# PREVALENCE OF CERVICAL CYTOLOGY ABNORMALITIES AMONG HIV INFECTED WOMEN AT RWANDA MILITARY HOSPITAL: A CROSS-SECTIONAL DESRIPTIVE STUDY.

A RESEARCH DISSERTATION SUBMITTED FOR THE AWARD OF MASTER OF MEDICINE IN OBSTETRICS AND GYNAECOLOGY


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# DEDICATION

To my late father John, for the challenges you met to earn me a place in school.

# DECLARATION

I declare that this dissertation is my original work and it has not been presented for the award of a degree at any other university.

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**LIST OF ABBREVIATIONS**

AGUS – Atypical Glandular Cells of Undetermined Significance

ASCUS - Atypical Squamous Cells of Undetermined Significance

CAP - College of American Pathologists

CHUB - University Central Hospital of Butare

CHUK - University Central Hospital of Kigali

CIN- Cervical Intra epithelial Neoplasia

DNA - Deoxyribonucleic acid

ERC- Ethics and Research Committee.

FIGO – International federation of Gynecology and obstetrics

HAART – Highly Active Anti-retroviral Therapy

HIV - Human Immunodeficiency Virus

HPV - Human Papillomavirus

HSIL - High grade Squamous Intra epithelial Lesion

ICC - Invasive Cervical Cancer

KNH - Kenyatta National Hospital

LEEP - Loop Electrosurgical Excision Procedure

LSIL - Low grade Squamous Intraepithelial Lesion

MOH-Ministry of Health

NHRC/RBC- National Health Research committee /Rwanda Biomedical Centre

SPSS - Statistical Package for Social Sciences

SIL- Squamous Intra epithelial Lesion

SCC- Squamous cell carcinoma.

WHO - World Health Organization

## Abstract

### Background

Cervical cancer is the second most common cancer in women worldwide and it is ranked second to cancer of the breast in developing countries whereas in developed countries cervical cancer is ranked fifth.

Studies now clearly demonstrate an increased risk of precancerous cervical lesions and a more rapid progression to cancer amongst HIV infected women particularly those with low CD4 cell counts or decreasing immunity.

Effective cytological screening and follow up intervention programs have been credited for the sharp decline in its prevalence in Europe and North America. This has not been the case in the developing world where resources and infrastructure have proved insufficient to offer quality screening and appropriate follow-up.

In Rwanda, there is no study that has previously determined the prevalence of abnormal Pap smear in HIV infected women hence a reason why we carried out this study.

**Objectives:**

To determine the prevalence of abnormal Pap smears in HIV-positive women attending HIV- clinic at Rwanda Military Hospital.

To determine the correlation between CD4+ cell count and abnormal Pap smear among HIV infected women at Rwanda Military Hospital.

To determine the correlation between WHO-HIV staging and abnormal pap smear among HIV-infected women at Rwanda Military Hospital.

**Methods:** This was a cross-sectional descriptive study which was aimed at determining the prevalence of cervical cytology abnormalities among HIV-infected women at Rwanda Military Hospital. Women who were eligible for the study and willing to participate consented. They were recruited by consecutive sampling. After filling the questionnaire that had social demographics and also other data were collected from their Medical records, a Pap smear was done to whoever fulfilled the study criteria.

**Results:** Between March and June, 2013 a total of 293 women infected with HIV had cervical smear taken for cytology. Of the 293 women who were recruited for the study, cervical SIL were present in 58 (20%). Of those with cervical SIL, 33 (56.89%) women had low-grade SIL, 15(25.86%) had ASCUS, 6(10.34%) had high-grade SIL, 3(5.17%) had SCC and 1(1.72%) had AGC-H.

A CD4 lymphocyte count of <200 cells/mm3 was found to be significantly associated with cervical SIL.

In the current study, use of ARV drugs was not associated with a reduction in the risk of cervical SIL

**Conclusion:** A high prevalence of cervical SIL was found among HIV-infected women at Rwanda Military Hospital-Rwanda. Increased immune suppression was significantly associated with cervical SIL.

**Recommendation:**

Due to the high prevalence reported in this study, routine screening of all women should be done with much emphasis to be put in for the HIV-infected group.

Patients who were found to have an abnormal Pap smear were referred to the hospital's Gynecology Out Patient Clinic for further follow up.

The government through the ministry of Health should create awareness to the public about cancer of the cervix.

## Literature review

Cervical cancer is the second most common cancer in women worldwide, and the seventh most common overall (in both sexes combined). In developing countries however, cancer of the uterine cervix is ranked second to cancer of the breast, whereas in developed countries cervical cancer is ranked fifth [1]. Worldwide, cervical cancer accounts for almost half a million (529,800) new cases annually of all cancers diagnosed in women. More than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers [2].

Cervical cancer mortality rates varies in different geographic regions. The extent to which carcinoma of the cervix is a cause of mortality among HIV infected patients in Rwanda is not known but the World Health Organization ranks Rwanda among the countries worldwide with the highest cervical cancer incidence, estimated at 34.5/100,000 (IARC 2008). This incidence estimate is consistent with cervical cancer incidence found in other East African countries overall (34.5/100,000 women/year) while in Northern Africa the incidence is lower [2].

Annually, cervical cancer is responsible for 275,100 deaths, about 88% of which occur in developing countries: 53 000 in Africa, 31 700 in Latin America and the Caribbean, and 159 800 in Asia [1, 2]. In many parts of the developing world, age standardized incidence rates of ICC are ≥ 4-fold higher than what is reported in North America and Western Europe, reaching values in excess of 30-to-50 per 100,000 women in large areas of sub-Saharan Africa [3].The large differences in mortality, with estimates of 11.2 and 4 deaths per 100,000 women-years in less developed and more

developed countries respectively point to the persisting major survival differences [3].

Most women who die from cervical cancer, are in the prime of their life. They may be raising children, caring for their family, and contributing to the social and economic life of their town or village. Their death is both a personal tragedy and a sad and unnecessary loss to their family and their community [4].

Invasive cancer of the cervix is considered to be a preventable condition, given that it is associated with a long pre-invasive stage, making it amenable to screening and treatment as long as it is detected early and managed effectively [4,5].

Cancer of the cervix has been classified as an acquired immune deficiency syndrome (AIDS) defining cancer by the US Centers for Disease Control and Prevention [6].

As more women contract the virus, the risk of cervical squamous intraepithelial lesions (SIL) or cervical intraepithelial neoplasia and ultimately cervical cancer increases [7].

In many African countries, the true incidence of cervical cancer is not known as there is gross under-reporting and lack of vital cancer registration. Some of the figures quoted in the literature are hospital-based data, constituting only a small fraction of women dying from cervical cancer, as most women lose their lives without receiving any hospital care (Anorlu 2008).

Although national incidence rates for Rwanda are unknown, as there is no population based cancer registry but the data from a population-based

cancer registry in Butare in the early 1990s showed cervical cancer to be responsible for 22.5% of cancers among women. In a retrospective study of cancer cases from two university teaching hospitals; (University Central Hospital of Kigali [CHUK] and University Central Hospital of Butare [CHUB]) seen from 2000 through 2004, cervical cancer accounted for 27.3% of cancers among the women and was the most common malignancy encountered in all age groups. In Rwanda, cervical cancer is in fact one of the most common cancers among women, it is therefore of important national public health concern [8]. The incidence of cervical cancer has remained high in sub-Saharan Africa; the rate can be up to several-fold greater in poor countries compared with industrialized ones. The incidence rates in some countries (Uganda, Mali and Zimbabwe) appear to be on the rise [9].

Studies have shown that the prevalence of cervical intraepithelial lesions and ICC differ in different geographical regions of the world but also differ in HIV infected and those who are not infected of the same geographical, social and economic background.

In a study done in Thailand by Chalermchocharoenkit et al (2010) to establish the prevalence, and factors associated with cervical cytology abnormalities in 821 HIV infected Thai women at a female sexually transmitted disease clinic, Faculty of Medicine Siriraj Hospital , Mahidol University, the prevalence of sqaumous cell abnormalities was 15.4%(SCA); ASCUS:2.8%,ASC-H:0.6%, LSIL:8.5%, HSIL:3.5%[10].

In another study done in Thailand in 2008 published in 2009, the prevalence of abnormal cervical cytology from Pap smear in 280 HIV-infected women was 21.3%(60/280) of which 0.7%(2/280) had atypical squamous cells

exclude high grade lesion (ASC-H), 6.4%(18/280) had low grade squamous intraepithelial lesion (LSIL), 12.1%(34/280) had high-grade squamous cell intraepithelial lesion (HSIL) and 2.1%(6/280) had squamous cell carcinoma (SCCA) [11].

In a study that was done in Brazil by **Patricia Abrue et al**, 2006, looking at the cervical cytopathology in a Population of HIV-Positive and HIV-Negative Women, a total of 237 study population was investigated of which 125 were HIV positive and 112 were HIV negative. Abnormal cervical cytology was found to be 12.1% Vs 5.4% (p= 0.113) in HIV positive and HIV negative women respectively. ASCUS: 4.8%, LSIL: 6.4% HSIL: 0.8% for HIV positive group. ASCUS: 2.7%, LSIL : 2.7%, HSIL: 0% for HIV negative group [12].

In a study done in the USA- at an infectious diseases clinic at the princess Margaret Hospital, Nassau, Bahamas by Dionne N Dames et al (2008) published in 2009, to determine the prevalence of cervical cytology abnormalities and human papillomavirus in 100 HIV infected women, the prevalence of cervical abnormalities were noted in 44% of the study population. Seven patients (7%) had ASCUS, 31 (31%) had LGSIL and 6 (6%) participants had HGSIL [13].

In another USA study by L. Stewart. Massad et al (1999), this was a multicentre prospective cohort study which was conducted in six U.S cities to determine the prevalence and predictors of sqaumous cell abnormalities in Papanicolaou smear from 1713 women infected with HIV and 482 of HIV negative control group. Cervical cytology was abnormal in 38.3% of HIV-infected women VS 16.2% of HIV-uninfected women [14].

In a study done in Nigeria by Terrumun Z Swende et al (2008) published in 2012 to determine the prevalence and risk factors for cervical squamous intraepithelial lesions among women infected with HIV-1 in Makurdi, Nigeria Of the 253 women, cervical SIL were present in 45 (17.8%). However, abnormal cervical cytology was noted in 146 (57.7%). Of those with abnormal cervical cytology, 101 (39.9%) women had atypical squamous cells of undetermined significance, 16 (6.3%) had low-grade SIL and 29 (11.5%) women had high-grade SIL [15].

In a study by Joke A. M. Dols et al (2010) published in 2012, "HPV Type Distribution and prevalence of abnormal Cervical Cytology among HIV-Positive Tanzanian and South African Women'', the prevalence of abnormal cervical cytology was 28 and 31% respectively [16].

In a study done in Kenya by Kevin P McKenzie et al published in 2011 to determine the prevalence of cervical squamous intraepithelial lesions among HIV-positive women on ART. Abnormal cytology was found in 123 women (46%) with 70 women (26%) having low grade squamous intraepithelial lesions (LSIL), 22 (8%) high grade squamous intraepithelial lesions (HSIL), 30(11%) atypical squamous cells of unknown significance (ASCUS) and 1 (0.4%) atypical glandular cells (AGC) [17].

**Human Papillomavirus (HPV) in cervical Neoplasia**

Human papillomavirus (HPV) is known to play an important etiological role in the development of cervical cancer. To date more than 100 HPV types have been characterized based on nucleotide sequence and approximately 40 distinct HPV types are known to infect the genital tract. Based on the strength of their association with cervical cancer, mucosal types of HPV are

classified as low-risk or high-risk [18]. HPV genotypes that have only rarely or not been found in invasive cancer of the cervix are defined as low risk types they include HPV 6 and HPV 11. High-risk types such as HPV (16, 18, 45, 31, 33, 45, 52, 58, 35, and 51) are among most common types found in invasive cervical cancers and are the main factors implicated in cervical carcinogenesis [19].

In a study of about 2000 women, histologicaly diagnosed with invasive cervical cancer (ICC) in 22 countries, using a standard protocol by the International Agency for Research on Cancer (IARC) for the detection of HPV-DNA using PCR-based assays, Munoz et al discovered that HPV were present in 99.7%(95- 100%) of invasive cervical cancer, leading to the conclusion that HPV is a necessary cause of cervical cancer [20].

Although HPV types causing cervical cancer varies from one country to another, over 70% of all cervical cancer cases, in any given country, are attributed to only 2 types, HPV 16 and HPV 18, where between 41% and 67% are of high-grade cervical lesions and 16-32% of low-grade cervical lesions. After HPV-16 and 18, the six other most common HPV types are the same in all world regions, namely 31, 33, 35, 45, 52 and 58. These account for an additional 20% of cervical cancers worldwide [21].

There are four major steps in cervical cancer development: infection of metaplastic epithelium at the cervical transformation zone, viral persistence, progression of persistently infected epithelium to cervical pre-cancer, and invasion through the basement membrane of the epithelium. Infection is extremely common in young women in their first decade of sexual activity. Persistent infections and pre-cancer are established, typically within 5–10 years, from less than 10% of new infections. Invasive cancer of the cervix

(ICC) arises over many years, even decades, in a minority of women with pre-cancer, with a peak or plateau in risk at about 35–55 years of age [22].

**Risk factors**

Factors that contribute to the development or cervical cancer after infection with HPV include immunosupression. Immunosuppression by HIV infection is a strong risk factor for abnormal cytology (SIL).

In a recent review in Jos, Nigeria, Agaba et al found that 60.9% of their 369 HIV-positive women had initial CD4 counts less than 200 cells/mm3 [38]. Prolonged CD4 lymphopenia in patients infected with HIV results in defective T-cell proliferation regardless of the current CD4 count or viral load [38]. Davis et al reported that the strongest predictor of genital dysplasia was a nadir CD4 and CD4 count less than 200 cells/mm³ [39]. Other risk factors include; Multi-parity, early age at first delivery, cigarette smoking, long term use of hormonal contraceptives, co infection with Chlamydia trachomatis and herpes simplex virus among others.

**HPV-HIV co-infection**

Epidemiological evidence suggests that natural immunosurveillance mechanisms normally operate to control HPV infection. Hence immunocompromised individuals such as transplant recipients and human immunodeficiency virus-infected individuals are more prone to HPV infections and HPV-associated diseases. HIV infection results in a progressive reduction in the number of CD4 T helper lymphocytes and impairment of T-cell functions. Both oral and anogenital HPV infections have been shown to be more prevalent in HIV-infected individuals than in the

general population and in Rwanda the prevalence of HIV infection is estimated at 2.9% [2009]. [23].

In immunocompetent individuals, HPV infections normally clear in six to twenty-four months in 70% of females [24].

The natural history of HPV infection is altered in persons infected with the human immunodeficiency virus (HIV) and there is an increased likelihood of persistent HPV infections in this population. This persistent infection increases their risk of having cervical dysplasia and cervical intraepithelial neoplasms (CIN).

High HPV load in HIV- positive women is associated with a 10-fold increase risk of CIN in severe immunosuppressions. Recent studies have indicated that plasma HIV (Ribonucleic acid) RNA levels and CD4+ cell counts are strong determinants of the ability to detect HPV suggesting that as the immune system weakens, it facilitates reactivation of the HPV thus helping to explain the increase rates of HPV infection in women with HIV. Additionally, Highly Active Antiretroviral Therapy (HAART) does not seem to impact this increased rate or persistence of HPV infection in this population. Available data suggest that the widespread use of HAART has not resulted in a decrease in prevalence of genital HPV-infection in HIV-positive patients [25].

In a French cohort, the prevalence of HPV infection remained unchanged at 81%, five months after the initiation of HAART in HIV sero-positive women. In an Italian study after a medium follow-up of 15.4 months, no difference was observed in persistence of infection with high risk-HPV genotypes among HAART- treated women compared to untreated women [25].

## Prevention of Cervical cancer

### Primary prevention

Primary prevention of cervical cancer involves prevention of HPV infection. Preventing HPV infection is important in preventing cervical cancer because almost all cervical cancer cases are caused by HPV, a virus transmitted through sexual contact [20].

Primary prevention can be achieved through; Behavioral change approaches and the use of biological mechanisms, including HPV vaccination. Behavioral change approaches include abstinence from sexual exposure, being mutually faithful and consistent condom use which can reduce the risk of HPV transmission. HPV vaccination is the biological mechanism for primary prevention of HPV infection and cervical cancer. Currently, there are two types of HPV vaccines that provide protection against HPV subtypes 16 and 18: the quadrivalent vaccine (Gardasil), which protects against HPV subtypes 6, 11, 16 and 18, and the bivalent vaccine (Cervarix), which protects mainly against HPV subtypes 16 and 18. These vaccines also provide cross-protection against other oncogenic HPV subtypes.

Both Gardasil and Cervarix have been shown to be effective in preventing cervical precancerous lesions in the past eight years that they have been used. Both vaccines are given in a series of three 0.5 ml intramuscular injections within six months [26].

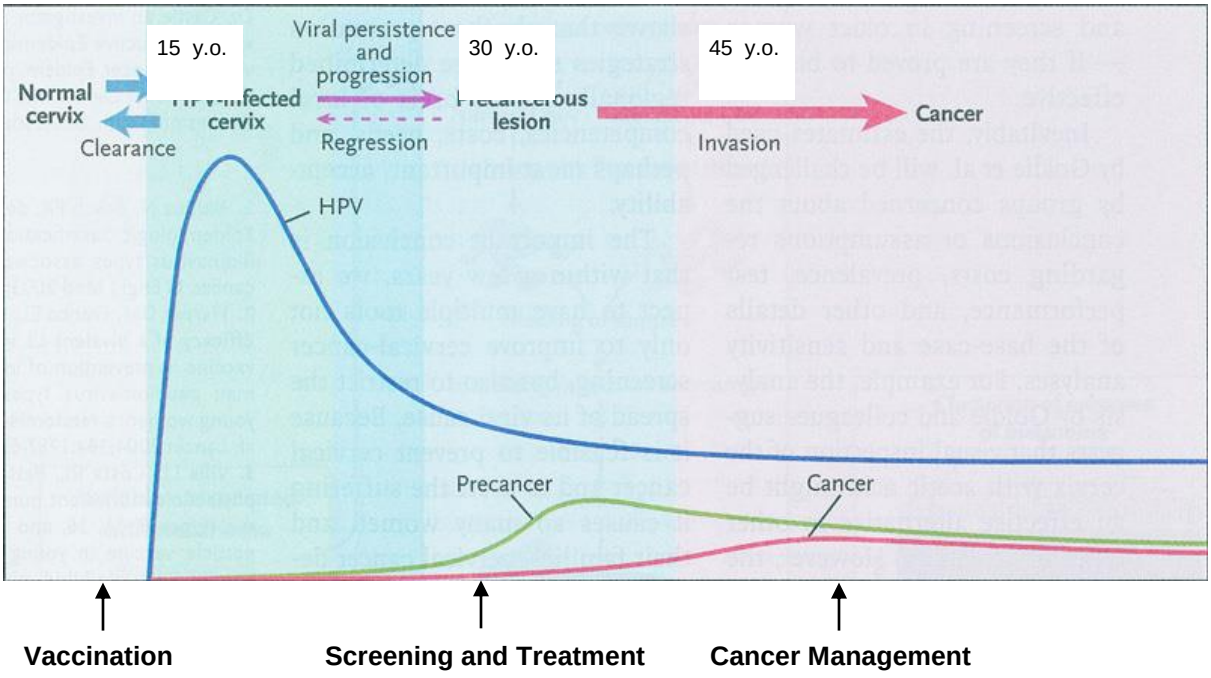
### Secondary prevention

### Screening:

Secondary prevention aims at preventing invasive cervical cancer by detecting and treating precancerous lesions of the cervix before they progress to cancer. Cervical cancer has a long precancerous period, usually

taking more than 10 years to progress from precancerous lesions to invasive cancer. As a result, it is rare for cervical cancer to develop in a woman less than 30 years of age (WHO 2006). This long precancerous stage provides an excellent opportunity for effective intervention measures as shown in the figure below

**Figure1. Continuum of Care for HPV Infection to Cervical Cancer (WHO 2006)**




The main objective of screening for cancer is to reduce morbidity from the disease. Cervical cancer is the most effectively controlled by screening comparing to other cancers because pre-cancerous lesions are detected and treated. In developed countries where there is a successful screening programs, mortality from cervical cancer seldom exceed 5 per 100,000 women, while in Africa, especially in East Africa, a mortality rate of 35 per 100,000 has been reported [3].

In the past 40 years, the number of cases of invasive cervical cancer in developed countries has decreased significantly and this decline largely is the result of existing screening routine tests in regard to cytology, colposcopy, or HPV DNA testing for identifying the population at risk [27].

**Cytology**

Screening by cytology (the Pap smear), through well-run screening programs, is the mainstay of primary screening for cervical cancer. Although the Pap test has never been examined in randomized controlled trials, consistent observational data however supports its effectiveness in reducing both incidence and mortality from cervical cancer. In Iceland, the mortality rate declined by 80% for more than 20 years, and in Finland and Sweden by 50% and 34%, respectively. Similar reductions have been observed in large populations in the United States and Canada. Reductions in cervical cancer incidence and mortality were proportional to the intensity of screening Mortality in the Canadian provinces was reduced most remarkably in British Columbia, which had screening rates two to five times those of the other provinces.

Case-control studies have found that the risk of developing invasive cervical cancer is three to ten times greater in non-screened compared to screened women. Other studies also found that cervical cancer risk increases with long duration following the last normal Pap test or with decreasing frequency of screening. Nonetheless, screening every 2 to 3 years has demonstrated not to increase the risk of finding invasive cervical cancer above the risk expected with annual screening. In low-resource settings, cervical cancer screening program using Pap smear test has failed to demonstrate cancer prevention for many reasons: little or no access to screening program, costs,

lack of well-trained personnel causing sampling and interpretation errors, inadequate cytology laboratory infrastructure, and lack of appropriate follow up of abnormal results [28].

In the US, similarly, more than a half of all invasive cancers occur in women that have never had a Pap smear; an additional 10 to 20% of cancers occur in women who spent more than five years following the last normal Pap test. Another proportion of one-quarter of US cervical cancers were in women that had an abnormal Pap smear, but did not get appropriate follow-up [28].

Various screening approaches like visual inspection after application of acetic acid or Lugo's iodine which offer a low cost alternative to cytological screening and have the advantage of immediate results, and, if indicated, treatment in one visit; have been shown to significantly reduce cervical cancer morbidity and mortality in a large randomised controlled trial in resource limited countries [28].

**Cytology abnormalities and management modalities**

Although precise figures are not available, laboratory surveys from the College of American Pathologists (CAP) indicate that more than 1 million women in the united states are diagnosed with low-grade intraepithelial lesions annually, referred to as Cervical Intraepithelial Neoplasia grade 1(CIN 1), and 500,000 will be found to have high-grade cervical cancer precursor lesions, referred to as CIN-2 and CIN-3 [29, 20]. The prevalence of CIN in Rwanda in not known. It is estimated that 3-7 million women worldwide may have high-grade dysplasia. According to the Bethesda classification system, cervical cytological abnormalities of the Squamous cells are uniformly reported as Low grade Squamous Intraepithelial Lesions (LSIL) representing mild cervical dysplasia, High grade Squamous Intraepithelial Lesion(HSIL) representing moderate to severe dysplasia or

Atypical Squamous cells of Undetermined Significance (ASCUS) that comprise a category that is suspicious but not conclusive for cellular dysplasia. A further category of glandular cell abnormality named Atypical Glandular cells of Undetermined Significance (AGUS) denotes an inconclusive appearance of glandular cells that are neither normal nor clearly dysplastic. In general terms, a cytological diagnosis of LSIL represents a histological diagnosis of CIN1 whereas a cytological diagnosis of HSIL would represent CIN2 or CIN 3 lesions on histology [29].

The objective of treatment of CIN is the prevention of invasive cancer of the cervix. Limited data are available to calculate the risk of invasive disease in women with untreated CIN [30]. The natural history of untreated CIN1 is characterized by high rates of spontaneous regression and low rates of progression to cancer. In his review, Ostor A, G found that in patients with CIN1, spontaneous regression occurs in 57% cases whereas 11% progress to CIN2 and CIN3 or cancer. Overall, the rate of progression to invasive cervical cancer observed in these studies was 0.3%. Independent recent meta-analysis of the natural history of CIN1 arrived at similar conclusions [30].

Follow-up studies have found that despite marginal relative differences, CIN2 and CIN3 lesions are more likely to persist or progress than to regress. Review of the published natural history literature indicates that 43% of untreated CIN-2 lesions will regress in the absence of treatment, whereas 35% will persist and 22% progress to carcinoma in situ or invasive cervical cancer. For comparison, 32% of CIN-3 lesions spontaneously regress, 56% persist, and 14% progress [30].

Both ablative treatment methods that destroy the affected cervical tissue in vivo and excisional modalities that remove the affected tissue are utilized for

treating CIN lesions [31]. Ablative methods include cryotherapy, laser ablation, electro-fulguration, and cold coagulation. Excisional methods that provide a tissue specimen for pathological examination include cold-knife conization, loop electrosurgical excision procedures (LEEP), laser conization, and electrosurgical needle conization. Although various studies show that both ablative and excisional modalities have a similar efficacy in eliminating CIN and reducing a woman's risk of future invasive cervical cancer [32, 33], a diagnostic excisional procedure is recommended for women with recurrent CIN 2 and CIN 3. Ablation is also unacceptable and a diagnostic excisional procedure is recommended for women with a histological diagnosis of CIN 2 and CIN 3 with unsatisfactory colposcopy [34]. There are no accepted nonsurgical therapies for CIN.

Acceptable post treatment management options for women with CIN 2, 3 include Human Papillomavirus (HPV) detection by HPV DNA testing at 6-12 months. Follow-up using either cytology alone or a combination of cytology and Colposcopy at 6 month intervals is also acceptable. Colposcopy with endocervical sampling is recommended for women who are HPV DNA positive or have a repeat cytology result of Atypical Squamous cells of Undetermined Significance (ASCUS) or greater. If the HPV DNA test is negative or if 2 consecutive repeat cytology tests are negative for intraepithelial lesion or malignancy, routine screening for at least 20 years commencing at 12 months is recommended. It is therefore unacceptable to offer repeat treatment or hysterectomy based on a positive follow up HPV DNA test alone [34].

Outpatient therapy employing methods such as cryotherapy and LEEP combined with proper follow-up, is appropriate for dealing with visible lesions on the ectocervix when invasive cancer and endocervical involvement have been ruled out. Cryotherapy and LEEP hold out particular promise for

developing countries because of their effectiveness, simplicity, minimal side effects and low cost. Cure rates range from 80% to 95%, depending on the method used and the severity of the lesions. However, each method has advantages and disadvantages that demand consideration [34].

**Justification/ Rationale**

The prevalence of cervical cancer is exacerbated by the burden of HIV/AIDS epidemic, which is highest in sub-Saharan Africa where more than half of the people infected with HIV are women who have limited access to cervical cancer screening programs. The association between HIV infection and invasive cervical cancer is complex, but several studies now clearly demonstrate an increased risk of precancerous cervical lesions and a more rapid progression to cancer amongst HIV-infected women.

As there is no available data on the prevalence of cervical cytology abnormalities in HIV-infected women at Rwanda Military Hospital and/or in Rwanda, this motivated us to carry out the research. Therefore this study may assist policy makers to develop guidelines for prevention and treatment strategies for cervical cancer among HIV-infected women which is currently based on limited evidence and is yet to start in Rwanda.

## Conceptual framework

Cancer of the cervix is a major Public Health concern in the world over and more so in Sub-Saharan Africa. HIV-infection is an important contributing factor. Women living with HIV are 2-5 folds likely to develop cancer of the cervix compared to those who are not infected by HIV. Other risk factors to the development of cancer of the cervix are; multi-parity, oral contraceptive use for a long period of time, early sexual debut, having multiple sexual partners, smoking has also been shown to increase a woman's risk of developing cancer of the cervix, low socioeconomic conditions, immunosuppression, low CD4+ cell count, high viral load.

Without any interventions, precancerous lesions of the cervix lead to invasive cancer and all its co-morbidities including death.

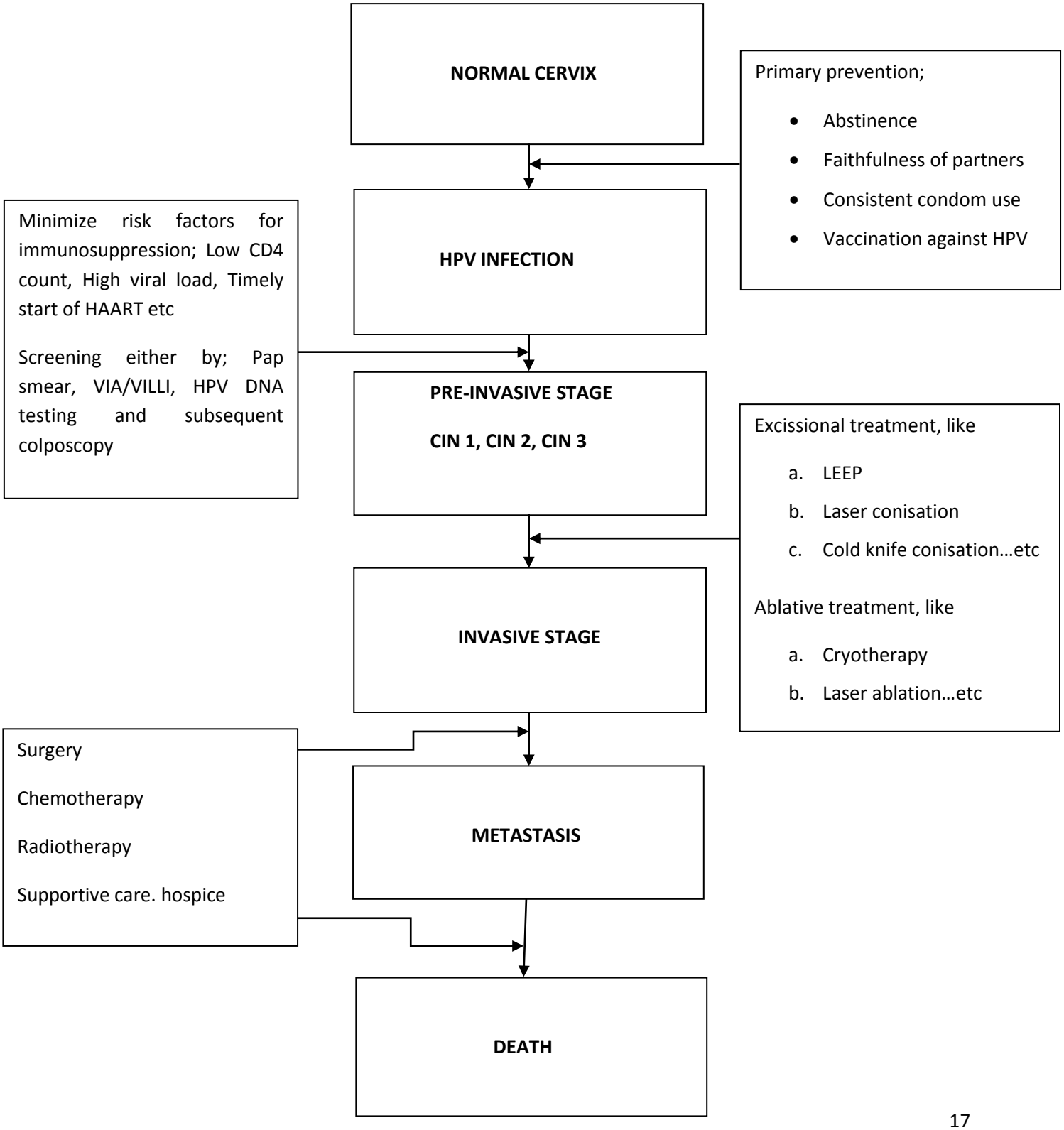
This grave condition can be halted by immunization of young girls (before sexual debut generally 9-15years) against high risk HPV, sex education programs aimed at sexual behavioral change (abstinence, consistent condom use and mutual faithfulness amongst partners) and dual contraception.

Timely screening of all sexually active women particularly those infected with HIV by use of Pap smear, VIA/VILLI, HPV DNA testing and subsequent colposcopy to avert precancerous lesion from progressing to invasive cancer. This can be achieved either by excissional treatment like LEEP, Laser conisation and cold knife conisation or by Ablative treatment like cryotherapy, laser ablation and electro fulguration. However, once the disease has progressed to invasive stages or metastasis, surgery, chemotherapy, radiotherapy and supportive care are the treatment options.

This can also be improved by carrying out studies on the cancer of the cervix to determine the actual prevalence, sociodemographic factors predisposing women to cervical dysplasia and cancer and thus estimate burden of disease. From studies, policies and interventions would be formulated for corrective action in terms of either prevention or timely screening and treatment of precancerous lesions especially in HIV-infected women.

With good policy formulation, HIV-infected women would be encouraged to have good health seeking habits including regular check up for cancer of cervix and in so doing pre-invasive cancer will be detected and treated on time.

**SCHEMATIC REPRESENTATION OF THE CONCEPTUAL FRAMEWORK**



## Research question

What is the prevalence of abnormal cervical cytology smears in HIV-positive patients at Rwanda Military Hospital?

## Objectives

### a) Broad

The objective of this study was to establish the prevalence of cervical cytology abnormalities among HIV infected women attending HIV clinic at Rwanda Military Hospital.

### b) Specific objectives

- To determine the prevalence of abnormal pap smears in HIV-positive women attending HIV- clinic at Rwanda Military Hospital.
- To determine the correlation between CD4+ cell count and abnormal Pap smear among women attending HIV-clinic at Rwanda Military Hospital.
- To determine the correlation between WHO-HIV staging and abnormal pap smear among women attending HIV clinic at Rwanda military hospital.

## CHAPTER 2: METHOLOGY

### 1. Study site

The study was done at Rwanda Military Hospital**.** Rwanda Military Hospital is the largest hospital located in Kicukiro District of Kigali city. It is located in Kanombe sector about five kilometers from the Kigali International Airport. It is run by the Ministry of Defense. The hospital serves both the military and the general public. The hospital have departments of; Internal medicine, Pediatrics, Surgery, Obstetrics and Gynecology ophthalmology among others. It has been recently approved to be a referral and teaching Hospital.

The facility's HIV clinic serves as both a primary care center and public referral center for women, men and children affected and infected by HIV/AIDS from around the District and it is one of the biggest HIV clinics in country. Currently, the center has approximately 3200 HIV infected adults enrolled for care. The clinic is run by three medical officers and six nurses who are all trained to manage HIV and related diseases. The clinic operates on daily basis (Monday –Friday) and on average fourty patients are seen and majority is women.

The fact that there was no cervical cancer screening program at the hospital and in the country in general this motivated us to carry out the research hence the site was suitable because of the large numbers of HIV-infected women and lack of screening program at the facility.

## 2. Study population

The study population comprised of all HIV-positive women, 18-69 years who had been or were sexually active and were attending the HIV-clinic and consented to participate in the study.

Women on their routine follow up for HIV who met the inclusion criteria and consented to participate in the study were screened for cervical cancer using conventional pap smear.

## 3. Study design

This was a Cross-Sectional Descriptive Study whose aim was to determine the prevalence of cervical cytology abnormalities in HIV-infected women at Rwanda Military Hospital.

## 4. Inclusion and exclusion Criteria

### 4. a. Inclusion criteria

All HIV-positive women, 18-69 years who had been or were sexually active and were attending the HIV-clinic and consented to participate in the study and have a pap smear done to them.

### 4. b. Exclusion criteria

- History of hysterectomy
- Clients who were not willing to participate in the study
- Women with obvious cancer of the cervix (were referred to GOPC for further management)
- Pregnant and postnatal mothers were excluded from our study.

## 5. Sample size determination

Literature review done in Africa and the world as a whole show that prevalence of cervical cytology abnormalities in HIV-infected women ranges between 12.5% to 38.3%. For purposes of this study, prevalence of abnormal cervical cytology in HIV-positive women was taken as an average of 12.5% and 38.3% thus 25.4%. The formula below was used to determine the sample size.

$n=1.96^2 x\ p\ (1-p)/d^2$

n=minimum sample size

p=prevalence of abnormal cytology in HIV infected women at 25.4%

d=precision/reliability to determine p=5%

n=1.96 x 1.96 x 0.254 (1-0.254) / 0.05 x 0.05

n=0.9757664 (0.746) / 0.0025

Thus n=292

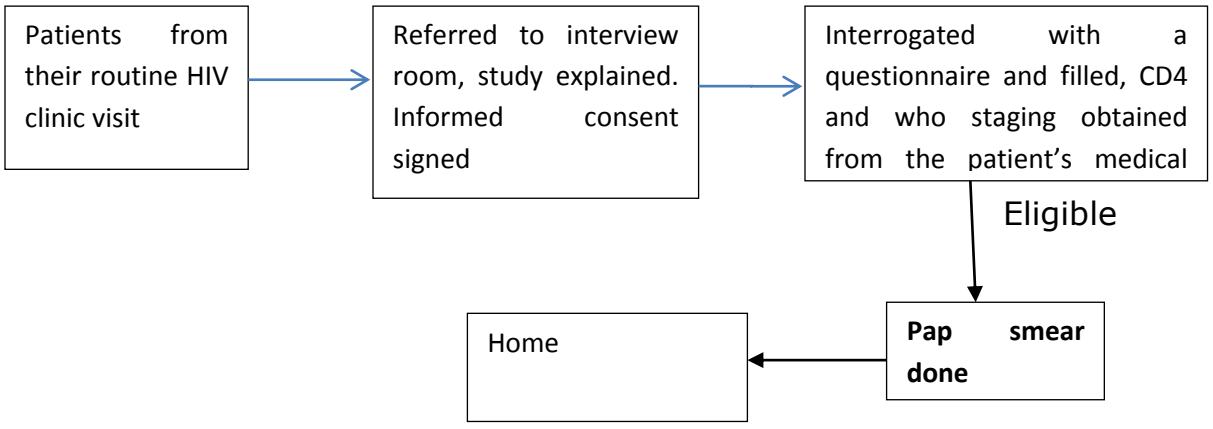
A minimum sample of 292 women was appropriate and was targeted.

## 6. Recruitment and consenting procedure

Study participants from their routine HIV clinic were referred to the study room, the study was explained to them, those who were found to be eligible and were willing to participate in the study were recruited. Interviews were conducted in a safe, secure and confidential environment for those who consented to participate.

The participants were recruited by consecutive sampling. The researcher/assistant was responsible for conducting all interviews. Once in the interview room, the participant was informed about the study, its objectives, risks and benefits. Those who were willing to participate were requested to sign a written informed consent. Participants were interviewed using a questionnaire but also their medical records were checked for CD4 cell counts, if they were on HAART or not, and WHO-HIV staging. Double recruitment of participant was prevented by enquiring from the client if they had completed the interview before. In addition, since there was no monetary incentive given to the participants, it was unlikely that a study participant would go through the process more than once.

The client flow is provided below.



## 7. Study instrument

The study instruments constituted of a questionnaire and the patient's medical records. The questionnaire had structured questions which were both categorical and open ended about the sociodemographic data and sexual history while the CD4 count, HAART status and WHO stage were obtained from medical records. The questionnaire is attached as appendix I.

## 8. Data management

### a) Data collection

Data was collected by the principal investigator and the research assistant. After training of the research assistant, the questionnaire was pre-tested in order to determine its applicability. The questionnaire was also examined for clarity, ambiguity, time taken to fill it out and analyzability. Appropriate adjustments were then made to research. The researcher and the assistants introduced themselves to the study participants and the purpose of study was explained. Ultimate benefits to the patients were stressed upon after which an informed consent in a language clear to the patient either English or Kinyarwanda was signed (Appendix II). The questionnaire was filled by the researcher or the assistant together with patient in a private room to ensure confidentiality. During the interview, bilateral conversations were encouraged. All specimen collected were stored in a safe place awaiting transfer to the pathologist.

b).Quality control and assurance procedures

Due to financial constraints, quality control and assurance procedure to ensure the quality of the results of Pap smears by at least 10% re-read of the slides by a different Pathologist was not possible. But the fact that the Pap smear were stained and interpreted by qualified/experienced pathologist, are to be considered appropriate.

**c).Data management**

Data collected was entered into an SPSS database by the statistician. Each record was assigned a unique identifier and names were dropped so as to maintain participants' confidentiality. Quality of data was assessed by conducting consistency checks. Data were stored in a password protected computer.

**d).Data analysis**

The data collected was transferred into a Microsoft Access database and then analyzed using SPSS software version 17.0. A descriptive analysis included measures of central tendency like mean for age, age at sexual debut, number of lifetime sexual partners and duration since diagnosis of HIV in years, measures of variability; standard deviation, range univariate analysis and also inferential analysis using chi square and T-test was done.

## Ethical Considerations

- Approval to carry out research was sought from the KNH/UON Ethics and Research committee at Kenyatta National Hospital and also from the National Health Research committee of the Rwanda Biomedical Centre (RBC) and the National Ethics and Research Committee (ERC) - Rwanda.
- Informed written consents were obtained from all study participants.
- Records were coded and patient's names were not used.
- No incentives were given to study subjects.
- Participation was purely voluntary and at any stage the participant was free to withdraw from the study or not answer some questions without penalty.
- It was capitalizing on events taking place during routine HIV clinic and it did not interfere with the already laid down HIV clinic protocol at the Hospital.
- Information collected remained confidential and was only be used for purposes of the study only.
- Patients who were found to have lesions necessitating treatment were referred appropriately to the facilities GOPC.

## Plans for dissemination and time line

The plans are as follows:-

- Presentation as a dissertation in partial fulfillment for the award of the degree of master of medicine in the Department of obstetrics and gynecology at the University of Nairobi. October/2013
- Give to Rwanda Military Hospital HIV clinic for follow up and further management and to adopt appropriate changes. November/2013
- Share with MOH to advice on policy and further research. March/2014
- Publication in local and international journals. 2014

# CHAPTER 3: RESULTS

**Table 1: Socio-Demographic Characteristics**

| Factor | N | % (95% CI) | Mean (SD) |
|---|---|---|---|
| **Age** | | | |
| < 20 | 1 | 0.3 (0.0 - 1.0) | |
| 20 - 29 | 68 | 23.2 (18.3 - 28.1) | |
| 30 - 39 | 127 | 43.3 (37.6 - 49.1) | 36.3 (8.2) |
| 40 - 49 | 78 | 26.6 (21.5 - 31.7) | |
| 50 - 59 | 19 | 6.5 (3.6 - 9.3) | |
| **Total** | **293** | | |
| **Age at 1st Sexual Intercourse** | | | |
| < 16 | 36 | 12.3 (8.5 - 16.1) | |
| 16+ | 257 | 87.7 (83.9 - 91.4) | 18.9 (3.6) |
| **Total** | **293** | | |
| **Number of lifetime Sexual Partners.** | | | |
| 1 | 42 | 14.3(10.3 - 18.4) | |
| 2-3 | 96 | 32.8 (27.4 - 38.2) | 4.2 (3.8) |
| 4 + | 155 | 52.9 (47.2 - 58.7) | |
| **Total** | **293** | | |
| **Duration since diagnosis of HIV (yrs)** | | | |
| < 1 | 5 | 1.7 (0.2 - 3.2) | |
| 2-3 | 63 | 21.5 (16.8 - 26.2) | |
| 4-5 | 54 | 18.4 (13.9 - 22.9) | 6.9 (4.0) |
| 6+ | 171 | 58.4 (52.7 - 64.0) | |
| **Total** | **293** | | |
| **Ever Been screened for Cancer of the cervix.** | | | |
| Yes | 2 | 0.7 (0.0 - 1.6) | |
| No | 291 | 291 (99.3 - 100.0) | - |
| **Total** | **293** | | |

A total of 293 women were enrolled in the study. The mean age of our participants was 36.3 (SD 8.2). Youngest was 19 yrs and the oldest was 59yrs. Majority of the women 127 (43.3%) were

aged between 30-39yrs. Majority of our study participants had sexual debut after 16 yrs 257(87.7%) with a mean age at sexual debut of 18.9. Most participants in our study had more than 1 sexual partner 251(85.7%) and those who had more than 4 lifetime sexual partners were the majority155 (52.9%). Majority of the patients 225(76.8%) were on follow up for more than 4 yrs and 171(58.4%) were on follow up for more than 6yrs.

Only 2 out of 293 patients had had cervical cancer screening done prior to this research and neither of two knew about her results.

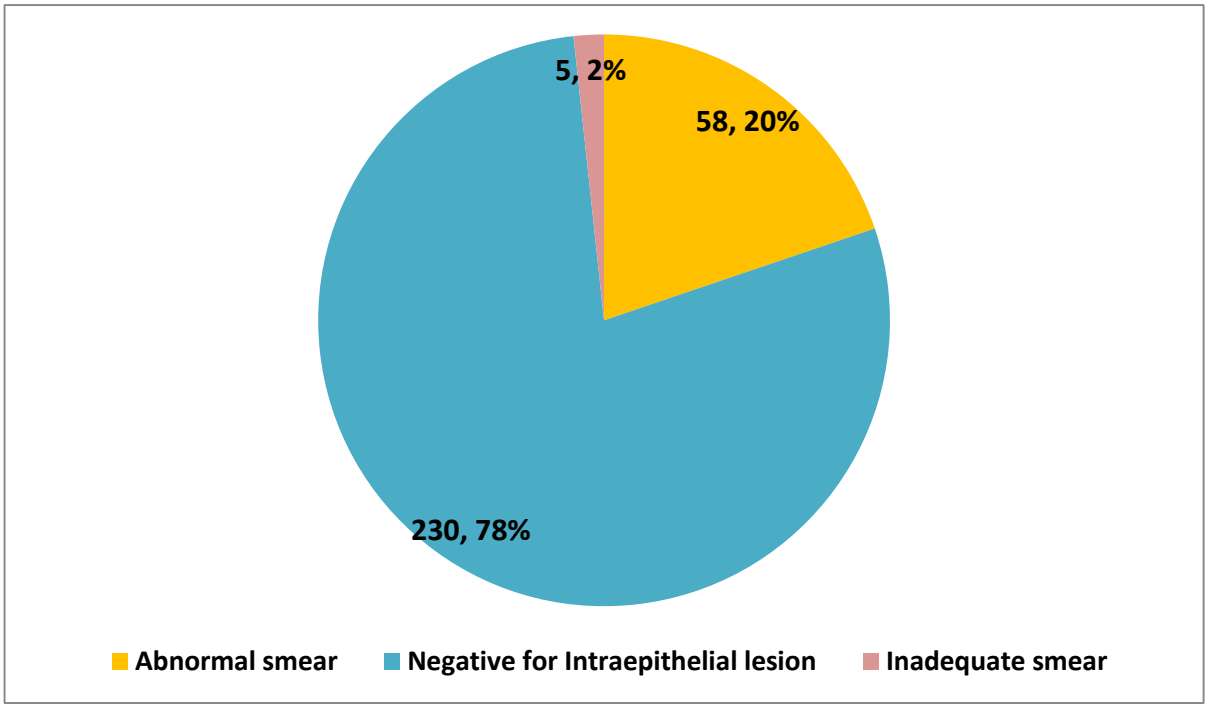
**Table 2: Clinical Findings**

| Findings | N | % (95% CI) | Mean (SD) |
|---|---|---|---|
| **Initial CD4 Count** | | | |
| < 200 | 143 | 48.8 (42.8 - 54.7) | 223 (162) |
| 200 + | 150 | 51.2 (45.3 - 57.2) | |
| **Total** | **293** | | |
| **Current CD4 Count** | | | |
| < 200 | 21 | 7.2 (2.7 - 7.9) | 497 (209) |
| 200 + | 272 | 92.8 (92.0 - 97.3) | |
| **Total** | **293** | | |
| **WHO Staging** | | | |
| I | 217 | 74.1 (69.0 - 79.1) | |
| II | 31 | 10.6 (7.0 - 14.1) | |
| III | 37 | 12.6 (8.8 - 16.5) | - |
| IV | 8 | 2.7 (0.9 - 4.6) | |
| **Total** | **293** | | |
| **On ART** | | | |
| Yes | 284 | 96.9 % | |
| No | 9 | 3.1 % | |
| **Total** | **293** | | |

The mean CD4 count was 223 (SD 162) at the beginning of follow up with 143 (48.8%) patients having CD4 count less than 200/mm3 and the current mean CD4 count was 497 (SD 209) with only 21 (7.2%) having CD4cell count less than 200/mm3.

Majority of our patients 217 (74.1%) in this study were in WHO HIV/AIDS class 1 at the time of the study. Most of the patients 284 (96.9%) were on HAART during the time of the study.

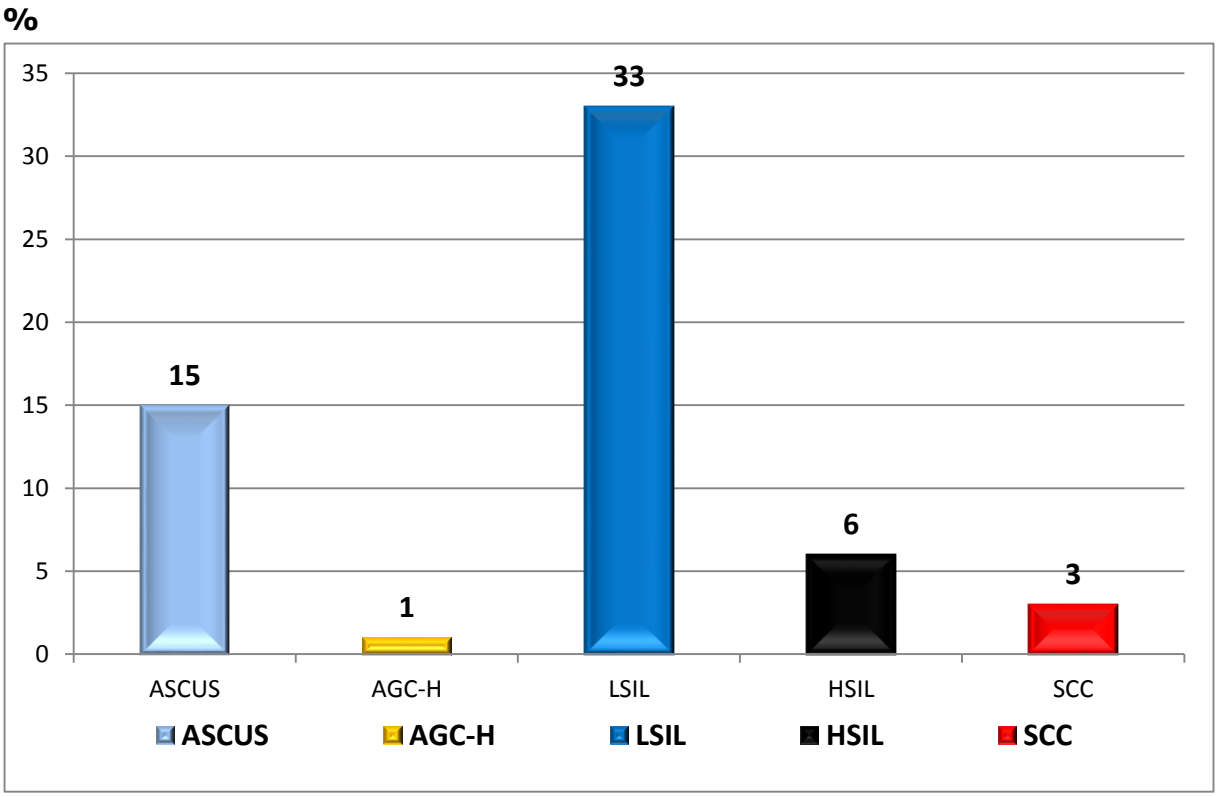
**FIGURE 2: PREVALENCE OF ABNORMAL CYTOLOGY.**




A total of 293 women were enrolled in the study. Five were excluded from the analysis due to inadequate smear or missing cervical cells at all.

The prevalence of cervical cytology abnormalities in this research was 58 out of 288 (20%) with LSIL being the most prevalent at 33 out of 288 (11.30%), ASCUS 15 out of 288 (5.13%), HSIL 6out of 292 (2.05%), SCC was seen in 3 out of 288 (1.02%) and lastly AGC-H was 1 out of 288 (0.34%).

**Figure 3: Bethesda classification N=58**




LSIL was the most common lesion seen among the abnormal Pap smears.

**Table 3: CD4 cell count and abnormal Pap smear, N=288, P value =0.033**

| | Abnormal Pap smear | | Negative for IE lesion | | P value | OR(95%CI) |
|---|---|---|---|---|---|---|
| | Freq | % | Freq | % | | |
| Current CD4 count | | | | | | |
| <200 cells/mm³ | 8 | 13.8 | 13 | 5.7 | | |
| >200 cells/mm³ | 50 | 86.2 | 217 | 94.3 | 0.033 | 2.7(1.1-6.8) |

Women whose current CD4+ cell count was less than 200 cells/mm³ were 2.7 times more likely to have abnormal pap smear than women whose current CD4+cell count was above 200 cells/mm³ [Odds ratios (OR) = 2.7,95% CI (1.1-6.8)]. P = 0.033

**Table 4: WHO-HIV classification and abnormal smear, N=288, P Value = 0.705**

| | | ABNORMAL CYTOLOGY | | NEGATIVE FOR INTRAEPITHELIAL LESION | |
|---|---|---|---|---|---|
| | | FREQ | % | FREQ | % |
| | | | | | |
| WHO-HIV CLASSIFICATION | I. | 46 | 79.3 | 168 | 73.0 |
| | II. | 6 | 10.3 | 24 | 10.4 |
| | III. | 5 | 8.6 | 32 | 13.9 |
| | IV. | 1 | 1.7 | 6 | 2.6 |

**The association between WHO-HIV classification and abnormal Pap smear was not found to be statistically significant. P value = 0.705.**

**Table 5: Other variables**

| | Results | | | | p value | OR (95% CI) |
|---|---|---|---|---|---|---|
| | Positive | | Negative | | | |
| | Freq | % | Freq | % | | |
| **Age** | | | | | | |
| < 30 | 15 | 25.9 | 53 | 23.0 | | |
| 30+ | 43 | 74.1 | 177 | 77.0 | 0.851 | 1.2 (0.6 - 2.3) |
| **On ART** | | | | | | |
| Yes | 54 | 93.1 | 225 | 97.8 | | |
| No | 4 | 6.9 | 5 | 2.2 | 0.065 | 0.3 (0.1 - 1.2) |
| **Age at 1st sexual intercourse** | | | | | | |
| < 16 | 7 | 12.1 | 29 | 12.6 | | |
| 16+ | 51 | 87.9 | 201 | 87.4 | 0.912 | 0.9 (0.4 - 2.3) |
| **No. of Sexual Partner** | | | | | | |
| 1 | 7 | 12.1 | 35 | 15.2 | | |
| 1+ | 51 | 87.9 | 195 | 84.8 | 0.544 | 0.8 (0.3 - 1.8) |
| **Duration since diagnosis** | | | | | | |
| 1 - 3 | 11 | 19.0 | 54 | 23.5 | | |
| 4+ | 47 | 81.0 | 176 | 76.5 | 0.462 | 0.8 (0.4 - 1.6) |

There was no statistically significant association between the variables in the table above (table 5) and abnormal Pap smear.

# CHAPTER 4: DISCUSSION.

## DISCUSSION

During the early days of the HIV epidemic, HIV-infected women who had cervical human papillomavirus infection and SIL frequently died of AIDS well before developing invasive cervical cancer [15]. However, following the introduction of HAART, the clinical course of HIV has been substantially prolonged, making HIV-infected women a clinically significant group of patients who have an increased risk of acquiring human papillomavirus infection and developing SIL and invasive cervical cancer [35].

According to the World Health Organization (WHO), invasive cervical cancer (ICC) is the second most common cancer in women worldwide and is more frequent in low income countries [9]. Recent guidelines recommend that, following two initial normal Pap-smears at a 6-month interval, all HIV-positive women should undergo annual cervical cytologic examination. In addition, it is recommended that all immunosuppressed women with atypical squamous cells undergo colposcopy [36]. This study provides the first comprehensive analysis of the prevalence of cervical cytological abnormalities in this population at Rwanda Military Hospital, Rwanda.

**Prevalence**

The prevalence of cervical cytology abnormalities in our study was (20%) 58/288, (fig 1). This is comparable to 21.3%(60/280) as documented in the study done in Thailand by Pimpika Tansupswatdikul, Somkid Piyaman MD et al in 2009 which was aimed at establishing prevalence of abnormal cervical cytology from Pap smear in HIV-infected women[11].

The reported prevalence in this study is however higher than the 2.9% and 13.3%, reported by Kapiga et al [37] among HIV-seropositive pregnant women in Tanzania and Chalermchockcharoenkit et al in Thailand [10] among HIV-infected women by postpartum Papanicolaou smear. The fact that the other studies were conducted among pregnant and postpartum women may have contributed to the observed variation.

The current study's prevalence is high compared to other researches done in Brazil (12.1%) by Patricia Abrue et al (2006) [12] and in Nigeria (10.9%) by Anorlu RI et al (2007). All studies sought to establish the prevalence, and factors associated with cervical cytology abnormalities in HIV infected women in which the prevalence of abnormal cytology was lower compared to our findings of 20%.

However, other researchers have reported higher prevalences in Africa involving HIV-positive women; In Makurdi, Nigeria (57.7%) [15], Tanzanian 28 % [16] and South African 31% [16], Kenya (46%) [17].

The difference between this current study and those of other researchers may be attributed to the different social backgrounds and sample size differences and possibly the different stages of HIV infection and specific age groups sampled like in the Kenyan cohort where only patients aged 30 to 39 were recruited.

Elsewhere, L. Stewart. Massad et al in their study, "Prevalence and predictors of sqaumous cell abnormalities in Papanicolaou smear from women infected with HIV" which was a multicentre prospective cohort study that was conducted in six U.S cities. Cervical cytology was abnormal in 38.3% of HIV-infected women VS 16.2% of HIV-uninfected women [14].

In a study by Dionne N Dames et al (2008) published in 2009 the prevalence of cervical abnormalities was reported to be 44% in the USA [13]. These two were high 38.3% and 44% compared to our findings 20%, this is probably due to the large numbers used in their studies.

The prevalence of cervical cytology in the Rwandan general population in not known but the World Health Organization ranks Rwanda among the countries worldwide with the highest cervical cancer incidence, estimated at 34.5/100,000 (IARC 2008).

**CD4 Cell count.**

Immunosuppression by HIV infection is a strong risk factor for abnormal cytology (SIL). In this study, 48.8% of HIV-positive women had baseline CD4 counts less than 200 cells/mm3, which is diagnostic of immunologic AIDS. In a recent review in Jos, Nigeria, Agaba et al found that 60.9% of their 369 HIV-positive women had initial CD4 counts less than 200 cells/mm3 [38]. The lower percentage of women with immunologic AIDS in this study may partly explain the lower prevalence of SIL of 20% in this study as compared with 29% in the Jos study. This study also showed that the CD4 count was inversely associated with cervical cytology abnormalities, and women with a CD4 count less than 200 cells/mm3 were at greater risk of abnormal cytology compared to women with CD4 counts greater than 200 cells/mm³. This finding is in accordance with several other studies involving HIV-positive women. Prolonged CD4 lymphopenia in patients infected with

HIV results in defective T-cell proliferation regardless of the current CD4 count or viral load [38]. Davis et al reported that the strongest predictor of genital dysplasia was a nadir CD4 and CD4 count less than 200 cells/mm³ [39].

**Use of HAART.**

Previous studies have not satisfactorily established a protective effect of antiretroviral treatment on the risk of SIL. HAART showed some potential effect in the Women's Interagency HIV study [40]. Heard et al [41] showed that HAART had a positive impact on regression of SIL, and this was associated with increasing CD4 cell counts.

In their study, Peter Memiah, wangeci Mbuthia et al found out that patients who were not on ART were 2.21 times more likely to have CIN infection than patients who were on HAART [42].

In other studies, the effect of HAART on the prevalence of SIL has not been significant [38, 43] or it has remained unchanged [44]. Similarly in this study, the use of HAART was not associated with a significant reduction in the risk of SIL.

In other studies, the effect of HAART on the prevalence of SIL has not been significant or the prevalence of SIL has remained unchanged [38]. Similarly in the current study, the use of HAART was not associated with a significant reduction in the risk of cervical cytology abnormalities.

## Study limitations

- The fact that this was hospital based cross-sectional study it does not reflect the actual national prevalence and therefore may lack the strength to affect national policy. However the Military Hospital serves a large proportion of HIV- infected women, these findings will inform about the cervical cancer screening practices within the facility and may be expanded nationwide.
- There was also no end-of-study colposcopy for those whose cytology was reported as ASCUS, HSIL+ to seek occult lesions; this leaves the possibility of underestimation of the endpoints of low-grade SIL and high-grade SIL at the time of the study.
- Sample size determination did not anticipate loss of results or inadequate smear as there were 5 Pap smears that were reported as inadequate.

## Conclusion

Cervical cancer is a leading cause of morbidity and mortality in countries with the fewest resources and these resources are often already over stretched by high levels of HIV infection. Virologic synergy between HIV and HPV infections further exacerbates the problem, and HIV-infected women are at increased risk for HPV and HPV-related diseases, including cervical cancer. Furthermore, unlike other typical opportunistic infections, there is no evidence that the use of effective ART reduces the burden of HPV or HPV related complications, possibly leading to increased numbers of women at risk for cervical cancer as HIV treatment programs become more accessible and successful. Fortunately, cervical cancer is preceded by an extended precancerous period that can be detected and treated to prevent the

development of invasive disease. Cervical cytology, which has revolutionized cervical cancer prevention in the U.S. and other developed countries over the past half-century, is simply not feasible for most countries with few resources. Alternatives such as VIA and HPV testing hold great promise as alternative screening strategies, coupled with the use of cryotherapy or LEEP to treat precancerous lesions. In the new WHO Global health sector strategy on HIV/AIDS an over-arching goal is to achieve universal access to Cervical Cancer Screening and Prevention for HIV-Infected Women in the Developing countries. Two of the four strategic directions noted in this strategy are to leverage broader health outcomes through HIV responses, including strengthening linkages between HIV and other related health programs, notably including cervical cancer screening and care, and to build strong and sustainable heath systems in which HIV and other essential services are available, accessible, affordable and sustainable.

In conclusion, a high prevalence (20%) of cervical cytology abnormality was found among HIV infected women at Rwanda Military Hospital, Rwanda. Decreased CD4 cell counts were associated with abnormal Pap smear. CD4 cell counts less than 200 cells/mm3 was significantly associated with positivity of the cervical cytology. There was no statistically significant association between WHO stage and abnormal Pap smear.

**Recommendation.**

- The government through the ministry of health should create awareness about the burden of cervical cancer to the public.
- Programs for cervical cancer screening and treatment should be developed.
- Programs to train health care providers on the cervical cancer screening.
- Due to the high prevalence reported in this study, screening of this high risk group (HIV-infected women) should be routine.

# CHAPTER 5: APPENDICES

## APPENDIX 1: REFERENCES


1. Parkin DM, Pasini P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int J Cancer 1999;54:827–41.

2. GLOBOCAN 2008. Ferlay J., Shin H.R., Bray F., Forman D., Mathers C. and Parkin D.M. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr.

3. Sankaranarayanan R and Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynaecol 2006;20:207–25.

4.World Health Organization. *Comprehensive Cervical Cancer Control*. *A Guide to Essential Practice*. Geneva, Switzerland: World Health Organization; 2006.

5.El-Ghobashy A, Herrington S. Cervical cancer: epidemiology and molecular characterization. In: Studd J, editor. *Progress in Obstetrics and Gynaecology*. *Vol 16*. London, UK: Elsevier Science Limited; 2005.

6.Centers for Disease Control and Prevention, "MMWR. Recommendations and Reports-1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults," January 2011, http://www.cdc.gov/mmwr/preview/mmwrhtml/ 00018871.htm.

7.Davis AT, Chakraborty H, Flowers L, Mosunjac MB. Cervical dysplasia in women infected with HIV: a correlation with HIV viral load and CD4 count. *Gynaecol Oncol*. 2001;80:350–354.

8.National cervical cancer screening and treatment guidelines; Rwanda. Version 2011.

9. Parkin DM, Whelan SL, Ferlay J, et al, editors. Cancer Incidence in Five Continents, Vol VIII. IARC Scientific Publication No.155. Lyon: IARC, 2002.

10. Chalermchockcharoenkit .A, Chenchit Chayachinda et al. Prevalence and cumulative incidence of abnormal cervical cytology among HIV-infected Thai women. BMC Infectious Diseases 2011, 11:8

11.Pimpika Tansupswatdikul, Somkid Piyaman MD et al. Prevalence and Predictors of Abnormal Cervical Cytology in HIV-Infected Patients at the Anonymous Clinic, Chonburi Hospital. Thai Journal of Obstetrics and Gynaecology January 2009, Vol. 17, pp. 51-5661-

12.Patr´ıcia Abreu Pinheiro de Lemos, Marco T´ ulio Antonio Garc´ıa-Zapata et al. Cervical Cytopathology in a Population of HIV-Positive and HIV-Negative Women . Journal of Tropical Medicine Volume 2012, Article ID 869758, 4 pages doi:10.1155/2012/869758

13.Dionne N Dames, Camille Ragin, Andrea Griffith-Bowe et al (2009). The prevalence of cervical cytology abnormalities and human papillomavirus in women infected with the human immunodeficiency virus. *Infectious Agents and Cancer* 2009, **4**(Suppl 1):S8 doi:10.1186/1750-9378-4-S1-S8

14. L stewart Massd, Catherina A Riester, Kathryn M. Anastos et al. Prevalence and predictors of sqaumous cell abnormalities in Papanicolaou smear from women infected with HIV-1. JAIDS Journal of Acquired Immune Deficiency Syndromes 1999,21: 33-41

15. Terrumun Z Swende, Stephen D Ngwan, Laadi T Swende et al (2012). Prevalence and risk factors for cervical squamous intraepithelial lesions among women infected with HIV-1 in Makurdi, Nigeria. The international journal of women's health, February 2012.

16. Joke A. M. Dols, Gregor Reid,Joelle M. Brown et al (2012). HPV Type Distribution and Cervical Cytology among HIV-Positive Tanzanian and South African Women**.** International Scholarly Research Network ISRN Obstetrics and Gynecology Volume 2012, Article ID 514146, 5 pages doi:10.5402/2012/514146

17.Kevin P McKenzie, Robyn K Rogers, Julia W Njoroge et al. Cervical squamous intraepithelial lesions among HIV-positive women on antiretroviral therapy in Kenya. Curr Hin res.2011 Apr;9(3):180-5

18. Munoz N, Bosch F & de Sanjose S. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *New England Journal of Medicine* 2003;348:518–527.

19. Clifford G, Smith J, Plummer M, Munoz N & Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. *British Journal of Cancer* 2003; 88:63–73.

20. Nubia Mu˜noz a,∗, Xavier Castellsagu´e b, Amy Berrington de Gonz´alez c, Lutz Gissmann, HPV in the etiology of human cancer Vaccine 24S3 (2006) S3/1–S3/10

21. Clifford G et al. Vaccine 2006;24(S3):26-34).

22. Melnikow J, Nuovo J, Willan AR, Chan BK, et al. Natural history of cervical squamous intraepithelial lesions: a meta analysis. Obstet Gynecology 1998;92:727-35.

23. King G, Healy C, Glover M, Kwan J, Williams D, Leigh I & Thornhill M. Prevalence and risk factors associated with leukoplakia, hairy leukoplakia, erythematous candidiasis, and gingival hyperplasia in renal transplant recipients. *Oral Surgery, Oral Medicine & Oral Pathology* 1994; 78:718–726.

24. Kanowitz S, Miller SB, Stone J, Hanson E: The Natural History of Human Papillomavirus Infection as Measured by Repeated DNA testing in Adolescent and Young Women. *J Pediatr* 1998, 132(2):277-84.

25. Lillo F, Ferrari D, Veglia F & Uberti-Foppa C. human papillomavirus infection and associated cervical disease in human immunodeficiency virus-infected women: effect of highly active antiretroviral therapy. *Journal of Infectious Diseases* 2001; 184:547–551.

26. World Health Organisation 2009B. Human papillomavirus vaccines. WHO positionpaper.Availableat:http://www.who.int/wer/2009/wer8415/en/index.html.

27. National Institutes of Health. Cervical Cancer. *NIH Consensus Statement.* 1996;14(1):1–38.

28. Sankaranarayanan R, Sellors J, Lauterbach M. (2005). Training for Cervical Cancer Prevention Programs in Low-Resource Settings: Focus on Visual Inspection with Acetic Acid and Cryotherapy. International Journal of Gynecology and Obstetrics 89,S30-S37.

29. Jones BA and Davey DD. Quality management in gynaecologic cytology using interlaboratory comparison. Arch Pathol Lab Med 2000;124:672-81.

30. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with cervical intraepithelial neoplasia or adenocarcinoma in situ; American Society for Colposcopy and Cervical Pathology–sponsored Consensus Conference; American Journal of Obstetrics & Gynecology OCTOBER 2007pg 340-345.

31. Martin-Hirsch PL, Paraskevaidis E and Kitchener H. Surgery for cervical intraepithelial neoplasia. Cochrane Database Syst Rev 2000:CD001318.

32. Kyrgiou M, Tsoumpou I, Vrekoussis T, et al. The up-to-date evidence on colposcopy practice and treatment of cervical intraepithelial neoplasia: the Cochrane colposcopy and cervical cytopathology collaborative group (C5 group) approach. Cancer Treat Rev 2006;32:516-23.

33. Kalliala I, Nieminen P, Dyba T, et al. Cancer free survival after CIN treatment: comparisons of treatment methods and histology. Gynaecol Oncol 2007;105:228-33.

34. Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with cervical intraepithelial neoplasia or adenocarcinoma in situ; American Society for Colposcopy and Cervical Pathology–sponsored Consensus Conference; American Journal of Obstetrics & Gynecology OCTOBER 2007pg 340-345.

35. Branca M, Garbuglia AR, Benedetto A, et al. Factors predicting the persistence of genital human papillomavirus infections and Pap smear abnormality in HIV-positive and HIV-negative women during prospective follow-up. *Int J STD AIDS*. 2003;14:417–425.

36. T. C. Wright Jr., L. S. Massad, C. J. Dunton, M. Spitzer, E. J. Wilkinson, and D. Solomon, "2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests," *American Journal of Obstetrics and Gynecology*, vol. 197, no. 4, pp. 346–355, 2007.

37. Kapiga SH, Msamanga GI, Spiegelman D, Mwakyoma H, Fawzi WW, Hunter DJ. Risk factors for cervical squamous intraepithelial lesions among HIV-1 seropositive women in Dar es Salaam, Tanzania. *Int J Gynecol Obstet*. 1999;67:87–94.

38. Agaba PA, Thacher TD, Ekwempu CC, Idoko JA. Cervical dysplasia in Nigerian women infected with HIV. *Int J Gynecol Obstet*. 2009;107:99–102.

39. Davis AT, Chakraborty H, Flowers L, Mosunjac MB. Cervical dysplasia in women infected with HIV: a correlation with HIV viral load and CD4 count. *Gynaecol Oncol*. 2001;80:350–354.

40. Minkoff H, Ahdieh L, Massad LS, et al. The effect of highly active antiretroviral therapy on cervical cytologic changes associated with oncogenic HPV among HIV-infected women. *AIDS*. 2001;15: 2157–2164.

41. Heard I, Tassie JM, Kazatchkine M, Orth G. Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV-seropositive women. *AIDS*. 2002;16:1799–1802.

42. Peter M, Wangeci M, Grace K et al. Prevalence and Risk Factors Associated with Precancerous Cervical Cancer Lesions among HIV-Infected Women in Resource-Limited Settings. Hindawi Publishing Corporation AIDS Research and Treatment Volume 2012, Article ID 953743, 7 pages doi:10.1155/2012/953743

43. Lehtovirta P, Paavonen J, Heikinheimo O et al. Risk factors, diagnosis and prognosis of cervical intraepithelial neoplasia among HIV-infected women. *Int J STD AIDS*. 2008;19:37–41.

44. Moore AL, Sabin CA, Madge S, et al. Highly active antiretroviral therapy and cervical intraepithelial neoplasia. *AIDS*. 2002;16:927–929.

**APPENDIX 2: QUESTIONNAIRE**

ART No……

STUDY SERIAL No..……

CONTACT MOBILE NUMBER ……..

General Information

1. Age……

2. Age at first coitus ……..

3. Number of life time sexual partners ……

4. No of CD4+ cell count

    a) Baseline…….

    b) Current……..

5. WHO staging

Stage 1

Stage 2

    Stage 3

    Stage 4

6. (a). HAART status (if the patient is on HAART or not). Yes/No

6. (b) Is it first line or second line ……...

6. (c) Duration of follow up in yrs ……..

7. Have you had a Pap smear or any other cervical cancer screening procedure done before?

a) YES/NO

b) If yes what was the result?

8.ResultsofthecurrentPapsmear……
……
……
……

**APPENDIX 2: CONSENT FORM**

## University of Nairobi

Study participation consent form

## Prevalence of cervical cytology abnormalities among HIV infected women attending HIV clinic at Rwanda Military Hospital

**Investigators**

Dr.Patrick Kayumba, MB.ChB, Student M.MED Obs/Gyn University of Nairobi

**Emergency telephone number**

Dr. Patrick Kayumba, (+250)788-666-163

**Investigators' statement**

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study. Please read this form carefully. You may ask questions about what we will ask you to do, the risks, the benefits and your rights as a volunteer, or anything about the research or in this form that is not clear. When all your questions have been answered, you can decide if you want to be in this study or not. This process is called "informed consent".

**Purpose and benefits**

This study will help us to know how many of the participants will have abnormal results of cancer screening among HIV infected women at Rwanda Military Hospital. Through this study we want to understand the burden of cervical cancer lesions in HIV infected women.

This study will benefit the society by providing information that can be used to improve services to ensure more HIV positive women are referred for

cervical cancer screening services as part of their routine care at the HIV clinic and even a push toward integration of these services and as a result, more HIV infected women will benefit from the screening once the routine screening is implemented in the routine care of HIV infected women.

At a personal level, participation in the study will provide an extra opportunity for women who did not know if they have precancerous or cancer lesions. Women identified as having abnormal results of the Pap smear will be referred to the hospital's gynecology outpatient clinic (GOPC) for further follow up and management using routine referral system of the hospital. Colposcopy and LEEP are available in Kigali particularly at King Faisal Hospital and at CHUK- University and central hospital of Kigali. Therefore with the routine referral system, patients with HSIL will be referred for managed.

**Procedures**

This is what will happen if you decide to participate in this study. I will ask you questions about yourself, your sexual history, I will also obtain some information about your HIV status such as use of ART or not, duration on HAART, if first line or second line drugs, and the number of CD4 cell count from your file.

After answering these questions, I, the researcher will proceed to do a pap smear in presence of a female assistant. The procedure will involve, introduction of disposable speculum in your birth canal and then taking some cells from your cervix using a cytobrush

**Risks, stress, or discomfort**

You may become embarrassed, worried, or anxious when answering some of the questions as they are of a personal nature e.g. the sexual history.

Participation in the study will require you to commit your time. Completing the questions will take 5-6 minutes. However, we will try to serve you as quickly as possible.

**Other information**

We will keep your identity as a research subject confidential. Only the principal investigator will have access to information about you. The information about you will be identified by the study number and will not be linked to your name in any records. Your name will not be used in any published reports about this study.

Although we will make every effort to keep your information confidential, no system for protecting your confidentiality can be completely secure. You may withdraw from the study, refuse to answer any of the questions asked or to have the test as described above at any time without loss of benefit or penalty.

No incentives will be given to study subjects.

If you have any questions regarding the study you can contact the investigator listed above. You are free to refuse to participate in the study, if you decide not to participate in the study you will receive similar care to that provided to HIV infected women participating in the study.

Signature of investigator _____Date_____

Name of Investigator_____

**Participant's statement:**

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later on about the research I can ask the investigator listed above. If I have questions about my rights as a research subject, I can call the National Ethics and Research Committee at (+250)255-107-884. I will receive a copy of this consent form.

Signature of the study participant----------Date----------

Or

Left thumbprint of the participant----------Date ----------

Name of the participant_____

Signature of witness (If thumbprint used) _____

Name of Witness_____

Rwanda National Ethics and Research Committee
P.O. Box 84
Kigali
Telephone (+250)255107884
Email: rnec@moh.gov.rw
Website: www.rnec.moh.gov.rw
Secretary, RNEC: PROF, WANE JUSTIN

**KINYARWANDA VERSION OF CONSENT FORM**

**UMUGEREKA WA 2**

**IFISHI YO KWEMERA KUGIRA**

**URUHARE MUBUSHAKASHATSI**

***Igipimo cy'ubwandu n'ubusembwa bw'indwara z'inkondo y'umura mu bagore babana n'ubwandu bw'agakoko gatera SIDA bakurikiranwa mu bitaro bya Gisirikare mu Rwanda***

**Abakora ubushakashatsi**

Dr.Patrick Kayumba, MB.ChB, Umunyeshuri wiga mu cyiciro cya gatatu cy'ubuvuzi bw'ababyeyi n' abagore batwite muri kaminuza ya Nairobi-Kenya.

**Inomero ya telefone**

Dr. Patrick Kayumba, (+250)788-666-163

**Intego n'inyungu**

Intego y'ubu bushakashatsi ni ukugirango hagaragazwe igipimo cy'uburwayi n'ubusembwa bw'inkondo y'umura mu bagore babana n'ubwandu bw'agakoko gatera SIDA mu Bitaro bya gisirikare I Kanombe. Binyuze muri ubu bushakashatsi, turashaka kumenya ubwinshi bwikibazo cy'uburwayi bwa kanseri y'inkondo y'umura mu bagore babana n'ubwandu bw'agakoko gatera SIDA.

Ubu bushakashatsi buzagirira akamaro umuryango nyarwanda kuko buzagaragaza amakuru n'imibare bishobora gukoreshwa mu kurushaho gutanga serivisi kubagore babana nubwandu bw'agakoko gatera sida. Ibi bizatuma Umubare wisumbuye w'abagore babana n'ubwandu bw'agakoko gatera SIDA basuzumwa bityo, bagire amahirwe yo gukurikiranwa. Ku rwego bwite, kugira uruhare muri ubu bushakashatsi bizaha amahirwe abagore batazi ko bafite ibisebe bishobora kuba biterwa cyangwa bifitanye isano na kanseri. Abagore bazagaragara ko bafite ibisubizo bitari byiza nyuma yo kubasuzuma hakoreshejwe uburyo bwabugenewe bita "Pap smear" bazoherezwa mu ishami rishinzwe ubuvuzi bwabagore (GOPC) kugira ngo bavurwe hakirikare.

**Uburyo buzakoreshwa**

Ibi ni byo bizakorwa kuwemera kugira uruhare muri ubu bushakashatsi. Azakubaza ibibazo ku buzima bwe bwite, imitwitire ye mu bihe byashize, ubuzima bw'imibonano mpuzabitsina ; na none kandi nzashakisha amakuru y'uko uhagaze mu birebana n'ubwandu bw'agakoko gatera SIDA nko kumenya niba unywa imiti igabanya ubukana bwa SIDA nigihe yayitangiriye, cyangwa kumenya umubare w'abasirikare bamurinda ubukana bwa virusi itera SIDA (umubare wa CD4) muri dosiye ye.

Nyuma yo gusubiza ibi bibazo, Umushakashatsi azapima kanseri akoresheje uburyo bwitwa "pap smear" ari ku mwe n'umuforomokazi .Uburyo buzakoreshwa nukwinjiza igipimo cya pulasitiki cyabugenewe gikoreshwa inshuro imwe mu nda ibyara ,akuremo uturemangingo duke ku nkondo y'umura akoresheje akaroso kabigenewe. Ntibibabaza kandi nta ngaruka mbi bifite ku buzima bw'umugore.

**Ese, amabanga y'ibyerekeye ubuzima bwanjye azahabwa agaciro?** Tuzakora ibishoboka byose kugirira ibanga ibyanditse ku ifishi yawe. Bishobora gutangwa gusa aruko bisabwe n'itegeko. Amakuru azava muri ubu bushakashatsi azatangazwa, ariko nta na hamwe amazina yawe cyangwa se andi makuru akwerekeye bizakoreshwa

**Ese, hari amafaranga nzacibwa kugira ngo ngire uruhare muri ubu bushakashatsi?** Nta mafaranga bisaba kugira uruhare muri ubu bushakashatsi.

**Byagenda bite mu gihe naba nkomeretse bitewe no kuba naragize uruhare muri ubu bushakashatsi?** Uretse utubazo duto tw'ingaruka bizwi nko kunva ubabaye akanya gato dushobora kugaragara mu ikorwa ry'ubu bushakashatsi, ni ngombwa rwose kumenyesha ukuriye ubushakashatsi igihe wumva waba wagize ikibazo gitewe no kugira uruhare muri ubu bushakashatsi. Ushobora kubibwira muganga imbonankubone cyangwa se ukamuhamagara kuri lejefoni +250 788 666 163.

**Mfite burenganzira ki mu gihe naba ngiye muri ubu bushakashatsi?** Guhitamo kugira uruhare muri ubu bushakashatsi ni uburenganzira bwawe busesuye. Kutajya muri ubu bushakashatsi kandi nta nkurikizi byakugiraho

**Ninde nshobora gusaba ibisobanuro kuri ubu bushakashatsi?** Ku birebana n'ubu bushakashatsi wabaza Uhagarariye ubushakashatsi: Dr. Patrick KAYUMBA: terefoni 0788666163.

Ku birebana n'uburenganzira bwawe, wabaza: Prof. Wane Justin, Perezida wa Komite ishinzwe uburenganzira bw'abakorerwaho ubushakashatsi mu rwego rw'Igihugu**,** kuri telefone igendanwa nomero 0788500499 cyangwa Dr. NKERAMIHIGO Emmanuel, Umunyamabanga Nshingwabikorwa w'iyo Komite, kuri telefone igendanwa nomero 0788557273.

Uzahabwa kopi y'iki cyemezo nyuma y'uko wowe cyangwa umubyeyi wawe/ugushinzwe n'umukozi ushinzwe kuvugana n'abakorerwaho ubushakashatsi muzaba mumaze kugishyiraho umukono.

**Umukono w'ukorerwaho ubushakashatsi –** Nahawe kopi z'amapaji yose y'iki cyemezo. Nagisomye cyangwa nagisomewe. Nasobanuriwe neza kandi ibibazo byose nari mfite byasubijwe. Nemeye ko nzagira uruhare muri ubu bushakashatsi. Nshyize umukono n'itariki kuri iki cyemezo ku giti cyanjye.

Izina n'umukono by'ukorerwaho ubushakashatsi _____Itariki_____

**Umukono w'umubyeyi/Ushinzwe ukorerwaho ubushakashatsi –** Nahawe kopi z'amapaji yose y'iki cyemezo. Nagisomye cyangwa nagisomewe. Nasobanuriwe neza kandi ibibazo byose nari mfite byasubijwe. Nemeye ko nzagira uruhare muri ubu bushakashatsi. Nshyize umukono n'itariki kuri iki cyemezo ku giti cyanjye.

Izina n'umukono by'umubyeyi/Ushinzwe ukorerwaho ubushakashatsi_____ Itariki____

**Umukono w'umukozi ushinzwe kuvugana n'abakorerwaho ubushakashatsi –** Nahaye ukorerwaho ubushakashatsi kopi z'amapaji yose y'iki cyemezo. Namusobanuriye amakuru yose ari muri iki cyemezo nawe yemera nta gahato kugira uruhare muri ubu bushakashatsi. Ukorerwaho ubushakashatsi yemeye kandi asinyira imbere yanjye iki cyemezo ku giti cye. Nanjye kandi nashyize itariki n'umukono kuri iki cyenezo ku giti cyanjye. Izina n'umukono by'umukozi wakiriye ifishi _____Itariki_____

**APPENDIX 3: CYTOLOGY REQUEST/REPORT FORM.**

TRACNET (FILE) No……..

RESEARCH No…….……..

AGE……..DATE……..

DATE OF SPECIMEN COLLECTION……

**CLINICAL OBSERVATION:**

NORMAL IFLAMMED ERODED SUSPICIOUS

OTHERS SPECIFY…….

PROVISIONAL DIAGNOSIS…….

**LAB REPORT**

**BETHSEDA CLASSFICATION**

Suitability Yes/No ASCUS ☐

Adequacy Yes/No AGC ☐

Negative ☐ LSIL ☐

Inflammatory ☐ HSIL ☐

Reactive ☐ Glandular Neoplasia ☐

**Comments……**
**……**
**……**
**……**

**Pathologist's Name……Sign……**

**Lab Number……Date……**

**APPENDIX 4: REFERRAL FORM FOR PATIENTS WITH ABNORMAL PAP SMEAR AFTER THE RESEARCH RESULTS.**

Name of the patient……..SEX……

AGE……

DATE…….

File number…….……..

Clinic referred from……..……

Clinic referred to…….

Results of the Pap Smear……...

……..….

Reason for referral……..

Name of the referring Clinician……

Sign……..

**APPPENDIX 5: RESEARCH TIME LINE**

| ACTIVITY | TIME FRAME |
|---|---|
| | |
| RESEARCH PROPOSAL WRITTING | JULY-OCTOBER (2012) |
| ETHICAL APPROVAL | NOVEMBER-MARCH (2012/2013) |
| DATA COLLECTION AND ENTRY | MARCH –JUNE (2013) |
| DATA ANALYSIS | JULY-AUGUST (2013) |
| DISSERTATION PRESENTATION | SEPTEMBER-OCTOBER (2013) |

## APPENDIX 6: PROJECT BUDGET

| NO | ITEM | QUANTITY | UNIT PRICE | TOTAL |
|---|---|---|---|---|
| A | **LABORATORY** | | | |
| 1 | Pap kits | 12x25 =300 | 2500 | 30,000 |
| 2 | Disposable speculum | 300 | 80 | 24,000 |
| 3 | Gloves in pairs | 300pairs=6boxes | 1000 | 6,000 |
| 4 | Pathologist fees | 293 Samples | 400 | 116,800 |
| B | **TRANSPORT** | | | |
| 1 | Researcher from Nairobi to Kigali | 1X3 Trips | 32,000 | 96,000 |
| C | **Research assistants fee** | Researcher | | 75,000 |
| D | **Communication** | 1x25 | 500 | 12,500 |
| E | **Statistician fee** | 1 | 30,000 | 30,000 |
| F | **Stationary/Printing** | | | |
| 1 | Questionnaire+ consent forms | 300x7pages | 10 | 21,000 |
| 2 | Pens | 6 | 100 | 600 |
| 3 | Notebooks | 2 | 150 | 300 |
| 4 | Final manuscript | 4 | 1000 | 4000 |
| G | GRAND TOTAL | 1 | 416,200KSH | 416,200KES |

## APPENDIX 7: ETHICAL APPROVAL