CHARACTERIZATION OF HUMAN PAPILLOMAVIRUS GENOTYPES AND THEIR CORRELATES AMONG WOMEN LIVING WITH HIV ATTENDING ANTIRETROVIRAL THERAPY CLINIC IN MUKONO, UGANDA

NANTALE PROSSY NABATTE

SHS/MPH/4977-1/2022

A THESIS SUBMITTED TO THE SCHOOL OF PUBLIC HEALTH, DEPARTMENT OF COMMUNITY HEALTH IN THE PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF A MASTER OF PUBLIC HEALTH DEGREE OF AMREF INTERNATIONAL UNIVERSITY

JULY 2023

DECLARATION AND APPROVAL

Declaration by Candidate:

I, **Nantale Prossy Nabatte**, possess the ultimate responsibility of the work constituted in this special project report and declare that this is original and has never been submitted to any university or institution for the award of any qualification.

_____ Date: 08/07/2023

Nantale Prossy Nabatte

SHS/MPH/4977-1/2022

Declaration by Supervisors:

This work has been submitted for examination with approval of:

_____ Date: 08/07/2023_____

Dr. Josephat Nyagero

Senior Lecturer, Amref International University

_____ Date: 08/07/2023

Dr. Elizabeth Kemigisha

Post-doctoral Research Scientist, African Population and Health Research Center

COPYRIGHT

THE REPUBLIC OF UGANDA

UGANDA REGISTRATION SERVICES BUREAU

THE COPYRIGHT AND NEIGHBOURING RIGHTS REGULATIONS, 2010

UNDER REGULATION 5 (1)

NOTICE OF APPLICATION FOR REGISTRATION OF COPYRIGHT OR NEIGHBOURING RIGHT

TAKE NOTICE THAT **Nantale Prossy Nabatte** of **P.O. Box 28437, Mukono, Uganda** lodged a Copyright Application Number **UG/C/ 2023/95** with the Registrar of Copyright for the registration of copyright for the following works:

Characterization of Human Papillomavirus genotypes and their correlates among women living with HIV attending antiretroviral therapy clinic in Mukono, Uganda Literary Works

Any person intending to object to the application for registration of copyright or neighboring rights may file a letter of objection with this office within 60 days from the date of this notice.

Dated this **13th day of June, 2023**

Registrar of Copyright

DEDICATION

I dedicate this thesis to the Capacity Development of Applied Epidemiologists in Eastern Africa, African Population and Health Research Center together with the Amref International University, Jaramogi Oginga Odinga University of Science and Technology, Lund University who granted me the opportunity to be part of the Fellowship and the great support they have rendered for my education. May the good Lord bless you.

ACKNOWLEDGEMENT

I owe a particularly large debt to Dr. Nyagero Josephat and Dr. Elizabeth Kemigisha for the guidance, support and encouragement they gave me during the data collection, analysis and the writing-up of the special project report. I sincerely appreciate their generous contribution in this regard.

I also wish to thank them for sparing their valuable time to read through the entire special project report and for giving me the benefit of their considerable experience in the field of public health. I extend my sincere regards to the doctor, clinical officer in Mukono General Hospital that is Dr. Sentenza Nicholas and Ms. Namata Davinia respectively who supported me during the data collection. May the Almighty God fully reward you all for your generosity. Great thanks to the management of Mukono General Hospital for giving me permission to collect data from the facility.

ABSTRACT

Background: Human Papilloma Virus (HPV) is a prevalent infection transmitted sexually worldwide. Studies have revealed a higher prevalence for HPV infection amongst HIV positive women. It is important to screen for HPV so that women found positive receive early treatment to prevent development of cancer for cervix. The broad objective of the research is to determine types, occurrence plus associated correlates of HPV infection by genotyping HPV among a group of WLHIV attending antiretroviral therapy clinic in Mukono, Uganda.

Methods: This cross sectional study involved collecting data for socio-demographic, sexual practices and medical history factors associated with HPV genotypes from a sample of 342 WLHIV. The HPV genotypes results were obtained retrospectively from the respective laboratory records. Epidata v4.6 was used for data entry and STATA V14 used for analysis. Analysis for the correlates of hr-HPV infection was done using modified poisson regression model.

Results: Slightly more than a half (56.7%) of the participants were aged below 35 years, married (52.6%), and with primary level of education (51.2%). The prevalence of hr-HPV was 39.8% (CI: 34.40- 44.78) with HPV16, HPV 18/45 and other hr-HPV types being positive in 23(6.7%), 21(6.1%) and 110(32.2%) respectively. Additionally, 17(12.5%) were infected with multiple hr-HPV genotype infections. The hr-HPV was higher among 30-34 years of age (n= 41, 30.2%) than 45-49 years (n=16, 11.8%). In terms of associated correlates, age 45-49 years (adjPR: 1.95, 95% CI: 1.41- 2.69), being married (adjPR: 1.30, 95% CI: 1.00, 1.69), condom use (adjPR: 1.31, 95% CI: 1.00 -1.71) and age of sexual debut (adjPR: 1.42, 95% CI: 1.08-1.87) were significantly related with HPV genotypes.

Conclusion and Recommendations: High-risk HPV infection prevalence was high, indicative of a risk to the health of WLHIV. Being aged 45-49 years, married, using condoms, age of sexual debut are the key correlates of hr-PHV. It is recommended that the implementing teams should educate the public on the key correlates to hr-HPV infection, emphasizing on the need for screening and treatment in this population.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS AND ACRONYMS

AdjOR Adjusted Prevalence Ratio

A LEVEL Advanced level

ALIS African Laboratory Information System

CACancer Cancer of the cervix

CACX Cancer of the cervix

CD38 Cluster of differentiation 38

CD4 Cluster of differentiation 4

CIN Cervical invasive neoplasia

CSV Comma Separate Value

CX Cervix

DNA Deoxyribonucleic acid

dsDNA double-stranded deoxyribonucleic acid

EA East Africa

GAA Glacial Acetic Acid

HIV Human immunodeficiency virus

HLA- DR Human Leucokyte Antigen-DR isotype

HPV Human Papilloma virus

hr High-risk

hr-HPV High risk Human Papilloma virus

HSIL High grade squamous intraepithelial lesion

HSV Herpes simplex virus

IARC International Agency for Research on cancer

LMIC Low- and middle-income countries

lr-HPV Low-risk Human papillomavirus

lr Low- risk

MGH Mukono General Hospital

MLR Multivariate Logistic Regression

mRNA Messenger Ribonucleic acid

O LEVEL Ordinary Level

PCC Probe check control

PCR Polymerase chain reaction

pRb Retinoblastoma protein

SAC Sample adequacy control

SIL Squamous intraepithelial cells

SPSS Statistical Package for the Social Sciences

SSA Sub-Saharan Africa

STD Sexually transmitted disease

STI Sexually transmitted infection

UNCST Uganda National Council for Science and Technology

VIA Visual inspection with acetic acid

VS Versus

WLHIV Women living with HIV

DEFINITION OF TERMS

Anogenital is an area consisting of the perianal skin, anus, adjacent external gentalia involving the vaginal introitus labia majora, mons pubis and labia minora.

Carcinogenic is an organism or agent capable of causing cancer.

CD38$^+$ is a a protein with sugar molecules located on the exterior of many white blood cells (WBCs) for example the natural killer, B lymphocytes and CD4$^+$ cells. It plays a role in calcium signaling, signal transduction and cell adhesion.

CD4$^+$T are glycoproteins located on the exterior of resistant cells for example monocytes, microphages, T helper and dendritic cells. They trigger the cells of the innate resistant system, B-lymphocytes, the nonimmune and cytotoxic T cells. They also suppress the immune reaction.

Cervical intraepithelial neoplasia is a condition where unusual cells grow on the exterior of the cervix thus if not managed, it can develop into cervical cancer.

Chlamydia trachomatis is a bacteria that is the utmost frequent result of curable bacterial sexually transmitted infections globally.

Condylomas is an elevated growth on the surface of the genitals produced by Human papillomavirus infection.

Dysplasia is the presence of abnormal cells within the tissue.

Genital herpes is produced by a herpes simplex virus (HSV) and it is an infection transmitted sexually.

High-grade squamous intraepithelial lesion is a condition of the cervix (CX) where there are moderate and severe changes in the cells lining it.

High-risk HPV is a subtype of HPV with high potential to cause cervical cancer.

Hormonal milieu is an environment of the maternal hormonal levels which is adverse during pregnancy which can result into abnormal growth of the fetal brain.

HPV is the utmost significant STD worldwide. It is a small, dsDNA virus and part of the family Papillomaviridae. It is categorized into lr (low-risk) and hr (high-risk) HPV according to the oncogenic possibility.

Human Leucokyte Antigen-DR isotype is a major histocompatibility complex class II antigen demonstration molecule. It supports the immune system to differentiate the body's individual proteins from the proteins prepared by external attackers for example viruses and bacteria

Intraepithelial cells are unusual cells on the exterior of the cervix and have not grown beyond it.

Low-risk HPV is a subtype of HPV which cause genital warts and does not cause cervical cancer.

Malignant neoplasm is a cancerous tumor. It can extent into neighboring tissues. It can also extent into further portions of the body via lymph and blood systems.

Neoplasia is the formation of new, abnormal growth of tissue.

Oncogenic are viruses that cause cancer.

Oncoproteins are proteins programmed by oncogenes that play a role in the guiding or production of proteins related with the growth of cancer tumor cells.

p53 and pRB are critical cell cycle points which suppress tumors that is suppressive tumor protein and retinoblastoma protein respectively.

Patient refer to a person who is sick.

Prevalence is a measure of the overall integer of people in an exact group who have a definite illness, disorder or threat at a specific point in time.

Squamous intraepithelial cells is a region of abnormal cells that form on the exterior of certain organs for example the cervix.

T cell is a form of WBCs that defends the body from contamination and support in preventing cancer (CA).

Visual inspection with acetic acid refers to examination of the uterine CX with a bare eye following application of 5% acetic acid then results explained at one minute thus used to detect cervical cancer precursors by a professional.

Xpert HPV Assay is a test which is computerized for qualitative recognition and variation of the DNA for HPV.

CHAPTER 1: INTRODUCTION

1.1 Overview

The most common gynecological malignancy is the cancer of the cervix. Sung et al. (2021) reported 604,000 new cases globally, leading to about 342,000 deaths in 2020. It has become the utmost frequent cancer in 23 countries as well as major outcome of cancer associated death in 36 countries. There is a remarkable difference of incidence rate for cancer of the cervix in low- and middle-income countries (LMICs) as related to that in developed countries, the extreme reported in Sub Saharan Africa (SSA), Southeast Asia, South America and South Polynesia. WHO/IARC, (2020) revealed that Uganda is one of the top 10 nations with the uppermost incidence of CACX 28.8/10000 every year worldwide plus it takes the second position in East Africa (EA) having approximately 6413 new patients and 4301 deaths in a year.

In addition, nearly 35.7% new cases of cancer in Ugandan women reported by WHO/IARC, (2020) were attributable to CACX, in addition about 11 million females of Uganda remain at a danger of CACX as a result of infection with sexual transmitted persistent carcinogenic sub-types of HPV. The higher frequency of persistent HPV infection is connected with HIV infection leading to quick growth, faster advancement, and malignant alteration of premalignant lesions and amplified forcefulness of the previously prevailing cancerous lesions. In Uganda one of the frequent infection transmitted sexually is HIV having the general prevalence of 6.2 percent and 7.2 percent in females who are 15 – 64 years as reported by Uganda population-centered Human immunodeficiency virus influence

evaluation 2016-2017 as reported by Sarah Maria et al. (2022). More so the prevalence of HIV is 7.4% in Mukono district as revealed by Kasibante et al. (2020).

1.2 Background of the Study

Cancer of the cervix (CACX) is a main problem in public Well-being. It is among the severe threats to women's lives (Torode et al., 2021). It takes the fourth position in cancer globally among females, Furthermore Sung et al. (2021) revealed that invasive CACX is amongst the primary outcome in women of cancer associated illness and death worldwide. It is the utmost fourth cancer generally frequent in females, about 600,000 women are detected with cancer and more than 300,000 death occur globally every year. Ferlay et al. (2019) predicted new cases of 570,000 women in 2018. The most significant number of patients is detected in the LMICs, over 85%, SSA having the greatest problem universally. Nevertheless, this problem is unevenly dispersed where out of 10 deaths 9 of them happen in LMICs then 6 of these happening in only Sub- Saharan Africa. Hence its greatest effect internationally experienced by females living in LMICs where it is the primary outcome of CA related illness and death in women particularly SSA as reported by Ibrahim Khalil et al. (2022).

The current estimates according to (ICO/IARC, 2021) in Uganda show 6959 women are detected with CACX and causing 4607 deaths yearly. Risk factors for cervical cancer include age, marital status, educational level, parity, multiple sexual associates, infection with HIV and further infections transmitted sexually for example chlamydia trachomatis and genital herpes, smoking of cigarettes, use of hormonal and oral contraceptives, nutritional aspects, social class, origin, environmental difference (Bogale et al., 2020). In

addition, (Sarah Maria et al., 2022) mentioned that due to the great possibility of WLHIV developing CACX the Uganda national treatment strategies for HIV plus Centers for Disease control and Prevention recommend CACX screening annually in WLHIV.

The hr-HPV execute an essential part in the of cervical cancer progression (NCI, 2019). According to Groves and Coleman (2015) the carcinogenic forms of high-risk HPV as categorized by the IARC include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59. Karadža et al. (2021) revealed that infection which is persistent with one or more oncogenic HPV genotypes is the greatest important factor identified in causing cervical neoplasia. Almost all women who are active sexually are infected with HPV at one point, but the infection spontaneously clears in most of them in 24 months (Tam et al., 2018). However, 12% of these severe infections persist and develop into lesions which are precancerous or aggressive cancer with time if not identified and treated primarily in life (Adebamowo et al., 2017).

Prevention strategies for cervical cancer include screening which plays a part in early diagnosis (WHO, 2008). According to (Castle et al., 2021) CACX as a problem to public health can be eliminated through extended efforts to incorporate HIV care with CACX prevention and control. However, the achievement of CACX screening as examined by Raddi et al. (2012) is highly dependent on the full involvement of the target population influenced by individual aspects like demographic variation. In other wards vaccination and screening can entirely prevent CACX (Castle et al., 2021). The WHO suggests a screening and treatment plan to reduce the frequency of CACX. This plan involves screening with a high risk-HPV test tracked by visible examination using acetic acid, then management of

women with positive results for the two tests using thermal removal. Alternatively screening using high- risk HPV testing and management of all cases with positive results for high-risk HPV (WHO, 2013).

High- risk HPV testing for WLHIV provides a chance for women to self-collect the specimen, this reduces individual and health method obstructions to screening. The self-collected samples are then tested using Xpert HPV assay. High- risk HPV testing reduces cancer and related mortality more than visible examination with acetic acid (WHO, 2013). Furthermore, women easily accept self- collected high-risk HPV testing (Yeh et al., 2019). In addition, Bogale et al. (2020) revealed that there is higher positivity result with Xpert HPV assay testing as compared to the low sensitivity rate when using optical examination with acetic acid. This indicates that implementing Human papilloma virus DNA as a main screening test can help reduce CACX morbidity and mortality in Uganda.

The threat of cervical infection is increased by HIV infection because of hr-HPV oncogenic genotypes that bring about HSIL and invasive cancer (Gheit et al., 2006). HIV infection changes the normal history of HPV infection because it reduces the rate at which the infection clears naturally and rising the development to high grade and aggressive lesions (Stelzle et al., 2021). According to Gheit et al. (2006) HPV infection in WLHIV is three times higher and bring about cervical cancer than their counterparts (Dreyer, 2018). In addition, Stelzle et al. (2021) revealed that WLHIV have 6 times higher threat of developing CACX than the women without HIV.

However high- risk oncogenic HPV genotypes testing is not done on every woman living with HIV because of the limited resources thus this research seeks to show the burden of

hr-HPV subtypes for effective vaccination strategies against cervical cancer and the need for consistent resources for the timely diagnosis and management to prevent fatal aggressive cancer.

1.3 Statement of the Problem

High - risk oncogenic genotype human papillomavirus infection induces CACX which is a cancer commonly found in women internationally. Approximately 529,800 women are detected with CACX and 275,100 women die yearly worldwide (Sung et al., 2021). In Uganda CACX is the main cause amongst women of both CA associated incidence (54.8 per 100,000) and related CA death (40.5 per 100,000) (Ferlay et al., 2019).

WLHIV have an increased danger of infection with HPV and perseverance, enhancing the danger of defects in the cells of the CX and aggressive CACX. HIV leads to a decrease in CD4+ T cells increasing rate of infection with HPV and decreases the opportunity for its natural elimination (Lima et al., 2014).

There is a prevalence of 33.6% HPV in the general population in Uganda (Nakisige et al., 2017); which is above global average. Ferlay et al. (2019) estimated 570,000 new cases in 2018. SSA has a high infection of HIV in women who are young, and Uganda is among the highly affected countries. HIV causes severe immunosuppression. Many studies indicate that immunosuppression greatly elevates the threat of HPV infection (Lima et al., 2014). For effective vaccination strategies against CACX, there is a gap to generate data on the description of high-risk Human papilloma virus genotypes among the group that is most at risk (HIV positive women). Previous studies by ICO/IARC (2021) show that annually many women 6,969 are diagnosed in the advanced stage of cervical cancer and 4,607 women die

from the disease. However, the characterization of high-risk genotypes among the group that is most at risk (WLHIV) is not clear therefore this research sought to explore the types and occurrence of HPV infection by genotyping Human papillomavirus among a group of WLHIV attending antiretroviral therapy clinic in Mukono, Uganda.

1.4 Objectives of the Study

The broad purpose of the research is to determine the types and occurrence of HPV infection by genotyping HPV and related factors among a group of WLHIV attending antiretroviral therapy clinic in Mukono, Uganda. The specific objectives of the research include:

1. To define the characteristics of Human papillomavirus genotypes among a group of WLHIV attending antiretroviral therapy clinic in Mukono, Uganda.
2. To identify how socio-demographic factors predispose WLHIV to Human papillomavirus genotypes in Mukono.
3. To establish how sexual practices predisposes WLHIV to Human papillomavirus genotypes in Mukono
4. To assess how medical history predisposes WLHIV to Human papillomavirus genotypes in Mukono.

1.5 Research Questions

1. What is the prevalence of hr carcinogenic HPV genotypes among WLHIV in Mukono, Uganda?

2. How do socio-demographic factors predispose WLHIV to hr carcinogenic HPV genotypes?
3. How do sexual behavioral practices predispose WLHIV to hr carcinogenic HPV genotypes?
4. How does medical history predispose WLHIV to hr carcinogenic HPV genotypes?

1.6 Hypothesis

1. Ho: Socio-demographic factors do not predispose WLHIV to HPV genotypes in Mukono
2. Ho: Sexual behavioral practices do not predispose WLHIV to HPV genotypes in Mukono
3. Ho: Medical History does not predispose WLHIV to Human papillomavirus genotypes in Mukono

1.7 Justification of the Study

This research shows the characterization of HPV genotypes among WLHIV attending antiretroviral therapy clinic in Mukono, Uganda. The results of this study are useful in cervical cancer vaccination campaigns (strains that an effective vaccine should contain), which group needs to be given greatest attention. The results will also inform policy makers on how screening and vaccination for HPV will impact prevention of invasive cervical cancer. Further, it shows the necessity for consistent provision of resources for high-risk HPV testing for detection and early treatment to prevent the fatal invasive cervical cancer.

1.8 Significance of the Study

In Uganda, 6,969 women are detected with CA annually, and the majority are in the advanced stage; thus, 4,609 women die annually. This study shows the need for consistent provision of resources for high-risk HPV testing for the detection and early treatment to prevent fatal invasive cancer.

The results are helpful in the cervical cancer vaccination campaigns showing strains an effective vaccine should contain and which group needs to be given the most significant attention.

Furthermore, policymakers will be informed on how the vaccination and screening for Human Papillomavirus will impact prevention of invasive CACX.

1.9 Scope of the Study

This research was done in Mukono General Hospital a government health facility located on the Kampala-Jinja highway in Mukono town, Uganda. It was carried out for a period of one month.

1.10 Limitations of the Study

The general limitation in this study is that in cross sectional surveys direction of association cannot be confirmed, as such we cannot determine causality. There is potential for social desirable bias as some of the variables were about sexual history and the study participants were not comfortable when asked about the sexual behavior. The study population was from Mukono division and suburbs the results may therefore not be representative of across the country.

1.10.1 Mitigation

Despite these limitations, the data reported in this report remain important and there is currently no other report on hr-HPV prevalence in this population that is specific to Ugandan population.

Research assistants received a two days training about the interview guide. Furthermore, the research assistants were a medical doctor and clinical officer with good clinical practice training on handling human subjects in the studies more so the principal investigator also well trained in good laboratory clinical practice in handling human subjects. Standard pre-tested interview guides were used. The consent form and interview guide were translated using back to back translation to a local language (Luganda since majority of patients who attend the clinic speak Luganda).

1.11 Assumptions of the Study

The main assumptions that guided this study are that the study participants were WLHIV and HIV infection enhances infection with multiple Human papillomavirus genotyes.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

HPV is a prevalent sexually transmitted infection globally according to Kombe Kombe et al. (2021) disrupting individual social life. The women who are active sexually are infected with HPV at minimum one time in their lifespan which is spontaneously cleared by the resistant system although persistent infections due to high -risk Human papilloma virus can lead to CACX and death (Mousavi et al., 2020). HPV is considered to be a significant topic because of the rates of the infections increasing rapidly. The epithelial cells of the human anal and genital area are invaded by the virus. The time between the development of symptoms and exposure can be three to four months though the virus can be spread to another person during this period as stated by (Ohihoin et al., 2022)

HPV is dsDNA virus which is small and part of Papillomaviridae family. It is classified into low-risk HPVs according to Martel et al. (2017) which cause cutaneous and anogenital warts and hr-HPVs that cause oropharyngeal cancers, cancers of the anogenital like CACX, vaginal, anal and penile vulvar cancer. CACX is the greatest third mutual CA in women as stated by Sung et al. (2021) which is an HPV related disease causing high mortality in women. Dereje et al. (2020) estimated new cases of 604,000 women with CACX and 342,000 death of women from CACX globally, of these about one-fifth occurred in Africa 117,000 women newly diagnosed cases and 77,000 women died. Nelson and Mirabello (2023) revealed that Human papillomavirus contributes to 4.5% of all human cancers for example the tumors of the oropharynx, penis, vagina, cervix, vulva, larynx. However, the most common of these is the cancer of the cervix caused by HPV.

Sub-Saharan Africa has the uppermost rates internationally, particularly in Uganda with incidence rates exceeding 40 per 100,000 women. CACX is the utmost prevalent CA in females occurring in 20 countries and the greatest frequent outcome of cancer death in females happening in 21 of the 48 Sub-Saharan African countries (Dereje et al., 2020). Uganda amongst the uppermost 10 nations with high incidence of CACX and the second in East Africa with 6413 new cases and 4301 deaths every year (Sarah Maria et al., 2022).

2.1.1 HPV Infection Associated with Cervical Cancer

Nelson and Mirabello (2023) indicates that hr-HPV types when incorporated into the genome of the host apply their oncogenic properties initially through constant manifestation of E6 and E7 protein for HPV. These interrupt development, support DNA duplication then invade the host immunity through interaction with other numerous host cell proteins. In addition, these oncoproteins express an essential part in HPV- dependent virulent alteration thus manifested in cervical cancer (Harężа et al., 2022). Furthermore, continuous manifestation of the E6 protein and E7 protein is required for the CACX maintenance.

The proteins which suppress tumors are attacked by E6 protein and E7 protein for example p53 and pRb hence causing cell multiplication, preventing cell death, thus promoting genome variability and avoiding the inborn resistant system according to Harężа et al. (2022). The infection of hr-Human papilloma virus plays an essential role in the CACX progression which is the greatest gynecological third malignancy frequent in women internationally. Nelson and Mirabello (2023) reported that Human papillomavirus uses the host polymerases to replicate their genomes which are usually manifested before development however the production of the virion needs factors for transcription for the host that are expressed during

differentiation. However, both necessities need to be accomplished without activating the response of the immune system which can led to cell death. These tactics used by Human papilloma virus to accomplish its contradictory objectives can unintentionally lead to CA since there is extensive similarity among the cellular purposes essential for viral achievement plus those that enhance the exposure of the cells for the host to the most common type in CA. This means that the reproduction approaches HPV displays enhance cancer. Evaluations of about 275,100 deaths and 529,800 new cases happen annually in the world (Sung et al., 2021).

Aggressive cancer of the cervix is introduced by lesions which are precursors identified by disorders of cellular development, covering and different nuclei. The lesions which are precursors are grouped through histology as CIN in three grades as follows: CIN I which is low grade, CIN II the moderate grade and CIN III the high grade to carcinoma in the original place of development. Alternatively, they can be categorized through cytology according to Badial et al. (2018) as SIL. WLHIV have a bigger threat of HPV infection and perseverance, enhancing the danger of defects in the cells of the cervix and invasive CACX. There is a reduction in the integer and purpose of $CD4^+$ T cells due to infection with HIV which can result into increased frequency of infection with Human papilloma virus thus decreasing the opportunity of its natural removal. However cervical cancer is controlled by screening because of the clearly defined premalignant stages. The detection tests for HPV DNA can be applied as supplementary device coupled with cytology of the cervix to enhance managing patients in danger for cervical cancer (Mousavi et al., 2022). The vaccination and screening can entirely prevent CACX (Castle et al., 2021). The WHO suggests a screening and treatment plan to reduce the frequency of CACX that is the 90-70-90 approach by 2030. This

entails having 90% of girls vaccinated by the age of 15 years, 70% of women screened using highly sensitive test by the age of 35 years and again at 45years. Finally having 90% of those with pre-cancers treated.

2.2 Theoretical Framework

2.2.1 Human Papillomavirus as a Medical Problem

Haręża et al. (2022) revealed that Human papilloma virus is the greatest public infection transmitted sexually which happens through uninterrupted mucosa to mucosa or skin to skin connection. The nonthreatening cutaneous expressions of Human papillomavirus mainly involve papillomas normally called warts. Human papillomavirus can present as an uninterrupted carcinogen by contaminating cells that later experience neoplastic alteration. It shows detailed unintentional development for squamous epithelium. Particular type of the infection develops in the skin whereas others develop in the mucosa membranes for example the vagina. The medical outcome of the contamination in the skin and mucosal lesions present as warts and condylomas, also appear as both low- grade and high - grade dysplasia referred to as premalignant lesions. The new cancer cases approximately 690,000 every year which occur globally are caused by HPV infections. In addition, HPV is the succeeding primary reason of cancer where out of the 690,000 new CA cases that happen yearly, 570,000 are CACX cases.

Hewavisenti et al. (2023) reported that Human papillomavirus is prevalent virus transmitted sexually causing mucosal or cutaneous stratified epithelial infection, involved in increasing associated cancers universally. Human papillomavirus infection can be removed by enough resistant response, but immunocompromised people can undergo insistent, treatment

resistance plus advanced disease. According to Morshed et al. (2014) papillomaviruses are viruses comprising of double-stranded deoxyribonucleic acid (dsDNA). They are circular with an eight kilobases genome. They are viruses which are not enveloped and can give rise to squamous epithelial tumors (warts and papillomas) in various body parts. They comprise of open reading frames eight in number which include, possible early (E1-E2, E4-E7), long control region (LCR) and Late (L1 and L2). The constant manifestation of E6 protein and E7 protein genes is connected to prompt cellular alteration carcinogenesis plus immortalization. The primary composition of HPVs is the protein referred to as L1 which can gather itself into particles like virus as reported by Wang et al. (2022).

The HPV comprises of about 200 identical viral types by Alemi et al. (2014) that are categorized into two groups, hr and lr according to their relationship with cancer progression. The utmost frequent categories of hr-Human papilloma virus include HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68. These are related with moderate and high- grade cervical lesions and CACX (Zhao et al., 2020). According to Haręża et al. (2022) among the 690,000 cancer cases caused by HPV infection five hundred seventy thousand are CACX cases of which five hundred thousand cases are caused by hr-Human papilloma virus 16 and Human papilloma virus 18 and 120,000 cases are caused by HPV31, 33,35,45,52 and 58.

The greatest frequent types of lr-HPV include HPV6, 11, 40, 42,43,44,54,61,70,72 and 81. They bring about Low-grade cervical lesions for example warts of the genital (condyloma) and nonthreatening cervical lesions. They are hardly identified in neoplasms which are malignant (Badial et al., 2018). HPVs only contaminate basal cells of the epithelium which are undifferentiated deeper layers of the mucous membrane, they have high mitotic capacity.

The specific molecular relations containing the viral antigens and host receptors determine the HPV entry into the basal epithelial cells (Kombe Kombe et al., 2021).

The epithelial cell differentiation determines the HPV replication thus by infecting homogenous basal cells increases the virus's proliferation and perseverance. Continuous dedifferentiating the basal cells simultaneously ensure viral protein synthesis successively hence ensuring viral accumulation and elevated danger of Human papilloma virus infection and related CACX (Kombe Kombe et al., 2021).

2.2.2 Socio-Demographic Factors Associated with HPV Genotypes

Socio-demographic factors for example age, education and marital status are related with HPV infection. Studies by Shahid et al. (2021) on women living with HIV in Kenya showed women who were 30 to 39 were most probable to have high- risk infections than those who were older. This is because HPV contamination is common amongst young adults who are active sexually and there is simultaneous infection of single or multiple strains of Human papilloma virus oncogenic types in WLHIV as related to those who are negative for HIV. The occurrence of HPV infection in women who were 30-39 years was 65.50% as compared to the 33.52% of those who were 40-49 years of age and the 3.98% of those who were 50 years and above. In addition, women who were single and less than 40 years had an elevated danger of HPV16 disease with cervical lesions than their counterparts. More studies by Swai et al. (2022) in Tanzania revealed possibility of 42.9% perseverance of hr-HPV infection in older WLHIV than the 28.0% of the HIV negative women. Additionally, Aziz et al. (2023) reported an important association of Human papilloma virus infection with age ≤ 35 years. The women who were 35 years or less were 1.21 times more probable to have Human

papilloma virus infection than those who were above 35 years. There was higher prevalence of hr-Human papilloma virus DNA of 57 percent in women less than thirty years as shown by Tiiti et al. (2022) and decreased to 45.6 percent in women 30 to 39 years and elevated to 48.8% in women 40-49 years. In addition, Tiiti et al. (2022) showed that the prevalence of hr-Human papilloma virus E6/E7 messenger RNA elevated with age highest in women greater than or equal to thirty years than those less than thirty years. This is because the HPV infection in young women is short-term with no symptoms where as in advanced age there is persistence of HPV infection due to hormonal changes and hr-Human papilloma virus E6/E7 messenger RNA identifies vigorous Human papilloma virus infection and a higher danger of CACX progression. Additional studies by Khaali et al. (2019) in Morocco showed that women aged 30-45 years had four times elevated danger of genital HPV disease.

It was also reported by Tiiti et al. (2022) that women with only high school education had an HPV prevalence of 58% than college educated women. It has been noted that women with this level of education have sexual behaviors which put them at high-risk (hr) of contracting diseases which are transmitted sexually thus have reduced approach of seeking medical help in case of being infected. More so Ashaka et al. (2022) reported a higher danger of Human papilloma virus infection in women with primary level and secondary level of education in Lagos, Nigeria. The women who had a primary level and secondary level of learning had a twofold increased threat of HPV infection than the ones who had tertiary level of learning. Aziz et al. (2023) also reported 1.92 times possibility of HPV infection in women who are uneducated and with incomplete secondary level of education than those with secondary and higher education in Pakistan.

Studies by Roik et al. (2018) show marital status is related with decreased hr-HPV infection. The women who are single have greater threat of infection with HPV as compared to those who are married because of unsafe sexual behavior for example having sexual companions who are not consistent (Tiiti et al., 2022). There was also an association of marital status with HPV infection in a study conducted by Ashaka et al. (2022). The females who were single, separated, widowed were extra susceptible to HPV contamination than the married women. This is because women in these groups are likely to have new companions which positions them at a danger of HPV contamination. According to Karuri et al. (2017) women without employment are considerably related with infection of hr-HPV because of the low income earning leading to poverty hence having multiple sexual partners.

In developing countries, the biggest number of women who are pregnant are within the age of 20 to 35 years. The extreme threat of Human papillomavirus disease is in women who are younger in this age group but most of these infections have no signs and symptoms thus most of the infections clear naturally due to the immune system which is strong. However, in the course of pregnancy the altered hormonal milieu and response of the immune system influence the incidence or persistence of the Human papillomavirus infection. This HPV infection prevalence is 40% high in pregnancy due to these hormonal changes and the altered response of the immune system which enhances perseverance of infection with HPV elevating the danger of CACX (Pandey et al., 2019). In addition, high occurrence of Human papillomavirus infection was reported by McClymont et al. (2022) in pregnant women living with HIV above the incidence of Human papilloma virus infection among pregnant women who are HIV negative. The pregnant WLHIV had 54% increased risk of being HPV positive

than their counter parts. The HPV16 was the utmost dominant type detected in the pregnant women living with HIV which is oncogenic.

2.2.3 Sexual Practices Associated with HPV Genotypes

Studies by Itarat et al. (2019) show that sexual behavior increases the risk of 16/18 carcinogenic HPV infections. Early sexual behavior increases the threat of HPV 16 infection and many sexual associates enhance the danger of HPV 18 infection. HPV disease in women with more than 11 sexual partners was 5.77 times extra probable than those with 0 -1 partner. A higher threat of Human papilloma virus infection was also reported by Ashaka et al. (2022) in Lagos, Nigeria where there were more than four life time sexual partners. The women who had more than four sexual companions were 1.21 times more probable to have HPV contamination than their counterparts. Furthermore, there is an increasing trend of HPV infection with multiple sexual partners. The number of lifespan sexual companions according to Pedroza-Gonzalez et al. (2022) among university female students in Mexico, has an important relationship with HPV infection. There was an important relationship of Human papilloma virus infection with the integer of sexual partners. There was a 2.6-fold increased threat of having Human papilloma virus infection in women who had >3 sexual companions than those who had ≤3 sexual partners. More so there was 83% prevalence of HPV in the women who had more than three sexual partners as compared to the 66% of the women who had ≤ 3 sexual partners. The HPV 18 was the most prevalent in this population which is a high-risk HPV genotype. Other studies reported 48.1% HPV prevalence in women with multiple sexual associates in contrast to 15% in women with one sexual partner. Multiple sexual associates are an important threat aspect of acquiring HPV infection because an

increased number of sexual companions increases the probability of interacting with a contaminated partner (Monteiro et al., 2021). Recent studies in Africa by Mekonnen and Mittiku, (2023) reported 2.95 times bigger threat of CACX in women who had early sex debut before 18 years of age than their counter parts. This indicated that females who had early sexual experience had an amplified danger of CACX development than women who started sex contact far ahead in life. This is because of the immature cervix which is susceptible to HPV infection the leading cause of CACX. More studies reported elevated prevalence of HPV infection in teenage girls of Tanzania about the period of the stated sexual introduction. About 56% were diseased with high-risk and multiples Human papilloma virus genotypes with 51% of them infected with more than one type of the genotypes (Baisley et al., 2019).

2.2.3 Medical History Associated with HPV Genotypes

According to Zhu et al. (2019) warts of the genital are a sort of infection transmitted sexually brought about by particular types of Human papilloma virus. They are regular signs of HPV infections. The principal medical indicator for warts of the genital is nonthreatening hyperplasia of the mucus membrane and skin in the genitalia, perineum, and anus. They affect the physiological function as well triggering psychological stress. They are normally related with HPV 6 and HPV11. Previous studies by Dareng et al. (2019) show that they are mostly common with HPV11 in SSA. In addition, various other types of Human papilloma virus in genital warts have been identified like HPV 54, 42, 2, 43 and 40. Zhu et al. (2019) revealed that the major pathogens of genital warts are lr- HPV types nevertheless high- risk HPV types and coinfections with multiple Human papilloma virus types are as well frequent in genital warts. HPV 6, HPV 52 and HPV 11 are the dominant Human papilloma virus types in warts

of the genital in Xian, China. Recent studies by Ashaka et al. (2022) observed that women infected with genital warts had a greater possibility of Human papilloma virus infection.

The use of condoms consistently shields against HPV infections and related cervical neoplasia (Lam et al., 2014). However current studies by Monteiro et al. (2021) indicate a statistically important relationship among HPV infections and using condoms. There was a two times higher possibility of infection with HPV in women who were consistently using condoms during sexual interaction as related to their counterparts. This is because the use of condoms does not guarantee complete protection against microbial infection because they do not entirely shield the reproductive male organ thus parts not covered shelter communicable particles or asymptomatic lesions in Human papilloma virus infection. On contrary other recent studies by Ashaka et al. (2022) revealed an important decrease in the likelihood of HPV infection with the use of condoms which highlights the significance of condom use during sexual intercourse as a way of defense against sexually transmitted infection for example Human papillomavirus.

Recent studies by Yang et al. (2022) reported a significant relationship of Human papilloma virus infection with the hormonal and non-hormonal contraceptives. The women who were using hormonal and non-hormonal contraceptives had 1.26 times bigger threat of HPV infection as related to those who were using barrier methods. This is because the hormonal contraceptives contain oestrogen and progesterone which directly affect cervical cells increasing cell multiplication and stimulating Human papillomavirus transcription. Taku et al. (2020) revealed a considerably elevated threat of high-risk HPV infection amongst women

who were using any contraceptives. The women who were currently using contraceptives were 1.85 times probable to have hr-HPV infection as compared their counterparts.

2.3 Review of Empirical Related Literature

WLHIV have a greater threat of developing CACX due to the extreme danger of Human papilloma virus infection and persistence as a result immune suppression. There is also a greater incidence of wide variety of HPV genotypes according to Pala et al. (2021) because of the simultaneous various infection. Tiiti et al. (2022) showed 73.5% prevalence of HPV in WLHIV which is high. This matched with earlier studies in Brazil where the majority was 48% to 68% for example Monteiro et al. (2021) revealed a prevalence of 63.3% in a study which was cross sectional conducted on WLHIV in Belem, para, Amazon region in brazil. Similar studies by Chachage et al. (2023) in a cohort study in Africa which is observational in many sites including Uganda, Kenya, Tanzania and Nigeria found the high- risk HPV prevalence in WLHIV to be 50.9% as compared to 38.1% among the Human immunodeficiency virus negative women.

The hr- HPV subtypes prevalence in WLHIV was 57.5% in a prospective study conducted in Brazil. In addition, there was a greater occurrence of HPV in particular HPV56 and HPV16. However, HPV56 is not incorporated in the quadrivalent vaccine. It's essential to closely monitor HPV56 infected patients to inhibit cervical cancer thus enhance improved prognosis (Badial et al., 2018). According to Aziz et al. (2023) the prevalence of Human papilloma virus in WLHIV was confirmed to be 36.9% as related to the 4.4% in the Human immunodeficiency virus negative women in Pakistan in a local population of federal capital territory. The hr-HPV types were identified in 15.39% as compared to the 21.54% detected

lr- HPV types. The hr- HPV types were discovered in 62.5% women identified with low grade SIL. The HPV18, 16, 58, 68, HPV33 and HPV45 were detected amongst the hr-Human papilloma virus types. More so there was a bigger threat of Human papilloma virus infection with Age ≤ 35years and incomplete secondary education.

Tiiti et al. (2022) showed an important relationship between the high-risk HPV infection with employment, age, and marital status. Being married and age of 50-59 years were statistically protective for high-risk HPV infection whereas unemployment was predictive. Furthermore, age was related with hr-Human papilloma virus E6/E7 mRNA manifestation. Age of 40-49 years was suggestively related with enhanced threat of hr-Human papilloma virus E6/E7 Messenger RNA manifestation. The use of Contraceptive beyond 24 months was predictive for hr- Human papilloma virus E6/E7 Messenger RNA.

2.3.1 HPV and HIV Infection

Mbuya et al. (2020) stated that the burden of premalignant and malignant cervical lesions attributed to HPV infection remain high in WLHIV even on antiretroviral therapy management. Majority of HPV infections are asymptomatic but immunosuppressed individuals for example WLHIV have enhanced infection with Human papilloma virus and quickly advance from lesions associated with HPV infection to aggressive cervical cancer. HIV viral replication is prevented by antiretroviral therapy, rebuilding CD4 T cell totals and protection thus reducing the threat of infection to opportunistic infection but the HPV infection in WLHIV remains high regardless of the ART commencement as reported by Brickman and Palefsky (2015). It has been shown by Bere et al. (2014) that regularity of resistant cells and provocative cytokines in the interior of premalignant cervical lesions

associated with HPV infection are inhibited in WLHIV reflecting an uninterrupted outcome of Human immunodeficiency virus on uterine cervix resistant reaction. In addition, continuing HIV prompted immune stimulation, manifested by bigger percentage of CD38+ HLA-DR+ systemic T cells is related with resistant dysfunction and impairment of the mucous membrane causing increased HPV infection in WLHIV (Adler et al., 2015). Various previous studies by Chaturvedi et al. (2009) show altered risks of invasive CACX in association with HIV infection. Previous studies by Hagensee et al. (2004) mentioned that a probable elevation in WLHIV is due to enhanced prevalence of the infection for HPV or its persistence. Cervical intraepithelial neoplasia is not likely to clear thus the likelihood of developing into invasive CACX. WLHIV have a greater danger of developing cervical precancers and cancers thus a greater necessity to have preventive services available to them (Bukirwa et al., 2015).

2.3.2 Cervical Cancer

CACX is the unrestricted growth of cells on the cervix. WHO (2019) stated that cells begin to develop gradually and unusually on the cervix over many years, ten to twenty years, for aggressive cancer to advance after identifying precancerous lesions. According to Yang and Al-Hendy (2022) cancer of the cervix is a malignant neoplasm arising from the cells of the uterine CX. The CX comprises of two portions and is shielded by two categories of cells. The endocervix made up of glandular cells closer to the uterus and the exocervix comprising of squamous cells nearer to the vagina. The area where the two cell categories join, the alteration region, is the area where majority of CACX initiate. In regard to their place of origin they can be categorized as cancer of squamous cell ascending from the squamous cells of exocervix attributed to 80% of CACX cases.

The cancer of the adeno originating from the glandular cells of the endoCX causing 10 to 20% of the cancer cases. The adenosquamous carcinomas where the cancer contains the structures of the two cells types and it a rare type of cancer. It is spread sexually and brought about by the Human papillomavirus. CACX is the greatest frequently identified CA in 23 countries international. It is the major basis of CA death in 36 countries, with the enormous number of these nations found in SSA where the highest rates are particularly in Eastern Africa, middle Africa and southern Africa as revealed by Ferlay et al. (2019) . In SSA 34.8 new patients of CACX are identified per 100,000 women yearly and 22.5 percent death per 100,000 women occur due to the disease (WHO, 2013). One of the world's uppermost CACX occurrence rates of 45.6 per 100,000 women by WHO (2010) 25 per 100,000 women CACX deaths happen in Uganda.

The prevalence of HPV of 33.6% by Nakisige et al. (2017) together with low screening acceptance has led to Uganda experiencing the utmost incidence rates of cervical cancer. 80% of women have advanced stage disease who present with cervical cancer.

2.4 Identification of the Knowledge Gap

The WHO describes HPV as a causative agent of CACX. The HPV genotypes are grouped into lr and hr according to their potential to induce CACX (Dunne & Markowitz, 2006). The utmost prevalent high-risk forms are HPV16, 18, 31 and 45 by de Sanjose et al. (2010) and are commonly related with carcinomas of cervical squamous cell contributing to 80% cases. HPV16 and 18 occur in 50 and 20% cases respectively globally. The infection of HPV prevalence differs considerably according to the population under study plus the methods used to detect HPV (Ahmed et al., 2021).

In sexually active adolescent girls and WLHIV high proportions of HPV infection have been described. In HIV negative women, HPV infection clears within 2 years. But 10% of the women affected have an infection which is persistent (Wentzensen et al., 2009). The elevated occurrence of Human papillomavirus in WLHIV is said to be due to the immune system which is compromised because of infection with HIV hence enhancing the persistence of infection with HPV and elevating the chances of developing conditions from various HPV genotypes leading to an increased danger of advancing into CIN (Seyler et al., 2018).

The HPV genotypes related to the growth of high grade SIL and CIN in WLHIV attending antiretroviral therapy clinic in Mukono, Uganda are not characterized. In this case, the current study intended to describe the Human papilloma virus genotypes and their correlates among WLHIV attending antiretroviral therapy clinic in Mukono, Uganda.

2.5 Conceptual Framework

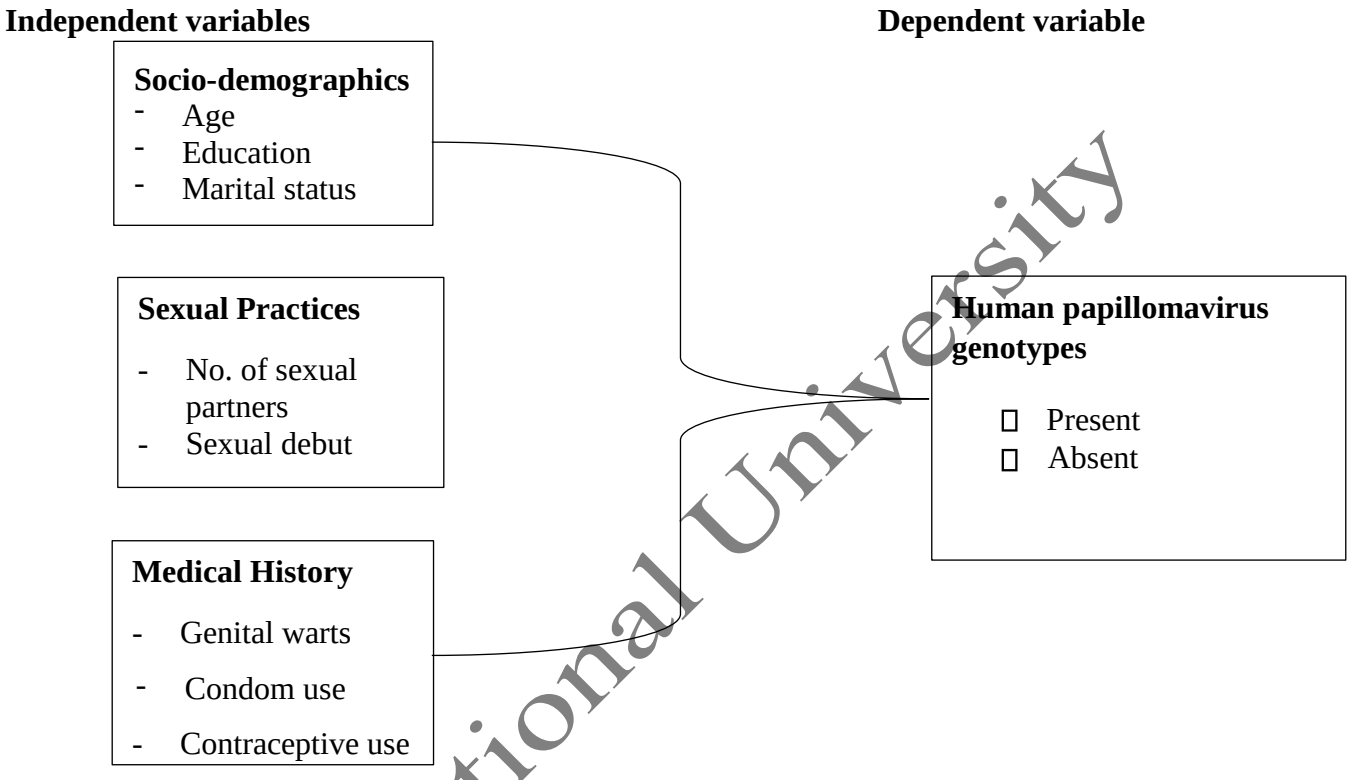

Figure 1: Conceptual Framework for the Study

CHAPTER 3: RESEARCH METHODOLOGY

3.1 Introduction

The chapter summarizes on how the study was conducted and covers: the study design, site, population, sample and sampling procedures, data collection instruments, validity and reliability, data collection procedures, data analysis and presentation, ethical considerations, study limitations and constraints. This study was cross sectional carried out in Mukono General Hospital for two months from December 2022 to January 2023 where WLHIV with an Xpert HPV test done were recruited using systematic random sampling and evaluated an interview guide. The respondents' results for HPV genotypes were obtained retrospectively from respective laboratory records.

3.2 Study Design

This study adopted a cross sectional study design because WLHIV with an Xpert HPV test done were recruited and then questioned using an interview guide. The respondents' results for HPV genotypes were obtained retrospectively from the respective laboratory records. This study design is the most appropriate as the main objectives was to determine the types and associated factors of HPV infection by genotyping Human papillomavirus factors among a group of WLHIV attending antiretroviral therapy clinic in Mukono, Uganda.

3.3 Study Site

This research was carried out in Mukono General Hospital a government Health Facility located on the Kampala – Jinja highway in Mukono town, Uganda. It has a bed capacity of 12 and it offers ART therapy, cancer screening, antenatal, deliveries and postnatal,

outpatients and in-patient services. About 3,000 WLHIV are regularly attending the ART clinic serving 47 lower facilities in Mukono district.

3.4 Study Population

The women between 25 - 49 years attending an antiretroviral therapy clinic in Mukono General Hospital were recruited for the study because Xpert HPV test was done on this group. Self-collected cervical specimens are collected by WLHIV and tested using a genexpert machine which is PCR that identifies and differentiate hr-HPV. The ART clinic is attended by 3,000 WLHIV who are always advised to have an Xpert HPV test done at the start, then every after 12 months. This test was carried out in Mukono General Hospital Laboratory in the Xpert HPV diagnostic section.

3.4.1 Inclusion Criteria

They were permanent residents of Mukono, having lived in Mukono for at least two years.

3.4.2 Exclusion Criteria

Those sampled but during data collection were too sick at the time to be interviewed.

3.5 Sample and Sampling Procedures

The participants of the study were recruited from women between 25 to 49 years of age living with HIV attending the ART clinic in Mukono General Hospital who have had an Xpert HPV test done from July 2021 to December 2022.

3.5.1 Sample Size Determination

There is a prevalence of 33.6% HPV in the general population in Uganda (Nakisige et al., 2017). A sample size of 342 women was used based on Cochran's sample size calculation formula (Cochran, 1963) at 95% confidence level with an error of 5 percent. $n = (Z\alpha/2)^2 p (1-p)/w^2$, where:

α = the level of significance which can be obtained as 1- confidence level.

P = best estimate of population proportions

W = maximum acceptable difference

Zα/2 = the value under standard normal table for the given value of confidence level

$n = (Z\alpha/2)^2 p(1-p)/w^2$

p = 100/33.6=0.336

$n = (1.96)^2 0.336(1-0.336)/0.05^2$

n = **342**

3.5.2 Sampling Procedures

The study participants were selected from the target group of 3,000 WLHIV between the ages of 25 - 49 years attending anti-retroviral Clinic in Mukono General Hospital Using systematic random sampling. Each woman of the sample group was uniquely labelled. The

sampling fraction was calculated using systematic random sampling method. Sampling Fraction = 342/3000 =1/8 (every 8^{th}) the first number was picked randomly followed by each 8^{th} member.

3.6 Data Collection Instruments

3.6.1 Interview Guides

An interview guide was developed which captured: Age, education, marital status, STI history (syphilis, warts), number of sexual companions, age of starting sexual activity, pregnancy, condom use, contraceptive use, and engagement in prostitution.

3.6.2 Results for Xpert HPV

The results from the Xpert HPV are recorded in the Health Management Information System (HMIS) registers and the African laboratory information system (ALIS). The results of 342 HIV positive women who were examined using an interview guide were obtained from the Comma Separate Values (CSV) downloaded from ALIS by the principal investigator. These results were examined for presence and absence of hr- HPV genotypes.

3.7 Validity and Reliability

Research assistants received a two days training about the interview guide. Standard pre-tested interview guides were used. A unique code was assigned to the participants for identification during extraction of information from the laboratory records. The consent form and interview guide were translated using back to back translation to a local language (Luganda since majority of patients who attend the clinic speak Luganda). The data was

double entered and double checked for completeness and correctness each day by the principal investigator.

3.8 Data Collection Procedures

Data was collected after obtaining IRB approval (Appendix III), site administrative clearance (Appendix IV), and national research permit (refer Appendix V) by medical officer, clinical officer and principal investigator who interviewed participants on socio-demographic factors, sexual practices and Medical history using a pretested interview guide. During the interview process, patients were given identification numbers. The results for Xpert HPV of the interviewed patients were extracted from the comma separate file download from the African laboratory information system in the laboratory.

3.8.1 Description and Measurements of Study Variables

3.8.1.1 Dependent variable

In this study, High Risk Human papillomavirus genotype was the dependent variable as a binary outcome. hr-HPV genotype presence was denoted by 1 and absence by 0. The hr-HPV genotypes were defined as present at the time of testing with a positive result and the type of hr-HPV well defined on the lab results.

3.8.1.2 Independent Variables

Patients' socio- demographic included age, level of education, marital status, parity, pregnancy. The sexual practices related variables are; sexually active, number of sexual companions, and age of sex debut. Lastly, the medical history variables included in this study are; genital warts, family planning, condom use.

Table 1: Description And Measurement Of Independent And Dependent Variable

Objective	Variable	Description	Type	Measurement
Dependent variable				
Broad objective	High-risk Human papillomavirus genotype	hr-HPV genotypes were defined as present at the time of testing with a positive result and the type of hr-HPV well defined on the lab results.	Categorical	1. Present 1 2. Absent 0
Independent variables				
Specific objective 1: on socio-demographics	Age	Completed years since birth	Numerical	Full integer number of years
	Level of education	Maximum level of education achieved by the respondents	Categorical	Primary 1 Secondary 2 Tertiary 3
	Marital status	Status of respondent in terms of marriage	Categorical	Single 1 Married 2 Previously married 3
	Parity	Number of children one has ever given birth	Numerical	Full integer number of children
	Pregnancy	Whether one was pregnant or not at the time of study	Categorical	Yes 1 No 2
Specific objective 2: on sexual practices	Sexually active	Whether one had a sexual partner and was engaged in sexual intercourse with the partner within the study period	Categorical	Yes 1 No 2
	Number of sexual companions	Integer of sexual companions in the last three months	Numerical	Full integer number of partners
	Age at sex debut	Age in complete years when someone had sex for the first time	Numerical	Full integer number of years
Specific objective 3: on medical history	Genital warts	If one has ever had or been infected with genital warts	Categorical	Yes 1 No 2
	Family planning	If one was using family planning (barrier, hormonal and non-hormal methods) at that time of the study or not	Categorical	Yes 1 No 2
	Condom use	If one was using condoms at that time	Categorical	Yes 1 No 2

3.9 Data Analysis and Presentation

This section outlines how data was analyzed and presented. It involves data management and analysis, describes how data was handled, cleaned giving details of software used for the exploration. Further giving explanations on how each variable was examined logically and in details, normally in order to describe and interpret it.

3.9.1 Data Management

A password protected laptop was used in backing up all the data and external drive. The consent forms which were completed were filed then stored under lock and key in protected location. Data was entered in Epidata software (Version 4.4.2.1). Double data entry was done, and query reports ran to facilitate consistency, accuracy and completeness. Data cleaning was done and transferred to Stata software (version 17.0) for statistical analysis.

3.9.2 Data Analysis

At univariate analysis, variables which were continuous were described using measures of central tendency such as: means (standard deviations) and medians (interquartile range) ranges while variables which were categorical were defined using frequencies, proportions and percentages. The prevalence of hr-HPV was determined by dividing the number of study participants with any of the mentioned hr-HPV with the total number of study participants.

For correlates of Human papillomavirus genotypes, a Modified Poisson regression model was used. Before running the model, data was checked for multicollinearity using the variance inflating factor (VIF) and tolerance (1/VIF). For variables that were found to be

collinear, one of them was included in the model and the other dropped. We then checked for outliers using DFbetas and leverage values and found no outliers in the data.

Bivariate analyses were done using the modified poisson model for each variable at a time and their p-values observed. Variables that had a p-value ≤0.2 were considered for multivariable analysis. Interaction was assessed using likelihood ratio tests that compared full models with interaction terms and reduced models without interaction terms. Confounding was then assessed where a variable was considered a confounder if the change in prevalence ratio (PR) was greater than 10%.

Where change in PR = [(Crude PR – Adjusted PR)/Crude PR] *100

In the multivariable analysis, if the p-value of a variable was significant statistically at 5% level of significance (p-value<0.05) it was considered a risk factor. Prevalence ratios and their 95% confidence intervals were reported.

3.10 Ethical Consideration

3.10.1 Ethical Approvals

Approval letter from the graduate school of Amref International University was obtained. This was then followed by obtaining ethical approval from the Uganda Christian University Research Ethical Committee. Chairperson, Prof. Peter Waiswa or Secretariat, Mr. Ahimbisibwe Osborn Reference number: UCUREC-2022-404. A Support letter was obtained from the Medical superintendent of Mukono general Hospital where the research was conducted, and national research permit was obtained from the UNCST Reference

number HS2550ES. The study participants had voluntary participation, with an informed consent being filled out by each respondent.

3.10.2 Consent Process

The participants were explained to the background and the reason of the study. This was then preceded by the explanation of expected welfares of conducting the study, comprising of potential support to the participant, public, and the scientific world. An explanation was also given of how confidentiality and privacy will be kept throughout the research and how delicate private data of the participant will be handled. Participants were informed that it was not a mandate to participate in the research. They were also informed that their time will be compensated. Participants were informed that it was voluntary to participate in the study that they are free to join willing with a right to pull out any moment without being penalized. A consent statement after understanding the study and a signature were obtained from the participant.

3.11 Study Constraints and Limitations

The general limitation in this study is that in cross sectional surveys direction of association cannot be confirmed, as such we cannot determine causality. There is potential for social desirable bias as some of the variables were about sexual history and the study participants were not comfortable when asked about the sexual behavior. The study population was from Mukono division and suburbs the results may therefore not be representative of across the country. Despite these limitations, there is currently no other report in this population that is specific to Ugandan population on hr-HPV prevalence thus the data reported in this report remain important.

CHAPTER 4: RESULTS

4.1 Introduction

This section presents the outcomes of the findings regarding the study objectives. It describes the characteristics of research participants through generated summaries of their sociodemographic, sexual practices and medical history of participants showing factors and their patterns. Furthermore, it entails the representation of hr-Human papilloma virus genotypes and its distribution among the study participants. In addition, it shows the correlation of the hr-HPV genotypes and the sociodemographic, sexual practices, medical history respectively among the study participants. Finally, it confirms the relationships of the correlates with the hr-HPV genotypes among the study participants.

4.2 Description of Study Participants

This section presents the univariate results that focus on the socio-demographic characteristics, sexual practices, and those related to the medical history of the study respondents.

4.2.1 Socio-demographic Characteristics

An overall of 342 participants were enrolled in the research. The median age was 33 years, the youngest being 25 years and the oldest being 49 years. One in every ten (30.4%) of the study participants were aged between 30-34 years, followed by 90(26.3%) in age group 25-29 years. Slightly more than a half (51.2%) of the participants had attained primary education and only 17 out of 342 (5%) had attained tertiary education. Slightly more than a half (52.6%) of the participants were married and 4 in every 10 (40.9%) were single. Majority 338(97.7%)

of the participants were not pregnant at the time of the survey as only 2.3% of them were pregnant. Almost universally (96.8%), had ever given birth to 1 or 3 children. – see Table 2.

Table 2: Percent distribution of Socio-Demographic Characteristics of Study Participants

Characteristic	n=342	%
Age (Years)		
25-29	90	26.3
30-34	104	30.4
35-39	66	19.3
40-44	54	15.8
45-49	28	8.2
Education level		
Primary	175	51.2
Secondary	150	43.9
Tertiary	17	5.0
Marital status		
Single	140	40.9
Married	180	52.6
Previously married	22	6.4
Ever given birth		
No	11	3.2
Yes	331	96.8
Parity		
0	11	3.2
1-3	263	76.9
>3	68	19.9
Currently pregnant		
No	334	97.7
Yes	8	2.3

n=number of participants, %-Percentage

4.2.2 Sexual Practices among Respondents

Regarding being sexually active, the biggest percentage of the study participants 327(95.5%) were currently sexually active. More than half, 193(56.4%) of the participants became

sexually active at 18 years and above. The reported sex debut ranged between 16 years and 19 years among the respondents with 18 years as the median age. Slightly more than a half of the participants 173(50.6%) had been sexually active for 15 years, with 169(49.4%) of them beyond 15 years. The biggest number of participants 256(74.9%) had one sexual partner in the last three months. Further, almost two thirds of the participants 223(65.2%) did not have protected sex consistently - see Table 3.

Table 3: Percent Distribution of Sexual Practices among Respondents

Characteristic	n=342	%
Currently sexually active		
No	15	4.4
Yes	327	95.6
Age of sex debut		
<18 years	149	43.6
≥18 years	193	56.4
Period being sexually active (Years)		
≤15 years	173	50.6
>15 years	169	49.4
≥ one sexual partner in last three months		
No	256	74.9
Yes	86	25.1
Consistent protected sexual intercourse		
Yes	119	34.8
No	223	65.2

n=number of participants, %-Percentage

4.2.3 Medical History of Respondents

A small percentage of participants 42(12.3%) had ever developed genital warts. Most of them 300(87.7%) had never been infected with genital warts and only 2 out of 42(4.8%) who

developed warts did not medically treat them. The genital warts reoccurred in 11(26.2%) out of the 42 who developed them and 31(73.8%) never had a reinfection.

Table 4: Percent Distribution of Medical History of Respondents

Characteristic	n=342	%
Ever developed genital warts		
No	300	87.7
Yes	42	12.3
Genital warts medically treated, *n=42*		
Yes	40	95.2
No	2	4.8
Genital warts reoccurred, *n=42*		
No	31	73.8
Yes	11	26.2
Use condoms		
No	158	46.2
Yes	184	53.8
Frequency of condom use		
Never	158	46.2
Always	123	36.0
Sometimes	61	17.8
Using family planning methods		
No	2	0.6
Yes	340	99.4
Current family planning method, *n=340*		
Barrier	54	15.9
Hormonal	245	72.1
Non-hormonal	41	12.1

n=number of participants, %-Percentage

Almost all participants 340(99.4%) were using family planning, only 2(0.6%) of them were not using family planning and the most commonly used method was the hormonal contraception 245(72.1%).

Most of the women 184(53.8%) were using condoms, with 123(36%) always using them and 61(17.8%) using them sometimes. However, 158(46.2) never used them – see Table 4.

4.3 Characterization of Human Papillomavirus Genotypes

Out of the total participants, 136(39.8%) were found to be high-risk HPV positive with Human papilloma virus 16, Human papilloma virus 18/45 and other hr-HPV types being positive in 23(6.7%), 21(6.1%) and 110(32.2%) correspondingly. Additionally, most of the participants 17(12.5%) were infected with more than one type of hr-HPV genotype in other words they had mixed hr-HPV infections - see Table 5.

Table 5: Percent Distribution of Prevalence of High-Risk HPV

High risk HPV	**n=342**	**%**
High risk DNA(Positive)	136	39.8
HPV type 16	23	6.7
HPV type 18/45	21	6.1
Other high-risk HPV	110	32.2

n-number of participants, %= Percentage

Among those with single hr-Human papilloma virus infection, HPV 18/45 (11%) (95% CI: 6.7 - 17.6) was prevalent compared to HPV 16 (7.4%) (95% CI: 4.0 - 13.2). Furthermore, amongst those with multiple hr-Human papilloma virus infections, HPV 16+other hr-HPV sequence was the most frequent (8.1%) (95% CI: 4.5 - 14.1) as compared to 2.9% (95% CI: 1.1 - 7.6) with HPV 18/45 + other hr-Human papilloma virus and 0.7% (95% Confidence

Interval: 0.1-5.1) with Human papilloma virus 16 + HPV 18/45. However, 0.7% (95% CI: 0.1-5.1) had a mixed infection of all the hr-HPV genotypes that is HPV16+ HPV18/45+other hr-HPV - see Table 6.

Table 6: Percent Distribution of Hr-HPV Types

hr-HPV types	hr-HPV -positive n=136 (%)	95% CI
Single Test Positive only		
HPV type 16 only	10 (7.4)	4.0 - 13.2
HPV type 18/45 only	15 (11.0)	6.7 - 17.6
Other high-risk HPV only	94 (69.1)	60.8 - 76.4
Multiple Tests Positive only		
HPV-16+18/45	1 (0.7)	0.1 - 5.1
HPV-16+Other hr-HPV	11 (8.1)	4.5 - 14.1
HPV-18/45+Other hr-HPV	4 (2.9)	1.1 - 7.6
HPV-16+18/45+Other hr-HPV	1 (0.7)	0.1 - 5.1

n-number of participants, %= Percentage, 95%CI- Confidence interval

4.4 Factors Related with Hr-HPV Infection among Study Participants

This section describes and confirms the correlation of the hr-HPV genotypes and the sociodemographic, sexual practices, medical history correspondingly among the study participants. It also shows and elaborates the non-correlates of hr-HPV infection.

4.4.1 Socio-Demographic Factors Related with Hr-HPV Infection

Table 7 indicates the sociodemographic factors related with hr-Human papilloma virus infection. According to the bivariate analysis age was suggestively related with hr-Human papilloma virus infection. Having the age of 45- 49 years was significantly related with the

enhanced threat (cPR: 1.56; 95% Confidence Interval: 1.02-2.37; p=0.039) of hr-HPV infection. Those who are ≤45years have 1.56 times possibility of developing hr-HPV infection than those below 45years. This variable was considered for multivariate analysis.

Furthermore, being married (cPR: 1.21; 95% Confidence Interval: 0.92-1.60; p-value=0.173) had a bigger threat of hr-HPV infection. The women who are married are 1.21-fold more probable to have hr-Human papilloma virus infection than those who are single and previous married. This variable was also considered for multivariable analysis – see Table 7.

Regarding the level of education, being of secondary school level (cPR: 1:17; 95% Confidence Interval: 0.89-1.52 p-value=0.256) was not scientifically connected with hr-Human papilloma virus infection in this research. Although those who had secondary level of education were 1.17 times more probable to have hr-HPV than their counter parts, but this was not remarkable because the p-value was greater than 0.05 and the 95% CI was crossing 1. In addition, Tertiary level of education (cPR: 0.95; 95% Confidence Interval: 0.48-1.86; p-value=0.882) was not considerably related with hr-Human papilloma virus infection. The women who had tertiary level of education had the same likelihood of developing hr-HPV infection as those with the primary and secondary level of education– see Table 7.

Ever given birth (cPR: 199; 95% Confidence Interval: 0.50- 2.43; p-value= 0.820) was not scientifically connected with hr-HPV infection. Those who have ever given birth were 1.99 times more like to have hr-HPV than those who had never given birth, but this was not significant because of p=0.820 and the 95% CI crossing 1- see Table 7.

On parity; the women who had 1 – 3 children (cPR: 1.11; 95% CI: 0.500- 2.46; p=0.800) had 1.11 times risk of having HPV than their counter parts, but this was not scientifically important because of a p>0.05 and 95% CI crossing one. More so those who had >3childern (cPR: 1.05; 95% CI: 0.45- 2.43; p=0.907) had 1.05 times possibility of developing hr-HPV than their counter parts but this was not statistically significant- see Table 7.

Currently pregnant (cPR: 1.27; 95% Confidence Interval: 0.62- 2.56; p-value=0.514) was not considerably connected with hr-HPV infection. The women who were pregnant had 1.27 times likelihood of having hr-HPV than those who were not, but this was not statistically important because of a p>0.05 and 95% CI crossing 1- see Table 7.

Table 7: Socio-Demographic Factors Related with Hr-HPV Infection

Characteristic	hr-HPV Prevalence n=136 (%)	cPR (95% CI)	p-value
Age (Years)			
25-29	33 (24.3)	Ref	
30-34	41 (30.2)	1.08 (0.75, 1.54)	0.695
35-39	29 (21.3)	1.20 (0.82, 1.54)	0.357
40-44	17 (12.5)	0.86 (0.53, 1.39)	0.533
45-49	16 (11.8)	1.56 (1.02, 2.37)	**0.039**
Education level			
Primary	110 (53.4)	Ref	
Secondary	85 (41.3)	1.17 (0.89, 1.52)	0.256
Tertiary	11 (5.3)	0.95 (0.48, 1.86)	0.882
Marital status			
Single	90 (43.7)	Ref	
Married	102 (49.5)	1.21 (0.92, 1.60)	0.173
Previously married	14 (6.8)	1.02 (0.56, 1.85)	0.953
Ever given birth			
No	7(3.4)	Ref	
Yes	199(96.6)	1.10 (0.50, 2.43)	0.820
Parity			
0	7 (3.4)	Ref	
1-3	157 (76.2)	1.11 (0.500, 2.46)	0.800
>3	42 (20.4)	1.05 (0.45, 2.43)	0.907
Currently pregnant			
No	202 (98.1)	Ref	
Yes	4 (1.9)	1.27 (0.62, 2.56)	0.514

n=number of participants, %-Percentage, cPR-crude prevalence ratio, 95%CI-confidence interval

4.4.2 Sexual Practices Associated with Hr-HPV Infection

Bivariate analysis revealed an increased risk of being currently sexually active (cPR: 3:07; 95% CI: 0.84-11.26, p=0.090) with hr-HPV infection. This result indicates that those who were sexually active were 3.07 times more probable to have hr-Human papilloma virus

infection than those who were not sexually active. This variable was considered for multivariable analysis.

There was an important relationship between infection of hr-HPV and age of sex debut (cPR: 1.42; 95% Confidence Interval: 1.07-1.87; p-value=0.015). The women who had sex debut at ≥18years were 1.42 times more probable to have hr-HPV infection than their complements. This variable was therefore included for multivariable analysis - see Table 8.

The period of being sexually active (cPR: 1.12; 95% Confidence Interval: 0.86-1.45; p-value=0.403) was not considerably connected with hr-HPV. This is because those who had been sexually active for more than 15 years were 1.12 times more probable to have hr-Human papilloma virus infection than those who had been sexually active ≤15 years but the p>0.05 at 95% CI crossing number 1.

More than or equal to one sexual partner in the last three months (cPR: 0.84; 95% Confidence Interval: 0.61- 1.16; p-value=0.300) was not considerably related with hr-HPV. This is because women who had ≥1 sexual partner in the last three months had the same possibility of developing hr-HPV infection with their counterparts.

Consistent protected sexual intercourse (cPR: 0.98; 95% Confidence Interval: 0.74 -1.29; p-value=0.875) was not considerably related with hr-HPV because the women who consistently had protected sex had the same possibility of having hr-HPV with their counter parts -see Table 8.

Table 8: Sexual Practice Factors Related with Hr-HPV Infection

Characteristic	hr-HPV Prevalence n=136 (%)	cPR (95% CI)	p-value
Currently sexually active			
No	13 (6.3)	Ref	
Yes	193 (93.7)	3.07 (0.84, 11.26)	0.090
Age of sex debut			
<18 years	101 (49)	Ref	
≥18 years	105 (51)	1.42 (1.07, 1.87)	**0.015**
Period being sexually active (Years)			
≤15 years	108 (52.4)	Ref	
>15 years	98 (47.6)	1.12 (0.86, 1.45)	0.403
≥ one sexual partner in last three months			
No	150 (72.8)	Ref	
Yes	56 (27.2)	0.84 (0.61, 1.16)	0.300
Consistent protected sexual intercourse			
Yes	71 (34.5)	Ref	
No	135 (65.5)	0.98 (0.74, 1.29)	0.875
Number of sexual partners, *median* *(IQR)*	1 (1, 1)	1.01 (0.86, 1.18)	0.906

IQR-interquartile range, n=number of participants, %-Percentage, cPR-crude prevalence ratio, 95%CI- confidence interval

4.4.3 Factors Associated with the Medical History of Respondents

Based on the bivariate analysis, ever developed genital warts (cPR: 0.95; 95% Confidence Interval: 0.63- 1.44; p-value=0.816) was not statistically related with hr-HPV. This means that those who have ever developed genital warts and their counter parts had the same risk of developing hr-HPV infection - see Table 9.

Use of condoms (cPR: 1.30; 95% CI: 1.00 - 1.71; p=0.054) had a bigger risk of hr-HPV infection. Those who were using condoms were 1.3 times more probable to have hr-HPV infection than their counter parts but not statistically important. Furthermore, there was an important association between the frequency of condom use (cPR: 1.44; 95% Confidence

Interval: 1.03- 2.01 p-value=0.033) and high risk-HPV infection. The participants who were sometimes using condoms were 1.44 times probable to have hr-Human papilloma virus infection as related to those who were always using condoms thus frequency of condom use was a predictive factor of hr-HPV. These variables were considered for multivariable analysis - see Table 9.

Using family planning methods (cPR: 0.79; 95% Confidence Interval: 0.20-3.20; p-value=0.746) was not considerably related with hr-HPV. The females who were using family planning had the same possibility of developing hr-HPV with those who were not using family planning methods - see Table 9.

Current family planning methods: hormonal methods (cPR: 1.08; 95% Confidence Interval: 0.75, 1.56; p-value=0.676) were not related statistically with hr-HPV. The participants who were using hormonal methods were 1.1 times more probable to have hr-HPV than the ones who were using barrier methods, but this was not statistically important because the p=0.676. In addition, non-hormonal methods (cPR: 0.69; 95% Confidence Interval: 0.38-1.27; p-value=0.231) were not considerably related with hr-HPV infection. The women who were using non-hormonal methods had the same likelihood of developing hr-HPV infection with those who were using barrier methods - see Table 9.

Years on family planning (cPR: 1.00; 95% Confidence Interval: 0.95-1.06; p-value=0.910) were not considerably related with high- risk human papillomavirus infection. Those who were using family planning for one year had the same possibility of having hr-HPV infection with women who were using family planning for two years - see Table 9.

Table 9: Medical History Factors Related with Hr-HPV Infection

Characteristic	hr-HPV Prevalence n=136 (%)	cPR (95% CI)	p-value
Ever developed genital warts			
No	180 (87.4)	Ref	
Yes	26 (12.6)	0.95 (0.63, 1.44)	0.816
Use condoms			
No	104 (50.5)	Ref	
Yes	102 (49.5)	1.30 (1.00, 1.71)	0.054
Frequency of condom use			
Never	54 (39.7)	Ref	
Always	52 (38.2)	1.24 (0.92, 1.67)	0.164
Sometimes	30 (22.1)	1.44 (1.03, 2.01)	**0.033**
Using family planning methods			
No	1 (0.5)	Ref	
Yes	205 (99.5)	0.79 (0.20, 3.20)	0.746
Current family planning method, *n=340*			
Barrier	33 (16.1)	Ref	
Hormonal	142 (69.3)	1.08 (0.75, 1.56)	0.676
Non-hormonal	30 (14.6)	0.69 (0.38, 1.27)	0.231
Years on family planning, *median (IQR)*	1 (1, 2)	1.00 (0.95, 1.06)	0.910

IQR-interquartile range, n=number of participants, %-Percentage, cPR-crude prevalence ratio, 95%CI- confidence interval

4.5 Model for Associated Factors with Hr-HPV Infection among Study Participants

Even after multivariable analysis age that is being 45-49 years (aPR: 1.95; 95% Confidence Interval: 1.41- 2.69; p<0.0001) was identified as significantly predictive factor of hr-HPV infection. The WLHIV aged 45-49 years were 1.95 times more probable to have high risk Human papillomavirus infection than those below 45 years. In addition, being married (aPR: 1.30, 95% CI: 1.00- 1.69; p=0.050), age of sex debut (aPR: 1.44, 95% Confidence Interval: 1.09-1.90; p-value=0.010), use condoms (aPR: 1.33; 95% Confidence Interval: 1.05-1.69; p-value=0.020) remained significantly related with hr-HPV infection hence were recognized as predictive factors of hr-HPV. In addition, married women were 1.32 times more probable to

have high risk Human papillomavirus infection than those who were not married – see Table 10.

The women who had their sex debut at 18 years and above were 1.44 times likely to have hr-HPV infection than their count parts. This could be because the majority of the women in this study population (193) had their sexual debut at 18 years and above which was almost twice the number of their counter parts. The participants who were using condoms were 1.33 times probable to have hr-Human papilloma virus infection as related to their counter parts. This means that women who were using condoms had 33% increased risk of getting hr-HPV infection as related to those who were not using condoms (143) - see Table 10.

Table 10: Model for Factors Related with Hr-HPV Infection

Characteristic	aPR (95% CI)	p-value
Age (Years)		
25-29	Ref	
30-34	1.11 (0.77, 1.60)	0.563
35-39	1.17 (0.79, 1.74)	0.435
40-44	0.87 (0.54, 1.41)	0.584
45-49	1.95 (1.41, 2.69)	**<0.0001**
Marital status		
Single	Ref	
Married	1.30 (1.00, 1.69)	**0.050**
Previously married	0.82 (0.39, 1.73)	0.605
Age of sex debut		
<18 years	Ref	
≥18 years	1.44 (1.09, 1.90)	**0.010**
Use condoms		
No	Ref	
Yes	1.33 (1.05, 1.69)	**0.020**

n=number of participants, %-Percentage, aPR-adjusted prevalence ratio

CHAPTER 5: DISCUSSIONS

5.1 Introduction

This chapter presents the discussions on the study results in comparison with previous studies. It includes the presentation of hr-Human papilloma virus genotypes in the study population elaborating the implication of the findings and suggestions of what is required to prevent or reduce the burden. This is preceded by the discussion of the socio-demographic factors in this research that are significantly and not significantly related with the high-risk Human papilloma virus infections in comparison with the previous studies and the reasons for differences in the findings. There are further discussions on the sexual practices statistically and not scientifically related with the hr-Human papilloma virus in the research population and comparison with the former studies and elaboration on variations. Finally, enlightenments of the medical factors significantly and not significantly related with hr-HPV infection in this study in comparisons with earlier studies and details of variations.

5.2 Characterization of High–Risk Carcinogenic Human Papillomavirus Genotypes

This research reveals a relatively high hr-Human papilloma virus prevalence among WLHIV (39.8%). The elevated hr-HPV prevalence with high load of HIV in Uganda are major public health challenges. WLHIV are more probable to have persistence high -risk Human papilloma virus and progress into CACX as compared to their counterparts.

The occurrence of hr carcinogenic HPV genotypes of 39.8% reported in this study was below that of a similar study which was 63.3% carried out in Brazil Monteiro et al (2021). The variations in the outcomes could be described by the small sample size of 169 women,

compared to our study with 342 participants. Furthermore, the results in this study were also contrary to 55.9% prevalence revealed by da Silva et al. (2020) in a prevalence survey on 270 WLHIV in Northeast Brazil. In addition, the findings in this research were different from what was reported by Okoye et al. (2021) were higher than the incidence of 28.9% reported in a 20-year systematic review of 16,237 participants in SSA. More so results of this research were contrary to what was revealed by Chachage et al. (2023) at twelve hospitals including Tanzania, Kenya Uganda and Nigeria in an African cohort study of 1002 women were the prevalence was 50.9% among WLHIV and 38.8% among HIV negative women.

However the present findings were consistent with reports in a research by Taku et al. (2020) in rural Eastern Cape, South Africa on 417 women which revealed that WLHIV had a suggestively higher hr-human papilloma virus prevalence than the Human immunodeficiency virus negative women (40.6%, 63/155 vs 21.4%, 56/262 respectively, p = 0.0001). Other similar studies by Zinzendorf (2022) have reported higher HPV rate among women living with HIV (39.1%) than Human immunodeficiency virus negative women (24.1%). The most prevalent were HPV 16 (20%) with multiple HPV infections among WLHIV (45.5%) than Human immunodeficiency virus negative women (12.7%) (Monteiro et al, 2021). The prevalence for this research was similar to that reported in a pilot CACX screening program in Uganda on WLHIV attending ART therapy clinics in 10 high volume hospitals by Lubega et al. (2022) where hr-HPV positivity rate was 30% (1,817), 214 (12%) were HPV16 positive, 187(20%) were HPV 18/45 positive and (66%) had other hr-HPV genotypes as a result including HPV 31, 22, 35, 39, 51, 52, 56, 58, 59, 66 and 68. 213(12%) of the women had multiple infections with hr-Human papilloma virus genotypes. The prevalence established in

this study implies that many WLHIV attending ART therapy clinics could be having a considerable burden of double disease which needs to be given due attention. Therefore, increase of Human papilloma virus vaccines and advancement of vaccines with extensive action against the less common hr-Human papilloma virus genotypes may improve CACX prevention in Uganda and Africa at large.

5.3 Correlates of Human Papillomavirus Genotypes

The hr- HPV infection was suggestively related with age, being married, and age of sex debut and condom use. However, a significant association between the level of education, number of sexual companions, and use of hormonal and non-hormonal methods with hr-HPV infection was not recognized.

5.3.1 Socio-Demographic Factors

In this study's sociodemographic aspects such as age and being married were significantly connected with high-risk HPV. This is because the hr-HPV infection in young women is short-term with no symptoms where as in advanced age there is more persistence of hr-HPV infection due to hormonal changes. This could be due to the collective lifetime contact and resistant system weakness to the perseverance or recurrence of the dormant disease. Furthermore, this is due to consequences of HIV infection and concomitant/related immunosuppression. More so advanced age is one of the reasons for insistent Human papilloma virus infection which results from increased E6/E7 messenger RNA manifestation which attack the proteins which suppress tumors for example p53 and pRB hence causing cell multiplication, preventing cell death, thus promoting genome variability and avoiding the inborn resistant system according to Harężа et al. (2022).

In summary, this shows impairment of the immune system with increasing age as revealed by Swai et al. (2022). Findings in this study were consistent with what was described by Tiiti et al. (2022) in a study which was cross- sectional in a tertiary hospital Guateng, province, South Africa. These findings were also similar with what was revealed by Taku et al. (2020) in a study which cross-sectional carried out at a community health clinic in Eastern Cape Province of South Africa. However, the findings in this study are contrary to what was revealed by Shahid et al. (2021) in a research conducted in Kenya on 331 WLHIV. In this study being married was a statistically associated with hr-HPV. This is because most of the participants in this research were married and hr-HPV infection is favored by the immunosuppression which enhances the infection by multiple hr- Human papilloma virus genotypes which may to lead to progression of the intraepithelial lesions to cervical intraepithelial neoplasia as reported by Monteiro et al. (2021). The findings in this study are similar with what was revealed by Tiiti et al. (2022) in a study which was cross- sectional carried out in a tertiary hospital Guateng, province, South Africa where significant relationship of hr-Human papilloma virus infection was reported with marital status however being married was a protective factor. On the other hand, these results were contrary to what was revealed by Mandiriri et al. (2020) in the analytical cohort study of 321 WLHIV in Harare, Zimbabwe.

In this study level of education, ever given birth, parity, currently pregnant were not significantly associated with hr-HPV. The findings were consistent with what was revealed by Monteiro et al. (2022) in a study which was cross-sectional conducted in Belem, Para, in Amazon region of Brazil. These findings were also like those by Taku et al. (2020) that revealed no outstanding association between level of education and hr-Human papilloma virus infection. However, the findings in this study were contrary to what was revealed by Yang et

al. (2022); Aziz et al. (2023) were education was reported to be significantly related with hr-Human papilloma virus. In addition, McClymont et al. (2022) revealed significant association of pregnancy with hr-HPV infection. The difference could be due to the organized evaluation and multiple analysis of 10 studies as compared to the present cross-sectional study.

5.3.2 Sexual Practices

In this cross-sectional study, it was discovered that age of sexual debut was considerably related with hr-HPV infection. This shows that late commencement of sexual action does not control the danger of Human papilloma virus infection far ahead in life. Furthermore, this is because of the compromised resistant system caused by Human immunodeficiency virus infection supporting viral perseverance of hr- Human papilloma virus infection and increasing the risk of contracting the infection from multiple Human papillomavirus genotypes. Findings in this study were also similar to the study which showed that WLHIV who had sexual debut above 15 years were 1.2 times probable to have hr-HPV infection though it was not statistically significant as compared to those below by (Monteiro et al, 2021). However, this result is contrary to what was revealed by Monteiro et al. (2022) in a study conducted in Belem, Para, Northern Brazil on 169 women which was cross sectional.

In this study currently sexually active and integer of sexual companions were not considerably related with hr-Human papilloma virus infection. These findings are consistent with those revealed by Tiiti et al. (2022) in a study which was cross-sectional in a tertiary hospital Guateng, province, South Africa. However, this was contrary to what was revealed by Megersa et al. (2023) in a study which was cross-sectional conducted among WLHIV in Southern Ethiopia.

5.3.3 Use of Condoms

The current study confirmed that condom use was considerably associated with hr-HPV infection. This is because most of the women in this population were not using them consistently thus if not consistent, use of condoms does not guarantee complete protection against microbial infection and most women using condoms have multiple sexual companions which exposes them to danger of getting hr-Human papilloma virus infection. The findings are consistent with what Monteiro et al. (2021) reported in the observational population based cross sectional study conducted on WLHIV from Belem Para in Amazon Brazil. This was contrary to what was revealed by Ashaka et al. (2022) that condom use is a protecting factor in a cross sectional study on 165 women in Lagos, Nigeria.

5.3.4 Use of Family Planning

The present study shows that there was no significant association of use of family planning with hr-HPV infection. The findings were also related to what was stated by Monteiro et al. (2022) that revealed no significant association of use of family planning with hr-HPV infection. However, Yang et al. (2022) revealed significant association of hormonal, non-hormonal methods with hr-HPV infection in large-scale population screening study of 10, 628 women. The variations in the findings could be due to the bigger variance in the sample size between the two studies.

5.3.5 Medical History

In this research there was no important association of ever developed genital warts with hr-HPV infection. These findings were also similar to those by Taku et al. (2020) that revealed no significant association between self-reported warts with hr-HPV infection. However other

studies conducted in Lagos, Nigeria by Ashaka et al. (2022) hospital based cross-sectional study conducted on 165 participants reported significant associations of history of STI with HPV infection. The controversy in the findings could be due to the greater variance in the sample size among the two studies. In addition, the studies were done on different study population, where the previous study was done on women who sought medical help in a hospital and their HIV status was not determines as compared to the current study conducted on WLHIV.

5.5 Strength of the Study

The desired sample size was achieved in adherence to designed sampling procedure leading to the study having an adequate power. Further, the study was conducted in large HIV treatment center in Mukono General Hospital which serves majority of patients in Mukono division and suburbs. It therefore generated results that could be representative of the targeted study population,

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Introduction

In this section, summaries have been made in relation to the study findings and suggestions according to the results reported, clearly indicating the relevance of the research and impact in the body of knowledge to the field of study. These are based on the study hypotheses and objectives.

6.2 Conclusions

6.2.1 High Prevalence of Human Papilloma Various Infection Among WLHIV

This research confirmed a high prevalence of Human papilloma virus infection among more than one third of participants and this underscores the need to frequently screen and diagnose cervical cancer pre-cancerous lesions for effective prevention of CACX among WLHIV.

6.2.2 Socio-Demographic Characteristics

Among socio-demographic features of participants in this study, it was confirmed that women of late age (between 45 to 49years) and those who are married were more probable to have HPV infection. Other social demographic factors were not significant. This is related to the literature where the peak of CACX diagnosis among WLHIV slightly lower than the general population in the late 40s.

6.2.3 Sexual Practices

It has also been shown from the study results that late commencement of sexual action does not control the danger of Human papilloma virus infection far ahead in life, as sexual practices predispose WLHIV to hr-HPV genotypes while the period of being sexually active does not.

6.2.4 Medical History

In regard to the results reported, it has been confirmed that the use of condoms as medical history related factors predisposes women living with HIV to high-risk HPV genotypes while pregnancy, parity, family planning, history of ever developing genital warts do not.

Based on the conclusions summarized in sections 6.2.1 – 6.2.4, we can therefore reject the hypotheses that socio-demographic, sexual practices and medical history related factors do not predispose WLHIV to hr carcinogenic HPV genotypes and accept the alternative hypotheses that socio-demographic, sexual practices and medical factors do predispose WLHIV to hr carcinogenic HPV genotypes. Specifically, age, being married, age of sexual debut, condom use is confirmed in this study as factors that predispose WLHIV to hr-HPV genotypes.

6.3 Recommendations

6.3.1 Implementation of the HIV Treatment Programs

It is very important for the implementers of HIV treatment programs to health educate the public that even the use of condoms, advanced age, being married and later sexual debut does not guarantee safety to hr-HPV infection thus emphasize screening and treatment in this population.

In addition, there is the need to ensure that techniques for diagnosis of hr-HPV genotypes are continuously maintained because of their early detection of the oncogenic HPV genotypes thus necessitating early treatment and prevention of progression to invasive cancer hence promoting health.

Furthermore, through emphasis on implementing more successful programs for the identification of hr-Human papilloma virus infection and observing and management of WLHIV with cytological variations of the CX and especially with CACX, as well as regular inhibition and health-promotion activities for the populations of the town of Mukono, and Other Towns in Uganda.

6.3.2 Community and Hospital Related Recommendations

To the community or hospital and health facility environments, more emphasis should be put on sensitization of persistence of hr-HPV and development of CACX to WLHIV and need for continuous CACX screening and treatment.

In addition, continuously health educate WLHIV on the risk factors of hr-Human papilloma virus for example inconsistency use of condoms, advanced age, being married and the need to continuously adhere to annual CACX screening as suggested by WHO to maintain health and prevent fatal invasive cervical cancer.

6.3.3 Recommendations for Further Research

In this research the prevalence of hr-Human papilloma virus in WLHIV attending ART therapy clinic in MGH was confirmed to be 39.8% which is relatively high compared to the 33.6% in the general population. This indicates that even though the population of WLHIV attend the ART therapy in MGH the prevalence of hr-Human papilloma virus among them is high. This shows a threat to the health of WLHIV in Mukono, Uganda. There is therefore the need to conduct more research to determine the effect of ART therapy on hr-HPV persistence and the risks this may pose to the health providers.

REFERENCES

Adebamowo, S. N., Olawande, O., Famooto, A., Dareng, E. O., Offiong, R., Adebamowo, C. A., & H3Africa ACCME Research Group. (2017). Persistent low-risk and high-risk human papillomavirus infections of the uterine cervix in HIV-negative and HIV-positive women. *Frontiers in Public Health*, *5*, 178. https://doi.org/10.3389/fpubh.2017.00178

Adler, D., Wallace, M., Bennie, T., Abar, B., Sadeghi, R., Meiring, T., Williamson, A.-L., & Bekker, L.-G. (2015). High risk human papillomavirus persistence among HIV-infected young women in South Africa. *International Journal of Infectious Diseases*, *33*, 219–221. https://doi.org/10.1016/j.ijid.2015.02.009

Ahmed, A., Saqlain, M., Bashir, N., Dujaili, J., Hashmi, F., Mazhar, F., Khan, A., Jabeen, M., Blebil, A., & Awaisu, A. (2021). Health-related quality of life and its predictors among adults living with HIV/AIDS and receiving antiretroviral therapy in Pakistan. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *30*(6), 1653–1664. https://doi.org/10.1007/s11136-021-02771-y

Alemi, M., Mohabatkar, H., & Behbahani, M. (2014). In silico comparison of low- and high-risk human papillomavirus proteins. *Applied Biochemistry and Biotechnology*, *172*(1), 188–195. https://doi.org/10.1007/s12010-013-0479-5

Ashaka, O. S., Omoare, A. A., James, A. B., Adeyemi, O. O., Oladiji, F., Adeniji, K. A., Okunade, K. S., & Agbede, O. O. (2022). Prevalence and risk factors of genital human papillomavirus infections among women in Lagos, Nigeria. *Tropical Medicine and Infectious Disease*, *7*(11). https://doi.org/10.3390/tropicalmed7110386

Aziz, H., Sattar, A. A., Mahmood, H., Fatima, S., Khurshid, M., & Faheem, M. (2023a). Prevalence of HPV types in HIV-positive and negative females with normal cervical cytology or dysplasia. *Journal of Clinical Laboratory Analysis*, *37*(4), e24851. https://doi.org/10.1002/jcla.24851

Aziz, H., Sattar, A. A., Mahmood, H., Fatima, S., Khurshid, M., & Faheem, M. (2023b). Prevalence of HPV types in HIV-positive and negative females with normal cervical cytology or dysplasia. *Journal of Clinical Laboratory Analysis*, *37*(4), e24851. https://doi.org/10.1002/jcla.24851

Badial, R. M., Dias, M. C., Stuqui, B., Melli, P. P. dos S., Quintana, S. M., do Bonfim, C. M., Cordeiro, J. A., Rabachini, T., Calmon, M. de F., Provazzi, P. J. S., & Rahal, P. (2018). Detection and genotyping of human papillomavirus (HPV) in HIV-infected women and its relationship with HPV/HIV co-infection. *Medicine*, *97*(14), e9545. https://doi.org/10.1097/MD.0000000000009545

Baisley, K., Andreasen, A., Irani, J., Nnko, S., Changalucha, J., Crucitti, T., Francis, S., Holm Hansen, C., Hayes, R., Buvé, A., & Watson-Jones, D. (2019). HPV prevalence around the time of sexual debut in adolescent girls in Tanzania. *Sexually Transmitted Infections*, *96*(3), 211–219. https://doi.org/10.1136/sextrans-2019-054012

Bere, A., Tayib, S., Kriek, J.-M., Masson, L., Jaumdally, S. Z., Barnabas, S. L., Carr, W. H., Allan, B., Williamson, A.-L., Denny, L., & Passmore, J.-A. S. (2014). Altered phenotype and function of NK cells infiltrating Human Papillomavirus (HPV)-associated genital warts

during HIV infection. *Clinical Immunology*, *150*(2), 210–219. https://doi.org/10.1016/j.clim.2013.12.005

Bogale, A. L., Belay, N. B., Medhin, G., & Ali, J. H. (2020). Molecular epidemiology of human papillomavirus among HIV infected women in developing countries: Systematic review and meta-analysis. *Virology Journal*, *17*(1), 179. https://doi.org/10.1186/s12985-020-01448-1

Brickman, C., & Palefsky, J. M. (2015). Human papillomavirus in the HIV-infected host: Epidemiology and pathogenesis in the antiretroviral era. *Current HIV/AIDS Reports*, *12*(1), 6–15. https://doi.org/10.1007/s11904-014-0254-4

Bukirwa, A., Mutyoba, J. N., N. Mukasa, B., Karamagi, Y., Odiit, M., Kawuma, E., & Wanyenze, R. K. (2015). Motivations and barriers to cervical cancer screening among HIV infected women in HIV care: A qualitative study. *BMC Women's Health*, *15*, 1-11.

Castle, P. E., Einstein, M. H., & Sahasrabuddhe, V. V. (2021). Cervical cancer prevention and control in women living with human immunodeficiency virus. *CA: A Cancer Journal for Clinicians*, *71*(6), 505–526. https://doi.org/10.3322/caac.21696

Chachage, M., Parikh, A. P., Mahenge, A., Bahemana, E., Mnkai, J., Mbuya, W., Mcharo, R., Maganga, L., Mwamwaja, J., Gervas, R., Kibuuka, H., Maswai, J., Singoei, V., Iroezindu, M., Fasina, A., Esber, A., Dear, N., Imbach, M., Crowell, T. A., … AFRICOS Study Group. (2023). High-risk human papillomavirus genotype distribution among women living with and at risk for HIV in Africa. *AIDS (London, England)*, *37*(4), 625–635. https://doi.org/10.1097/QAD.0000000000003437

Chaturvedi, A. K., Madeleine, M. M., Biggar, R. J., & Engels, E. A. (2009). Risk of human papillomavirus-associated cancers among persons with AIDS. *Journal of the National Cancer Institute*, *101*(16), 1120–1130. https://doi.org/10.1093/jnci/djp205

Cochran. (1963). *Cochran, W. G.: Sampling Techniques, 2. Aufl. John Wiley and Sons, New York, London 1963. Preis s—Heinisch—1965—Biometrische Zeitschrift—Wiley Online Library*. https://onlinelibrary.wiley.com/doi/abs/10.1002/bimj.19650070312

da Silva, B. E. B., Santos, V. S., Santos, I. E. R., Araujo, E. D., Alves, M. V., Silva, L. A. D. S., ... & de Lemos, L. M. D. (2020). Prevalence and genotype distribution of human papillomavirus in women living with HIV/AIDS in an area of Northeast Brazil. *Journal of Medical Virology*, *92*(12), 3279-3287. https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25935

Dareng, E. O., Adebamowo, S. N., Famooto, A., Olawande, O., Odutola, M. K., Olaniyan, Y., ... & Adebamowo, C. A. (2019). Prevalence and incidence of genital warts and cervical Human Papillomavirus infections in Nigerian women. *BMC infectious diseases*, *19*(1), 1-10.

De Sanjose, S., Quint, W. G., Alemany, L., Geraets, D. T., Klaustermeier, J. E., Lloveras, B., ... & Bosch, F. X. (2010). Human papillomavirus genotype attribution in invasive cervical cancer: A retrospective cross-sectional worldwide study. *The Lancet Oncology*, *11*(11), 1048-1056.

Dereje, N., Gebremariam, A., Addissie, A., Worku, A., Assefa, M., Abraha, A., Tigeneh, W., Kantelhardt, E. J., & Jemal, A. (2020). Factors associated with advanced stage at diagnosis of cervical cancer in Addis Ababa, Ethiopia: A population-based study. *BMJ Open*, *10*(10), e040645. https://doi.org/10.1136/bmjopen-2020-040645

Dreyer, G. (2018). Clinical implications of the interaction between HPV and HIV infections. *Best Practice & Research. Clinical Obstetrics & Gynaecology*, *47*, 95–106. https://doi.org/10.1016/j.bpobgyn.2017.08.011

Dunne, E., & Markowitz, L. (2006). Emerging infections: Genital human papillomavirus infection. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, *43*, 624–629. https://doi.org/10.1086/505982

Ferlay, J., Colombet, M., Soerjomataram, I., Mathers, C., Parkin, D. M., Piñeros, M., Znaor, A., & Bray, F. (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *International Journal of Cancer*, *144*(8), 1941–1953. https://doi.org/10.1002/ijc.31937

Gheit, T., Simoes, R. T., Tommasino, M., Donadi, E. A., & Gonçalves, M. A. G. (2006). HPV16 variants in squamous intraepithelial lesions in human immunodeficiency virus-negative and -positive Brazilian women. *Viral Immunology*, *19*(2), 340–345. https://doi.org/10.1089/vim.2006.19.340

Groves, I. J., & Coleman, N. (2015). Pathogenesis of human papillomavirus-associated mucosal disease. *The Journal of Pathology*, *235*(4), 527–538. https://doi.org/10.1002/path.4496

Hagensee, M. E., Cameron, J. E., Leigh, J. E., & Clark, R. A. (2004). Human papillomavirus infection and disease in HIV-infected individuals. *The American Journal of the Medical Sciences*, *328*(1), 57–63. https://doi.org/10.1097/00000441-200407000-00008

Haręża, D. A., Wilczyński, J. R., & Paradowska, E. (2022). Human papillomaviruses as infectious agents in gynecological cancers: Oncogenic properties of viral proteins. *International Journal of Molecular Sciences, 23*(3), 1818. https://doi.org/10.3390/ijms23031818

Hewavisenti, R. V., Arena, J., Ahlenstiel, C. L., & Sasson, S. C. (2023). Human papillomavirus in the setting of immunodeficiency: Pathogenesis and the emergence of next-generation therapies to reduce the high associated cancer risk. *Frontiers in Immunology, 14*, 1112513. https://doi.org/10.3389/fimmu.2023.1112513

Ibrahim Khalil, A., Mpunga, T., Wei, F., Baussano, I., de Martel, C., Bray, F., Stelzle, D., Dryden-Peterson, S., Jaquet, A., Horner, M., Awolude, O. A., Trejo, M. J., Mudini, W., Soliman, A. S., Sengayi-Muchengeti, M., Coghill, A. E., van Aardt, M. C., De Vuyst, H., Hawes, S. E., … Clifford, G. M. (2022). Age-specific burden of cervical cancer associated with HIV: A global analysis with a focus on sub-Saharan Africa. *International Journal of Cancer, 150*(5), 761–772. https://doi.org/10.1002/ijc.33841

ICO/IARC. (2021). Uganda: Human Papillomavirus and Related Cancers, Fact Sheet 2022. *Fact Sheet*, 2.

Itarat, Y., Kietpeerakool, C., Jampathong, N., Chumworathayi, B., Kleebkaow, P., Aue-Aungkul, A., & Nhokaew, W. (2019). Sexual behavior and infection with cervical human papillomavirus types 16 and 18. *International Journal of Women's Health*, 489-494.

Karadža, M., Židovec Lepej, S., Planinić, A., Grgić, I., Ćorušić, A., Planinić, P., Ćorić, M., Hošnjak, L., Fujs Komloš, K., Poljak, M., & Vince, A. (2021). Distribution of human papillomavirus genotypes in women with high-grade cervical intraepithelial lesions and cervical carcinoma

and analysis of human papillomavirus-16 genomic variants. *Croatian Medical Journal*, *62*(1), 68–79. https://doi.org/10.3325/cmj.2021.62.68

Karuri, A. R., Kashyap, V. K., Yallapu, M. M., Zafar, N., Kedia, S. K., Jaggi, M., & Chauhan, S. C. (2017). Disparity in rates of HPV infection and cervical cancer in underserved US populations. *Frontiers in Bioscience*, *9*, 254–269.

Kasibante, P., Kiboss, J., Atuhairwe, C., & Taremwa, I. (2020). Individual, health facility-related, and psychosocial determinants of retention in chronic HIV care among HIV-positive young people in Mukono Municipality, Uganda. HIV & AIDS Review. *International Journal of HIV-Related Problems*, 19(2), 99-105.

Khaali, W., Gihbid, A., Elamrani, A., Chaoui, I., Attaleb, M., Benhassou, M., Belghmi, K., El Mzibri, M., & Khyatti, M. (2019). Prevalence, genotype distribution and risk factors of human papillomavirus in Moroccan women. *Archives of Clinical and Biomedical Research*, *03*. https://doi.org/10.26502/acbr.50170083

Kombe Kombe, A. J., Li, B., Zahid, A., Mengist, H. M., Bounda, G.-A., Zhou, Y., & Jin, T. (2021). Epidemiology and burden of human papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation. *Frontiers in Public Health*, *8*, 552028. https://doi.org/10.3389/fpubh.2020.552028

Lam, J. U. H., Rebolj, M., Dugué, P.-A., Bonde, J., von Euler-Chelpin, M., & Lynge, E. (2014). Condom use in prevention of Human Papillomavirus infections and cervical neoplasia: Systematic review of longitudinal studies. *Journal of Medical Screening*, *21*(1), 38–50. https://doi.org/10.1177/0969141314522454

Lima, M. D. M., Braz-Silva, P. H., Pereira, S. M., Riera, C., Coelho, A. C., & Gallottini, M. (2014). Oral and cervical HPV infection in HIV-positive and HIV-negative women attending a sexual health clinic in São Paulo, Brazil. *International Journal of Gynaecology and Obstetrics: The Official Organ of the International Federation of Gynaecology and Obstetrics*, *126*(1), 33–36. https://doi.org/10.1016/j.ijgo.2014.01.017

Lubega, M., Okiira, C., Nabaggala, A., Achola, C., Kamuntu, Y., Musoke, A., Abala, A., & Ndidde, S. (2022). *Epidemiology of Human Papillomavirus genotypes and prevalence of cervical precancerous lesions among women with HIV results from a pilot cervical cancer screening program in Uganda*. Retrieved February 19, 2023, from https://programme.aids2022.org/Abstract/Abstract/?abstractid=3317

Mandiriri, A. M., Pascoe, M. J., Shamu, T., & Lowe, S. (2020). Cervical human papillomavirus prevalence, risk factors and outcomes in a cohort of HIV-infected women in Harare, Zimbabwe. *Southern African Journal of HIV Medicine*, *21*(1), 1123. https://doi.org/10.4102/sajhivmed.v21i1.1123

Martel, C., Plummer, M., Vignat, J., & Franceschi, S. (2017). Worldwide burden of cancer attributable to HPV by site, country and HPV type. *International Journal of Cancer, 141*. https://doi.org/10.1002/ijc.30716

Mbuya, W., Mcharo, R., Mhizde, J., Mnkai, J., Mahenge, A., Mwakatima, M., ... & Chachage, M. (2020). Depletion and activation of mucosal CD4 T cells in HIV infected women with HPV-associated lesions of the cervix uteri. *Plos One*, *15*(10), e0240154.

McClymont, E., Faber, M. T., Lindquist, S., Bone, J. N., & Kjær, S. K. (2022). Human papillomavirus infection among pregnant women living with HIV: A systematic review and meta-analysis. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *91*(2), 122. https://doi.org/10.1097/QAI.0000000000003050

Megersa, T., Dango, S., Kumsa, K., Lemma, K., & Lencha, B. (2023). Prevalence of high-risk human papillomavirus infections and associated factors among women living with HIV in Shashemene town public health facilities, Southern Ethiopia. *BMC Women's Health*, *23*(1), 125. https://doi.org/10.1186/s12905-023-02279-2

Mekonnen, A. G., & Mittiku, Y. M. (2023). Early-onset of sexual activity as a potential risk of cervical cancer in Africa: A review of literature. *PLOS Global Public Health*, *3*(3), e0000941. https://doi.org/10.1371/journal.pgph.0000941

Monteiro, J. C., Fonseca, R. R. D. S., Ferreira, T. C. D. S., Rodrigues, L. L. S., Da Silva, A. R. B., Gomes, S. T., ... & Machado, L. F. A. (2021). Prevalence of high risk HPV in HIV-Infected women from Belém, Pará, Amazon region of Brazil: A cross-sectional study. *Frontiers in Public Health*, *9*, 649152.

Monteiro, J. C., Tsutsumi, M. Y., de Carvalho, D. O., da Silva Costa, E. do C., Feitosa, R. N. M., Laurentino, R. V., de Souza Fonseca, R. R., Silvestre, R. V. D., Oliveira-Filho, A. B., & Machado, L. F. A. (2022). Prevalence, diversity, and risk factors for cervical HPV infection in women screened for cervical cancer in Belém, Pará, Northern Brazil. *Pathogens*, *11*(9), 960. https://doi.org/10.3390/pathogens11090960

Morshed, K., Polz-Gruszka, D., Szymański, M., & Polz-Dacewicz, M. (2014). Human Papillomavirus (HPV)—Structure, epidemiology and pathogenesis. *Otolaryngologia Polska = The Polish Otolaryngology*, *68*(5), 213–219. https://doi.org/10.1016/j.otpol.2014.06.001

Mousavi, A.-S., Pouryasin, A., Yarandi, F., Pirzadeh, L., Alipour, A., Khodadad, S., & Pouryasin, M. (2020). Assessment of cervical cancer molecular-based screening tools: HPV-DNA detection versus E6/E7 mRNA testing; First report of a prospective cohort study among Iranian Women. *Iranian Journal of Public Health*, *49*(9), 1734–1742. https://doi.org/10.18502/ijph.v49i9.4093

Nakisige, C., Schwartz, M., & Ndira, A. O. (2017). Cervical cancer screening and treatment in Uganda. *Gynecologic Oncology Reports*, *20*, 37–40. https://doi.org/10.1016/j.gore.2017.01.009

NCI. (2019, March 1). *HPV and Cancer—NCI* (nciglobal,ncienterprise) [CgvArticle]. https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer

Nelson, C. W., & Mirabello, L. (2023). Human papillomavirus genomics: Understanding carcinogenicity. *Tumour Virus Research*, *15*. https://doi.org/10.1016/j.tvr.2023.200258

Ohihoin, A. G., Okwuraiwe, P. A., Musa, A. Z., Olorunfemi, G., Onwuamah, C. K., Ige, F., Amoo, O. S., Audu, R., Okogbo, F., Daniyan, B., Swende, T., Onyemelukwe, G. C., Daru, H., Usman, H., Shittu, O., Musa, J., Ezechi, O. C., & Ujah, I. A. (2022). Prevalence and predictors of high-risk HPV in Nigeria. *Advances in Infectious Diseases*, *12*(04), 745–757. https://doi.org/10.4236/aid.2022.124052

Okoye, J. O., Ofodile, C. A., Adeleke, O. K., & Obioma, O. (2021). Prevalence of high-risk HPV genotypes in Sub-Saharan Africa according to HIV status: A 20-year systematic review. *Epidemiology and Health*, *43*, e2021039. https://doi.org/10.4178/epih.e2021039

Pala, V. S., Patil, C., Nagmoti, M. B., Dalal, A. D., & Mane, A. (2021). Detection of human papillomavirus genotypes in human immunodeficiency virus-negative women in Belagavi, Karnataka. *Indian Journal of Health Sciences and Biomedical Research kleu*, *14*(3), 322-327.

Pandey, D., Solleti, V., Jain, G., Das, A., Shama Prasada, K., Acharya, S., & Satyamoorthy, K. (2019). Human Papillomavirus (HPV) Infection in early pregnancy: Prevalence and implications. *Infectious Diseases in Obstetrics and Gynecology*, *2019*, 4376902. https://doi.org/10.1155/2019/4376902

Pedroza-Gonzalez, A., Reyes-Reali, J., Campos-Solorzano, M., Blancas-Diaz, E. M., Tomas-Morales, J. A., Hernandez-Aparicio, A. A., Montes de Oca-Samperio, D., Garrido, E., Garcia-Romo, G. S., Mendez-Catala, C. F., Alvarez Ortiz, P., Sánchez Ramos, J., Mendoza-Ramos, M. I., Saucedo-Campos, A. D., & Pozo-Molina, G. (2022). Human papillomavirus infection and seroprevalence among female university students in Mexico. *Human Vaccines & Immunotherapeutics*, *18*(1), 2028514. https://doi.org/10.1080/21645515.2022.2028514

Raddi, S. A., Dalal, A., & Castillino, R. B. (2012). Assessment of knowledge and perceived barriers to prevention of cervical cancer among women attending gynecology OPD at KLE's Dr Prabhakar Kore Hospital and Medical Research Center, Belgaum, Karnataka, with a view to develop an information booklet. *Journal of South Asian Federation of Obstetrics and Gynaecology*, *4*(3), 169–171. https://doi.org/10.5005/jp-journals-10006-1206

Roik, E., Sharashova, E., Kharkova, O., Nieboer, E., Postoev, V., & Odland, J. Ø. (2018). Sociodemographic characteristics, sexual behaviour and knowledge about cervical cancer prevention as risk factors for high-risk human papillomavirus infection in Arkhangelsk, North-West Russia. *International Journal of Circumpolar Health*, *77*(1), 1498681. https://doi.org/10.1080/22423982.2018.1498681

Sarah Maria, N., Olwit, C., Kaggwa, M. M., Nabirye, R. C., & Ngabirano, T. D. (2022). Cervical cancer screening among HIV-positive women in urban Uganda: A cross sectional study. *BMC Women's Health*, *22*, 148. https://doi.org/10.1186/s12905-022-01743-9

Seyler, L., Lacor, P., & Allard, S. D. (2018). Current challenges in the treatment of HIV. *Polish Archives of Internal Medicine*, *128*(10), 609–616. https://doi.org/10.20452/pamw.4357

Shahid et al. (2021). The relation of age on HIV-positive women's cluster of differentiation 4, antiretroviral therapy, Papanicolaou test, Human Papillomavirus test and visual inspection with Acetic Acid. *Journal of Healthcare, Science and the Humanities*, *11*(1), 37–50.

Stelzle, D., Tanaka, L. F., Lee, K. K., Khalil, A. I., Baussano, I., Shah, A. S. V., McAllister, D. A., Gottlieb, S. L., Klug, S. J., Winkler, A. S., Bray, F., Baggaley, R., Clifford, G. M., Broutet, N., & Dalal, S. (2021). Estimates of the global burden of cervical cancer associated with HIV. *The Lancet Global Health*, *9*(2), e161–e169. https://doi.org/10.1016/S2214-109X(20)30459-9

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide

for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

Swai, P., Rasch, V., Linde, D. S., Mchome, B., Manongi, R., Wu, C. S., Waldstrom, M., Iftner, T., Mwaiselage, J., & Kjaer, S. K. (2022). Persistence and risk factors of high-risk human papillomavirus infection among HIV positive and HIV negative Tanzanian women: A cohort study. *Infectious Agents and Cancer*, *17*(1), 26. https://doi.org/10.1186/s13027-022-00442-2

Taku, O., Businge, C. B., Mdaka, M. L., Phohlo, K., Basera, W., Garcia-Jardon, M., Meiring, T. L., Gyllensten, U., Williamson, A.-L., & Mbulawa, Z. Z. A. (2020a). Human papillomavirus prevalence and risk factors among HIV-negative and HIV-positive women residing in rural Eastern Cape, South Africa. *International Journal of Infectious Diseases*, *95*, 176–182. https://doi.org/10.1016/j.ijid.2020.02.051

Tam, S., Fu, S., Xu, L., Krause, K. J., Lairson, D. R., Miao, H., ... & Dahlstrom, K. R. (2018). The epidemiology of oral human papillomavirus infection in healthy populations: A systematic review and meta-analysis. *Oral Oncology*, *82*, 91-99.

Tiiti, T. A., Selabe, S. G., Bogers, J., & Lebelo, R. L. (2022b). High prevalence of and factors associated with human papillomavirus infection among women attending a tertiary hospital in Gauteng Province, South Africa. *BMC Cancer*, *22*(1), 854. https://doi.org/10.1186/s12885-022-09964-9

Torode, J., Kithaka, B., Chowdhury, R., Simelela, N., Cruz, J. L., & Tsu, V. D. (2021). National action towards a world free of cervical cancer for all women. *Preventive Medicine*, *144*, 106313. https://doi.org/10.1016/j.ypmed.2020.106313

Wang, X., Han, S., Li, X., Wang, X., Wang, S., & Ma, L. (2022). Prevalence and distribution of human papillomavirus (HPV) in Luoyang city of Henan province during 2015–2021 and the genetic variability of HPV16 and 52. *Virology Journal*, *19*, 37. https://doi.org/10.1186/s12985-022-01759-5

Wentzensen, N., Schiffman, M., Dunn, S. T., Zuna, R. E., Walker, J., Allen, R. A., Zhang, R., Sherman, M. E., Wacholder, S., Jeronimo, J., Gold, M. A., & Wang, S. S. (2009). Grading the severity of cervical neoplasia based on combined histopathology, cytopathology, and HPV genotype distribution among 1,700 women referred to colposcopy in Oklahoma. *International Journal of Cancer*, *124*(4), 964–969. https://doi.org/10.1002/ijc.23969

WHO. (2008). *Comprehensive cervical cancer control—A guide to essential practice*. WHO | Regional Office for Africa. https://www.afro.who.int/publications/comprehensive-cervical-cancer-control-guide-essential-practice

WHO. (2013). *WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention: Supplemental material: GRADE evidence-to-recommendation tables and evidence profiles for each recommendation*. World Health Organization. https://apps.who.int/iris/handle/10665/96735

WHO. (2019). *Report of the Regional meeting on prevention of cervical cancer through HPV vaccination New Delhi, India, 5–7 June 2018*. World Health Organization. Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/333279

Yang, D., Zhang, J., Cui, X., Ma, J., Wang, C., & Piao, H. (2022). Risk factors associated with human papillomavirus infection, cervical cancer, and precancerous lesions in large-scale population

screening. *Frontiers in Microbiology*, *13*. https://www.frontiersin.org/articles/10.3389/fmicb.2022.914516

Yang, Q., & Al-Hendy, A. (2022). The regulatory functions and the mechanisms of long non-coding RNAs in cervical cancer. *Cells*, *11*(7). https://doi.org/10.3390/cells11071149

Yeh, P. T., Kennedy, C. E., de Vuyst, H., & Narasimhan, M. (2019). Self-sampling for human papillomavirus (HPV) testing: A systematic review and meta-analysis. *BMJ Global Health*, *4*(3), e001351. https://doi.org/10.1136/bmjgh-2018-001351

Zhao, D., Zhang, L., Xie, F., Peng, D., Wei, J., Jiang, L., Zhang, S., & Qi, D. (2020). Outcomes of prior cervical cytology and HR-HPV testing in women subsequently diagnosed with CIN1, CIN2/3, and invasive cervical cancer: A 4-year routine clinical experience after implementation of systematic training and quality control programs. *BMC Cancer*, *20*, 810. https://doi.org/10.1186/s12885-020-07321-2

Zhu, C., Wang, Y., Mao, W., Zhang, H., & Ma, J. (2019). Prevalence and distribution of HPV types in genital warts in Xi'an, China: A prospective study. *BMJ Open*, *9*(5), e023897. https://doi.org/10.1136/bmjopen-2018-023897

Zinzendorf, N. Y. (2022). Prevalence and human papillomavirus genotypes distribution among HIV-positive and -negative young women aged 20 to 37-years-old with cervical cancer in Abidjan, Côte d'Ivoire. *International Journal of Virology and AIDS*, *9*(1), 080. https://doi.org/10.23937/2469-567X/1510080

Appendix I: Informed Consent (English Version)

TITLE OF THE STUDY: Characterization of Human Papillomavirus Genotypes and their correlates among women living with HIV Attending antiretroviral therapy clinic in Mukono, Uganda

INSTITUTIONS: Amref international university (AMIU), African population and health research council (APHRC)

PRINCIPAL INVESTIGATOR: Ms. Nantale Prossy Nabattte

CO-INVESTIGATORS: Dr. Josephat Nyagero (AMIU), Dr. Elizabeth Kemigisha (APHRC)

STUDY LOCATION: The study is to be carried out at Mukono General Hospital in Mukono town, Uganda

Explanation of the purposes of research

You have been asked to participate in this study. The information below involves things you should consider before participating in the study. You are free to ask any questions about the study. You are free inquire to from your doctor, family or friends before you join.

Important information to consider before you join.

Voluntary consent: You have been asked to join the study. It is upon you to decide to join or not. There are no penalties if you join or not or if you choose to leave after joining the study.

Purpose of this research: The research is being done to describe HPV genotypes and their correlates among WLHIV attending antiretroviral therapy clinic in Mukono, Uganda

Duration: Your part in this study will only take about 30 minutes with the interviewer.

Procedures

We will ask you to provide us with information through a series of questions to know your risk of developing HPV infection. The study you are going to participate in will help us to understand the presentation of HPV genotypes and their correlates among WLHIV attending the antiretroviral therapy in Mukono, Uganda.

What is HPV infection?

Human Papillomavirus infection is the most common sexually transmitted infection worldwide. It is the cause of cervical cancer which is fatal.

Why do we want to conduct the study?

In this study we are going to explore the HPV genotypes and their correlates among WLHIV attending the antiretroviral therapy clinic in Mukono, Uganda. Previous studies have shown that cervical cancer is the leading cause of cancer morbidity and mortality among women worldwide. In Uganda many women are diagnosed in the late stage which is fatal. But cervical cancer can be prevented through early screening and treatment. Therefore, this study will help generate data about the Characterization of the HPV genotypes and their correlates in WLHIV attending antiretroviral therapy clinic in Mukono, Uganda. This will help in the vaccination campaigns giving information about the strains the effective vaccine should contain and which group needs the greatest attention. It will also inform policy makers of the importance of screening and vaccination for HPV infection.

Procedures to be followed

To conduct this study, we will need a face to face interview with you which will take a few hours where we shall ask for your personal and sensitive information. About your age, marital status, education and your social life.

You may choose to withdraw from the study at any time without penalty. You will be assigned a study number and the links between the name and the number. All the data collected will be confidential and none of the data collected will be told to other people.

Risks Involved

The risks involved while you take part in this study is the violation of privacy while the interview is going on. The interviewer will be well trained and will change the topic as soon as this happens. You will be informed of the prevention steps before the interview begins. You can choose any area of your convenience to take the interview.

Potential benefits

You will receive counselling on ways to avoid exposure to HPV infection.

Compensation

An amount of 20,000ugx will be given as a compensation for your transport and time.

Confidentiality

We will maintain confidentiality and privacy throughout the entire process. The interviews will be conducted in the private room. All the data collected will be coded to protect your identity. Only the interviewer will have access to your information. After the study there will be no connection between your name and information given. In case of any changes there will be communication.

Questions about research

If you have any questions about this study, you can contact Ms. Nantale Prossy Nabatte

Contact 0782050026 or Dr. Nyagero Josephat Dean of students Amref International University Contact: +254722301689 or Dr. Elizabeth Kemigisha APHRC contact 0772858818

This study was reviewed and approved by Uganda Christian University Research Ethical Committee, in case of ethical concerns and participants' rights contact Uganda Christian university Research Ethical Committee chairperson, Prof. Peter Waiswa Contact: 0772405357 Email: pwaiswa@musph.ac.ug Or Secretariat, Mr. Ahimbisibwe Osborn Contact: 0775737627, Email: oahimbisibwe@ucu.ac.ug

Consent

Statement of the consent after understanding the study and signature portion

STATEMENT OF CONSENT

I (respondent's Name) _____ agree that the benefits, risks and my rights regarding this study have been explained to me.

I understand that my decision to participate in this study will not change my usual medical care. In the use of the information my identity will be concealed. I am aware that I may withdraw anytime. I understand that by signing this form I do not waive any legal rights but indicate that I have been informed about the study in which I am voluntarily agreeing to participate. A copy of this form will be provided to me.

Name……Signature/ thumb print of the participant……Date.....

or Witness…….. Signature/ thumb print of the Witness……Date.....

Name…….....Signature of the interviewer/ Person obtaining the informed

consent……. Date……..

Appendix II: Informed Consent (Luganda Version)

OKUKKIRIZIBWA OKUMANYIDDWA

OMUTWE GWOKUNONYEREZA / Omusomo: Eneeyisa y'e bika bw'obuwuka obulwaza kkookolo w'omumwa gwa nabaana ne ngeri gy'ekosaamu abakyala abafuna obujjanjabi obukakkanyaku akawuka ka mukenenya mu ddwaliro e Mukono.

EBITONGOLE: AMREF International University (AMIU), African population and health research council.

OMUNONYEREZA OMUKULU: Mukyala Nantale Prossy Nabatte

BAANANONYEREZA NABO: Dr. Josephat Nyagero (AMIU)

: Dr. Elizabeth Kemigisha (APHRC)

EKIFO AWANABEERA OMUSOMO

Okunonyereza kwa kubeera ku ddwaliro ku lya Mukono general hospital mu Kibuga kye Mukono mu Uganda.

Okunyonyola Ensonga Y'okunonyereza

Osabiddwa okwenyigira mu musomo guno.

Obubaka wammanga bulimu ebintu byolina okufaako nga tonenyeginra musomo. Oliwaddembe okubuuza ebibuuzo ebikwata ku musomo. Oli waddembe okubuuza ebibuzo ebikwata ku musomo. Oli waddembe okwebuuza ku musawo omukugu (Doctor), ab'enju

yo oba mikwano gyo nga tonaba kwegatta ku musomo.

Obubaka Bw'omugaso Bw'otekeddwa Okufaako Nga Tonaba Kwegatta Musomo.

Okukkiriza kwa kyeyagalire: Osabiddwa okwegatta ku musomo. Kiri eri gwe okusalawo okugwegattako oba akugaana. Tewali bibonerezo singa ogwegattako oba nedda oba singa osalaawo okuguvaamu nga obadde omazze okugwegattako.

Ensonga y'okunonyera kuno:

Okunonyereza kukolebwa okunyonyola ebika by'obuwuka obulwaaza kkookolo w'omumwa gwa nabaana ne ngeri gyebikosaamu abakyala abafuna obujjanjabi obukkakanya ku kuwuka ka mukenenya mu ddwaliro e Mukono mu Uganda. **Obudde Bwonomala**

Kijja kutwalirira eddakika asattu (30min) gokka ng'oli noyo akubuuza ebibuuzo.

Enkola ezinagobererwa

Tujja kukusaba otuuwe obudde oba amawulire nga tuyita mu nkalala ze bibuuzo okumanya akatyabaga oba obulabe bw'olina ku kukwatibwa akawuka aleeta kkookolo w'omumwa gwa nabaana.

Omusomo gwogenda okwetabaamu gujja kutuyamba okutegera enneyoleeka y'obuwuka obulwaaza kkookolo w'omumwa gwa nabaana ne ngeri gyebukosaamu abakyala abafuna obujjanjabi obukkakanya akawuka ka mukenenya mu Uganda.

Akawuka akalwaza kkookolo w'omumwa gwa nabaana kye ki?

Akawuka akalwaza kkookolo w'omumwa gwa nabaana y'eddwadde ekyasinze okusigibwa okuyita mu kwegatta. Kekaleetera kkookola w'omumwa gwa nabaana namutta.

Lwaki twagala okukola omusomo guno?

Mumusomo guno tugenda kwongera kuvvumbula ebika by'obuwuka obuleta kkookolo gw'omumwa gwa nabaana n'engiri gyebikosaamu abakyala abaali mu kufuna obujjanjabi obukkakanya akawuka akaleeta mukeneya mu Uganda. Emisomo egyakakolebwa emabegaako jiraze nti kkookolo w'omumwa gwa nabaana y'eddwadde esinga okutta abakyala munsi yonna. Ekyobulabe, mu Uganda obulwadde buno bugenda okuzulibwa mu bakyala nga buli mumutendera ogusembayo. Naye kkookolo asobola okuziyizibwa singa omuntu aba akebereddwa nga bukyali naafuna obujjanjabi. N'olwekyo omusomo guno gujjakuyamba okufuna amawulire agakwatta kuneyiisa n'ebika by'obuwuka obulwaaza kkookolo w'omumwa gwa nabaana n'engeri gyebikosaamu abakyala abafuna obujjanjabi obukkakanya akawuka ka mukenenya mu ddwaliro e Mukono mu Uganda.

Enkola ezinaagobererwa

Okukola omusomo guno, tujja kwetaaga okukubuuza ebibuuzo maaso ku maaso nga kijja kututwalira essaawa ntono nga tujja kukubuuza ebikukwatako gwe nga omuntu, emyaka gyo, oli mufumbo oba toli, obuyigirize n'obulamu bwo obwa bulijjo. Osobola okusalawo okuva mu

musomo wonna woyagalidde, tewali kibonerezo kyonna mu kino. Ojja kuweebwa ennamba kwonoosomera nennyungiro y'erinnya n'ebbanga. Byonna ebinaakubuuzibwa bijja kuba bya kyama era teri kijja kugambibwa bantu balala.

Obulabe obukirmu

Obulabe obuyinza okubaawo nga wenyigidde mu musomo guno kwe kutyoboola eddembe ly'obuntu eryekyama nga akubuuza ebibuuzo kugenda mu maaso. Abuuza ebibuuzo ajjakutendekebwa nga singa kino kibaawo, akyusizaawo omulamwa mangu nnyo. Ojakutegezeebwa emitendera gyokuziyiza kino ng'okubuuza ebibuuzo tekunaabawo. Osobola okwerondera ekifo ekikuwa emirembe woyinza okubuuzibwa ebibuuzo.

By'oyinza okufunamu

Ojjakufuna okubuddabudibwa kungeri yokwewalamu akawuka akaleeta kkookolo w'omumwa gwa nabaana.

Okuliyilirwa

Siringi emitwalo ebiri eja Uganda (20,000/=) zijja kuweebwa okukuliyilirwa ssente zonaaba osasanyiza mu ntambula n'obudde bwo.

Okukuma ebyama

Tujjakukuma ebyama mu musomo guno gwona. Okubuuza ebibuuzo kujja kubeera mu kasenge akekyama. Byona byonotubuulira bijja kuwebwa ennamba so ssi mannya go okusobola okukuma ebikukwatako. Akubuuza ebibuuzo yekka yajja okufuna ebikukwatako. Era mu musomo nga guwedde tewajja kuba kakwatte ku linnya lyo

nebyotubulidde. Singa wanabeerawo enkyuka kyuka zonna tujjakuba tukutegeza.

Ebibuuzo ebikwata kukunonyereza

Singa oba n'ebibuuzo ebikwata ku musomo guno, osobola okukubira Mukyala Nantale Prossy Nabatte ku number 0782-050026 oba Dr. Nyangero Josephat atwala abayizi ku ssettendekero lya Amref International University ku nnamba +254 722301689 oba Dr. Kemigish (APHRC) ku nnamba 0772-858818.

Omusomo guno gwekenezedwa era negukkakasibwa akakiiko ku ssettendekero lya Uganda Christian University akakola kubyekikugu mu kunoonyereza. Singa oba n'ensonga yona ekwata ku neeyisa eyekikuggu ssaako n'eddembe ly'abo abeetabye mu kunoonyereza, kubira ssentebe wa kakiiko omukenkufu (Professor) Waiswa ku nnamba y'essimu 0772405357 oba omuwandiikire obubaka nga oyita kumutimbagano ku pwaiswa@musph.ac.ug oba okubiire omuwandiisi Mw. Ahimbisibwe Osborn ku nnamba y'essimu 0775-737627 oba muwereze obubaka obuwandiike ku mutimbagano ku oahimbisibwe@ucu.ac.ug.

Okukkiriza

Obuwandiike obukkiriza oluvanyuma lwo kutegera n'okunyonyoka omusomo n'okusaako omukono.

Obuwandiike obukkiriza

Nze (erinnya ly'oyo addamu ebibuuzo) ..... nzikirizza nti, emiganyulo, obulabe n'eddembe lyange ebikwata ku musomo guno binnyinyonyodwa. Nkitegeera nti

okusaalawo kwange okwetaba mu musomo guno tekijja kukyusa bujjanjabi bwange obwa bulijjo. Mu kukozesa ebivvude mu musomo ebinkwatako byakozesa mu kukwekebwa si bya kulagibwa. Nkimanyi bulungi nti nsobola okuva musomo guno obudde bwonna. Nkitegeera nti okussa omukono ku kiwandiiko kino sirina ddembe lyenzijjaawo naye mbeera ndaga nti ntegezeddwako ku musomo nze kenyini kyeyagarire gwenzikiriza okwetabamu. Kkopi ku kiwandiiko kino ejjakumpeebwa.

Erinnya ..... Omukono / Ekyenkumu ky'oyo eyeetabye mu musomo ..... Ennaku z'omwezi .....

Erinnya ..... Omukuno gw'oyo abuuza / omuntu anonya okukkiriza kw'oyo eyeetabye musomo..... Ennaku z'omwezi.

Appendix III: Approval and Authorization Licenses

UGANDA CHRISTIAN UNIVERSITY
A Centre of Excellence in the Heart of Africa

04/11/2022
To: PROSSY NANTALE

AMREF INTERNATIONAL UNIVERSITY
0782050026

Type: Initial Review

Re: UCUREC-2022-404: CHARACTERIZATION OF HUMAN PAPILLOMAVIRUS GENOTYPES AND THEIR CORRELATES AMONG WOMEN LIVING WITH HIV ATTENDING ANTIRETROVIRAL THERAPY CLINIC IN MUKONO, UGANDA, 1, 2022-10-31

I am pleased to inform you that the Uganda Christian University REC, through expedited review held on **04/11/2022** approved the above referenced study. Approval of the research is for the period of **04/11/2022** to **04/11/2023.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re-review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **04/11/2023** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.

6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by Uganda Christian University REC:

No.	Document Title	Language	Version Number	Version Date
1	Prior Ethical Approval	English	1	2022-10-31
2	Protocol	English	1	2022-10-31
3	Informed Consent forms	English	1	2022-10-31
4	Data collection tools	English	1	2022-10-31

Yours Sincerely

Peter Waiswa For: Uganda Christian University REC

MUKONO GENERAL HOSPITAL
MUKONO DISTRICT
PO BOX 472
MUKONO.

The Republic of Uganda

MUKONO GENERAL HOSPITAL
MUKONO DISTRICT
PO BOX 472
MUKONO.
Email: mukonogeneralhospital@gmail.com
For any correspondence on this Note, please quote ref No…….

The Republic of Uganda

09 NOVEMBER 2022

EXECUTIVE SECRETARY
UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

Dear Sir/Madam

RE: PERMISSION TO CONDUCT RESEARCH AT MUKONO GENERAL HOSPITAL

I am writing this reference at the request of Prossy Nantale who is doing her Master's degree in Epidemiology and Biostatistics under public Health at Amref International University.
I have known Ms. Nantale for over three years in my capacity as a Medical Superintendent of Mukono General Hospital. She was employed as a Laboratory Technologist by Makerere University Walter Project and attached to Mukono General Hospital in 0ctober 2018. She is a very proactive and hardworking employee and this has prompted management to delegate more responsibilities of a Deputy Quality Manager which she has performed and additional responsibilities of a Hub Coordinator which she is doing diligently. Basing on Prossy's Performance, attendance and participation, I would rate her job performance in the Lab as Excellent.

She showed interest to conduct her research on Characterization of Human Papillomavirus Genotypes and their Correlates among women attending Antiretroviral Therapy clinic in Mukono, Uganda at Mukono General Hospital for the award of Master's degree in Epidemiology and Biostatistics under Public Health at Amref International University.

This research will entail collecting data from the Mukono General Hospital Laboratory for Xpert Human Papillomavirus results and also women attending Antiretroviral Therapy clinic in Mukono General Hospital will be invited to participate in this study. If they agree, they will be interviewed for 30 minutes and data will be filled in the interview guide which will be used. Participants will be asked to give their written or verbal consent before the research begins. Their responses will be treated confidentially, and identities (their names and the name of the organization) will be anonymous. Individual privacy will be maintained in all published and written data resulting from the study. The results will be communicated through dissertation and academic journals.

The research participants will not be advantaged or disadvantaged in any way. They will be reassured that they can withdraw their participation at any time during this project without any penalty. There are no foreseeable risks in participating in this study. The participants will not be paid for this study.

The research has been approved by the Uganda Christian University Research Ethical Committee (REC) to be conducted at Mukono General Hospital. And as management, we have cleared the researcher to conduct this research at the hospital.

This therefore serves to request you to permit Nantale Prossy (the Researcher) to carry out the above titled research in Uganda as a requirement by the University in which she is pursuing her Master's degree.

Yours Faithfully,

Dr. Kasirye Geoffrey
Medical Superintendent
Mukono General Hospital
Email; kasirye2004@gmail.com,
Mob No. +256774555542

Appendix V: National Permit

Uganda National Council for Science and Technology

(Established by Act of Parliament of the Republic of Uganda)

PROSSY NANTALE Makerere University Walter Reed Project
Kampala

Re: Research Approval: CHARACTERIZATION OF HUMAN PAPILLOMAVIRUS GENOTYPES AND THEIR CORRELATES AMONG WOMEN LIVING WITH HIV ATTENDING ANTIRETROVIRAL THERAPY CLINIC IN MUKONO, UGANDA

I am pleased to inform you that on **23/11/2022**, the Uganda National Council for Science and Technology (UNCST) approved the above referenced research project. The Approval of the research project is for the period of **23/11/2022** to **23/11/2023**.

Your research registration number with the UNCST is **HS2550ES**. Please, cite this number in all your future correspondences with UNCST in respect of the above research project. As the Principal Investigator of the research project, you are responsible for fulfilling the following requirements of approval:

1. Keeping all co-investigators informed of the status of the research.
2. Submitting all changes, amendments, and addenda to the research protocol or the consent form (where applicable) to the designated Research Ethics Committee (REC) or Lead Agency for re-review and approval **prior** to the activation of the changes. UNCST must be notified of the approved changes within five working days.
3. For clinical trials, all serious adverse events must be reported promptly to the designated local REC for review with copies to the National Drug Authority and a notification to the UNCST.
4. Unanticipated problems involving risks to research participants or other must be reported promptly to the UNCST. New information that becomes available which could change the risk/benefit ratio must be submitted promptly for UNCST notification after review by the REC.
5. Only approved study procedures are to be implemented. The UNCST may conduct impromptu audits of all study records.
6. An annual progress report and approval letter of continuation from the REC must be submitted electronically to UNCST. Failure to do so may result in termination of the research project.

Please note that this approval includes all study related tools submitted as part of the application as shown below:

No.	Document Title	Language	Version Number	Version Date
1	Data collection tools	English	1	31 October 2022
2	Informed Consent forms	English	1	31 October 2022
3	Project Proposal	English	1	
4	Approval Letter	English		
5	Administrative Clearance	English		
5	Interview guide	Luganda	1	15 November 2022
6	IPC PLAN	English	1	17 November 2022

Yours sincerely,

Hellen Opolot
For: Executive Secretary

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda
P.O. Box 6884
KAMPALA, UGANDA

COMMUNICATION

TEL: (256) 414 705500
FAX: (256) 414-234579
EMAIL: info@uncst.go.ug
WEBSITE: http://www.uncst.go.ug

Appendix VI: Interview Guide (English Version)

Factors associated with HPV- HIV Coinfection

This section asks about conditions that may predispose you to HPV infection.

Socio-Demographics

Q1. How old are you? _____in complete

years Q2. What is your level of education?

a) PLE certificate
b) O level certificate
c) Advanced level Certificate
d) Diploma
e) Degree

Q3 What is your marital status?

a) Single
b) Married
c) Divorced
d) Widowed

Sexual Activity

Q4. Are you sexually active?

a) Yes

b) No

Q5. If yes, at what age did you become sexually active? _____years

Q6. How long have you been sexually active? _____years

Q7. Have you had more than one sexual partner in the last three months?

a) Yes

b) No

Q8. How many sexual partners have you had in the last three months? _____

partners Q9. Have you consistently had protected sexual intercourse?

a) Yes

b) No

Q10. At what age did you become sexually active? _____ years

Medical History

Q11. Have you ever developed genital warts?

a) Yes

b) No

Q12. If yes, were they medically treated?

a) Yes

b) No

Q13. Did the genital warts reoccur?

a) Yes

b) No

Q14. Are you currently pregnant?

a) Yes

b) No

Q15. Have you ever given birth?

a) Yes

b) No

Q16. If yes, how many children do you have? _____ children

Q17. How old is the youngest? _____ years

Q18. Do you use condoms?

a) Yes

b) No

Q19. If yes how often if having multiple partners?

a) Never

b) Always

c) Sometimes

d) Others, specify _____

Q20. Have you ever used family planning methods?

a) Yes
b) No

Q 21. If yes, which family planning method are you currently using?

a) Condoms
b) Oral Contraceptives

c) Injectaplan

d) Norplant

e) Others specify _____

Q22. How long have you been on family planning? _____year

Appendix VII: Interview Guide (Luganda Version)

ENNAMBIKA Y'EBIBUUZO

Ensonga ezzetolera ku kawuka akalwaza kkookolo w'omumwa gwa nabaana n'akamukenenya.

Ekitundu kino kibuuza ku mbeera eziyinza okukussa mu mbeera ekwatibwa akawuka akalwaza kkookolo w'omumwa gwa nabaana.

Embeera z'abantu

Ekib: 1. Olina emyaka emeeka? ..... Emyaka mu bujjuvu.

Ekib: 2. Oli kumutendera ki oba ddaala ki ery'obuyigirizze?

a. PLE (P.7 – Kyamusanvu)
b. O'level (S.4- Siniya ey'okuna)
c. A'level (S.6 – Siniya ey'omukaaga)
d. Dipulooma
e. Digguli esooka

Ekib: 3. Oli mufumbo oba toli?

a. Ndi nzekka
b. Ndi mufumbo
c. Nanoba
d. Ndi namwandu

Ensonga Z'omukwano / Ez'omukisenge.

Ekib: 4. Okola bulungi bwekituuka munsonga zomukisenge oba mu by'okwegatta? Mu mukwano

a. Yee nkola bulungi
b. Nedda

Ekib: 5. Bwoba nga okola bulungi, watandikira ku myaka emeka okufuna obwetaavu bw'okwetaba mu bikolwa ebyokwegatta? Emyaka .....?

Ekib: 6. Omaze bbanga ki nga weetaba mu nsonga z'omukwano oba nga wegatta? Emyaka.....

Ekib: 7. Obaddeko n'ababeezi mu by'omukwano abasukka mw'omu mu myenzi esatu egiyise

a. Yee
b. Nedda

Ekib: **8**. Obadde n'ababeezi bameka mu by'omukwano mu myezi esatu egiyise? Ababeezi .....

Ekib: 9. Obaddenga weekuma buli lwobaddenga ogenda okwegatta mu mukwano?
a. Yee
b. Nedda

Ebyafaayo by'obulamu bwo
Ekib: **10.** Wali ofunyeeko ku bulwadde mu bitundu eby'ekyama abuleetebwa kkookolo w'omumwa gwa nabaana?
a. Yee
b. Nedda

Ekib: **11**. Bwoba nga wali obulwaddeko, wafuna obujjanjabi obwekikugu mu ddwaliro.
a. Yee
b. Nedda

Ekib: **12**. Obulwadde buno mu bitundu ebyekyama bwa ddamu nebulabika nate?
a. Yee
b. Nedda

Ekib: 13. Oli lubuto mu kaseera kano?
a. Yee
b. Nedda

Ekib: **14**. Wali ozaddeko?

a. Yee
b. Nedda

Ekib: 15. Oba wazaalako, olina abaana bameeka? Abaana .....

Ekib: 16. Omwana asembaayo omuto wamyaka emeka?
Emyaka .....

Ekib: 17. Okozesa obupiira bukalimpitawa?

a. Yee
b. Nedda

Ekib: 18. Bwobanga obukozesa, obukozesa emirindi emeka bwoba nga olina ababeezi abenjawulo?

a. Ssibukozesa
b. Mbukozesa bulijjo
c. Lumu na lumu
d. Ekirala, nnyonnyola.....

Ekib: 19. Wali okozesezza ku nkola eyekizaala ggumba?

a. Yee
b. Nedda

Ekib: 20. Bwobanga wazikozesaako, mu kiseera kino okozesa nkola ki

a. Obupiira bu kalimpiitawa
b. Empeke ez'okumira
c. Empiiso
d. Obuti obuteekebwa ku mukono okuziyiza okuzaala
e. Ekirala, Nnyonnyola .....

Ekib: 21. Omaze bbanga ki ku nkola ey'ekizaala ggumba
Emyaka .....

Appendix VIII: Originality Report

Characterizations of HPV5

ORIGINALITY REPORT

10%	9%	5%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.science.gov Internet Source	1%
2	dspace.mak.ac.ug Internet Source	<1%
3	www.researchgate.net Internet Source	<1%
4	www.mdpi.com Internet Source	<1%

e