THE PREVALENCE OF HPV AND ASSOCIATED FACTORS AMONG YOUNG WOMEN LESS THAN 25 YEARS IN RWANDA A CASE STUDY: KIGALI CITY

Dissertation submitted in partial fulfillment of the requirements for the degree of Master of Science in Epidemiology in the college of Medicine and Health Science

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DECLARATION

I, Marie Chantal UMULISA, hereby declare that the thesis has been written by me without any external unauthorized help, that it has been neither presented to any institution for evaluation nor previously published in its entirety or in parts.
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Signature : .....
Marie Chantal UMULISA
Date...../...../.....

DEDICATION

To my family (my husband; Alphonse MANIRAREBA, my daughter UWASE TETA Anne Chloe and my son MANZI Alpha Colin) for your love, encouragement and patience during my absence.

This work is mostly dedicated to you

ACKNOWLEDGEMENTS

To God, my creator, the source of wisdom and love,

The success of this work has been a joint effort made by various people to whom I owe thanks

My sincere thanks are addressed to the supervisor Prof NTAGANIRA Joseph for their help in design and analysis of this work.

Your interminable patience in guiding me paved a way and encourages me to complete my dissertation.

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To my prayer partners, my lecturers at UR-SPH, and my classmates especially Anne Marie UWITONZE and Michael MUGISHA whoever has contributed in any or other way to my success in studies as well as to the present dissertation. I could not have done this without your constant support.

May God bless you.

SUPERVISOR'S APPROVAL

DECLARATION AND AUTHORITY TO SUBMIT THE THESIS

Title of the thesis/Dissertation:

THE PREVALENCE OF HPV AND ASSOCIATED FACTORS AMONG YOUNG WOMEN LESS THAN 25 YEARS IN RWANDA.
A CASE STUDY: KIGALI CITY.

Declaration by Student

I, **Prof NTAGANIRA Joseph,** in my capacity, I do hereby authorize the student to submit his/her Thesis to the school ready for its defence.

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……../……/……./

ABSTRACT

Background

Cervical cancer is the mainly frequent female cancer in Rwanda, the first country in African to introduce human papilloma virus (HPV) vaccination programme in 2011.

Methods

To identify the prevalence and risk factors of HPV infection among young women in Rwanda, secondary data used from IARC survey database. Data selected were 1177 women aged less than 25 years from the general population in Kigali, period of 2013/14.Samples were tested for HPV by using GP5+/6+ PCR. Univariate, bivariate and multivariate logistic regression analyses were performed to assess the prevalence of HPV for single or multiple types of HPV and risk factors.

Results analysis

HPV prevalence was 42.84%. 238 (20.3%) women had single-type and 256 (22.9%) had multiple-type infections. HPV16 was the most popular type in women with normal cytology with multiple (10.4%) and single (6.6 %) infection respectively.

Several determinants were associated to HPV infection and increase such as having more than two partner, age >19, age at first sex intercourse, , HIV positive, Chlamydia negative, tobacco use and vaccination status (OR 1.48, 95% CI [1.13-1.93], OR 0.73[0.54-0.99], OR 2.34 95% CI [1.55-3.53], OR 0.46 95% CI [0.31-0.69], OR 0.41 95% CI [0.21-0.77], OR 2.86 95% CI [1.31-6.25], respectively, were significantly associated to HPV infection.

Conclusion

The findings of this study confirm Rwanda to be a setting of high prevalence of HPV among women less than 25 years.

HPV HPV16, 52, 45, 35, 58 and 18 were the most common HR HPV infections in the population between 15 to 24 years. The risk associated to HPV infection were HIV, factors, age at first sex intercourse, chlamydia and tobacco use.

This information will help for further studies and planning in country by using this data.

RESUME

Contexte

Le cancer du col est le cancer féminin principalement fréquent au Rwanda, le premier pays africain à introduire le programme de vaccination papillomavirus humain (VPH) en 2011.

Méthodes

Pour identifier la prévalence et les facteurs de risque de l'infection du HPV chez les jeunes femmes au Rwanda, les données secondaires utilisées à partir de la base de données de l'enquête du CIRC. Les données sélectionnées sont 1177 femmes âgées de moins de 25 ans de la population générale à Kigali, période 2013/14. Samples testé en utilisant GP5 + / 6 + PCR. Bivariées et des analyses de régression logistique multivariée ont été réalisées pour évaluer les facteurs de risque.

L'analyse des résultats

La prévalence du VPH était de 42.84%. Dans l'échantillon total de 238 (20.3%). Femmes avec unique type infection et 256 (22.9%) de type multiple infections. HPV16 était le type de VPH le plus populaire chez les femmes avec une cytologie normale (6,6%) et (10.4%) avec de multiples et uniques infections respectivement.

VPH avec risque élevé chez les femmes avec une cytologie normale dans l'infection unique et de multiples infections à VPH 35 (3,4%), VPH 56 (3%), VPH 58 (2,7%) et VPH 45 (2%). VPH 66, (2,8%), 70 et 6 types à faible risque avec (2%) ont été les plus fréquemment détectés.

Plusieurs déterminants ont été associés à l'infection avec VPH et augmentent avec l'âge du début de l'acte sexuel, HIV, chlamydia trachomatis, l'usage du tabac et l'état de vaccination a VPH étaient associe à l'infection du VPH (OR 1.48, 95% CI [1.13-1.93],

OR 0.73[0.54-0.99], OR 2.34 95% CI [1.55-3.53], OR 0.46 95% CI [0.31-0.69], OR 0.41 95% CI [0.21-0.77], OR 2.86 95% CI [1.31-6.25] respectivement.

Conclusion

Cette étude confirme le Rwanda a une haute prévalence du VPH. Chez les jeunes femmes de moins de 25 ans.

HPV16, 52, 45, 35, 58 and 18 étaient les plus communs dans l'étude chez les enfants entre 15- 24 ans. Les facteurs de risqué associe a infection de HPV étaient ; âge catégories, le début de relation sexuel, HIV positive, chlamydia et utilisation du tabac.

Cette information servira pour d'autres études et la planification en se référant sur ces informations

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ACRONYMS AND ABBREVIATIONS

CIN: Cervical intraepithelial Neoplasia

EPI: Expanded Program on Immunization

FIGO: International Federation of Gynaecology and Obstetrics

HIV: Human Immunodeficiency Virus

HPV Human papillomavirus

HPV–DNA: Human papilloma virus–deoxyribonucleic

HR HPV High-risk human papillomavirus

IARC: International Agency for Research on Cancer

IEC: Information Education Communication

ICC: Invasive cervical cancer

ID: Identification number

LBC: liquid-based cytology

LMIC: Low- and middle-income countries

MoH: Ministry of Health

NCDs Non-communicable diseases

OC: Oral contraceptive

PCR: Polymerase chain reaction

RBC: Rwanda Biomedical Centre

STI: Sexually transmitted infection

UICC: International Union against Cancer the WHO and the International

VIA: Visual inspection with acetic acid

WHO: World Health Organisation

DEFINITION OF KEYS TERMS

Human Papilloma Virus (HPV): Human Papilloma Virus (HPV) is viral infection and the most risk factor of cervical cancer that is transmitted between people through physical contact. HPV has multiple types of more than 100. HPV affect and spread by genitals, mouth, anal and throat through sexual contact. It's mainly visible by warts (1)(2).

Invasive cervical cancer (ICC) / cervical cancer: If the high-grade precancerous cells invade deeper tissues of the cervix or to other tissues or organs, then the disease is called invasive cervical cancer or cervical cancer.

Invasive squamous cell carcinoma: Invasive carcinoma composed of cells resembling those of squamous epithelium.

Adenocarcinoma: Invasive tumour with glandular and squamous elements interacted.
Parity: Refers to the number of times a woman has been pregnant

VIA (Vision Inspection with Acid Acetic): This is an attractive screening method for early-phase cervical cancer in underdeveloped countries. This technique is used by Acid acetic or Vinegar for visualization of cervical lesions.

LEEP: It is an abbreviation for loop electrosurgical excision procedure. It is a way to test and treat abnormal cell growth on the surface tissue of the cervix. LEEP may be recommended after abnormal changes in the cervix are confirmed by Pap tests and colposcopy biopsies.

Cryotherapy: This technique consists of applying for a short time on the skin up to the painful area, carbon dioxide at −78.3°C with a pressure. Cryotherapy is used to treat a variety of benign and malignant tissue damage, medically called lesions. The term "cryotherapy" comes from the Greekcryo(κρύο) meaning cold, and therapy (θεραπεία) meaning cure.

Young women: In this study young women are defined as women below 25 years and sexually active.

Prevalence: Prevalence is the real number of cases living with the disease; either during a period of time (period prevalence) or at a particular date in time (point prevalence). Period prevalence provides the better measure of the disease load since it includes all new cases and all deaths between two dates, whereas point prevalence only counts those alive on a particular date. Prevalence is also most significantly reported as the number of cases as part of the total population at risk and can be further categorized according to different subsets of the population.

GP5+/6+: The name of the PCR primers used in the assay to detect HPV, performed at Vrije University, Amsterdam

CHAPTER 1: INTRODUCTION

1.1 Background

Human papillomavirus (HPV) is the most common viral infection of the reproductive tract. It is transmitted by contact and is mainly sexually transmitted, although penetrative sex is not necessarily required for HPV transmission. Almost all women and men sexually active are exposed to be infected by HPV infection. HPV has variety of types and many do not cause problems. The most frequent type to be the main cause of cervical cancer are type 16 and 18 and genital warts by HPV types 6 and 11. HPV infections usually clear up without any intervention within a few months after acquisition, and about 90% clear within 2 years. A small proportion of infections with certain types of HPV can persist and progress to cancer (3)(4)(5)(6). HPV infection can vary significantly between regions with similar resemblances likes ethnic and cultural identities, owing to recent social and political interruption, as observed in North and South Vietnam (7)(8).

Human papillomavirus (HPV) infection is actually a well-established cause of cervical cancer and there is increasing proof of HPV being a suitable factor in other anogenital cancers (anus, vulva, vagina and penis) and head and neck cancers. HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide. HPV vaccines that prevent against HPV 16 and 18 infections are now available and have the potential to reduce the incidence of cervical and other anogenital cancers(9).

The estimate in 2012 shows that globally HPV related cancer is the 4th cause of cancer death worldwide in general female, and the 2nd among women between 15 to 44 years where cancer from HPV remains higher about 265,672 deaths and 527,624 new cases diagnosed annually in the World, and it's the most frequent cancer among women in Low and Middle income Country(LMIC) (2)(3)(9)(10)(11)(12)(13).

HPV is also most common in developing countries where there is no regular screening on human papilloma virus. In sub–Saharan Africa in East Africa, cervical cancer is also the

most common in women with the highest age standardized incidence at over 30 per 100 000 person-years (14).

Natural history studies have shown that the probability of acquiring HPV in young women is higher and that it usually remains positive for a period of less than a year. Countries in sub-Saharan Africa declare that the prevalence is highest among sexually active young women below 25-35 years, usually declining thereafter 25-35 years but around 12% persist and can develop into cervical cancer (5)(15)(13). Thus, the study conducted in Rwanda in 2005 found that cervical cancer represented 27% of diagnosed cancer cases among women (16)(17), while the study on HPV and Cervical Cytology in HIV-Infected and HIV-Uninfected Rwandan Women published in Rwanda, showed that among the highly-risked women are aged below 24 to 35 years of age. And they have HPV52 with highest incidence. In addition to that, HPV 52 and HPV 58 were also the most prevalent in Rwandan women with HIV positive and IST(C. trachomatis) than women with HIV negative(18)(19).

Also another study on Human papillomavirus infection in Rwanda showed that multiples variables were associated with HPV like occupation, tobacco use, marital status, number of lifetime sexual partners, history of receiving cash for sex, the presence of ano-genital warts, HIV positive, number of pregnancies and contraceptive use in the last year. (17).
After introduction of HPV vaccine (Gardasil which protect against HPV types 6,11,16,18, Rwanda initiated a study to evaluate the early impact of HPV vaccine to last for 5 years.
For this purpose, the study aimed at assessing the main factors associated with HPV infection among young women (women less than 25 years).

1.2 Problem statement and justification

HPV infection is a major problem in Rwanda and it is the second most cancer in women.
The overall attribution portion of cervical cancer due to any type of HPV infection in developed countries and low developed countries is 100 HPV types, where HPV prevalence in adolescent girls from sub-Saharan Africa was higher.at 8.4% of girls who -

reported themselves not having had sex, but surprisingly, the study showed they can be affected by HPV during delivery (20). The persistence of HPV infection is precondition for the abnormal ano-genital cytology. It is estimated at 12% worldwide, 5% in America and 3 % East Africa. Most of uninfected young women are limited to histological lesion and the HPV infection regresses spontanely (15,18).

HPV prevalence in Rwanda is still unknown. Looking at the latest data in Human Papillomavirus and Related Cancers, Fact Sheet 2016, Rwanda still has a problem of data for prevalence in general women, the same as women less than 25 ages. However, the latest data shows the overall prevalence was highest at (54%) among women aged below 20 years and this is the reason why this study is focused among young women aiming at finding out the prevalence of HPV and its associated factors((17)(18).

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1.3 Research Objectives

1.3.1 General Objective

The main objective is to assess factors associated with HPV infection among young women (women less than 25 years) in Rwanda.

1.3.2 Specific objectives

The specific objectives of this study will be to:

i. To determine the prevalence of HPV infection among young women less than 25 years of age in Rwanda.
ii. To identify associated factors with HPV Infection among women less than 25 years of age in Rwanda.

1.4 Research questions

i. What is the prevalence of HPV infection among women below 25 years in Rwanda?
ii. What are the factors associated with HPV infection among women below 25 years in Rwanda?

1.5 Justification of the study

The findings of the present study will give deep information on HPV status among young women for more prevention.
The interpretation of results, will help to reduce the burden of maternal mortality after people getting information about risk factors of HPV, they will perform regular early screening and will adhere to HPV vaccine.

CHAPTER2: LITERATURE REVIEW

2.1 Factor s associated with HPV young among women under 25

HPV is a main cause of cervical cancer, but it is not the sufficient cause. There are other co factors which can be associated with HPV infection to cervical cancer. Some of them are Tobacco smoking, parity (fertility), oral contraceptive use, some genital infections due to sexual behaviour (Chlamydia), HIV infection. Thus HPV important risk factors, is for anyone who had sexual intercourse is at risk to be infected on HPV infection. It can also not be possible to know people who will affect to this infection but people with weak immune system can be also at risk (1)(19)(3)(5).

In addition to the above mentioned risk factors, others have been scientifically shown such as tobacco smoking, marital status, wealth, number of sexual partners, oral contraceptive use, uncircumcised penis, early pregnancy(18).

a) Demographic factors

Several studies say that a socio demographics factor influences the increase of HPV. For women starting sexual intercourse at early age increase risk of HPV infection but the reason behind still unknown (3).
Prevalence of HPV varies with age. Study done on age distribution and analyses by non-parametrical models shown the peak of HPV infection in young women and decrease regularly at ages due to characteristics of their cervical epithelium and sexual behaviour and increase again on age greater than 60 (21).

HPV infection is high in young women less than 25 years old transient or decreased following some persistence which refers on immunity response, cervical epithelium characteristics and sexual behaviour where some studies reported the age of theirs first intercourse was from 9 years also the HPV increase in older women at age over 60 years (3)(21)(22)(23)(24)(25)(26). Others studies on women Mexican America showed the high association (age interval 18–19, 16–17, 9–15) for 12.9%, 15.1%, 16.3 respectively) between age at first sex intercourse and HPV infection(27).

Young women with her first full term pregnancy at early age (17ages) are most doubly to be affected to HPV infection than women with full pregnancy on more than 25 years. (2)
K. Singh et al on Human Papillomavirus Infection and Cervical Cytology in HIV-Infected and HIV-Uninfected Rwandan Women, showed that there is no risk on HPV related to all ages, mean that HPV can affect any age group which is different of women with sex at the early age also study done at the moment of HPV implementation in countries explain the highest percentage among women below 19 age (54%). The above mentioned study showed that the prevalence of HPV and carcinogenic among HIV women were higher in age group between 25 to 34 year age (17)(19).

According the marital status, the study conducted by Houlihan et Al on Prevalence of Human Papillomavirus in Adolescent Girls Before Reported Sexual Debut established

that single women are more associated on HPV infection than married women (OR = 1.41) (27)(26) (28).

Also being divorced or widowed, are associated to genital infection including HPV.(28) Thus being single is more risked than married women regarding the frequented partners in general, mean that married women in general have one partner which is different to single women who is not engaged can have more than one partner in his life.

For occupational activities, studies showed that women occupied by work outside home had higher infection than those who stay at home. Women without occupation mean poverty are at risk than those with occupation. They can be have a challenge to access on Pap test or treat themselves seeks the lack of income the poverty is associated with increasing of HPV. Logically women with low income have no access to the regular screening as recommended reason why HPV infection is increasing in some classification with low income(2)(29).

The study done in Sub-Saharan Africa in Uganda country on Factors associated with high-risk HPV positivity in a low-resource setting in sub-Saharan Africa by Sheona M. Mitchell at Al explain that women with low education are more affected by HPV infection (23.4%) than women with high education (13.2%). Mean that more education less HPV infection (29).

b) Sexual behaviors

Sexual intercourse is the main source of HPV infection. Sexual behaviour at early age increase the risk of HPV, prevalence, persistence and possibility to get ano-genital cancers when there are no preventives measures (3)(6)(14).

Sexual behaviour including having sex by cash is the main risk to influence genital infections which are correlated with history to increase HPV infection. Studies in Cambogia and Mexique showed that women received cash for sex was higher

(80.8%)than those who did not have received cash for sex like for their own husband or boyfriends (16.8%) and the majority of them had STI (58.7%) (10)(27)(29).

Worldwide and Sub-Saharan Africa women sexually active and who have more than one partner have higher incidence and prevalence of HPV infection. Many studies revealed that increased number of sexual partner is the most risk factor for HR HPV than women with LR HPV and if not followed refers to cervical cancer development of cervical lesions occurs (5)(12)(21).

There is study in Rwanda, study on HPV also shows the strength relationship between C. trachomatis and N. gonorrhoea with persistence of HPV infection (10)(18)(26).

For Rwanda as country the association of lifetime number of sexual partner and receiving cash for sex even its rarely reported but they strongly associated with acquisition of HPV prevalence and other genital infection(17)(18).

Some studies have also shown that the movement of men linked to sex behaviour change which forward to have multiple partners, these character augments the of HPV exposure to their regular partners(19).

Human immunodeficiency virus (HIV), the virus destroys the immune system and increase the risk of HPV infections. Although, women taking some drugs which suppress the immune system response or whose with transplant organs are more likely to be affected by HPV(2).

HIV and HPV are both sexual transmitted infection and share several risk factors for having infection Several study found that an increased risk of HIV infection increase HPV infection, and decrease the possibility to clear infection in body of human than women with HIV negative (1) (6). (18) (19) (22) (30).

According the study done in Spanish on HIV infected women found high prevalence of HR HPV over 40 prevent in observed, studies speak that HPV16 is most prevalent in HIV women and study done in Maroco showed the high prevalence in HPV with 42.5% and the most were women over 45 years (30).

Recently study shown that the presence of HIV for women with CD4+ T lymphocyte count between 200–350 cells/mm3 are less great to be affected the HPV than those with CD4+ T lymphocyte greater than 350 cells/mm3. This increase is due to severe immunodeficiency of the body's capacity to suppress latent infection although women with HIV negative the HPV frequency is very less although many studies said that the HPV prevalence in women HIV positive is two times than women with HIV negative (3)(31)(19).

In sub-Saharan Africa study showed the interaction between HIV HPV and cervical cancer. HIV is also as one of strong associated factors of HPV infection and increase the persistence of HPV which lead to precancerous lesion or invasive cervical cancer and other genital cancer but some strategies set to prevent cervical cancer actually many country in sub Saharan Africa introduced HPV vaccine which cover two types of HPV (16 and 18) (32)(22)(26).

In Rwanda the status of prevalence of HPV in HIV women was not different with others studies from others countries. HPV prevalence was higher (69%) in HIV women immunosuppressed and risk of HPV carcinoma (46%) although people with HIV positive have possibility to get more than 1 types of HPV. study at the moment of HPV vaccine implementation showed also strong relationship between HIV and HPV infection (17)(18)(19)(31).

c) Reproductive factors

Several studies discussed on number of pregnancy or parity (3 delivery or more) and find an associated risk factor to HPV. Women with more than 3 pregnancies full term, an increased risk to be affected on invasive cervical cancer because of transformation zone of exo cervix (hormonal factors) can make easily to be exposed on HPV (31)(33).

The reason behind it still unknown but the is research said that the changes of hormonal during pregnancy facilitate to be more susceptible to HPV infection(2).

Thus other recent study showed that multiparty and recent use of contraceptives were also significantly and negatively associated with HPV positivity(3)(17).

In Africa and worldwide, many women under oral contraceptive use in long duration has a relationship to influence the risk of invasive cervical cancer.(3)(31)(29) also few studies talk on the Intrauterine Device to be a risk of women ever used than women never used.
The risk is to progress for invasive cervical cancer, the mechanism behind is the traumatism of cervical or inflammation due to strange objects induced in cervix can facilitate the risk of HR HPV(2)(26).

Study done in Nigeria, showed that women with more miscarriages (5 or more) with some sign of vaginal abnormality increase risk of having cervical cancer or pre cancer lesions differently with pilot study on HPV for women with normal cytology showed that the lower risk to get HPV infection (5)(24). Thus, others showed that having the first child at later age had a lower risk to get HPV infection (23).

However, many studies showed the strong correlations between HPV infection and women on oral contraceptive use with long duration. Those women are greater risk to get HPV infection than women who were not used it OR with confidence interval 1.60 (1.03-2.50) (23).
Recent studies in Rwanda on HPV demonstrate the difference with the previous study shown (17).

d) Others health behaviour factors

Tobacco smoking as cofactors in different cancers, Tobacco use kills around 6 million in the word from cancer and others disease. The smokers inhale the nicotine. The majority of smokers start to smoke at early age (teenagers). The smoke is addictive by Nicotine. The inhalation of nicotine facilitates the absorption of toxic mixture containing different unknown carcinogenic. Simple mechanism the tobacco increases the risk of cancer through inflammation and epigenetic change, stress oxidative. Smoking is one of the factors associated to cancers, smoker's women and non-smokers are differently to have a risk of cervical cancer (34)(35)(36).

Studies had shown strengths association between tobacco use and different types of cancer where cervical cancer is included. Thus some researcher also associated the power nutrition with risk of cancer. We can explain that nutrition rich in fruit reduce risk ok cancer, for the people living with poverty is hard to have enough nutrition rich in vegetables and fruit that reason why also can influence the risk of cancer by low immunity (37).

As study conducted by Salvatore Vaccarella et Al on Smoking and human papillomavirus infection: pooled analysis of the International Agency for Research on Cancer HPV Prevalence Surveys Revealed that Tobacco smoking is suspected to facilitate the acquisition or persistence of an HPV infection through a reduced number of Langerhans cells and CD4 lymphocytes, which are markers of local immune response in the cervix. Also other research said that smoking affect immune system and cannot combat HPV infection (2). Tobacco smoking reduces the capacity of natural killer cell which refers to create the weak immune system and increase HPV acquisition.

Although the association of tobacco with HPV is focused on HPV type 16 which linked to carcinogenic (38). The HPV infection decrease with age, for smokers with more than 3 cigarettes per day, the persistence of HPV is higher than ever smokers. There are studies studies showed that smoking is closely to sexual behaviour (38)(39)(40).
Salvatore Vaccarella at al said “It is not clear whether smoking is associated with inincreased acquisition or persistence of human papillomavirus (HPV)”.Also said that among current smokers, HPV prevalence increased with smoking intensity, but a clear dose–response relationship was exclusively seen among women who declared one lifetime sexual partner(41).

For behaviour change in tobacco use, some studies ask to some countries to increase the tax of industries hope that will reduce the tobacco users(42). There is a limit in research related on related on smoking and HPV in Rwanda except study mixed with others factors.

Normally the prevention of HPV is not complicated. Several countries in word launched the cervical cancer epidemiology and prevention in close collaboration with the educational branch at (IARC, (FIGO), (UICC), and IAEA in 2011(3).

HPV is prevented by several things vaccinate boys and girls between 11 and 12 years old, use of condom or limit sexual partners and regular screening with pap smear for adult women(1). Thus reinforce strategies of behaviour change on sexual intercourse can be one of strategies for preventives against ano-genital cancers(3).

Vaccination is the primary prevention for HPV; several studies shown that HPV vaccine is effective and safe when used at the right time. It can protect both males and females against HPV infection which lead to cervical cancer. Worldwide women at risk for invasive cervical cancer, can spread on the 8 most common HPV types worldwide, with specific rank order, are HPV16, 18, 33, 45, 31, 58, 52 and 35. HPV16 and HPV18 are generally consistently and most common type to increase number of cervical cancer. Others can be ressemblably across the world and change or differs according the regions(3).

In developing countries Preventives, a measure is possible to vaccinate for adolescents girls before starting sexual intercourse but countries still have some challenges to limited medical services for girls, to strength high quality standards of screening by cytology in developing countries costly, and too often ineffective. Where have possibility of HPV vaccine, girls are vaccinated and are protected, thus to be successfully and cost effective its need to reach all targeted population which need the high logistic for deliverable service, access and compliance, for women already infected will be followed and treated according the protocol or guideline of cervical cancer treatment. Although if women screened early are reduced the burden of invasive cancer(32).

In Africa Actually there are two available vaccines. HPV vaccine bivalent and quadrivalent. The bivalent cover HPV types 16 and 18(Cervarix) and the quadrivalent (Gardasil) protect against HPV 16, 18, 11, 6. HPV types 6 and11 are the most causes the genitals warts and HPV 16, 18 for invasive cervical cancer. Those vaccines are cost

effective for women non-exposed to protect against HPV and cervical cancer and are prophylactic not curative (43)(44).

HPV vaccine 16 and 18 are the most preventable vaccine to reduce the burden of invasive cervical cancer, which contribute to cover over 70% of all cervical cancer cases. There are others HPV types which are exposed to cause cervical cancer on minim proportion (20%) like 31, 33, 35,45, 52, and 58(3). The government of Rwanda introduced HPV vaccine by in 2011 as the first country in Africa for cancer prevention.
It started by HPV quadrivalent which cover 4 relevant vaccines (HPV types 16, 18, 11, 6) with coverage of >90% in school girls aged 9-15. This will offer an excellent opportunity to assess vaccine effectiveness for country (45)(46).

WHO recommend screening for women age between 21 to 65 years old can prevent cervical cancer. For those with sexually active it recommends also the correct use of condoms for each sex intercourse and awareness of male circumcision to reduce the chance of getting HPV, but the condom protect the space covered by condom, which mean that the condom is not protected fully against HPV since it cannot cover the area of all pubis but it can be the alternative preventive method. Awareness on male circumcision can help also it recommend fidelity in couple have sex with one person (1)(3)(23).

Cervical screening programs are still needed for women already infected or unimmunized with the potential for future infection. Several methods are currently used in developing countries for cervical cancer screening. The most used is pap smear (Papanikolaou) which is most cost effective.Is the cervical cancer screening procedure and its supply the information of early detection of precancerous lesions or cancerous after testing on microscope. This method was the main method used to decrease the prevalence of cervical cancer.
Human papilloma virus–deoxyribonucleic *(*HPV–DNA) approach is a recent and first method for cervical cancer screening. this test help to reduction of mortality for invasive cervical cancer (ICC) by detecting the high risk damage of HPV and detect overall HPV DNA(47)(41). Message behind of this preventive method is that when screening is early

more curable precancer lesions which lead to cervical cancer. When pre-cancer lesions detected it can be treated (2).

Study done on Human Papillomavirus Infection and Cervical Cytology in HIV-Infected and HIV-Uninfected Rwandan Women, explain the high morbidity and mortality of women who have never screened and acquired the abnormalities and HPV infection (19).

The main implication in this study will contribute to increase Knowledge on prevalence of HPV among young women, to describe and identify the main risk factors among young women in Kigali, the information will help or contribute for government/MOH or leaders in decision making regarding data available to advocate on cervical cancer prevention and possible treatment; (regular screening and vaccination on young age even it's already started to increase the coverage on all doses).

2.2 Conceptual framework

Below is the figure of the concept framework of study, it's explained briefly the assumed factors associated to HPV infection.

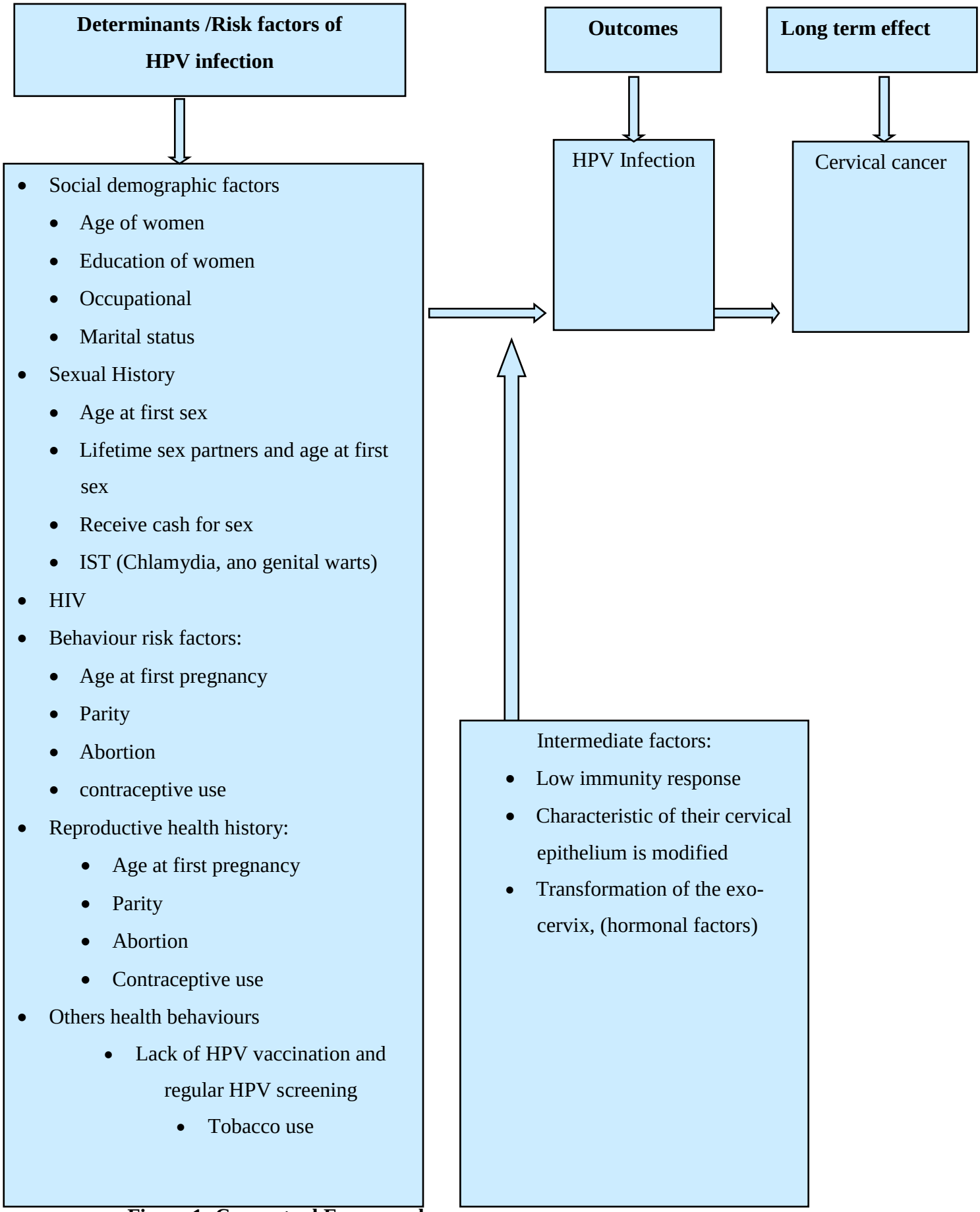

Figure 1: Conceptual Framework

CHAPTER 3: RESEARCH METHODOLOGY

3.1. Study design

This was a retrospective cross sectional study. It was based on data collected at Muhima District Hospital in order to assess early impact of HPV vaccine and screening in Rwanda, from 2013 to 2014.

3.2. Target population

All women under 25 years of age, sexually active, were eligible in this study.

3.3. Source of data

Using 2508 data collected in the study conducted by MoH with the support of IARC from 2013 to 2014, we selected data of women age 25 years old, making a sample population of 1177. The IARC team had given permission to use their data for secondary analysis.

3.4. Description of the sample (study participants)

Between July 2013 and May 2014, a survey was conducted by the Ministry of Health of Rwanda in collaboration with the IARC, Lyon, France. The study aim was to enrol 2,500 women from the general population using an age-stratified approach, namely 1,000 women aged below 25 years old, 500 women aged 25 to 29 years old, 200 women in each five-year age group between 30-34 and 45- 49 years, and 200 women aged >50 years.

All mentally and physically competent women were eligible for the study, regardless of their marital status, with exception of those who were known to be pregnant. At that time, 2508 were included in the study. For the present study, we selected women aged below 25 years which made a total of 1177. The data were extracted on an excel sheet and computed through STATA.

Inclusion criteria: Data from all mentally and physically competent and sexually active women aged below 25 years were eligible for the study, regardless their marital status.
Exclusion criteria: Data of women aged 25 years and above. A census approach was adopted where all women aged below 25 years were selected. The study participant comprised of 1177 women.

3.5 Data collection and instruments development procedures

Socio demographic factors, sexual behaviour factors, reproductive health history and other independent variables were retrieved from IARC database based on the initial questionnaire used in the baseline study.

3.6 Ethical considerations

Before doing the research, an official permission was request from IARC and received. Rules of confidentiality were respected.no identifier was attached to any participant data during collection, cleaning, analysing as well as displaying results. All data were password protected and only the data analyst had access to the password.

3.7 Data management and processing

Data were acquired on an excel sheet and then imported in STATA13.0 for further processing and analysis.Results are presented in statistical tables and HPV infection and its associations between independent variables and HPV infection.

3.9 Data Analysis

Analysis included descriptive statistics where frequency tables were presented in order to provide information on HPV prevalence infection. Bivariate analysis using OR, P value, Chi 2 or fisher's exact tests were performed between independent variables and HPV infection for eventual statistical significance of the proportion. Multivariate logistic

regression was performed for statistically significant variables to determine main predictors of HPV infection. The significance level was put to ($P< 0.05$) at the confidence level of 95%.

The measurements focused specifically on HPV infection and its related determinants among young women. The main variable of interest (dependent variable) is HPV infection, which is binary variable where those who has HPV infection responded yes and those who don't have responded no (yes or no).

The explanatory (independent) variables that maybe associated to the HPV among young women were:

- socio demographic factors such as age, marital status, education level, and occupation,
- sexual behaviour such as life time sexual intercourse, age at first sexual intercourse, years since first sexual intercourse, number of sexual partners that women had in life, IST like chlamydia or ano-genital warts and HIV, having sex by cash and sexual activity,
- reproductive health history such as menarche, year since first menarche, number of pregnancy, contraceptive use
- Other independent variables which are part of this study to check the risk of HPV infection include smoking, and history of lack of prevention such as vaccination and screening.

CHAPTER 4: RESULTS

4.1. Descriptive analysis

4.1.1 Prevalence of HPV and HPV types

A total of 1177 women aged 15-24 provided cervical cell samples and were included in study. Data of 1177 was computed and analyzed.
Women were systematically tested with GP5+/6+. The overall prevalence of HPV among young women (15-24 years) in Rwanda is 42.8%. Table 1; shows in details the different types of HPV by single and multiple.

In total, the prevalence was higher in single and multiple HPV type. 240 (20.4%) women had single-type and 260 (22.9%) had multiple-type HPV infections. HPV16 was the most prevalent type in women with normal cytology (6.6%) and (10.4%) with single and multiple infections respectively.

The most prevalent high-risk HPV types were; HPV52 (2.6% for single 7.8%for multiple types), HPV58 (2.2% for single and 6.4% for multiple), HPV 45 (2.2% single and5.4% multiple), and HPV 18 (2.2% single and 4.8% multiple).

For Low risk HPV, the common types were; HPV66, (1.6 % single and5%for multiple), HPV 70 (1.2% single and3.4 %for multiple) and HPV 6 with (0.8%single and 4% for multiple).

Table 1: HPV prevalence and its types by single and multiples infections among young women 15-24 years (n=1177)

HPV Positive						
HPV type	**Single**		**Multiple**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**
	240	**20.39**	**260**	**22.09**	**500**	**42.48**
High-risk						
16	33	6.6	52	10.4	85	17
18	11	2.2	24	4.8	35	7
31	10	2	22	4.4	32	6.4
33	3	0.6	19	3.8	22	4.4
35	10	2	40	8	50	10
39	4	0.8	22	4.4	26	5.2
45	11	2.2	27	5.4	38	7.6
51	8	1.6	23	4.6	31	6.2
52	13	2.6	39	7.8	52	10.4
56	8	1.6	35	7	43	8.6
58	11	2.2	32	6.4	43	8.6
59	8	1.6	15	3	23	4.6
68	3	0.6	7	1.4	10	2
Possibly high-risk and low risk						
6	4	0.8	20	4	24	4.8
11	2	0.4	11	2.2	13	2.6
26	4	0.8	8	1.6	12	2.4
30	3	0.6	10	2	13	2.6
53	3	0.6	11	2.2	14	2.8
66	8	1.6	25	5	33	6.6
70	6	1.2	17	3.4	23	4.6
73	2	0.4	9	1.8	11	2.2

4.1.2 Prevalence of HPV according to socio-Demographic factors

The study presented demographic, sexual behavioral, reproductive and other factors related to HPV among women between 15-24 years.

In socio demographic characteristics, HPV was most prevalent among women below 20 years with 53.8% in all women tested HPV positive. Women with low education had high HPV with 48.1%. HPV was most prevalent among women with professional occupation 49.1%. HPV was high in women with single marital status, 50.7%. Table 2 below shows different detailed demographic factors in relation to HPV.

Table 2 : HPV Prevalence according to demographic factors

	HPV status				
Variables	**Negative**		**Positive**		**Total**
	n	**%**	**n**	**%**	
Age categories					
<20 (n=197)	91	46.2	106	53.8	197
20-24 (n=980)	586	59.8	394	40.2	980
Education categories					
No Education (n=104)	54	51.9	50	48.1	104
Primary (n=771)	457	59.3	314	40.7	771
Secondary and higher (n=302)	166	55	136	45	302
Occupation categories					
Domestic service (n=567)	309	54.5	258	45.5	567
Sales and services (n=137)	75	54.7	62	45.3	137
Manual worker (n=235)	114	62.6	68	37.4	182
Professional (n=60)	28	46.67	32	53.3	53
Agriculture (n=231)	151	65.4	80	34.6	231
Marital status					
Single/Widow/Separate (n=388)	196	50.52	192	49.48	388
Married/Cohabiting (n=789)	481	61	308	39	789

Residence					
Kigali, Nyarugenge (n=1,045)	615	58.9	430	41.1	1045
Kigali, Gasabo or Kicukiro (n=114)	55	48.2	59	51.8	114

4.1.3 Prevalence of HPV according to Sexual behavior factors

About sexual behavior factors; lifetime sexual partners as described in table 3, women who had more than 2 partners had a higher HPV infection than women with one partner (51.1% vs 35.8%) respectively. Age at first sexual intercourse as shown, women who had her first sex intercourse at age below 20 have HPV higher compared to women over 20 years (46.2% vs 33% respectively).

Women that started their sexual activity last year prior to study period had more risk to be affected by HPV infection than women who started sexual activity late (42.6% vs 39.2%). Among women who receive cash for sex, out of 11 women who responded yes, 3 of them were HPV positive. This study also showed that among 23 cases of genital warts found in women tested, 16 cases (69.6%) had HPV infection.

For HIV status, 126 women self-reported to be infected by HIV, among them 78 (61.9%) were HPV positive. Similarly, for chlamydia status, among 1177 women tested, 120 women were chlamydia positive, and among them 69 (57.5%) were HPV Positive.

Table 3: Prevalence of HPV according to sexual behaviour

Variables	HPV status Negative		Positive		Total
	n	%		%	
Number of partner					
<=1 Partner (n=560)	360	64.3	200	35.7	560
2-5 Partners(n=468)	302	52.4	274	47.6	576
> 6 Partner (n= 41)	15	36.6	26	63.4	41
Prefer not answer (n=108)	68	13.6	40	8	108
Age at first sex					
<20 (n=847)	456	53.8	391	46.2	847
>=20 (n=330)	221	67	109	33	330
Sexual activity last year					
(Yes=1,115)	640	57.4	475	42.6	1115
(No=62)	37	59.7	25	40.3	62
Receive cash for sex					
Never (n=1,165)	668	57.3	497	42.7	1165
Ever (n=11)	8	72.7	3	27.3	11
Genital warts					
Yes (n=23)	7	30.4	16	69.6	23
No (n=1,154)	670	58.1	484	41.9	1154
HIV status					
Positive (n=126)	48	38.1	78	61.9	126
Negative (n=821)	509	62	312	38	821
Unknown (n=230)	120	52.2	110	47.8	230
Chlamydia status					
Negative (n=1,053)	626	59.4	427	40.6	1053
Positive (n=124)	51	41.1	73	58.9	124

4.1.5 Reproductive factors

Table 4, shows the reproductive factors which assessed in this study. Age at menarche, the study showed that women who had their menstruation in age group of 14 to 18, among 723 women tested HPV, 320(44.3%) were HPV positive. Among women, who had no pregnancy (n=143), 76 (53.1%) were HPV positive. About the history of use of contraceptives, it was found that among women who don't use the contraceptive method (n=513) 48.1% had HPV positive.

Table 4: Prevalence of HPV according to reproductive factors

Variables	HPV Status				
	Negative		Positive		Total
	n	%		%	
Age at menarche					
9-13 (n=379)	224	59.1	155	40.9	379
14-18 (n=723)	403	55.7	320	44.3	723
Unknown (n=75)	50	66.7	25	33.3	75
Number of pregnancy					
<1 (n=811)	451	38.32	360	30.59	143
>1 (n= 366)	226	19.2	140	11.89	668
Use contraceptive					
Yes (n=662)	411	62.1	251	37.9	662
No (n=515)	266	51.7	249	48.3	515
contraceptive categories					
Hormonal contraceptive (n=571)	356	62.3	215	37.7	571
Intra-uterine device (n=59)	36	61	23	39	59
Others (n=34)	19	55.9	15	44.1	34

4.1.6. Prevalence of HPV according to others health behavior factors

We assessed other factors such as tobacco use and history to vaccination of HPV; as shown in table below, among 52 women used tobacco, 36 (69.2%) were HPV positive. Vaccination status to HPV also showed that among women who self-reported to have been vaccinate (n=30), 20 of them were found to be HPV positive.

Table 5: Prevalence of HPV according other health behavior

	HPV status				
Variables	**Negative**		**Positive**		**Total**
	n	**%**	**n**	**%**	
Tobacco use					
No (n=1,124)	660	58.7	464	41.3	1124
Yes (n=52)	16	30.8	36	69.2	52
Vaccinated on HPV					
Yes(n=30)	10	33.3	20	66.7	30
No(n=1,144)	667	57.52	480	41.8	1144

4.2 Bivariate analysis

4.2.2 Demographic factors associated to HPV

HPV positivity was computed and compared to the demographic factors. Age category of women (p=0.001), occupation (p=0.005), marital status (p=0.01),
HPV was not associated with education category.
We have not compute the residence because all lived in Kigali city.

Table 6: demographic factors associated to HPV

Variables	n	%	OR	95%CI	P-value
Age categories					
<20 (n=197)	106	53.8	1.73	[1.27 - 2.36]	**0.00**
20-24 (n=980)	394	40.2	1		
Education categories					
No Education (n=104)	50	48.1	1		
Primary (n=771)	314	40.7	0.74	[0.49-1.12]	0.15
Secondary and higher (n=302)	136	45	0.88	[0.57 - 1.38]	0.59
Occupation categories					
Domestic service (n=567)	258	45.5	1		
Sales and services (n=137)	62	45.3	0.99	[0.68-1.44]	0.96
Manual worker (n=235)	68	37.4	0.71	[0.51-1.00]	0.05
Professional (n=60)	32	53.3	1.37	[0.80-2.33]	0.25
Agriculture (n=231)	80	34.6	0.63	[0.46-O.87]	**0.005**
Marital status					
Single/Widow/Separate (n=388)	192	49.48	1.53	[1.20-1.95]	**0.00**
Married/Cohabiting (n=789)	308	39	1		

4.2.3 Sexual behavior associated to HPV infection

HPV positivity was computed and compared to the sexual behavior, life partner ($p<0.001$), age at first sexual intercourse ($p<0.001$), ano-genital warts ($P=0.012$), HIV status ($p<0.001$), chlamydia trachomatis status ($p<0.001$), number of sexual partners Sexual activity for the last year, receive cash for sex.

Table 7: sexual behaviour to HPV infection

Variables	n	%	OR	95%CI	P-value
Number of partner					
<=1 Partner (n=560)	200	35.71	1		
2-5 Partners(n=468)	234	50	1.63	[1.29-2.07]	**0.00**
> 6 Partner (n= 41)	26	63.4	3.12	[1.61-60.2]	**0.001**
Age at first sex					
<20 (n=847)	391	46.2	1.74	[1.33- 2.27]	**0.00**
>=20 (n=330)	109	33			
Sexual activity last year					
(Yes=1,115)	475	42.6	1		
(No=62)	25	40.3	0.91	[0.54 -1.53]	0.72
Receive cash for sex					
Never (n=1,165)	497	42.7	1		
Ever (n=11)	3	27.3	0.50	[0.13- 1.91]	0.313
Genital warts					
Yes (n=23)	16	69.6	1		
No (n=1,154)	484	41.9	0.32	[0 .13-0 .77]	**0.012**
HIV status					
Positive (n=126)	78	61.9	2.65	[1.80- 3.90]	**0.00**
Negative (n=821)	312	38	1		
Unknown (n=230)	110	47.8	1.5	[1.11- 2.01]	**0.007**
Chlamydia status					
Negative (n=1,053)	427	40.6	1		
Positive (n=124)	73	58.9	2.098452	[1.44- 3.06]	0.00

4.2.4 Reproductive health behavior associated to HPV infection

HPV positivity was computed and compared to reproductive and other factors to determine the association. The number of pregnancy ($p<0.001$), use of contraceptive ($p<0.001$), type of contraceptive use ($p<0.001$), were found to be associated with HPV positivity

Age at menarche was not associated to the HPV infection.

Table 8: Reproductive health factor associated to HPV

Variables	n	%	OR	95%CI	P-value
Age at menarche					
9-13 (n=379)	155	40.9	1		
14-18 (n=723)	316	44.3	1.15	[0.89-1.48]	0.27
Unknown (n=75)	29	34	0.75	[0.46-1.22]	0.25
Number of pregnancy					
<1 (n=811)	360	30.59	1		
>1 (n= 366)	140	11.89	0.78	[0.60-0.99]	**0.05**
Use contraceptive					
Yes (n=662)	251	37.9	0.54	[0.36-0.80]	**0.00**
No (n=515)	249	48.3	1.00		
contraceptive categories					
Hormonal contraceptive (n=571)	15	44.1	1		
Intra-uterine device (n=59)	23	39	1.53	[1.21-1.94]	**0.00**
Others (n=34)	215	37.7	1.52	[1.2-1.9]	**0.00**

4.2.5: Other health behavior factors associated to HPV

HPV positivity was computed and compared to health behavior, tobacco use (p=0.001) and HPV vaccination status (p=0.009) were found to be associated with HPV positivity.

Table 7: Other health behavior risk factors associated to HPV

Variables	n	%	OR	95%CI	P-value
Tobacco use					
No (n=1,124)	464	41.3	0.31	[0.18 -0.57]	**0.00**
Yes (n=52)	36	69.2		1	
Vaccinated on HPV					
Yes(n=30)	20	66.7	1		
No(n=1,144)	478	41.8	2.72	[1.29-5.99]	**0.009**

4.3. Multivariate analysis

In the full model analysis, we considered all 11 variables that were significant in the bivariate analysis above. Lifetime partners, age at first sex, HIV status, chlamydia status, tobacco use, vaccination status were left in logistic regression model and obtained corresponding adjusted odds ratios for each variable.

Women with partner between 2 to 5partner, 46.8% more likely to be HPV positive compared to women with one partner (OR=1.48[1.13-1.93). Women who had sex after 20 years of age were 0.73 times more likely to be HPV positive compared to women who had sex before 20 years of age (OR=0.7395% CI [0.54-0.99]). Women who self-reported to be HIV positive were, 2.34 times more likely to be HPV positive compared to those who self-reported to be HIV negative (OR=2.34, 95% CI [1.55-3.53]).

Similarly, women with unknown HIV status were 1.41 times more likely to be HPV positive compared to women with self-reported HIV negative (OR=1.41, 95% CI [1.03-1.90]. Women who tested chlamydia trachomatis negative were 4.46 more likely to be HPV positive compared to women who tested chlamydia trachomatis positive (OR=0.46, 95% CI [0.31-0.69]Women who do not used tobacco were 0.41 time more likely to be HPV positive compared to women who never smoked (OR=0.41, 95% CI [0.21-0.77]. Women who do not received HPV vaccine were 2.86 time more likely to be HPV positive compared to women who never vaccinated (OR=2.89, 95% CI [1.31-6.25].
The following variable: Uses of contraceptive and contraceptive categories were dropped from full model due to collinear of these variables.

Table 8: Odds ratios (OR) and 95% confidence intervals (CI) for human papillomavirus (HPV) positivity and its Factors associated

Variables	n	%	Adjusted full model OR (95%CI)	P-Value	adjusted final model OR(95%CI)	p-value
Age categories						
<20 (n=197)	106	53.8	1			
20-24 (n=980)	394	40.2	0.81[0.57-1.16]	0.25		
Occupation categories						
Domestic service (n=567)	258	45.5	1			
Sales and services (n=137)	62	45.3	1.08[0.73-1.60]	0.70		
Manual worker (n=182)	68	37.4	0.75[0.51-1.09]	0.13		
Professional (n=60)	26	49.1	1.06[0.60-1.87]	0.85		
Agriculture (n=231)	80	34.6	0.79[0.56-1.12]	0.19		
Marital status						
Single/Widow/Separate (n=388)	192	49.48	1			
Married/Cohabiting (n=789)	308	39	1.21[0.92-1.60]	0.16		
Lifetime Partner						
<=1 Partner (n=560)	200	40	1			
2-5 Partners(n=468)	234	46.8	1.28[0.99-1.67]	**0.059**	1.48[1.13-1.93]	**0.004**
> 6 Partner (n= 41)	26	5.2	1.03[0.47-2.22]	0.94	1.48[0.71-3.06]	0.29

Age at first sex						
<20 (n=847)	391	46.2	1			
>=20 (n=330)	109	33	0.70[0.51-0.96]	**0.02**	0.73[0.54-0.99]	**0.045**
genital warts						
Yes (n=23)	16	69.6	1.92[0.75-4.94]	0.17		
No (n=1,154)	484	41.9	1			
HIV status						
Negative (n=821)	312	38	1			
Positive (n=126)	78	61.9	2.31[1.52-3.50]	**0.00**	2.34[1.55-3.53]	**0.00**
Unknown (n=230)	110	47.8	1.31[0.96-1.80]	0.08	1.41[1.03-1.90]	**0.03**
Chlamydia status						
Negative (n=1,053)	427	40.6	0.46[0.30-0.68]	**0.00**	0.46[0.31-0.69]	**0.00**
Positive (n=124)	73	58.9	1			
Number of pregnancy						
<=1 (n=811)	360	30.59				
>1 (n= 366)	140	11.89	0.83[0.62-1.10]	0.2		
Tobacco use						
(n=1,124)	464	41.3	0.44[0.23-0.85]	**0.01**	0.41[0.21-0.77]	**0.006**
(n=52)	36	69.2	1			
Vaccinated on HPV						
Yes(n=30)	20	66.7	2.21[0.98-5.01]	**0.06**	2.86[1.31-6.25]	**0.008**
No(n=1,144)	478	41.8	1			

4.4 Discussions

HPV among women between 15-24 years is less documented in Rwanda. To our knowledge we are not aware of any study done in Rwanda investigating the prevalence and risk factors of HPV among women between 15-24 years. This study is aimed at investigating the prevalence of HPV and its risk factors among women between 15-24 years of age in Rwanda. We used data extracted from a cross sectional study done in Rwanda which aimed at assessing the early impact of HPV vaccine among women between 18-65 years in Kigali city, Rwanda.

A sample of women between 15-24 equal to 1,177 were extracted and all corresponding factors related to demographic, sexual behaviours, reproductive and other factors were analysed using STATA 13.

HPV prevalence among women with 15-24 years of age was 42.48%. and those with HPV positive (n=500), 240 (20.4%) had a single type of HPV and those with 260 (22.9%) had multiple types of HPV. Similary the same study inin Nigeria showedthe same results but with a difference in HPV prevalence of 26.3% (48). And in Colombian (20.4%) of women less than 20 years were found with big prevalence of (53.8%).

A study done in Kenya on distribution of HPV where the prevalence was (44.3%) (49) and in Cambodia was 40.9% (10).In Colombia, women aged less than 25 years had almost five times higher prevalence rates of multiple infections (9.6%) than women aged 35 years(7).

HPV type-specific prevalence rankings can vary by regional or country. The most prevalent high-risk of HPV types in our study were; HPV52 (2.6% for single 7.8% for multiple types), HPV58 (2.2% for single and 6.4% for multiple), HPV 45 (2.2% single and 5.4% multiple), and HPV 18 (2.2% single and 4.8% multiple). Same as it was done in Nigerian on the burden, distribution and risk factors for cervical oncogenic human papilloma virus infection in HIV positive Nigerian women where. HPV 16 (3.9%), 35 (3.5%), 58 (3.3%) and 31 (3.3%) were the most common hr HPV infections detected (22).

However, different findings from the hr HPV distribution patterns describ other sub-Saharan African regions as, Americas, Asia and Europe (50)

For Low risk HPV, the common types were; HPV 66, (1.6 % single and 5% for multiple), HPV 70 (1.2% single and 3.4 % for multiple) and HPV 6 with (0.8% single and 4% for multiple). The HPV types with low risk in our population were 6, 11, 26, 53, 66, 70 and 73. In a similar study in Colombia with 6, 11, 26, , 61, 70, 73 except HPV 66 (7).

HPV-16 (6.6%), was the most prevalent HPV type detected, while other common high-risk types included 45(2.2%), 52(2.2%), 18(2.2%), and 58(2.2%), 35(2%) 51(1.6%), 31(2%) (22). A similar study in Nigeria found out the same HPV type as in our findings 16 (3.9%), 35 (3.5%), 58 (3.3%), 31 (3.3%), 18 (2.3%), 52 (2.3%), 51 (1.9%)). Although, the difference in this studies like HPV 51 and HPV 101arenot found in our findings (22).

As seen above some findings in various studies (24)(49)are similar with other previous study where HPV 16 is higher at (12.1%) from 14 sites of HPV vaccine trial among young girls, Nigeria 3.9% (14)(22).
HPV 18 was not exclusively biggest type in our population, which differs from other studies conducted in both random populations and selected cervical cancer or pre-cancer populations which is detected highly at 18 HPV type (17) (21) (22)(51).

Regarding the factors associated to the HPV infection, we computed demographic factors, sexual factors, reproductive factors and others. From demographic factors, our findings show that HPV prevalence was highest at (53.8%) among women $\leq$19 with normal cytology. This is similar in Colombia where HPV prevalence was higher 26.1%.(26) whereas other studies have showed HPV prevalence remaining equally high, or even growing in middle and old age, this is different from our findings, age was not statistically significant in adjusted full model (14) (15) (51) (52).

The literature explained shows the progressive decrease with age which is similar with several studies in sub-Saharan African populations and other countries have reported diminishing of HPV prevalence with age (7) (15)(18) (53).
Even if it declined as said, HR HPV prevalence remained 10-15% in women aged 35 or older as explained in the literature; HPV prevalence decreased less with age for people living with HIV than among HIV-negative women (5)(15)(13).

On sexual behaviour as predictor factor, age at first sex, the prevalence of HPV was predominant in women who debuted sex at below age of 20 with 46.2 % (54). This is the same as a study done in Mwanza region of Tanzania where sex debut remained a high prevalence in girls with age between 15 and 16 with 31.8%. Several literature confirmed that early age at first sex intercourse has been identified as risk factor of Invasive Cervical Cancer (ICC) (14) (55).

The study found out that the HIV infection had significantly higher risk of HPV than negative women (61.9%, 38%) respectively OR: 2.34 95% CI [1.55-3.53], a similar study in Nigerian women had a higher prevalence of HPV among HIV women confirming previous findings from Rwanda (56)(16)(18); sub-Saharan Africa and Cambodia, the HPV prevalence was very high among women with HIV positive 78.8% (10) and elsewhere (24)(23)(31).

There is several meaning which explains the increase of HPV among people with HIV and other genital infectious diseases. HIV, chlamydia and HPV have the same way of transmission, as well as behavioural risk factors, seems to facilitate the transmission of HIV or HPV acquisition. In the same way, HPV replication appears more efficient in immunosuppression individual than individuals with normal immune or 52 people used tobacco, 69.2% had HPV infection, which confirms that the smoking prevalence is 5.6% among Rwandan women and risk factor to cervical cancer, it remains different from our findings (23)(54).
We also found that using Tobacco among women has a high risk of getting the HPV infection 2.55[1.37- 4.74] and as literature says tobacco smoking is suspected to facilitate

the acquisition or persistence of an HPV infection through a reduced number of Langerhans cells and CD4 lymphocytes, which are markers of local immune response in the cervix and the association of tobacco with HPV lead to HPV type 16 which linked to carcinogene (2)(38).

In addition to that, Tobacco smoking is suspected to facilitate the decrease of immune system function. the 23 epidemiological study work on smoking and cervical cancer showed that smoking increase risks of having squamous cell carcinoma and other studies showed people who smoke, have feasibility declining HPV (41).

A pooled analysis on smoking and human papilloma infection confirmed the strong association among people who smoke(OR 1.18, 95% CI 1.01–1.39) contrary to study done on modifiable risk factors associated to student university where the non-smokers had an increase HPV infection.(57)

The findings for factors associated with HPV infection are likely to have the same study on Human papillomavirus infection in Rwanda. (17).

4.4.1 Study limitations and implications for future research

This study had strengths and weaknesses.

Strengths were

- The possibility of acquiring data and other necessary information was easy
- The study includes a relatively large number of young women especially those below 25 years
- The Study includes high-quality HPV testing and liquid-based cytology.
- Test used was of high-quality GP5+/6+ HPV, and it is clinically validated.
- The study population represented the general female population in Kigali.

Weakness was:

- It is difficult to evaluate women by level of HPV due to asymptomatic infection.
- In our findings some variables such as number of pregnancy, being vaccinated, genitals warts were not significant which is different from others studies, the constant might be the sample small size.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

The findings of this study confirm Rwanda to be a setting of high prevalence of HPV. HPV HPV16, 52, 45, 35, 58 and 18 were the most common HPV infections in the population between 15 to 24 years. The risk associated to HPV infection were HIV, age at first sex intercourse, Chlamydia and tobacco use and not being vaccinated.

This information will help for further studies and planning in country by using this data.

5.2 Recommendations

To the Ministry of Health:

- From the information of this research, strengthen early screening program among young women
- Reinforce awareness and Information, Education and Communication (IEC) on determinants of HPV in order to reduce the risk factors.
- Strengthen vaccination program in the country.

For further studies:

- Perform further studies on cervical cancer.
- Include a larger number of participants and extend it to the whole country.
- Perform cohort studies to evaluate whether detection of HR-HPV in women with normal cytology can predict development of cervical cancer over time.
- Perform longitudinal studies to evaluate whether detection of HR-HPV in HIV-infected women despite normal cytology predicts development of cervical dysplasia and/or cervical cancer over time.

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APPENDICES

A. Ethical approval

B. Author's approval if secondary data analysis or use of standards questionnaires

C. Informed consent form

D. Data collection Tools (questionnaires)