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PREVALENCE AND RISK FACTORS ASSOCIATED WITH HUMAN PAPILOMAVIRUS AMONG CERVICAL CANCER PATIENTS ATTENDING PARIRENYATWA GROUP OF HOSPITALS FROM JANUARY TO MAY 2023

BY

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A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF BACHELOR OF MEDICAL LABORATORY SCIENCES (HONOURS) IN THE COLLEGE OF HEALTH, AGRICULTURE AND NATURAL SCIENCES

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Abstract

HPV is the most common sexually transmitted infection and the most significant risk factor of cervical cancer. Every year, thousands of women are diagnosed with cervical cancer and die from the disease in Zimbabwe and worldwide. This cross sectional research was done to determine the prevalence of HPV in cervical cancer patients at PGH Harare, Zimbabwe with special attention on the risk factors, clinical manifestation, methods of screening diagnosing and prevention of HPV in cervical cancer patients.The study was done at PGH using preexisting data to estimate the prevalence of HPV in cervical cancer patients. From the study HPV DNA was identified in 85 % of the patients samples. HPV type 16 and 18 were the most common strains of HPV causing cervical cancer identified. The most common method used for diagnosis and screening for cervical cancer was the convectional pap smear. Other methods included; liquid based cytology, HPV testing and visual inspection on acetic acid. Majority of the subjects presented with abnormal vaginal bleeding and discharge. Smoking habits, use of oral contraceptives, having multiple sex partners were also contributing factors to the disease. Methods of prevention for HPV in cervical patients included; HPV vaccination and frequent screening for early detection and treatment. Patients with minor HPV infections were given topical treatments while those with invasive forms were put through surgery, radiation or chemotherapy depending on the severity of the disease. The researcher recommends, improved screening and vaccination programs, proactive campaigns to raising awareness on HPV and improved healthcare accessibility.

Key words; Prevalence, HPV, Cervical Cancer

Declarations

I Lucy Wangari hereby declare that this study is my original work and has not been submitted to any other university for any award. Other author's work used in this proposal have been acknowledged accordingly.

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List of acronyms and abbreviations

AUREC: Africa University Research Ethics Committee

ACIP: Advisory Committee on Immunization Practices

WHO: World Health Organisation

ICO: Catalan Institute of Oncology

IARC: International Agency for Research on Cancer

CDC: Center for Disease Control

DNA: Deoxyribonucleic acid

MOH: Ministry of health

PGH: Parirenyatwa Group of Hospitals

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CHAPTER 1 INTRODUCTION

1.0 Introduction

Human papilloma virus (HPV) infection is recognized as a primary etiological factor in the development of cervical cancer, one of the leading causes of cancer-related mortality among women worldwide (Cancer research UK,2023 and Statista, 2022). This chapter aims to provide a comprehensive review of the prevalence and risk factors associated with HPV infection in cervical cancer patients. Through a systematic review of literature and empirical research, this chapter gives a brief background on the disease examining; the epidemiology of HPV, exploring its molecular mechanisms in cervical carcinogenesis, evaluating the prevalence rates of HPV in cervical cancer patients in Zimbabwe and globally, as well as highlighting the significance of this study in provoking the establishment of health intervention aimed at implementing effective prevention strategies and improve cervical cancer screening and treatment outcomes. Furthermore, the chapter sets the study's goal as well as research questions to be used in subsequent chapters.

1.1 Background of the Study

Human papillomavirus (HPV) is the most common sexually transmitted infection and a known risk factor for cervical cancer (CDC, 2023). According to WHO, the human papillomavirus (HPV) is a tiny, non-enveloped DNA virus that infects skin or mucosal cells (WHO,2022). The circular, double-stranded viral genome is around 8 kb long. The genome encodes six early proteins involved in virus replication as well as two late proteins, L1 and L2, which are viral structural proteins. Additionally, according to the WHO, at least 13 of the more than 100 known HPV genotypes have

been associated to head and neck malignancies in addition to being known to cause cervical cancer.

HPV 16 and 18 are the two most frequent "high-risk" genotypes, accounting for over 70% of all cervical cancers. Two "low-risk" genotypes (HPV 6 and 11) cause genital warts, a typical benign disorder of the external genitalia that generates major morbidity (Juckett, 2020). Most individuals become infected with HPV at some point in their life because it is very contagious and reaches its peak occurrence soon after the start of sexual activity(GLOBACAN, 2012).

In 2020, there were over 500,000 reported cases of cervical cancer worldwide, with over 300,000 deaths (WHO, 2022). Ninety percent of these deaths occur in low-income nations where cancer prevention and control strategies remain inadequate (Globocan,2020). A study conducted by Karanja-Chege et al., (2022), reports that Kenya recorded over 5,000 new cases of cervical cancer and around 3,000 deaths from cervical cancer complications in 2020. About 2,270 new cervical cancer cases are diagnosed annually in Zimbabwe and 1,451 women are estimated to die of cervical cancer annually. This being a 2012 statistics. This figure continues to rise as current estimates indicate that every year 3043 women are diagnosed with cervical cancer and 1976 die from the disease(ICO/IARC 2023).

HPV vaccination is one of the primary cervical cancer prevention strategies used in conjunction with the promotion of abstinence, faithfulness to one partner, and condom use. HPV vaccine protects against most HPV variants including, HPV types 16 and 18, which cause approximately 70% of cervical cancer cases. Vaccination is most effective in early adolescence, before sexual debut and probable HPV infection(ACOG, 2017. According to research, children who grow up in low-income

settlements are more likely to engage in sexual activity at a young age. Recent studies suggest that dysfunctional families and a lack of parental supervision are the main causes of early sexual activity.

In 2018, Zimbabwe introduced HPV vaccine for 10-14year-old girls. Only 33% of the targeted group received the first treatment in 2020, with 16% returning for the second dose. While the COVID-19 pandemic disrupted immunization programs, other factors such as low demand spurred by misconceptions due to misinformation also had a part in the low coverage. Other co-factors that have facilitated this increase include tobacco smoking, bearing multiple children, long-term use of hormonal contraceptives and HIV infection which is a big burden in the country(Mpata & Nkosi, 2021). Understanding of the prevalence and risk factors of HPV in cervical cancer patients, is hence very important as it may assist to guide future interventions and policies in the development of effective prevention and control strategies to mitigate the burden of cervical cancer in Zimbabwe.

1.2 Problem Statement

Zimbabwe is home to 5.24 million women aged 15 years and older who are at risk of having cervical cancer. According to current statistics, 3043 women are diagnosed with cervical cancer and 1976 die from the disease(ICO/IARC 2023). Cervical cancer is the second most common disease among women in Zimbabwe, and the second most common cancer affecting women aged 15 to 44. About 9.1% of women in the general population are expected to have cervical HPV-16/18 infection at any given time. The prevalence of HPV is highest in adolescents and young adults between the ages of 15 and 25 and it is estimated that more than 75% of new HPV infections occur in people in this age group (CDC, 2022). The lack of adaptive immune responses and/or the relatively large area of cervical epithelium undergoing squamous metaplasia in this

age group may make it easier for HPV DNA to infect the basal cell layer where it can then proliferate, contributing to the increased risk of infection in younger women (Trottier & Franco, 2006). While the burden of HPV associated cancers and mortality is relatively high in Zimbabwe, no recent studies have been done to access the current situation and not especially at Parirenyatwa group of hospitals. Assessing the current information on the risk factors and co-factors of HPV infection and its related diseases is therefore a very crucial step in helping to reduce HPV infection and cervical cancer prevalence.

1.3 Research Objectives

1.3.1 Broad objective

To assess the prevalence and risk factors associated with HPV infection among cancer patients attending Parirenyatwa Group of Hospitals from January to May 2023.

1.3.2 Specific objectives

- To determine the risk factors of HPV in cervical cancer patients at PGH January to May 2023
- To determine the clinical manifestation of HPV in cervical cancer patients at PGH January to May 2023
- To determine the methods of diagnosis, screening and treatment of HPV in cervical cancer patients at PGH January to May 2023
- To determine the prevention methods of HPV available at PGH
- To determine the HPV infection prevalence among cervical cancer patients at PGH

1.4 Research Questions

- What are the risk factors of HPV infection in cervical cancer patients attending PGH January to May 2023?
- What are the clinical manifestations of HPV infection in cervical cancer patients attending PGH January to May 2023?
- What are the methods used for diagnosis, screening and treatment of HPV in cervical cancer patients at PGH January to May 2023?
- What prevention methods of HPV are offered at PGH?
- What is the prevalence of HPV infection in cervical cancer patients attending PGH ?

1.5 Significance of the Study

The aim of this study is to investigate the current prevalence and risk factors of HPV infection in cervical cancer patients.Understanding the prevalence and risk factors of HPV, the primary causative agent, is a crucial public health concern for developing targeted prevention and control strategies to reduce the burden of cervical cancer.By identifying the prevalence and risk factors associated with HPV, healthcare policymakers can implement targeted vaccination programs to reduce the incidence of cervical cancer, particularly in high-risk populations. This knowledge can also inform the development of effective screening programs for early detection of cervical abnormalities and HPV infection. This will enable healthcare providers to identify individuals at high risk of developing cervical cancer and intervene promptly with appropriate diagnostic and therapeutic interventions.Understanding the socioeconomic and behavioral risk factors associated with HPV infection and cervical cancer can help address disparities in access to healthcare and screening services. By

targeting interventions towards vulnerable populations, such as those with limited access to healthcare or low socioeconomic status, public health efforts can reduce disparities in cervical cancer incidence and mortality.Evidence-based data on HPV prevalence and risk factors are also essential for informing public health policies and resource allocation for cervical cancer prevention and control. The government and healthcare organizations can use this information to prioritize funding for vaccination programs, screening services, and treatment initiatives aimed at reducing the burden of cervical cancer. In the same breath, it allows for proper planning by the Ministry of Health (MOH) to increase awareness and knowledge in an effort to sensitize and improve on self-informed decisions regarding use of protection during sexual contacts, vaccination, and early detection of cervical cancers, as cancer found in early detection is highly treatable and the outlook very positive (Behring, 2022). The findings will also reveal potential research gaps that may be valuable for future research projects in this area of study by scholars.

1.6 Delimitation of the Study

This study will only include cervical cancer patients at Parirenyatwa hospital in Harare. Harare being the capital city and a cosmopolitan town, will thus provide a partial reflection and representation of the country.

Furthermore, the study is delimited to prevalence and risk factors of HPV; other aspects, such as awareness and perceptions, were not covered in this research. Lastly, the study will run from January to May 2023.

1.7 Limitations

The researcher may encounter budget constraints while conducting the research due to increasing cost of living that is being experienced in Zimbabwe. Delays may also be

experienced in acquiring the letter of approval for collecting data because the study will take place in a big governmental institution which is hierarchical.

1.8 Summary

The chapter introduces HPV and the subject area which is the prevalence and risk factors of HPV in cervical patients. The chapter goes on to give a brief background on the disease and a clear illustration of the country's disease burden, as well as highlighting the significance of this study in provoking the establishment of health interventions aimed at improving screening and vaccination strategies, reducing health disparities, advancing scientific knowledge, and informing public health policies to effectively combat cervical cancer in Zimbabwe and globally. Finally, the chapter discusses the extent of the study's boundaries.

CHAPTER 2 LITERATURE REVIEW

2.0 Introduction

The literature review's goal is to critically analyse and synthesis existing research and scholarly articles in relation to the field of interest to identify strategies that can be used to address the topic at hand. Throughout this chapter the researcher will analyse and present a literature review on the prevalence and risk factors associated with HPV in cervical cancer patients in Africa and beyond. The researcher will also provide details on risk factors, clinical manifestation, diagnosis, treatment and prevention of HPV-related diseases.

2.1 Conceptual framework

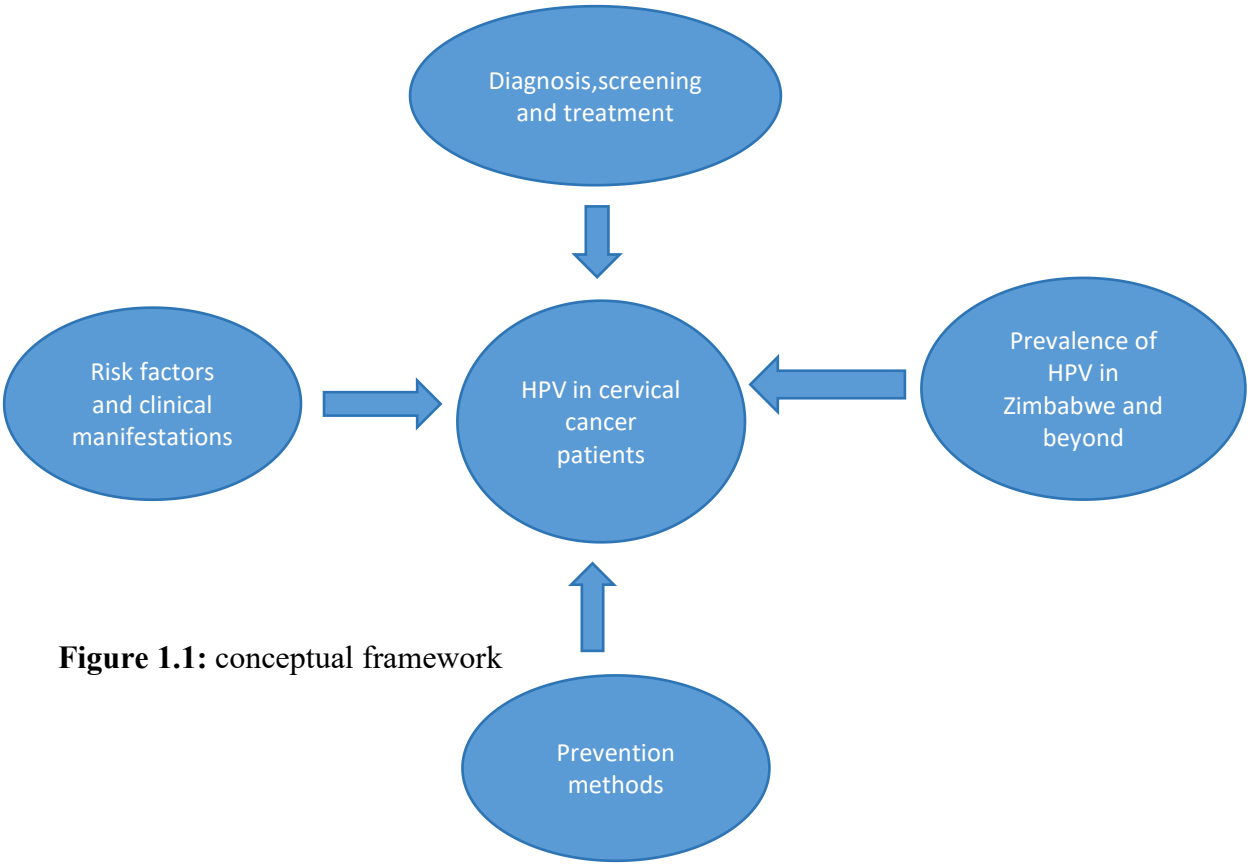

Figure 1.1: conceptual framework

(Jorg & Neringa,2024) describes a conceptual framework as a model that serves as a foundation for understanding and analyzing a particular phenomenon or topic by outlining the key concepts, variables or constructs, relationships and assumptions

underlying a study or research project. It acts as a road map by guiding the course of the research, directing what will be studied, and helping to organize and analyze the data.

Conceptual framework will help link the independent variables; risk factors and clinical manifestations, diagnosis, screening and treatment, prevention methods and prevalence of HPV in Zimbabwe and beyond to the dependent variable HPV in cervical cancer patients.

2.2 Risk factors and Clinical manifestations

HPV is transmitted through contact with infected genital skin or mucosa. Because of their high viral load, genital warts are extremely contagious; up to 66% of sexual contacts become infected (Winer et al., 2005). The typically incubation period for clinical warts is three weeks to eight months, with an average of 2.9 months (Winer et al., 2005). Oral infection with genital HPV strains is possible, but the chance of transmission is low. Perinatal transmission is also possible, but it is uncommon (Burchell, Winer, de Sanjosé, & Franco, 2006). Receptive anal intercourse has been linked to intra- and perianal warts, but these warts are not necessarily linked to anal intercourse. Importantly, cervical and anal infections frequently coexist in people who have never had an anal intercourse (Moscicki et al., 2004).

The most common risk factor for HPV acquisition is genital contact, and the risk increases with the number of sex partners. Other risk factors include having several partners, having sex at a young age, not using condoms consistently, and having a history of sexually transmitted infections. Because there is still touch with genital skin, condom use is only about 70% effective in preventing HPV transmission (Winer et al., 2006). A 2010 study by Maucort-Boulch et al., indicates that tobacco usage is related

with persistent HPV infection. Women who smoke more than 20 cigarettes per day are more likely to have persistent HPV infection than women who smoke fewer than 10 cigarettes per day. Likewise, men who smoke more than ten cigarettes per day are twice as likely to have genital warts than non-smokers.

Another study by Vinodhini et al., 2011 on the prevalence and risk factors of HPV recognized that first coitus at ≤15 years of age, increased number of pregnancies, increased number of sexual partners as mentioned earlier,use of contraceptives, smoking, chewing habit and early age marriage as significant risk factors for HPV infection.

HPV infection can be chronic, latent, or clinical. It could be a low viral-load infection with no clinical symptoms or a high viral-load infection with clinical disease. Genital warts or low or high-grade intraepithelial lesions might be symptoms of this condition. Up to 90% of people infected with high- or low-risk HPV will recover within two years(NYU Langone,n.d) . The small percentage of people who do not clear the infection are at risk of developing cervical cancer.

Other rarer HPV-induced cancers include those of the vagina, vulva, anus, and penis. Low-risk HPV genital infection can cause anogenital warts (condyloma acuminata), which appear as recurrent papules or cauliflower-like lesions, as well as flat genital warts (i.e., condyloma planum) (LabCE, n.d.).

2.3 Methods of Diagnosis, Screening and Treatment

HPV can be detected using polymerase chain reaction or DNA testing (ASCCP, 2020). A study done by Stoler, Castle, Solomon& Schiffman (2007) suggest that testing for low-risk HPV types that do not cause cervical cancer has no clinical benefit; thus, the currently available DNA tests detect only high-risk HPV types. The HPV test is

primarily available to women; no HPV test for men is currently available. The Hybrid Capture II High-Risk HPV test is a signal amplification-based solution hybridization assay that detects 13 high-risk and 5 low-risk HPV types. This assay is simple to perform and produces good results, making this test the best standardized HPV detection method. While the exact HPV type cannot be identified, “low-risk” (6, 11, 42, 43, 44) and “high-risk” (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) HPV genotype groups (HR HPV and LR HPV) are detected(Dixit et al., 2011).It has a sensitivity of about 90% and can be paired with cytology for women aged 30 and up. In case both tests come out negative, they can be redone three years later (Wright et al., 2006).

Another test for diagnosis of HPV is colposcopy and acetic acid test. In colposcopy, a low-powered microscope called a colposcope is used in the outpatient procedure, which is carried out by specially trained medical professionals. Colposcopy as defined by (Gearhart, 2020) is the examination of the cervix, vagina, and occasionally the vulva following the use of an acetic acid solution. It is also the process of taking colposcopically guided biopsies of any lesions that are thought to be neoplastic. Grading of colposcopic findings is based on surface contour, punctuation, mosaic pattern, and degree of acetowhite lesion. Higher deviations from these findings correspond to more severe lesions. This test however, is reserved for suspicious lesions and should not be used for routine screening. Some of the cases where colposcopy is used include: when dealing with immunosuppressed transplant recipients, HIV positive women and when the cervical cytology results are positive for malignant or suspicious cells, yet the cervix appears clinically normal among other phenomena(Dixit et al., 2011).

A biopsy may also be used for postmenopausal women and women with a history of vulvar dysplasia as well as females in whom clinical ambiguity regarding the diagnosis persists after medical therapy.

Currently, the doctor may likely offer the HPV test if the patient's Pap test was abnormal;revealing atypical squamous cells of clinical significance. The HPV test is a cervical cancer screening test. Although the test does not diagnose the disease, it reveals the presence of HPV strains including 16 and 18, which increase the risk of cervical cancer.

As for the management and treatment of HPV infection,all medicines used to treat the infection are applied topically but not on the mucosal surfaces. These medicines should not be used to treat dysplastic lesions, squamous cell carcinoma, verrucous carcinoma, or Bowenoid papulosis. Gearhart, 2020 et al., recommends the following 2 broad categories of medications:Immune response modifiers such as imiquimod and interferon alfa to be used in treatment of external anogenital warts or condylomata acuminata and Cytotoxic agents such as antiproliferative drugs (podofilox, podophyllin, and 5-fluorouracil [5-FU]) and chemodestructive or keratolytic agents (salicylic acid, trichloroacetic acid [TCA], and bichloracetic acid [BCA]); the latter are the only agents recommended for treatment of nongenital cutaneous warts. The article also recommends the use of surgical interventions in cases where large number of warts are present, a large area is affected, or the patient has refractory disease.

Knowing whether the patient has a kind of HPV that puts them at high risk of cervical cancer allow them and their doctor to make more informed decisions about their health care. These measures might involve additional monitoring, further testing, removal or treatment of the abnormal cells.

2.4 Prevention methods for HPV

The two approved HPV vaccines (Cer varix and Gardasil) are made up of non-infectious virus-like particles derived from the HPV L1 capsid protein. The quadrivalent recombinant HPV vaccination (Gardasil) was approved in 2006 for girls and women aged 9 to 26. It protects against HPV strains 6, 11, 16, and 18 (Saslow et al., 2007). It is given as a series of three shots to prevent genital warts and cervical cancer (at months 0, 1 to 2, and 6). The bivalent HPV vaccine (Cer varix) protects against types 16 and 18, but not types 6 and 11 (CDC, 2010). It is recommended for girls and women aged 10 to 25 and is administered in three doses ((at months 0, 1 to 2, and 6).

The three-year phase 3 FUTURE I (Females United to Unilaterally Reduce Endo/Ectocervical Disease) trial assessed the effectiveness of the quadrivalent vaccine in preventing genital infections caused by HPV types 6, 11, 16, and 18. When administered to women who had never been exposed, the vaccination was nearly 100% effective in preventing genital warts and precancerous lesions (CIN 2 and CIN 3). Another study, the FUTURE II trial, found that the quadrivalent vaccine is 98 percent effective in preventing high-grade precancerous cervical lesions (HPV 16, 18) in unexposed women during a three-year period. However, data from the intention-to-treat group (which includes sexually active, HPV-exposed women) imply that the vaccine is less protective in this cohort.

According to the PATRICIA (Papilloma Experiment Against Cancer in Young Adults) trial, the bivalent vaccine is 98 percent effective in preventing precancerous cervical lesions (CIN 2 and CIN 3) caused by HPV types 16 and 18, and may provide some cross-protection against strains 31, 33, and 45(Paavonen et al., 2009). According to a study done by (Bornstein, 2009) the bivalent vaccine adjuvant may result in a faster

immune response with larger titres. There have been no direct comparisons of the bivalent and quadrivalent vaccines.

The ACIP and the Centers for Disease Control and Prevention advises routine HPV vaccination of girls aged 11 to 12 years old, with catch-up immunization for females aged 13 to 26 years old (CDC, 2010). Both vaccines appear to be safe and immunogenic, with the most common side effects being local injection responses, dizziness, nausea, and syncope (Slade et al., 2009). Even after vaccination, it is critical to continue cervical cytologic monitoring because the vaccine is unlikely to change the course of pre-existing infections or treat all HPV-associated illness.

ACIP recently approved the nonroutine (permissive) use of the quadrivalent vaccine to prevent genital warts in males aged nine to eighteen. Despite the fact that males serve as a reservoir for female HPV infection, the lack of cost-effectiveness research makes vaccination of this demographic problematic. According to another study done by Auvert et al., (2009), circumcision appears to reduce HPV infection in men; in South Africa, the prevalence of HPV in circumcised men is 14.8 percent, compared to 22.3 percent in uncircumcised men.

HPV vaccination is controversial because of its high cost, unknown length of protection, and worries that it provides tacit permission of sexual activity and a false sense of security. Furthermore, many parents are concerned about the need to vaccinate girls as young as nine to eleven years old before they become sexually active. In countries where cervical screening is already established, HPV vaccination will only reduce the number of women who have abnormal screening tests, not the number of women who have cervical cancer (Harper and Williams 2010). The developing world has the greatest need for HPV vaccination because most women

never have Pap tests and cervical cancer is a leading cause of death. A vaccine that protects against the four or five most frequent high-risk HPV strains could prevent 80 to 90% of cervical malignancies worldwide (zur Hausen H, 2002).

Promoting behaviour change as a sole method for avoiding sexually transmitted infections has been found to be inefficient in reducing transmission and thus ineffective for HPV infection prevention as well. Other preventative techniques, including as condom use and screening, must therefore be linked to behaviour change.

2.5 HPV Prevalence in Zimbabwe and beyond

In 2023, the International Agency for Research on Cancer (IARC) estimated that 3043 women receive a cervical cancer diagnosis and 1976 of them pass away from the illness each year in Zimbabwe. Cervical cancer is ranked as the most common cancer among females in Zimbabwe and the most common cancer among those in the 15–44 age range(ICO/IARC, 2023). It is the fourth most diagnosed cancer among females worldwide (Bruni L. et., 2016).Information regarding the prevalence of HPV in Zimbabwe's general population is currently unavailable.Nonetheless, it is estimated that 4.7% of women in the general population of Eastern Africa of which Zimbabwe belongs to have a cervical HPV-16/18 infection at any given time, and that HPVs 16 or 18 are responsible for 67.9% of invasive cervical malignancies.

Global trends indicate that the majority of high-risk countries for cervical cancer are in Africa, particularly Malawi, Mozambique, Zambia, and Zimbabwe(Africa Coalition on Maternal Newborn and Child Health, 2014). The burden and mortality rate of cervical cancer is most likely to be greater than that listed in the national cancer registry because some cases, particularly in rural regions with limited access to healthcare facilities, go unreported (Chi'nombe et al., 2014). In Zimbabwe, the high

incidence of HIV exacerbates the high burden of cervical cancer, which is primarily caused by delayed disease manifestation, inadequate screening, diagnostic, and treatment facilities (Kuguyo et al., 2017). The high prevalence of HPV underscores the importance of cervical cancer prevention efforts, including vaccination and screening programs.

Globally, HPV is one of the most common sexually transmitted infections(CDC, 2022). According to WHO, approximately 80% of sexually active individuals will acquire HPV infection at some point in their lives. The prevalence of HPV varies by region, age group, and other factors. In many low- and middle-income countries, including those in sub-Saharan Africa, HPV prevalence tends to be higher due to limited access to healthcare, lack of awareness, and other socioeconomic factors.Contrary, due to the availability of effective and accessible screening programs as well as diagnostic and treatment facilities, the morbidity and death rate of cervical cancer is significantly lower in developed countries

Efforts to combat HPV-related diseases, such as cervical cancer, include vaccination programs targeting adolescents to prevent HPV infection, as well as cervical cancer screening programs to detect and treat precancerous lesions early. These efforts aim to reduce the burden of HPV-related diseases and improve public health outcomes globally.

2.6 Summary

To summarize, despite considerable advances in HPV infections treatment, vaccination programs and screening HPV related cancer continues to be a burden worldwide and especially in Zimbabwe. Assessing the risk factors that are contributing to this burden could be the missing link in reducing HPV mortality hence the purpose of this study.This chapter compared and contrasted several studies to

provide an overview of the risk factors, diagnosis, clinical manifestations, treatment, prevalence of HPV, its related diseases, and vaccine across several countries and demographics.

The literature review however, failed to bring to light the prevalence and risk factors among cervical cancer patients at PGH Harare. This hospital is particularly important because being the largest government hospital,it is home to the most qualified specialist in the country. Patients from all over Zimbabwe also visit this hospital on a daily basis hence conducting the research here will further shed light to the subject matter.

The current study hence intends to bridge this gap while also setting a precedent for the development of health interventions and future research.

CHAPTER 3 METHODOLOGY

3.0 Introduction

In accordance with the study's purpose, this chapter will discuss the research design, study setting, study target population, sample size, measurement method and data collection method that validates the research instrument to be utilized when conducting the study. The chapter will also give the data analysis strategy as well as the ethical considerations put in place for conducting this study. Finally, the researcher will give a summary of the chapter.

3.1 Research design

A research design is a road map for achieving objectives and answering questions. It is the plan for data collection,measurement and analysis. To generate relative information for the study, a retrospective cross sectional research design will be followed. Cross-sectional studies are useful for characterizing the prevalence of a condition or risk factor in a particular population(Tamara et al., 2012). (Patricia, 2005) also adds that when assessing the prevalence of disease or features, attitudes, and knowledge, a cross-sectional design is most appropriate.

The information gathered with this design essentially depicts what is happening at one point in time. This study type will provide a "snapshot" of the prevalence and risk factors of HPV in cancer patients at PGH, at that precise point in time, allowing for the production of a seamless illustration of the study objective in real time. Furthermore, the study design will allow the research to be completed in a short amount of time and at a low cost. In this study, patients request forms for cancer patients that were also diagnosed with HPV from January to May 2023 will be retrieved and analyzed .

The variables to be analyzed in this study include the dependent variable: prevalence of HPV in cervical cancer patients. This will indicate the presence of HPV in patients diagnosed with cervical cancer. The independent variables include; demographic variable(age, ethnicity) of the cervical cancer patients, behavioral variable of the cervical cancer patients(smoking status, number of sexual partners, use of contraceptives), HPV genotype and clinical variables related to cervical cancer and their association with HPV(histopathological type of cervical cancer, stage diagnosed, presence of co-infections that may influence prevalence of HPV).

3.2 Methodology

The data collection method that will be used in this study is the observational method. This method will be applied while reviewing request forms for patients with HPV related cervical cancer at PGH from January to May 2023.

3.3 Study Population

The study participants for this research will be cervical cancer patients with HPV co-infection whose samples were processed at PGH laboratory Harare from January to May 2023.

3.4 Sampling

The sample population will be selected at random (simple random sampling) from individuals who meet the inclusion criteria for this study.

3.5 Inclusion criteria

- All cervical cancer patients with HPV co-infection whose samples were processed at PGH laboratory Harare from January to May 2023.
- Cervical cancer patients without HPV co-infection

3.6 Exclusion criteria

- Cervical cancer patients whose age were not mentioned on the clinical request forms
- Cervical cancer patients with HPV infection whose samples were processed at PGH Laboratory earlier than January 1 2023 or later than May 31 , 2023

3.7 Sample size

The sample size will be 385 participants. It is calculated using a 95% confidence interval, 0.5 standard deviations, and a margin of error of 5% of the total population of cervical cancer patients with HPV co-infection to be involved in the study.

Using:

$$n = \frac{z^2 (p)(1-p)}{C^2}$$

$$= \frac{(\text{Z-score}^2) \times \text{standard deviation} \times (1-\text{standard deviation})}{(\text{Margin of error})^2}$$

Where:

Z= Z score for 95% Confidence Interval which is 1.96

P =estimated prevalence of 80 % expressed as a proportion which is 0.8

C= 0.0784

The above formula yields the sample size for my study as follow:

$$n = \frac{(1.96)^2 \times (0.8)\ (1-0.8)}{(0.0784)^2}$$

sample size = 100

3.8 Study Setting

This research study will be carried out at PGH Laboratories and some of the data shall be obtained from the Family planning clinic, Harare Zimbabwe .

3.10 Data analysis and organization of data

Descriptive analysis for all collected variables, including demographics, target population, and information on vaccination will be completed. Graphs, tables and charts will be used to display the obtained data sets. Microsoft Excel and Access will be used to organize, clean, and delete duplicated or incomplete data from a database and to illustrate data statistics.

3.11 Ethical considerations

The Africa University Research Ethics Committee will be consulted prior to data collection for ethical approval (see appendix B). Following approval, the AUREC will provide a letter of approval that will assist the researcher in obtaining authorization to perform the study at the chosen site. Participants' names will remain anonymous in order to preserve their identity. Information obtained from this study will be used for research purposes only.

3.12 Summary

This chapter discusses the cross-sectional study design as the framework that the researcher plans to use to obtain the objective of this study. Upon reviewing preexisting patients clinical data, the researcher will be able to collect the required information about the prevalence and risk factors of HPV infection among cancer patients at the target site. With this information, the researcher will obtain answers to the research questions, through analysis and interpretation of the data collected.

Additionally, the chapter discusses the sampling strategies to be used in this procedure including the sample size to be used, inclusion and exclusion criteria as well as the ethical consideration that the researcher plans to put in place.

CHAPTER 4 DATA PRESENTATION

4.0 Study findings

Out of the 100 cervical cancer patients tested for HPV, the study found out that 85 of them tested positive while 15 tested negative for HPV.

4.1 Distribution of HPV genotype in cervical cancer patients

By analyzing the available data at PGH the researcher found that 85% (85/100) of the patients had HPV DNA. These results were obtained through the use of PCR analyzer for DNA testing after the pap smear revealed atypical squamous cell of clinical significance. The six main HPV types found in the investigation were 16, 18, 31, 33, 35, and 58. The most common kind, found in 49% of the cases, was HPV-16. In 18% of the samples, HPV-18 was detected. 11% had Type 33 present.HPV-31 was found in 5% . For 35 and 58, there was one positive instance each. 15% of patients, were infected by mixed types of HPV. Table1.1 below is a representation of the data.

4.1.1 Table 1.1: distribution of HPV types at PGH Harare from January to May 2023

HPV TYPES	N%
HPV 18	18(18%)
HPV 31	5(5%)
HPV 33	11(11%)
HPV 35	1(1%)
HPV 58	1(1%)
Mixed HPV types	24(24%)

4.2 Characteristics of study population

The table 1.1 below illustrates an overview of the distribution of the study's sample characteristics. It is clear from this table that the typical patient fell within the fourth decade age group and going upwards. According to the table, increased risk of HPV infection and cervical cancer increased with the number of sexual partners a patient had. Other contributing risk factors for cervical cancer include, vaccination status, level of education, smoking history, and use of oral contraceptives. A small percentage of the patients had a history of STI and others were HIV positive. This may be attributed to overall sexual behaviour observed in most of the participants.

This information was obtained from participants' answers to questionnaires given to them during their visit to the Department of Obstetrics and Gynecology at PGH.

4.2.1 Table 1.1: characteristics of the study participants at PGH from January to May 2023

Variable	HPV negative	Percentage	HPV positive	Percentage
Age(years)	44±9.28		50±9.28	
Education level				
• None	2	2%	15	15%
• Elementary school-	5	5%	30	30%
• High School	7	7%	33	33%
• ≥High School	1	1%	7	7%
Age of sexual debut				
• < 15 years	6	6%	11	11%
• 15-20 years	7	7%	69	69%
• >20 years	2	2%	5	5%
Number of sex partners > 1	7	7%	17	17%
Smoking habits	14	14%%	17	17%
Use of oral contraceptives	15	15%	23	23%
Any history of STIs	20	20%	17	17%
HPV vaccination	0	0%	0	0%
HIV status	6	6%	11	11%

4.3 Clinical manifestation

The table below shows a list of the clinical symptoms experienced and completed by the subjects upon admission to the hospital. The most frequently experienced symptoms by all the subjects as shown in the table included; vaginal bleeding, abnormal vaginal discharge, fatigue and pelvic discomfort. The least experienced symptom was limb edema and fistula ranging at 7% and 5% respectively.

4.3.1 Table 1.2: clinical manifestations of the study participant at PGH from January to May 2023

Variable	N %
Vaginal bleeding	80(80%)
Post coitus bleeding	51(51%)
Post menopause bleeding	46(46%)
Abnormal vaginal discharge	81(81%)
Fistula	6(6%)
Back pain	59(59%)
Pelvic pain	70(70%)
Loss of appetite	40(40%)
Limb edema	7(7%)
Fatigue	74(74%)

Of the patients, 6% had stage I cancer, whereas 39% had stage II and 51% had advanced stage III or IV disease. Histological analysis of all 100 cases revealed the existence of invasive cervical carcinoma. 98% of the cases, had squamous cell carcinoma. While the remaining two had cervical adenocarcinomas.

4.4 Methods of diagnosis, screening and treatment used at PGH

Efforts to combat HPV related cervical cancer at PGH involves a range of methods. The methods used for diagnosis include; Pap smear test (most commonly used), followed by HPV DNA testing to identify the high risk HPV strains for cervical cancer. HPV DNA testing was found to be more precise as compared to the pap smear.

Last method of diagnosis used is the Visual Inspection with the Acetic Acid (VIA). This method is low cost and yet very effective.

As for screening PGH recommends regular screening for women especially between the ages of 21-65. Pap smear test is the most commonly used for screening. VIA is also used especially because its cheaper and easier to use as compared to other methods.

The treatment methods for HPV related cervical cancer involved; Cryotherapy to freeze precancerous lesions detected during screening. The other method is the Loop Electrosurgical Excision Procedure(LEEP) for removing abnormal tissue from the cervix during the precancerous stage. Radiotherapy and chemotherapy were the most commonly used methods of treatment of advanced cases cervical cancer. Hysterectomy which involves surgical removal of the cervix after diagnosis with cervical cancer is also used at PGH.

4.5 Prevention methods

PGH in conjunction with other health care ministries in Zimbabwe have implemented vaccination programs that target young girls typically 10-15 years before they become sexually active. This is meant to protect them against the high risk HPV types which lead to cervical cancer. PGH is also helping prevent HPV related cervical cancer through education and raising awareness. Women visiting the family planning clinic are encouraged to participate in screening programs which is available on set and free of charge and to get vaccinated, they are also promoting condom use as well as raising awareness on the factors that contribute to the susceptibility of getting HPV related cervical cancer such as having multiple sexual partners and smoking.

CHAPTER 5: DISCUSSION AND RECOMMENDATION

The goal of this study was to investigate the prevalence of HPV in cervical cancer patients . Major carcinogenic HPV types were present as seen in nearly all the cervical cancer patients. HPV type 16 was the most common infection at 49%. These results concur with other results from different parts of the world that HPV-16 plays a major role in the oncogenesis of cervical cancer.

With a frequency of 76.36%, HPV-16 is the most frequent cause of cervical cancer this is according to a study conducted in Manado in Indonesia. According to Langheden et al. (2018) through a study he conducted in Sweden, HPV-16 accounts for 60% of all instances of HPV, followed by HPV type 18 (19%), and the remaining kinds account for less than 10% of cases. Meanwhile, Zhang conducted a study in China and found different results, with HPV-52 being the most common kind (2,04%), followed by HPV-16 (1,81%) (Wang et al., 2016).

Awua evaluated 256 Ghanaian patients with cervical cancer and found similar outcomes. Awua et al. (2016) reported that 230 individuals tested positive for HPV, with the most common strains being HPV18 (47.4%), HPV59 (42.2%), HPV45 (37.4%), and HPV16 (9.0%). Additionally,Volpini through a study he did in southeastern Brazil found differences in the kinds of high-risk HPV, with HPV types 16 having the highest prevalence (8.9%), followed by HPV types 45 and 18, which had values of 6.7% and 4.4%, respectively (Volpini et al., 2017). According to this study's findings, the typical patient was in the early geriatric age range. A study done by Gokhan Boyraz et al. (2016) in Turkey on 126 women with cervical cancer reported similar outcomes. The patients' ages ranged from 29 to 83 years old, with an average age of 52. However, this is not the same as research done on 524 women in Puerto Rico, where the majority of the population is under 35 (Perez et al 2018).

The public's knowledge of seeking medical attention from professionals is strongly correlated with educational attainment. The majority of patients, as indicated by the results, did not pursue education beyond high school. Highly educated individuals are more mindful of their health and are more than likely to engage in safer sexual practices. This is consistent with systematic review research conducted in Sub-Saharan Africa by Lim, J, which indicates that inadequate awareness of cervical cancer poses a significant personal barrier to cervical screening as well as vaccination and prevents women from preventing cervical cancer (Lim & Ojo, 2016).

According to this study, women under the age of twenty-one are disproportionately affected by cervical cancer. Mitiku's research revealed a high correlation between sexual behavior such as having several partners, starting sexual activity at a younger age and the prevalence of cervical cancer. Women who have sexual interaction before the age of twenty-one are more than six times more likely to develop cervical cancer (Mitiku & Tefera, 2016).The typical lady in this study gave birth four times, ranging from two to six.

Women with more than three times the parital status have a five times higher risk of developing cervical cancer, according to a different study by Setyarini. One extrinsic factor that is strongly associated with a higher risk of cervical cancer is parity this is most especially if the intervals between labors are too close together. The explanation for this phenomena may be a link between pregnancy hormones and the promotion of cancer cell formation. During childbirth, women tend to have suppressed immunity and uterine cervical cell metaplasia. However, women with parity of 0 or >5 as get cervical cancer. Hence according to Harayani et al. (2012), this suggests that parity is not the only cause of cervical cancer.

Liu Chang studied the relationship between the number of sexual partners and the prevalence of cervical cancer in 2015. The findings indicated that whether or not the HPV DNA was found, women with four to seven sexual partners were at risk of acquiring cervical cancer. Transmission from men is linked to the incidence of cervical cancer ((Morris et al., 2019).This investigation revealed that sixteen patients had many sexual partners. The study also identified IUD use and smoking history as risk factors. Another research by Zidi et al., suggest that the biggest environmental risk factor for cervical cancer is smoking. It has been demonstrated that the chemical carcinogen benzopyrene, which is found in cigarettes, increases the synthesis of HPV in cervical cells and frequently results in viral persistence (Zidi et al., 2020). According to other research, there is a favorable correlation between long-term hormone use and the incidence of CIN 2/3 cervical cancer (Oh et al., 2016).

According to the findings, vaginal bleeding is one of the symptoms that all of the participants in this study complained of the most. Six percent of cervical cancer deaths are related to vaginal bleeding. There are numerous obstacles in the therapy process, and the incidence ranges from 0.7% to 100% (Eleje et al., 2015).

Patients with cancer, especially those with cervical cancer, may face additional symptoms such weight loss, exhaustion, and lack of appetite.

One unusual kind of problem from the course of cervical cancer is the existence of fistulas manifesting as leaking feces or pee. If this fistula is not treated, fluid will continuously leak from the vagina. The best course of action for closing the fistula is surgery. Giving a cream or lotion to lessen fluid leakage and avoid irritation and tissue damage to the vagina and surrounding tissue is sometimes included in the course of treatment. Additionally, around 4.5% of the patients in this study had a urine or feces leak.

According to this study, among the 100 women, 85 (85%) tested positive for HPV, and HPV type 16 (48.8%) is the most prevalent HPV genotype in PGH. Aside from that, vaginal bleeding, fluor albus, pelvic discomfort, and exhaustion are the most typical clinical signs of patients with cervical cancer.

Lastly, most of the patients who had HPV have not been vaccinated against the infection. This is unfortunate, bearing in mind that HPV vaccination is one of the primary cervical cancer prevention strategies.

5.1 Conclusion

The study on the prevalence of HPV among 100 patients with cervical cancer concludes by highlighting the substantial impact of HPV infection on cervical cancer incidences. In order to lessen the effect of HPV on cervical cancer incidence and mortality, the findings highlight the significance of comprehensive cervical cancer control methods that include vaccination, screening, and health education programs.

This chapter adds insightful information to the body of knowledge on HPV and cervical cancer, guiding the development of evidence-based strategies for the prevention and management of the disease.

In doing so, the researcher hopes to assist the health policy makers in evaluating the burden associated with HPV infection and hence allocate resources effectively. This in turn will allow for the development of targeted interventions especially to the high risk population and preventive measures to address significant health issues in the community.By tracking changes in prevalence rates, health authorities can identify emerging health threats, assess the effectiveness of interventions, and allocate resources where they are most needed. This information will also enable healthcare providers to implement targeted screening and prevention strategies for the high risk

groups groups, which will potentially lead to earlier detection and intervention. Lastly,understanding the risk factors for the disease will allow individuals to make informed decisions about their health behaviors and lifestyle choices by empowering them to adopt preventive measures, to reduce their risk of developing HPV related diseases.

This valuable information will hence assist in combating the high levels of mortality and morbidity related to HPV in Zimbabwe.

5.2 Limitation

The retrospective nature of the study may restrict the generalization of the findings because the sample size of 100 cervical cancer patients might not accurately reflect the larger population, care must be taken when extrapolating the findings.

5.3 Recommendations

Improved HPV Vaccination Programs

To lower the incidence of HPV infection and, in turn, the burden of cervical cancer, there is need to develop and promote HPV vaccination programs aimed at adolescents and young people.

Enhanced Screening Programs

In order to identify precancerous lesions and cervical cancer at an early stage when treatment is more effective, the cervical cancer screening programs, including HPV testing when practical should be enhanced.

Better Healthcare Service Access

To address inequities in cervical cancer outcomes,the ministry of health and the government must increase healthcare facilities, improve the infrastructure to ensure equitable access to services for cervical cancer screening, diagnosis, and treatment,

especially in underprivileged communities.

Public Education and Awareness

Raise public knowledge and understanding of the connection between HPV infection and cervical cancer, as well as the significance of immunization, routine screening, promoting abstinence in young people and faithfulness to one partner in older individuals and early detection in the fight against HPV related cervical cancer.

Further research could explore the effectiveness of HPV vaccination in reducing the cervical cancer incidence.

5.4 Dissemination of the data

The researcher made a report on the research findings, and shared it with the clinical director at PGH. This information is important as it can provide a base upon which other researches can undertake further studies and initiation of intervention strategies at the hospital for better healthcare.

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APENDICES

Appendix I: Budget

Transport	$ 100
Internet	$ 150
Miscellaneous	$ 100
Total	$ 350

Appendix II: Timetable

Activity	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Identification, presentation and approval of research topic									
Proposal writing									
Submission and clearance of research									
Data collection & analysis									

Report writing									
Submission of complete dissertation									

Appendix III: Data collection form

Patient Information

Patient ID:……..

Date of Birth:……

Age:……..

Clinical Information

Date of Diagnosis:……

Histopathological Type of Cervical Cancer:……

Disease Stage at Diagnosis:……

Co-existing Medical Conditions:……

HIV/AIDS:……..

STIs:…….

Behavioral Factors

Sexual Behavior:

-Number of Sexual Partners if available:……

-Age at First Intercourse if available:……

-Use of Contraceptives: …….

-History of Sexually Transmitted Infections:…….

Smoking Status:

-Current Smoker(yes/no)……..

-Frequency of Smoking……

-Duration of Smoking……

HPV Related Information:

HPV Genotype:

- Type(s) of HPV Detected……

- High-Risk or Low-Risk HPV……

HPV Vaccination History:

- Vaccination Status……

Presence of HPV-related Symptoms:

- Abnormal Pap Smear Results (Yes/No)……..

Environmental Factors:

Access to Healthcare Services:

- Regular Check-ups(Yes/No)……

- Participation in Screening Programs(Yes/No)……

Information collected here will be strictly confidential and ethical guidelines and regulations will be adhered to.

Appendix IV: Study site approval letter

All communications should be addressed to
"CLINICAL DIRECTORS OFFICE"
Telephone: 701502-7/4
Fax: 702227
Website:www parihosp.org

PARIRENYATWA GROUP OF HOSPITALS
P.O Box CY 198
Causeway
Zimbabwe

22 January 2024

RE: REQUEST FOR PERMISSION TO CONDUCT RESEARCH STUDY AT PARIRENYATWA GROUP OF HOSPITALS: LUCY WANGARI WANGUI

The above matter refers

The Parirenyatwa Group of Hospitals hereby grants you permission to conduct research on: -

PREVALENCE AND RISK FACTORS ASSOCIATED WITH HPV IN CERVICAL CANCER PATIENTS

The permission is granted subject to the following conditions: -

1. The researcher will provide all sundries necessary for sample collections. ☑
2. The researcher sponsors all payments for the tests involved. ☑
3. The hospital incurs no cost in the course of the research. ☑
4. All relevant departments are notified in advance and the Head of section/ward signs acknowledgement of such notification. ☑
5. The conduct of the research does not interfere or interrupt the daily service provision by the hospital. ☑
6. Formal written feedback on research outcomes must be given to the Director of Clinical Services. ☑
7. Permission for publication of research must be obtained from the Director of Clinical Services. ☑

PARIRENYATWA GROUP OF HOSPITALS
CLINICAL DIRECTOR
22 JAN 2024
P O BOX 198 CAUSEWAY
HARARE ZIMBABWE

DR M. MHLANGA
ACTING CLINICAL DIRECTOR

Appendix V: Approval letter from AUREC

Investing in Africa's future

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU3246/24

27 March, 2024

LUCY W WANGARI
C/O Africa University
Box 1320
MUTARE

RE: **PREVALENCE AND RISK FACTORS ASSOCIATED WITH HUMAN PAPILLOMAVIRUS AMONG CERVICAL CANCER PATIENTS ATTENDING PARIRENYATWA GROUP OF HOSPITALS FROM JANUARY TO MAY 2023**

Thank you for the above-titled proposal that you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following.

a) Research proposal

- **APPROVAL NUMBER** AUREC3246/24
  This number should be used on all correspondences, consent forms, and appropriate documents.
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** March 27, 2024
- **EXPIRATION DATE** March 27, 2025
- **TYPE OF MEETING**: Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

AFRICA UNIVERSITY
RESEARCH ETHICS COMMITTEE (AUREC)
APPROVED
P.O. BOX 1320, MUTARE, ZIMBABWE

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE