical examination including a speculum examination. Visual examination of the vagina and the cervix was done after insertion of a cuscos speculum. After obtaining cervical smear by use of a cytobrush, 5% acetic acid was applied on to the cervix with a cotton tip swab. The cervix was then examined with a bright source of light and reported as positive or negative VIA depending on presence or absence of distinct acetowhite areas. The smear was made on labeled slide, fixed with 95 % ethyl alcohol. The prepared smear was then stored and later transported to the laboratory for analysis. A fully completed request form accompanied each slide. Each patient was requested to come back for results after 1 month and depending on the results was advised and or referred accordingly.

Laboratory procedures

The Cytotechnologist based at the University of Nairobi, Department of Obstetrics and Gynecology, stained, read and reported on the pap smears. Staining was done with papanicolaou stains and reporting based on Bethesda 2001 classification.[72] A university of Nairobi pathologist re-read all abnormal smears and 10 thsmear of those reported as normal.

Data Instrument

The study instruments comprised a questionnaire, which was completed by the investigator or assistant. This questionnaire comprised of the socio-demographic characteristics, risk factors for CIN, HIV disease, ARV use and the CD4 counts report. A laboratory request and report form was used to report the clinical and cytological findings.

Data Collection and Management

Completed questionnaires were coded and sorted out for completeness. Serial numbers was used to link Pap smear result to participant questionnaire Data was entered and a data base designed in MS Access. Data cleaning was done before analysis.

Analysis was done using SPSS data analysis programme (SPSS-version 12.0).

The data was presented in tables and figures where applicable. Chi-square was used to establish the significant associations between the categorical variables. Odds Ratios (OR) and associated 95% Confidence interval (CI) was calculated to identify the factors that are more likely to explain the explanatory variable (associated with CIN). P-value of less than 5% ($P<0.05$) is considered statistically significant.

Ethical Considerations

Approval to conduct the study was obtained from Kenyatta National Hospital Ethics and Research Committee. Informed consent was obtained from the client before being recruited. This involved signing a consent form after an explanation by the investigator about the details of the study. This included the facts and basis, the risks and benefits and confidentiality and voluntary nature of the study. The contact address of the investigator was given to the client incase she needed further details about the study or wished to withdraw from the study. The information was communicated both verbally and in writing (appendix 1)

Refusal to participate in the study did not deny the patient appropriate management for their visits as per hospital protocol. The client bore no costs for Pap smear screening test. The Pap smear results was communicated to the clients during subsequent visits and care advised based on the practices at the Kenyatta National Hospital depending on individuals result.

RESULTS

Between the months of April and October 2008, One hundred and seventy five (175) subjects were enrolled.

Table 1: Socio-Demographic characteristic of the study population. (n = 175).

Characteristic	Frequency	Percent
Age		
• < 20	6	3.4
• 20-24	21	12.0
• 25-29	66	37.7
• 30-34	53	30.3
• 35-39	25	14.3
• 40+	4	2.3
Religion		
• Catholic	52	29.7
• Protestant	98	56.0
• Other	25	14.3
Education		
• None	5	2.9
• Primary	39	22.3
• Secondary	86	49.1
• College/University	45	25.7
Employment Status		
• Salaried Job	38	21.7
• Self-employed	56	32.0
• Unemployed	81	46.3
Marrital Status		
• Single	29	16.6
• Married (Mono.)	121	69.1
• Married (poly.)	15	8.6
• Separated	6	3.4
• Windowed	4	2.3
Smoking of Cigarettes		
• Yes	5	2.9
• No	170	97.1

The study subjects had a mean age of 29.5 years, range 17 to 40 years and 68% were 25-34 years. One hundred and twenty six (78%) were married, 69 % were in monogamous marriage and 2% were widowed.

Ninety four (54%) were employed with 60% being self employed while 81 (46%) were unemployed.

One hundred and thirty one (75%) had secondary education and above and 44(25%) had primary education and below. Only five (3%) had ever smoked cigarettes (Table 1).

Table 2: Obstetric characteristics (n = 175)

History	Frequency	Percent
Number Of Pregnancies		
• 1 - 2	100	57.1
• 3 - 4	72	41.1
• 5+	3	1.7
Mode of Delivery in last pregnancy	39	22.3
• SVD	136	77.7
• C/S		
Pregnancy Outcome		
• Live term birth	136	77.8
• Live pre-term	6	3.4
• Still birth	9	5.1
• abortions	24	13.7
Currently BF		
• EBF	60	42.3
• Formular	79	55.6
• Mixed	3	2.1
• N/A (SB,abortions)	33	

Most women were para one or two (57%) and majority (78%) had deliverd by caeserian section. One hundred and forty two (81%) had live births and 56 % were using formulae milk and only 2% reported were mixed feeding (Table 2).

Table 3: Contraceptive use by method. (n = 175)

FP method	Current Use	Ever used, n (%)
Any FP method	78 (44.6%)	123 (70.3%)
Pills	5 (2.9%)	32 (18.3%)
Mini Pills	2 (1.1%)	5 (2.9%)
Injectables	7 (4.0%)	43 (24.6%)
Barrier (Condom)	69 (39.4%)	28 (16.0%)
Implant	2 (1.1%)	22 (12.6%)
IUCD	1 (0.6%)	7 (4.0%)
Other	28 (16.0%)	4 (2.3%)
Dual method	17 (9.7%)	9 (5.1%)

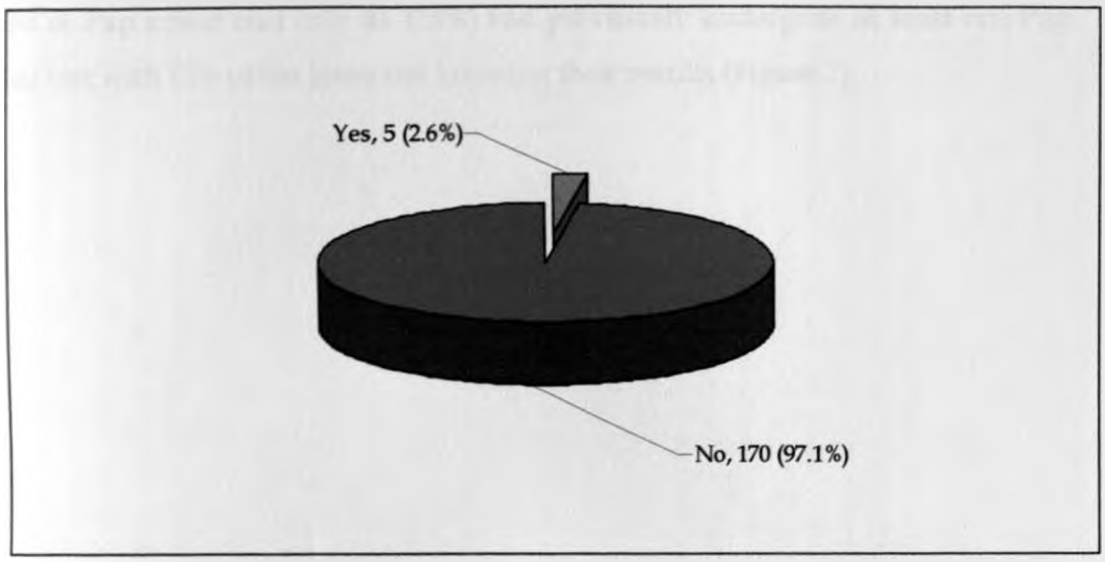
Although 70% of women had ever used contraceptives ony 45% were current users. Hormonal injectable contraceptive was the most common method ever used at 25%, however barrier methods was common among current users(39%). Only 17 (10%) of the subjects were on dual method of contraception. Contraceptive use has significantly reduced(p value<0.005) among HIV positive women attending post natal clinic. There is no significant differences by method used. More women are currently using IUCD (Table 3).

Table 4: Sexual characteristic (n = 175)

History	frequency	Percent
Age at 1st Sexual contact (in years)		
• ≤ 15	21	12.0
• 16-20	113	64.6
• 21-25	36	20.6
• 26 +	5	2.9
Ever had STD		
• Yes	24	13.7
• No	151	86.3
Number of Sexual Partners		
• 1	31	17.7
• 2-3	99	56.6
• 4 +	45	26.7

Sexual debut for most women (77%) was below 20 years and 83% reported having had 2 or more sexual partners and 27% , four or more sexual partners. Twenty four (14%) women reported having suffered from a STI (Table 4).

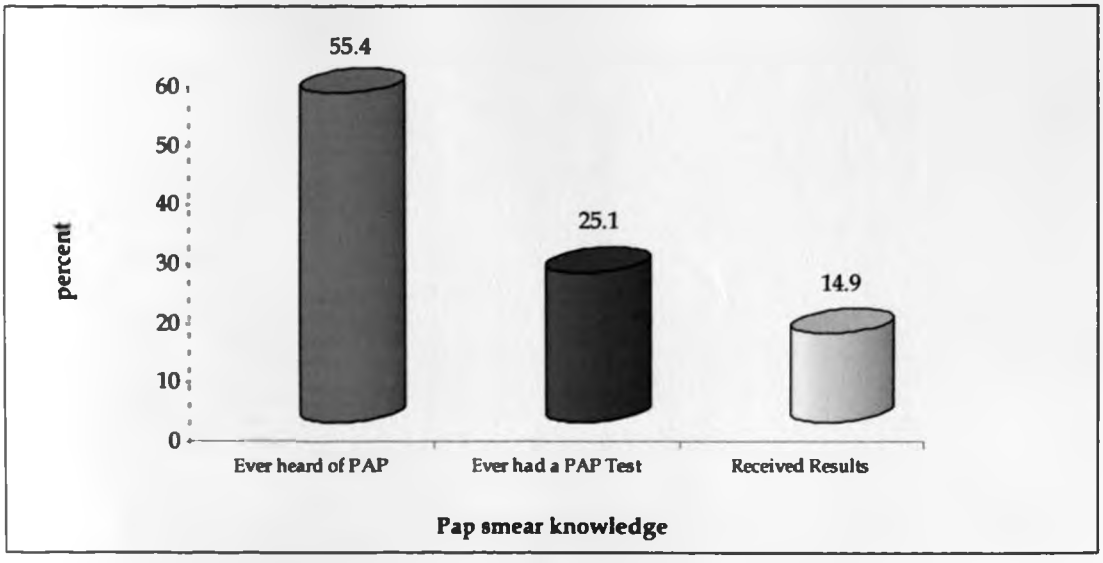
Figure 1: Family History of Cervical Cancer



Five (3%) of women had a family history of cervical cancer. All the women with a family

history of cervical cancer had had cervical cell abnormalities (p value <0.005) (Figure 1).

Figure 2: Pap smear Knowledge



Knowledge and utilization of Pap smear test was low, only 97 (55%) women had heard of Pap smear and only 44 (25%) had previously undergone at least one Pap smear test with 52% of the latter not knowing their results (Figure 2).

Table 5: ARVS and CD4 count levels (n = 175)

Factors	Count	Percentage
On HAART		
• Yes	68	38.9
• No	107	61.1
ARV's currently on (n=68)		
• D4T+3TC+NVP	30	44.1
• D4T+3TC+EFV	2	2.9
• AZT+3TC+EFZ	24	35.3
• AZT +3TC +EFV	3	4.4
• 3TC + NVP+TDF	1	1.5
• TDF/KALETRA/3TC	1	1.5
• Not Known	7	10.3
CD4 Count (latest)		
• ≤ 200	18	10.3
• 201-500	64	36.6
• 500 +	65	37.1
• Not Known	28	16.0

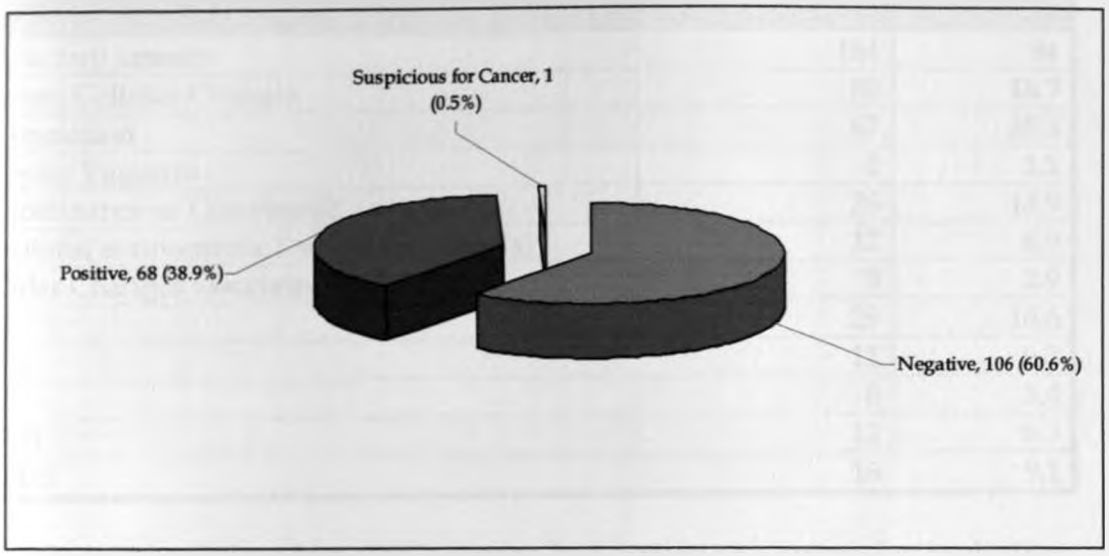
Sixty eight women (40%) were on HAART, with 87% being on first line regimes of D4T or AZT plus 3TC plus NVP or EFV. One hundred and fourty seven (84%) obtained their CD4 results, 16% did not know the results mostly because their results had been misplaced. Of those who had CD4 results 12% had a count of 200 cells/ul or less while 88% had more than 200 cells/ul (Table 5).

Table 6: Abnormal findings on Physical Examination

Findings	Frequency	Percentage
General examination		
• Wasting	9	5
• Pallor	2	1
• Body rash	5	3
Genital examination		
• External genital warts	2	1
• Vaginal warts	2	1
• Abnormal discharge	16	9
• Eroded cervix/cervicitis	33	29
• Cervical polyp	4	2
• Suspicious for cancer	2	1

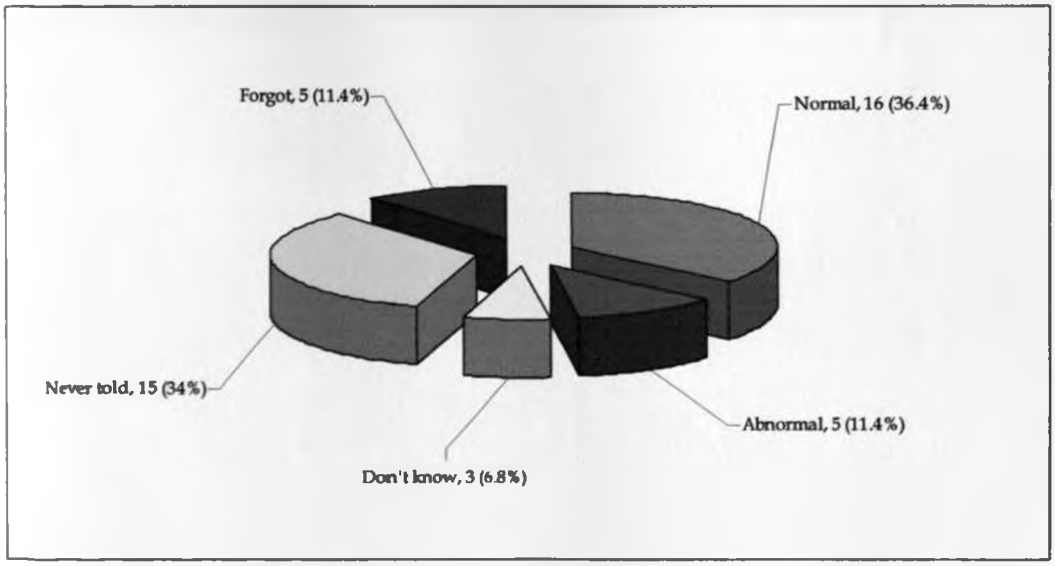
Most women (94%) had normal general exam findings,2% had vulval and vaginal warts. One hundred and twenty (69%) had normal looking cervix while, 29% and 1% had eroded/cervicitis and suspicious looking cervix (Table 6).

Figure 3: Results of VIA



On visual inspection with acetic acid(VIA) 106 (61%) had negative VIA and one was suspicious for invasive cancer (Figure 3).

Figure 4: previous pap smear Results



Among those who had had a pap smear test 29 (85%) women were told their results, 11% forgot, 34% were never told and 7% did not know their results (Figure 4).

Table 7: Frequency of cytological findings at postpartum period (n = 175)

Cervical cytological findings	Frequency(cases)	Percentage
Satisfactory smears	164	94
Reactive Cellular Changes	80	45.7
Inflammation	67	38.3
Atrophic Vaginitis	2	1.1
Predominance of Coccobacilli	26	14.9
Infections(actinomyces,T.vaginalis,candida)	12	6.9
Cellular Changes associated with HSV	5	2.9
LSIL	29	16.6
HSIL	11	6.3
SCC	6	3.4
AGUS	12	6.9
ASCUS	16	9.1

One hundred and sixty four (94%) women had satisfactory smear for evaluation. Eighty (46%) had reactive cellular changes associated with inflammation and or infection. The common organisms were coccobacilli (15%), HSV (3%), Candida (3%), actinomyces (3%) and trichomonas (2%). Sixty five (37.1%) had cytological abnormalities, sixty two (95%) of these had squamous cell abnormalities. Nine women had both squamous and glandular cell abnormalities. The frequency of ASCUS,AGUS,LSIL,HSIL,SCC were9%,7%,17%,6% and 3% respectively (Table 7).

Table 8: Association between cervical cytological abnormalities & Socio-demographic Factors (n = 175)

Socio-demographic Factor	Cervical cytological findings		OR (95% CI)	P-value
	Abnormal, n (%)	Normal, n (%)		
Age				
• ≥ 30	29 (44.6)	53 (48.2)	0.9 (0.5 – 1.6)	0.648
• < 30[1]	36 (55.4)	57 (51.8)		
Education				
• Primary & Below	14 (21.5)	30 (27.3)	0.7 (0.4 – 1.5)	0.398
• Secondary & above[1]	51 (78.5)	80 (72.7)		
Marital				
• Unmarried	13 (20.0)	26 (23.6)	0.8 (0.4 – 1.7)	0.576
• Married [1]	52 (80.0)	8 (76.4)		
Smoking				
• Yes	3 (4.6)	2 (1.8)	2.6 (0.4 – 16.0)	0.283
• No[1]	62 (95.4)	108 (98.2)		

1- is the reference group

Age, marital status and level of education were not significantly associated with development of cervical cytological abnormalities. However, those who were smoking or had ever smoked had a twofold risk of developing abnormal cervical cytology {OR 2.6(0.4-16.0)} (Table 8).

Table 9: Association between cervical cytological Abnormalities & parity and mode of delivery (n = 175)

History	Cervical cytological findings		OR (95% CI)	P-value
	Abnormal, n (%)	Normal, n (%)		
No. pregnancies				
• > 3	13 (20.0)	12 (15.5)	1.4 (0.6 – 3.0)	0.441
• ≤ 3[1]	52 (80.0)	93 (84.5)		
Mode of Del.				
• SVD	16 (24.6)	23 (20.9)	1.2 (0.6 – 2.6)	0.569
• C/S[1]	49 (75.4)	87 (79.1)		

1- is the reference group

There was no statistically significant difference as regards parity or mode of delivery between those who had abnormal Pap smear and negative CIN (Table 9).

Table 10: Association between cervical cytological Abnormalities & contraceptive method (n = 175)

History	Cervical cytological findings		OR (95% CI)	P-value
	Abnormal, n (%)	Normal, n (%)		
FP				
• ever	48 (73.6)	75 (68.2)	1.3 (0.7 – 2.6)	0.428
• never[1]	49 (26.2)	35 (31.8)		
Type				
• Pills	15 (23.1)	22 (20.0)	1.2 (0.6 – 2.5)	0.630
• Injectables	15 (23.1)	28 (25.5)	0.9 (0.4 – 1.8)	0.724
• Implants	7 (10.8)	15 (13.6)	0.8 (0.3 – 2.0)	0.580
• IUCD	1 (1.5)	6 (5.5)	0.3 (0.2 – 2.3)	0.201
• Barrier (condom)	17 (26.2)	11 (10.0)	3.2 (1.4 – 7.3)	0.005

1- is the reference group.
For the types of FP the reference group was those who had not used the method.

Barrier method (condom use) was associated with increased risk for development of cervical cytological abnormalities. Most mothers may have begun consistent and correct use after diagnosis of HIV disease. The other methods did not significantly affect its development (Table 10).

Table 11: Association between Cytological Abnormalities & Sexual History (n = 175)

History	Cervical cytological findings		OR (95% CI)	P-value
	Abnormal, n (%)	Normal, n (%)		
Sexual Debut				
• < 15	6 (9.2)	3 (2.7)		
• 15 – 20	44 (67.7)	81 (73.6)	-	0.168
• > 20	15 (23.1)	26 (23.6)		
No. of Sexual Partners				
• > 2[1]	37 (8.9)	53 (48.2)	1.4 (0.8 – 2.6)	0.264
• ≤ 2	28 (43.1)	57 (51.8)		
History of CaCx				
• Yes[1]	5 (7.7)	0	-	***0.003***
• No	60 (92.3)	110 (100.0)		
Ever had STI				
• **Yes**[1]	5 (7.7)	19 (17.3)	0.4 (0.1 – 1.1)	0.075
• **No**	60 (92.3)	91 (82.7)		

1- is the reference group

Family history of cervical cancer was significantly associated with development of cervical dysplasia (p value=0.003). All five women with family history had cervical cell abnormalities (Table 11).

Table 12: Association between cervical cytological abnormalities & CD4 count (n = 175)

History	Cervical cytological findings		OR (95% CI)	P-value
	Abnormal, n (%)	Normal, n (%)		
On **HAART**				
• Yes[1]	29 (44.6)	39 (35.5)	1.5 (0.8 – 2.7)	0.230
• No	36 (55.4)	71 (64.5)		
latest **CD4**				
• < 200[1]	5 (27.8)	13 (72.2)	0.7 (0.2 – 2.2)	0.594
• ≥ 200	44 (34.1)	85 (65.9)		
Initial CD4 Count				
• < 200[1]	8 (19.0)	14 (19.2)	1.0 (0.4 – 2.6)	0.986
• ≥ 200	34 (81.0)	59 (80.8)		

1- is the reference group

Table 13: Comparison between the VIA and Pap smear cytology results

VIA	Pap		Total
	+Ve	-Ve	
+Ve	43(63%)	25(37%)	68(100%)
-Ve	22(21%)	85(79%)	107(100%)
Total	**65(37.1%)**	**110(62.9%)**	**175**

Of the 68 VIA positive results 43 (63%) had squamous cell abnormalities on Pap smear. Twenty five (27%) VIA positive had normal Pap smear. Eighty five (49%) of the mothers had normal results by both screening. The kappa statistic was 0.426 suggesting moderate agreement between the two cervical screening procedures and p value of 0.0001 (Table 13).

DISCUSSION

Cervical cancer is the commonest female reproductive tract cancers in developing world. Cervical intra-epithelial lesions precede invasive disease by 8-15 years. Several studies have documented an increased prevalence of CIN in HIV infected women. The presence of early CIN in women with HIV with greater chance for progression to more significant CIN or invasive cancer leads to increase in death by cervical cancer rather by AIDS per se. In Kenya the prevalence of HIV in women is 8.7 %[76] and Pap smear screening remains opportunistic.

We found a high prevalence (37.1%) of squamous cell abnormalities in HIV-infected women in the post partum period. Similar studies in Thailand [51] and Lusaka, Zambia [50]reported prevalence of 13.3% and 76% respectively. We found the relative frequencies of ASCUS, AGUS, LSIL, HSIL and SCC of 9%, 7%, 17%, 6% and 3% respectively. Lehtovirta et al reported a prevalence of 4%, 24%, 15% and 5% for ASCUS, AGUS, and LSIL and HSIL respectively.[49] In Kenya the prevalence of cervical dysplasia in family planning attendees is reported as 2-5%.[8, 9, 10] Fonk et al reported a prevalence of 13% among women seeking STD treatment in Nairobi.[11] Our findings are similar to those reported by lehtovirta but twice those reported in Thailand.
This difference may be due to the fact that more women are now on HAART and are more likely to live longer. The high prevalence reported in the Zambian study[50] may be due to the more immunosuppressed population, median CD4 was 165 cells/ul as opposed to 474 in our study. The prevalence reported by other researchers in this country is those of general family planning clinic attendees [8,9,10] or STI clients [11]who may not be HIV positive.

There was no significant difference in the prevalence of cervical epithelial abnormalities between those with low (<200cells/ul) and high CD4 counts (>200 cells/ul). However those who were on HAART were more likely to have abnormal cervical cytology by Pap smear {OR 1.5(0.8-2.7)}. Previous studies demonstrated that the risk of HPV and cervical neoplasia increases with increasing degrees of immunosupression. Aideeh et al reported that HIV infected patients were likely to

be repeatedly HPV positive over 6 year period than women without HIV infection and that a subsequent positive HPV test was most common in those with CD4 count <200/ul.[47] In our study the CD4 counts of those on HAART may have improved with treatment, since 39% were already on HAART.

The major risk factors associated with cervical cancer detection are similar in HIV infected and non HIV- infected women and also include the lack of screening and prolonged duration of precancerous or early cancerous lesions.[51] In our study only 55% had ever heard of a Pap smear test and only 25% had at least had one Pap smear test in their lives. Out of those who had done a pap smear only 21% were told their results. This is comparable to what was reported by Gichangi in his study where 51% of the cervical cancer and non cervical cancer respondents were aware of CACX and Pap smear but only 21% reported having done a pap smear in the past .[71] Similar findings were reported by Ayinde et al in Ibadan, 33.5% and 8.3% level of awareness among female medical and non medical students respectively.[72] Mutyabate et al in mulago hospital reported 81% of health workers had never been screened.[73] Despite cervical cancer being a major cause of morbidity and mortality among HIV women its level of awareness and pap smear screening remains low. Pap smear screening being dependant on other services in our setup and mothers presenting late for antenatal visits or no visits, postpartum provides an opportunity for Pap smear test.

In this study age, marital status, educational status, coitarche, no of sexual partners, contraceptive method, parity and mode of delivery were not statistically significant in development of CIN (P values>0.005). Family history of cervical cancer was found to be significantly associated with development of CIN (P value=0.003). Other studies elsewhere have demonstrated that sexual activity at an early age, history of STI, low social economic status and cigarette smoking are associated with increased risk of developing cancer of the cervix. High parity, combined oral contraceptive and vaginal delivery have also been demonstrated by some studies to be associated with cancer of the cervix. In our study only family history of cervical cancer was associated with increased risk of developing cervical abnormalities.

In our study, 99 women (56.6%) were negative for intra-epithelial lesions. Eighty (45.7%) had reactive cellular changes associated with inflammation and or organisms.

Although Pap smear is not a routine screening test for sexually transmitted disease, some specific infections were detected in our study. The organisms detected are coccobacilli, candida, actinomyces and trichomonas with prevalence of 14.9%, 2.7%, 2.3%, and1.7% respectively. Hence at least 31.7% of the mothers needed treatment before repeat of the Pap smear.

Cohen et al reported significant association between bacterial vaginosis and HIV sero-positivity (OR=4.0).[74] In the same study self reported history of an STI was significantly associated with HIV infection.

On visual inspection with acetic acid 68 (38.9%) mothers were reported to be positive for VIA and 1 (0.5%) as suspicious for cancer. Of the 68 reported as positive 43 (63.2%) were found to have cervical intra-epithelial lesion on Pap smear and twenty five (36.8%) were found to have normal pap smears. In a study in Zimbabwe by university of Zimbabwe and JHPIEGO VIA was abnormal in 20% of the women. This is lower than what we found in our study and this is explained by the fact that our population was that of HIV positive women in whom cervical dysplasia was common. The sensitivity of VIA in the Zimbabwe study was reported to be 76.6 %(CI 95% 70.3-82.3) and specificity 64.1 %(CI 95%61.9-66.2) compared to colposcopy and biopsy. In the same study the sensitivity of Pap smear and specificity was 44.3% and 90.6 5 respectively.[75] In our study we found only moderate agreement between VIA and Pap smear.

Study limitations.

Our study was underpowered to correlate risk factors and abnormal cervical cytology especially specific abnormalities (HSIL/LSIL). There were a high percentage of reactive cellular changes which may have obscured cellular detail. We also did not have gold standard when comparing Pap smear cytology and VIA findings.

CONCLUSION.

There is a high prevalence of abnormal cervical cytology among women attending post -delivery services in KNH. Despite high prevalence of abnormal cervical cytology among HIV positive women as demonstrated in this study the level of awareness and Pap smear screening remain low.

Postpartum visit offers an opportunity to do pap smears. Ninety three percent of the mothers had satisfactory smears. Genital infections are common in HIV positive mothers attending postnatal clinic. The prevalence of smears with infections was 25%.

RECOMMENDATIONS

1. There is need to increase knowledge and awareness about cervical cancer and screening among Kenyan women. This will increase uptake of the available hospital screening facilities.
2. Pelvic examination at postpartum in HIV positive mothers should be performed in order to offer treatment for STIs and bacterial vaginosis.
3. More research is needed on use of VIA in screening for cervical abnormalities vis-à-vis Pap smear cytology.

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Appendix 1: PATIENT INFORMATION AND CONSENT FORM.

Study on prevalence of abnormal cervical cytology in HIV positive mothers at 6 weeks after delivery at KNH

Principal investigator: Alfred Kiplangat Terer, MBCHB, Mmed student in the Department of Obstetrics and Gynecology, University of Nairobi .Tel. No. 0724238719

Chairperson KNH-ERC: Professor K. M Bhatt, 0202726300.

Introduction

The purpose of this consent form is to give you information about the study on abnormalities of cells in the birth canal. This information will help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer and anything else about the research or this form that is not clear. When we have answered all questions, you can decide if you want to be on the study or not. This process is called informed consent. If you wish, we will give you a copy of this form for your records.

Reasons for research

The purpose of this study is to document how common abnormal cells in the birth canal are in HIV positive women after delivery.

The abnormal cells in the birth canal can lead to cancer of cervix which is a major cause of illness and death among women. These abnormal cells occur many years before cancer and can be treated. However the disease progresses faster in those who are HIV positive.

Benefits

The results will be useful in determining extend of disease and designing of ways of Pap smear screening in women who are HIV positive.

In addition you will know your Pap smear status and be advised on follow up.

Possible risks.

There are no serious risks but you may experience some discomfort during speculum examination. You may experience slight bleeding after the procedure.

Confidentiality

The information given to researchers will be kept in strict confidence. This information will be part of your clinical records. However no information by which your identity can be revealed will be released or published.

Participant's agreement.

I voluntarily agree to participate in the study on prevalence of abnormal cervical cytology in women who are HIV positive at 6 weeks after delivery at KNH clinic 18. I understand that participation in the study does not entail financial benefit. I have been informed that the information obtained will be treated with utmost confidentiality and my treatment will not be compromised if I decline participation or withdraw from the study.

I have had a chance to ask questions, if I have questions later about the research I can ask the researcher. If I have questions about my rights as a research subject, I can call the ethical review committee at Kenyatta National Hospital on telephone number 726300. ext.44102

....

Signature of subject Date

....

Witness Date

I certify that the nature and purpose, potential benefits, possible risks associated with participating in this study have been explained to the above participant.

....

Signature of principal investigator. Date

Appendix 2: **DATA COLLECTION SHEET**

Section A: Socio-Demographic Data

1. Serial Number [ ][ ][ ][ ][ ]

2. Clinic Number [ ][ ][ ][ ][ ]

3. Age in Years [ ][ ]

4. What is your religion? (*Tick one*) [ ]

1. Catholic 2.Protestant 3.Muslim 4.Others, Specify_____

5. What is the highest education level you have completed?

1. None [ ]
2. Primary [ ]
3. Secondary [ ]
4. college/university [ ]
5. Don't know [ ]

6. What is your employment status?

1. Salaried job [ ]
2. Self employed [ ]
3. Unemployed [ ]

7. What is your marital status? (*Tick one)*

1. Single [ ]
2. married (monogamous) [ ]
3. married (polygamous) [ ]
4. Divorced [ ]
5. Separated [ ]

[ ]

6. Widowed

8. Do you currently Smoke cigarettes or use traditional tobacco? Yes ☐ No ☐

9. If yes for how long have you smoked? ☐☐ Years.

Section B: Obstetric History

10. How Many pregnancies have you ever had? ☐☐

11. Of the pregnancies you have ever had how many ended as:

Abortions? ☐☐

Still births? ☐☐

Live births? ☐☐

12. When was your last delivery? (*dd/mm/yy*) ☐☐ / ☐☐ / ☐☐

13. Mode of delivery

1) Spontaneous vertex delivery (SVD) ☐
2) Breech delivery ☐
3) Operative vaginal delivery (vacuum extraction) ☐
4) Caesarian section ☐

14. Pregnancy outcome

1) Live term birth (>=37 completed weeks) ☐
2) Live preterm birth (< 37 completed weeks) ☐
3) Stillbirth ☐

15. How are you currently feeding the baby?

1) Exclusive breastfeeding. ☐
2) Formulae milk feeding ☐
3) Mixed feeding ☐
3) Others (specify) _____ ☐

Section C: Gynecology History

16. Have you resumed your menstrual flow? Yes No

17. If yes when was your last menstrual period? (dd/mm/yy ☐☐/☐☐/☐☐

18. Have you ever used any family planning method? Yes ☐ No ☐

19. If yes to question 18 specify the method used. (*Please tick all that Apply*)

Pills (COC) ☐
Mini Pill ☐
Injectables ☐
Barrier (condom) ☐
Implants ☐
IUCD ☐
Natural ☐
Spermacides ☐
Other Specify _____

20. Which family planning method are you using now? (Please tick all that apply)

Pills (COC) ☐
Mini Pill ☐
Injectables ☐
Barrier (condom) ☐
Implants ☐
IUCD ☐
Natural ☐

Spermacides ☐

Other Specify _____

21. Have you ever heard of Pap smear test? Yes ☐ No ☐ (if no skip question 21-23)

22. Have you ever had a Pap smear test? No ☐ Yes ☐

23. When was your last Pap smear test? (*dd/mm/yy*) ☐☐ ☐☐ ☐☐

24. What was the result of Pap smear test? (*Tick one*) ☐

1. Normal 2.Abnormal, Specify_____ 3. I do not know 4.was never told 5.i have forgotten

Section D: Sexual History

25. At what age did you have your first sexual contact? (Completed years) ☐☐

26. Have you ever had sexually transmitted infection/diseases? No ☐ Yes ☐

27. In your lifetime, how many sexual partners have you had? ☐☐

28. Do you think or know whether your partner has or had other sexual partners? (*Tick one*)

1. Yes ☐ 2. No ☐ 3. I don't know ☐

29. For how long have you been married? (No of completed years) ☐☐

30. Is there a family history of cervical cancer? Yes ☐ No ☐

Section F: HIV Disease and ARV use.

31. When were you diagnosed with HIV infection? (*dd/mm/yy*) ☐☐ ☐☐ ☐☐

32. Have you been started on ARVS? No ☐ Yes ☐

If your answer is **No** skip question 33.

34. Which ARVS are you on? (*Refer below for regimens*)

First Line Regimens

1. Stavudine (d4T) + Lamivudine (3TC) + Nevirapine (NVP) ☐
2. Stavudine (d4T) + Lamivudine (3TC) + Efavivenz (EFV) ☐
3. Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP) ☐
4. Zidovudine (AZT) + Lamivudine (3TC) + Efavivenz (EFZ) ☐

Second Line

5. Didanosine (dd1) +Abacavir (ABC) + Kalctra (Lpr/r) ☐
6. Tenofir Disoproxil fumarate (TDF) + Abacavir (ABC) + Efavirenz (EFV) ☐
7. Others, Specify_____

35. When was your last CD4 test done? (*dd/mm/yy*) ☐☐ / ☐☐ / ☐☐

36. What is/was the CD4 count/ (Cells/ul?) ☐☐☐☐☐

Section E: present symptoms

37. Do you have any per vaginal bleeding?

1) Yes ☐

2) No ☐

38. Do you have any abnormal vaginal discharge?

1) Yes ☐

2) No ☐

If no skip question 39

39. Characteristics of the abnormal vaginal discharge

Yellow in color	Yes ☐	No ☐
Smelly	Yes ☐	No ☐
Associated vulva Itching	Yes ☐	No ☐
Increased in Volume	Yes ☐	No ☐

Stains underwear Yes ☐ No ☐

Others specify _____

40. Do you have abdominal pains? Yes ☐ NO ☐

41. for how many days? ☐

42. When do you experience the pain?

a) When passing urine? Yes ☐ No ☐

b) When having sex? Yes ☐ No ☐

c) All the time? Yes ☐ No ☐

Section F: Physical examination findings

43. General condition of the Patient

1. Wasted Yes ☐ No ☐
2. Pale Yes ☐ No ☐
3. Jaundice Yes ☐ No ☐
4. Oral thrash Yes ☐ No ☐
5. Febrile Yes ☐ No ☐
6. Lymphadenopathy Yes ☐ No ☐
7. Other (Specify) _____

44. State of external genitalia.

1. Normal ☐
2. Abnormal growth or ulcers. ☐
   Describe_____
3. Abnormal discharge. ☐ Describe
   _____

45. State of vaginal wall.

1. Normal ☐

2) Abnormal growth or ulcers. ☐
Describe_____

3) Abnormal discharge. ☐
Describe_____

46. State of the cervix

1) Normal looking cervix ☐

2) Eroded, cervicitis ☐

3) Presence of polyp, warts ☐

4) Suspicious (unhealthy looking, bleeding on touch. ☐
Describe_____
Hypertrophied elongated cervix, growth or ulcer)

5) Abnormal discharge. ☐
Describe_____

47. Is there uterine tenderness on palpation? Yes ☐ No ☐

Section H: clinical information extracted from patients file.

48. Date of HIV diagnosis

49. CD4 count at time of HIV disease diagnosis. _____

50. ARV regimen currently on (see regimens below)

First Line Regimens

1. Stavudine (d4T) + Lamivudine (3TC) + Nevirapine (NVP) ☐
2. Stavudine (d4T) + Lamivudine (3TC) + Efavivenz (EFV) ☐
3. Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP) ☐
4. Zidovudine (AZT) + Lamivudine (3TC) + Efavivenz (EFZ) ☐

Second Line

5. Didanosine (ddI) +Abacavir (ABC) + Kaletra (Lpr/r) ☐

6. Tenofir Disoproxil fumarate (TDF) + Abacavir (ABC) + Efavirenz (EFV) ☐

7. Others, Specify_____

Appendix 3: **CYTOPATHOLOGY REQUEST FORM**

PAT.NO:_____CLINIC:_____

NAME:_____

ADDRESS: _____

DOB:_____AGE:_____SEX:_____

DOCTOR:_____

DOCTOR'S NAME.....RECEIPT NO.....CHARGED BY.....

ADDRESS..... LAB REF.NO.....CHECKED BY.....

TEL..... PATIENT TEL:.....

L.M.P: PARITY: DATE OF SMEAR: PREVIOUS REPORT:

APPEARANCE OF CERVIX: NORMAL: ERODED: SUSPICIOUS:

OTHER CLINICAL DETAILS

REPORT

UNSATISFACTORY FOR EVALUATION: _____ ☐

SATISFACTORY FOR EVALUATION _____ ☐

DESCRIPTIVE DIAGNOSIS

Benign cellular changes _____ ☐

Reactive Cellular Changes _____ ☐

Trichomonas vaginalis _____ ☐

Inflammation _____ ☐

Fungal organisms consistent with Candida _____ ☐

Atrophy with inflammation (atrophic vaginitis) _____ ☐

Predominance of coccobacilli _____ ☐

IUD: _____ ☐

Bacteria consistent with actinomyces _____ ☐

Cellular changes associated with herpes simplex virus_____ ☐

Others _____ ☐

EPITHELIAL CELL ABNORMALITIES

Atypical squamous cells of undermined significance (ASCUS) _____ ☐

Atypicac squamous cells can not exclude high grade lesion (ASC-H)_____ ☐

Human Papillomavirus (HPV) with mild dysplasia (LSIL)_____ ☐

Low grade squamous intraepithelial lesion (LSIL)_____ ☐

High grade intraepithelial lesion previous termed

Moderate dysplasia, severe dysplasia and CIS, (CIN2 and CIN3) (HSIL)

_____ ☐

Squamous Cell Carcinoma_____ ☐

Recurrent Carcinoma_____ ☐

A typical glandular cells (AGUS) _____ ☐

Endocervical adenocarcinoma_____ ☐

Endometrial adenocarcinoma_____ ☐

Comments:_____

_____

_____

_____

_____

_____ _____ _____

Cytotechnologist **Date** **Pathologist**

Appendix 4: **THE 2001 BETHESDA SYSTEM FOR REPORTING CERVICAL CYTOLOGIC DIAGNOSIS.**

Specimen adequacy.

- Satisfactory for evaluation (note Presence or absence of endocervical transformation zone components or other quality indicators such as partially obscuring blood or inflammation).
- Unsatisfactory for evaluation. (Specify reason)
  Specimen rejected or not processed (specify reason).
  Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormalities (specify reason).

General categorization (optional)

- Negative for intra-epithelial lesion or malignancy.
- Epithelial cell abnormality.
- Other.

Interpretation/result.

- **Negative for intra-epithelial lesion or malignancy.**

  A. Organisms.

  i. Trichomonas vaginalis
  ii. Fungal organisms morphologically consistent with Candida species
  iii. Shift in flora suggestive of bacterial vaginosis
  iv. Bacteria morphologically consistent Actinomyces species.
  v. Cellular changes consistent with herpes simplex virus.

  B. Other non-neoplastic findings (optional)

  C. Reactive cellular changes associated with;

  i. Inflammation (includes typical repair).
  ii. Radiation.
  iii. Intrauterine contraceptive device.

D. Glandular cells status post hysterectomy.

E. Atrophy.

- **Epithelial cell abnormalities.**

A. Squamous cell.

i. Atypical squamous cells (ASC).

ASC of undetermined significance (ASC-US).

ASC can exclude high-grade squamous intraepithelial lesion (ASC-H).

ii. Low-grade squamous intraepithelial lesion (LSIL)-encompassing HPV, mild dysplasia and CIN 1.

iii. High-grade intraepithelial lesion (HSIL)-encompassing moderate and severe dysplasia, CIS, CIN11, CIN111.

iv. Squamous cell carcinoma.

B. Glandular cell.

i. Atypical glandular cell (AGC) (Specify endocervical, endometrial, or glandular cells not otherwise specified).

ii. Atypical glandular cells, favor neoplastic (Specify endocervical or not otherwise specified).

iii. Endocervical adenocarcinoma in situ (AIS).

iv. Adenocarcinoma.

C. Other.

Endometrial cells in women 40 years or older.

Appendix 5 **INTERPRATATION OF CERVICAL VIA FINDIGS.**

NEGATIVE VIA

- No acetowhite lesions.
- Nabothian follicles taking up acetowhitening.
- Faint line-like acetowhitening at the junction of columnar and squamous epithelium.
- Streak-like acetowhitening.
- Dot-like areas in the endocervix, which are due to grape-like formations of columnar epithelium staining with acetic acid.
- Aceto-white lesions far away from transformation zone.
- A poly protruding from the os taking up acetowhitening.

POSITIVE VIA

- Sharp distinct, well defined, dense acetowhite areas with or without raised margins.
- Lesions are close to sqamo-columnar junction in the transformation zone.
- Dense acetowhite lesions in the columnar epithelium or lesions are near the os.
- Condyloma and leukoplakia close to the squamo-columnar junction turn intensely white with acetic acid.

SUSPICIOUS FOR CANCER.

- Clinically visible ulcerative-proliferative growth.
- Oozing and or bleeding on touch.

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Ref: KNH-ERC/ 01/ 295

7th April, 2008

Dr. Alfred Kiplangat Terer
Dept. of Obs. & Gynae
University of Nairobi

Dear Dr. Terer

RESEARCH PROPOSAL: "THE PREVALENCE OF ABNORMAL CERVICAL CYTOLOGY IN HIV POSITIVE MOTHERS AT SIX WEEKS POSTPARTUM AT KENYATTA NATIONAL HOSPITAL"
(P11/1/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above cited research proposal for the period 7th April, 2008 – 6th April, 2009.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M. Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
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