ASSESSMENT OF RISK FACTORS ASSOCIATED WITH CERVICAL CANCER AMONGST WOMEN ATTENDINGTHE ONCOLOGY CENTRE AND HEALTH FACILITIES IN WINDHOEK, KHOMAS REGION

A CASE CONTROL STUDY

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ABSTRACT

Cervical Cancer is one of the leading causes of cancer related deaths in women worldwide. These deaths are unnecessary, as there is evidence that Cervical Cancer is preventable and treatable if detected early and managed effectively. Human Papilloma virus (HPV) is a well-known cause of Cervical Cancer with HPV genotypes 16 and 18 are responsible for 70% of all Cervical Cancer worldwide. However, there are other risk factors. Current estimates indicate that every year 527,624 women are diagnosed with Cervical Cancer and 265,653 die from the disease. In Namibia with a population of around 2.1 million, 632,000 women aged 15 years and above are at risk of developing Cervical Cancer. This study aimed to determine the risk factors associated with Cervical Cancer among women in Khomas region, Namibia.

The researcher conducted an unmatched 1:1 case control study. A sample size of 402; 201 cases of Cervical Cancer and 201 appropriate controls were chosen using a simple random sampling method. Data was analysed using Epi info 7. Bivariate analysis was done using odds ratio to determine association between suspected risk factors and Cervical Cancer. Significant associations at 5% on bivariate analysis was loaded into a logistic regression model to determine predictors of Cervical Cancer.

The multivariate logistic regression analysis found that after adjusting for HIV status, the following variables were significant risk factors of Cervical Cancer: family history of cancer (AOR:2.55; 95% CI, 1.64-3.95; p = 0.0004), unemployment (AOR: 2.56; 95% CI, 0.26-0.59; p = 0.0001), marital status (AOR: 1.90; 95% CI, 1.25-2.89;p=0.003), living in rural areas (AOR: 2.77; 95% CI, 1.26-4.21; p= 0.000002), use of contraceptive (AOR: 1.64; 95% CI, 1.08-2.49; p = 0.03), lack of secondary education (AOR: 2.49: 95% CI, 1.50-4.13; p = 0.0005) and not attending Pap smear screening (AOR: 1.92; 95% CI, 0.33-0.82; p = 0.007).

These risk factors associated with Cervical Cancer in our environment could be the basis for targeted screening and treatment programme. The introduction of routine HPV vaccination could reduce Cervical Cancer.

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LIST OF ABBREVIATIONS AND ACRONYMS

AFSI	Age at First Sexual Intercourse
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
CDC	Centres for Disease Control and Prevention
CIN3	High grade precancerous cells
CI	Confidence Interval
COR	Crude odd ratios
DNA	Deoxyribonucleic Acid
DHIS	District Health Information System
DVT	Deep Vein Thrombosis
FIGO	International Federation of Obstetrics Gynaecology
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
LLETZ	Large Loop Excision of Transformation Zone
NDHS	Namibian Demographic and Health Survey
MoHSS	Ministry of Health and Social Services
NNCR	Namibian National Cancer Registry

PCB	Post-Coital Bleeding
OR	Odds Ratio
ROS	Reactive Oxygen Species
RR	Relative Risk
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infections
TB	Tuberculosis
VIA	Visual Inspection with Ascetic Acid
WHO	World Health Organization

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DEDICATION

I dedicate this project to God Almighty my creator, my strong pillar, my source of inspiration, wisdom, knowledge and understanding. I also dedicate this work to my late parents Lizzy and Richard Louw, thank you for the life lessons learned. My husband, Johan Eiman, your continuous love and encouragement is what kept me motivated. To my children Jean-Lee my eldest son, Kylie my one and only daughter and Zachary John Eiman my last born, my prayer is that my studies will be a stepping stone in being a source of inspiration for all your academic and future career endeavours. My love for all of you can never be quantified. God bless you all.

DECLARATIONS

I, Elmarie Eiman, hereby declare that this study is my own work and is a true reflection of my research, and that this work, or any part thereof has not been submitted for a degree at any other institution.

Elmarie Eiman	……..……	April 2020
Name of Student	Signature	Date

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CHAPTER 1

1.1 INTRODUCTION

This chapter presents the background of the study, problem statement, purpose of the study, specific objectives and significance of the study, limitations and delimitations as well as definition of key concepts.

1.2 BACKGROUND OF THE STUDY

The term cancer covers well over 100 different medical conditions, all involving abnormal and excessive divisions of cells. It is initiated when genetic material, Deoxyribonucleic Acid (DNA), within a body cell is damaged and mutates. Cancer of the cervix occurs when abnormal cell growth takes place in the lower part of the uterus (cervix) [1,2]. It is one of the leading causes of cancer related deaths in women worldwide. Current estimates indicate that every year 527,624 women are diagnosed with Cervical Cancer and 265,653 die from the disease. Human Papilloma virus (HPV) is a well-known cause of Cervical Cancer, HPV types 16 and 18 are responsible for 70% of Cervical Cancer as well as pre-cancerous cervical conditions [3]. Cervical Cancer presents at various stages of precancerous neoplasia before it progresses into invasive cancer. Most women with Cervical Cancer experience a long asymptomatic period before the disease recognition characterised by abnormal cytological changes. Early detection and treatment of such abnormalities can prevent the development of cancer and is the principle behind cervical screening [4].

Namibia with a population of around 2.1 million, of which 632,000 are women aged 15 years and above are at risk of developing Cervical Cancer. Its prevalence is 26.4 per 100 000 women per year. According to the National Namibian Cancer Registry (NNCR), 117 women are diagnosed with Cervical Cancer every year and 63 died from

the disease between 2010-2014 [5]. The District Health Information System (DHIS) 2.0 data showed that in Windhoek Central Hospital (Khomas Region) in 2017, 765 women were admitted due to Cervical Cancer with 25 deaths. Data showed an increase in Cervical Cancer diagnosis with most deaths between 35 – 49 years [6]. These deaths are hardly necessary, as there is evidence that Cervical Cancer is one of the most preventable and treatable forms of cancer if it is detected early and managed effectively [4].

WHO factsheet in 2017 estimates, that 11 million people are diagnosed with cancer each year with 7 million deaths, more than the combined total deaths from HIV/AIDS, TB and Malaria. It is estimated that by 2020, there will be 15 million cases of cancer, annually, with 80% occurring in low- and middle-income countries. In sub-Saharan Africa, the disease increases with more than 75,000 new cases and 50,000 deaths yearly with HIV infections as a contributing factor. These figures indicate an increase of Cervical Cancer in the world [7].

The Cancer Association of Namibia, in collaboration with the Ministry of Health, has been involved in advocacy and provision of screening services in Namibia. Primary prevention strategies for HPV infection involve the provision of health education at various levels and HPV vaccination for girls 9-14 years as key measures to reduce the risk of Cervical Cancer in women [5]. The Namibia Demographic and Health Survey (NDHS) in 2013 showed that 66% of women 15-49 years are aware of Cervical Cancer screening but only 25% have taken part in the screening exercise [8]. Kangmennaang et al, investigated the disparities in Cervical Cancer screening among Namibian women and reported that only 39% of the women had undergone screening and the attainment of higher education level, health insurance scheme was associated with increase in cervical screening [9].

A recent study in Sub-Saharan Africa (SSA) indicated that Cervical Cancer remains the most prevalent malignancy in women, who only seek professional help when they are experiencing symptoms, implying late-stage presentation and higher mortality rates [10]. Another study in 2017 on the incidence mortality and risk factors of Cervical Cancer in the world suggested that the combination of biological, economic and health factors contribute to the incidence of the disease. The authors stated that the rise can be mitigated by preventive programs, life style changes, smoking cessation, early and effective treatment of precancerous lesions [11]. The main objective of this study was to determine the risk factors associated with Cervical Cancer among women attending the Oncology centre and Health facilities in Windhoek Khomas region, Namibia.

1.3 PROBLEM STATEMENT

The increased prevalence of Cervical Cancer in Namibia, being the second most common cancer among women is a cause for concern and there are no studies to determine the risk factors. Therefore, this study aimed to determine the risk factors of Cervical Cancer. Data from the Namibian National Cancer Registry (NNCR) showed that the age specific incidence rate for Cervical Cancer was 27.2 per 100 000 representing an almost two-fold increase since the previous reporting period when it was 15.6 per 100 000 [5].

Furthermore, the NDHS 2013 data showed low uptake of Cervical Cancer screening in Khomas region generally and especially among women with poor education [8]. The dearth of literature on the various risk factors make this study imperative in Khomas region against the background of rising incidence of the disease.

1.4 PURPOSE OF THE STUDY

To determine the risk factors associated with Cervical Cancer amongst women attending the Oncology Centre and Health Facilities in Windhoek, Khomas region.

1.5 SPECIFIC OBJECTIVES OF THE STUDY

The specific objectives of the study are:

- To identify the risk factors for Cervical Cancer amongst women attending the Oncology Centre and Health Facilities in Windhoek, Khomas region
- To determine the socio-demographic and medical characteristics of patients with Cervical Cancer

1.6 SIGNIFICANCE OF THE STUDY

The increase of Cervical Cancer cases in Namibia is a cause for concern. To address this problem, there is a need to determine the population at risk in the country to provide wide primary prevention strategies that could assist in programme planning and development. The findings could be useful to increase the knowledge of health care practitioners through early detection of the disease and contribute to a reduction in morbidity and mortality. It could go a long way in increasing the uptake of Cervical Cancer screening strategies among women and foster lifestyle changes in seeking early treatment as well as establish a foundation for further studies in Cervical Cancer research. Lastly, this study would generate region specific data which might be used in designing population specific interventions for control of Cervical Cancer in Khomas region and in the country at large.

1.7 STUDY LIMITATIONS

All the women attending the Oncology Centre, during the study period, might not be representative of Namibia as a whole because regions treat their cancer patients only those that need specialised treatment are referred to this facility.

1.8 DELIMITATIONS

All patients in this study were sampled from the patients seen at the Oncology Centre and health facilities in Windhoek, Khomas region, Namibia. The study focused on women with Cervical Cancer and the control group were women screened for Cervical Cancer who tested negative at the same health facilities in Windhoek.

1.9 DEFINITIONS OF KEY CONCEPTS

1.9.1 **Awareness** - means the knowledge and understanding that something is happening or exists [12]. In this study, the women's awareness about risk factors for Cervical Cancer will be determined

1.9.2 **Cancer** - The term cancer involves the abnormal and excessive divisions of cells. It is initiated when genetic material Deoxyribonucleic Acid (DNA) within a body cell is damaged and mutates [13] In this study, cancer refers to the abnormal growth of the cells in the cervix.

1.9.3 **Cervix** - the lowest part of the uterus to the vagina [13]. In this study, cervix refers to the area where Cervical Cancer screening tests are done.

1.9.4 **Cervical pre-cancer** – is the extensive multiplication of abnormal cells in the cervical epithelium prior to the development of cancer [13]. In this study, it refers to the mild, moderate and severe stages of cervical lesions caused by HPV.

1.9.5 **Cervical Cancer** - it occurs when abnormal cell growth takes place in the cervix of a woman, the lower part of the uterus (womb) [13] In this study, Cervical Cancer refers to the disease in which cancer cells form in the cervix.

1.9.6 **Cervical Cancer screening** - it involves the collections of cells from the cervix to detect and diagnose abnormal cancer cells in asymptomatic persons before it develops into cancer [13]. In this study, Cervical Cancer screening refers to women attending health facilities in Windhoek, Khomas region for diagnostic purposes.

1.9.7 **Human Papilloma virus** - the cause of nearly all Cervical Cancers [13]. It is strongly linked with a sexually transmitted genital infection thought to infect three quarters of the reproductive age population. In this study, it refers to the primary cause of Cervical Cancer.

1.9.8 **Risk factors** - is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury [13]. In this study, the identified variables will be assessed as they affect Cervical Cancer.

1.9.9 **Public health facility** - Public health is defined as the science of protecting the safety and improving the health of communities through education, policy-making and research for disease and injury prevention [14]. In this study, the public health facilities will be used to conduct the survey.

1.10 SUMMARY

The purpose of the study was to provide insight into the general pattern of risks associated with Cervical Cancer disease in Windhoek Khomas Region of Namibia by quantifying the major risk factors amongst women attending the Oncology Centre and Health Facilities. The researcher explained the research problem, purpose, specific objectives and significance of the study. The next chapter reviews available literatures on the risk factors of Cervical Cancer.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

The purpose of literature review is to search and evaluate published articles on the topic of interest. It conveys to the reader what is known regarding the topic, through identifying strengths and gaps to formulate areas for further research. It shows the readers that in-depth studies of the topic have been done and shows where the current research fits in. It helps the researcher to avoid duplication of work done by other researchers for new frontiers to contribute to knowledge [15].

Cancer of the cervix occurs when abnormal cell growth takes place in the lower part of the uterus (cervix) [8]. The cervix connects the body of the uterus to the vagina (birth canal) and has two different parts covered with two different types of cells. The part of the cervix closest to the body of the uterus is called the endocervix covered with glandular cells while the part to the vagina is the exocervix, and is covered by squamous cells. These two cell types meet at a place called the transformation zone and change as women get older and during labour. Most Cervical Cancers begin in the cells located in the transformation zone. These cells do not suddenly change into cancer. Instead, the normal cells of the cervix first gradually develop pre-cancerous changes that turn into cancer. The pre-cancerous cells become cancer. As mentioned in Chapter 1, these changes can be identified with appropriate screening and treated before becoming cancerous [16].

2.2 THE DEVELOPMENT OF CERVICAL CANCER

2.2.1 HPV infection

The primary cause of Cervical Cancer is HPV transmitted through skin-to-skin contact and is the most common sexually transmitted infection (STI). HPV does not always cause symptomatic disease in the early course in infected individuals. However, at a later stage an infected woman may develop abnormal vaginal bleeding, pelvic pain, or pain during sexual intercourse, unpleasant vaginal discharge and pain when passing urine. Many studies have shown that more than 97% of all cancers of the cervix are associated with persistent HPV infection. The accumulated data regarding HPV as a risk factor for Cervical Cancer are mainly from case-control studies [4,8,17-19].

2.2.2 The Stages of Cervical Cancer

Cervical Cancer is classified into stages according to the International Federation of Gynaecology and Obstetrics (FIGO) classification system and treatment outlined in the Ministry of Health's National Cervical Cancer Prevention Guidelines [13,20].

Table 2.2.2.1 The stages of Cervical Cancer

Staging	**Characteristics**	**Treatment**
Stage 1A	The cancer remains confined to the cervix only visible through the microscope but with a naked eye looks normal.	

Stage 1 A Divided into sub-stages 1A1 AND 1A2		
Stage 1A 1	The cancer has grown 3mm or less down into the stoma and extends up to 7 mm in width.	Stage 1A cancer is almost curable mostly treated with surgery.
Stage 1A 2	The cancer has grown more than 3mm into the stoma but not more than 7 mm in width.	
Stage 1B	The cancer is visible to the naked eye during clinical examination.	
Stage 1A Divided into sub-stages 1B1 AND 1B2		
Stage 1B 1	The cancer is more than 5mm deep or 7mm in width and has grown as 4cm in size.	Stage 1B cancer can be treated with surgery and radiotherapy. It is curable if adequate and timely treatment is available.
Stage 1B 2	The cancer has grown beyond 4cm in size.	
Stage 2A	The cancer has spread beyond the cervix down along the vagina, but not as far as the lower third of the vagina.	
Stage 2 A Divided into sub-stages 2A1 AND 2A2		
Stage 2A 1	The cancer is 4cm less in size.	Stage 2B cancer can be treated with radiotherapy sometimes combined with chemotherapy.
Stage 2A 2	The cancer is more than 4cm in size.	

Stage 2B	The cancer has spread into the tissues surrounding the cervix called the parametrium.	
Stage 3 is divided into stage 3 A and 3B		
Stage 3A	The cancer has spread into the lower third of the vagina.	Stage 3 cancer is treated with radiotherapy combined with chemotherapy. Radiation is also used for relief of symptoms in the advanced cases.
Stage 3B	The cancer has spread out of the pelvic wall or is blocking one or both of the tubes (ureters) that drain the kidneys.	
Stage 4A	The cancer has spread to the nearby organs such as the bladder or rectum.	
Stage 4B	The cancer has spread to faraway organs such as the lungs.	

2.2.3 Clinical features of Cervical Cancer

The symptoms associated with Cervical Cancer are very common and non-specific. Many of these symptoms are associated with Sexually Transmitted Infections (STI's) and therefore it is important for those infected, particularly young women in whom the cancer is highly prevalent, to seek medical attention. The most common signs and symptoms include [21-23].

- Abnormal vaginal bleeding
- Intermenstrual bleeding

- Post-menopausal bleeding
- Unusual vaginal discharge (blood-stained)
- Offensive vaginal smelling
- Pain when passing urine (dysuria)
- Pelvic pain
- Lower abdominal pain
- Suspicious cervix on examination

In later stages of Cervical Cancer other symptoms like:

- Loin pain from hydronephrosis due to obstruction of the uterus from lateral spread
- Sciatica as the cancer compresses nerve roots
- Swollen legs from deep vein thrombosis (DVT)

Post-coital or abnormal vaginal bleeding are known warning signs for Cervical Cancer and is the presenting symptom in 6-10% of patients. Women diagnosed with post-coital bleeding (PCB) over 40 years need referral to a gynaecologist within 2 weeks and all other cases with unexplained repeated PCB should be referred within 4-6 weeks. Post-menopausal bleeding is a sign of endometrial cancer and therefore these women need ultrasound to measure the thickness if more than >4mm a biopsy is needed [24]. Women with these aforementioned signs and symptoms often ignore them and only seek medical attention when the cancer is in advanced stages. Many studies on symptomatic presentation indicate that women misattribute their gynaecological

symptoms and experience long considerations and help seeking intervals [20-23]. These studies recommended targeted interventions such as community awareness campaigns about Cervical Cancer to promote prompt help-seeking behaviours.

2.2.4 Risk factors of Cervical Cancer

2.2.4.1 Human Papilloma Virus (HPV)

HPV is the primary risk factor for Cervical Cancer spread through sexual intercourse and associated with chronic inflammation of the cervix and vagina. HIV infection and other sexually transmitted diseases increase the risk of women getting invasive Cervical Cancer [7, 23]. Another result indicated that since the recognition of Acquired Immunodeficiency Syndrome (AIDS) in 1981, an increased burden of Cervical Cancer was identified among Human Immunodeficiency Virus (HIV)-positive women. The introduction of Antiretroviral Therapy (ART) decreased the risk of opportunistic infections and improved overall survival of HIV infected women [25]. Despite the associated risk of HPV with Cervical Cancer, studies show that women are not aware of the virus (HPV) or HPV vaccine. Their lack of awareness about this notable risk factor for Cervical Cancer may work as an obstacle in health services utilization[17,26]. Early Age at First Sexual Intercourse (AFSI) was associated with an increased risk of HPV infection. Sexual behaviour determines exposure to HPV because AFSI is of particular interest as it has been associated with riskier sexual behaviour, such as having unprotected sex, having multiple sexual partners, as well as a woman's partner having multiple sexual partners[27].

2.2.4.2 Cigarette smoking

Tobacco use is an important risk factor for cancer, accounting for 22% of global cancer deaths and 71% of global lung cancer deaths [28]. Each cigarette puff delivers a mixture of chemicals to the lungs where they are absorbed into the bloodstream and carried to

every organ in the body. These chemicals damage the DNA, which controls how cells reproduce and directs cells to carry out different tasks. The DNA damage can cause cells to mutate and grow uncontrollably and can start the body on the path to cancer. Tobacco smoke contains more than 7,000 chemicals, at least 70 of which are known to cause cancer [29].

A greater risk of high-grade cervical disease for current-smokers than never-smokers was reported; risk increased with increasing number of cigarettes smoked per day and longer duration of tobacco smoking. Long term smokers of ≥5 cigarettes per day had increased the risk of developing CIN 2/3 [31,32].

Epidemiological evidence for a relationship between tobacco and cervical carcinogenesis are supported by a number of studies. Several researchers demonstrated malignant transformations of papilloma and cervical tissue from exposure to chemical carcinogens contained in tobacco smoke. Others reported that smoking increase the risks of HPV infection and the likelihood of infection persistence through the suppression of cell mediated immunity. In a recent study on the progression of HPV infections in adult women, those who smoked were significantly less likely to clear an infection than non-smokers. The plausibility of a causal link between smoking and cervical carcinogenesis was strengthened by isolating tobacco-specific carcinogens in the cervical mucus of smokers [11,33,34].

2.2.4.3 Use of oral contraceptives

Oral contraceptive use has been reported as one of the risk factors of Cervical Cancer. An epidemiological survey that investigated the pattern of oral contraceptive use and Cervical Cancer confirmed that current and recent use of combined oral contraceptives was associated with an increase in the risk of invasive cancer of the uterine cervix. The

risk was said to increase with the duration of oral contraceptive use of 5 years; double the risk for longer uses. The hormonal influence of oral contraceptives increases the expression of HPV genes in the cervix thereby facilitating HPV persistence [35]. Similar results were obtained on long-term use of oral contraceptives from several studies [11,36-46].

This finding was corroborated by another epidemiological study which showed lower risk by 10 or more years of last use of oral contraceptives compared to that in never-users. The relative risks were broadly similar in women likely not to have been screened and in women likely to have been screened, in analyses restricted to high-risk HPV-positive women, and for CIN3/carcinoma in situ. A small increase in risk of invasive Cervical Cancer was associated with the use of progestogen-only injectable contraceptives for 5 years or more [30,38].

2.2.4.4 Positive family history of Cervical Cancer

Studies indicate that having a family history of Cervical Cancer can increase risk two to three times higher than those with no family history. However, some researchers suspect some of the familial tendency may be caused by an inherited condition that makes some women less able to fight off HPV infection compared with others [39].

2.2.4.5 Multiple pregnancies

A study in Kenya indicated that multiparous women were at an increased risk of Cervical Cancer. It was argued that it could be due to the enlargement of the transformation zone as a result of hormonal changes in pregnancy as well as frequent unprotected sex. The result from a pooled analysis of 25 epidemiological studies showed that the risk of Cervical Cancer increased to almost two-fold in women with more than 7 term pregnancies compared with those who had 1-2 full term pregnancies

(RR=1.76 95% CI: 1.53-2.02). In Kenya, the total fertility rate is 4.9% children per woman which represented a moderate risk of Cervical Cancer [38]. Some studies concurred with the findings of the Kenyan survey that women with multiple pregnancies are at increased risk for Cervical Cancer [30, 40-41].

2.2.4.6 Diet

Women with diets low in fruits and vegetables may be at increased risk for Cervical Cancer. A lower socio-economic status has been associated with a higher risk of developing Cervical Cancer, possibly due to lack of access to good health care and Papanicolaou ('Pap-smear') tests[1]. A reduction in total fat intake, increased consumption of whole grains, fruits and vegetables lower the risk of Cervical Cancer. Two studies concluded that a diet rich in vegetables and fruits prevented cancer due to their antioxidant properties, by reducing the toxic effects of reactive oxygen species (ROS) and possible enhancement of the immune response [42,43].

2.2.5 Primary prevention of Cervical Cancer

The rising incidence of Cervical Cancer can be mitigated in two ways namely, preventing the pre-cancers and secondly, detecting the pre-cancers before they become cancerous [44]. Since Cervical Cancer is preventable, therefore, if women at risk are adequately screened and treated for early changes then invasive cancer could almost be eradicated. Thus, if the screening coverage is high and women with positive results are reliably treated, then the secondary prevention component of the comprehensive strategy will show measurable impact [13]. With the causal link of HPV infection to Cervical Cancer, the main goal of primary prevention is to reduce acquisition of HPV infection. In Namibia, a number of methods are available, but HPV vaccination is the most effective and reliable primary prevention strategy [13].

The effective secondary prevention strategies are screening and treatment of pre-cancers such as Pap smear, Visual Inspection with Ascetic Acid (VIA), HPV DNA testing and large loop excision of transformation zone (LLETZ) (if the precancerous lesions are not appropriate for cryotherapy) [13].

2.2.5.1 HPV Vaccination

HPV vaccine prevents the infection by HPV types, before exposure to the virus through sexual contact [46]. Studies indicate that vaccinating girls from an earlier age of between 9-14 years against HPV infection could save up to 400 lives per year. The HPV vaccine targets the oncogenic HPV serotypes. The concept behind prophylactic vaccination is to achieve high levels of neutralizing antibodies against specific oncogenic HPV serotypes to prevent the infection in HPV immature individuals [47,48].

There are currently three vials available in the market:

Table 2.2.5.1 HPV Vaccine Vials available in the market

Name of vaccine	Type of vaccine	Protects against HPV
Cervarix	Bivalent	HPV 16 - 18
Gardasil	Quadrivalent	HPV 6,11,16-18
Gardasil	Nanovalent	6,11,16,18,31,33,45,52 -58

In Namibia, the Ministry of Health and Social Services (MoHSS) has chosen girls between the ages of 9-14 as the primary target population for HPV vaccination. The HPV vaccine consists of two doses given 6 to 12 months apart. In instances when girls are 15 years of age or older, three doses are needed: the initial dose, second dose one to two months later and the third dose 6 to 12 months later than the initial dose. At

present, the vaccine is only available in the private sector although the recent Namibian guidelines on Cervical Cancer indicate that the HPV vaccine will be delivered in the National school health programme [13].

A study showed that the UK used Gardasil, quadrivalent vaccine to vaccinate young girls aged 12 to 13 as part of childhood vaccination programmes by giving a series of two injections 6-24 months separately. Furthermore, the study stated that girls can have the vaccine up to the age of 18 years but if over 14 years, a series of three injections are needed because the immune response to the vaccination is not as good in older girls [49]. In Australia, the same vaccine has been used and a 90% reduction in genital warts in heterosexual men and women under the age of 21 years was reported. It stated that the vaccinations reduce the risk of Cervical Cancer by 70% [50,51]. The World Health Organisation in collaboration with the Ministry of Health and Social Services in Namibia apart from HPV vaccine recommend the following primary prevention strategies:

- Safer sex education for adolescents to reduce the risk of HPV infection and other infections, like HIV
- Male circumcision
- Condom promotion for sexually active individuals

2.2.5.2 Pap smear

Although there are various methods to detect Cervical Cancer, the most popular method is the Pap smear test because it is available in all public health facilities and in the private sector in Namibia. According to the NDHS 2013 data, 93% of women aged 15-49 years had Pap smear tests done although only 66% have heard about Cervical Cancer.

A Pap smear finds abnormal cervical cells before they turn into cancer cells rated from moderate to low sensitivity, detecting pre-cancer of grades Cin2 (moderate) and Cin3 (severe)[52]. Therefore, women must go frequently for Pap smears to identify lesions that may have been missed on the first screening. Recommendations on the frequency of Pap smear vary from country to country, but in Namibia the practice is that all women aged 21 or older who are sexually active should have Pap smear every year [13]. Pap smears have a high specificity meaning that women who do not have cervical pre-cancer will test negative 95% of the time[13,54]. The U.S. Centres for Disease Control and Prevention (CDC) recommends that all HIV-positive women get an initial Pap test and should be re-tested 6 months later. If both Pap tests are normal, such HIV-positive women can get yearly Pap tests in the future [54].

2.2.5.3 Visual Inspection with Acetic Acid (VIA)

The Visual Inspection with Acetic Acid (VIA) test is an alternative screening method to Pap smear test. The VIA test is performed by a trained health care provider applying diluted acetic acid (table vinegar) on a cotton swab on the cervix for visual signs of possible cancer during a vaginal examination. The result is available within a minute: if aceto-white changes occur (white colour that occurs after applying acetic acid) on the cervix and remains, it is associated with cervical pre-cancer. If these changes occur in the transformation zone, the results are positive; if no changes occur the results are negative. The advantage of VIA is that the result is immediately available and treatment can be provided [43]. A study conducted in Rwanda showed that VIA is effective for Cervical Cancer screening because it is practical and feasible even in rural settings [38].

2.2.5.4 HPV DNA Testing

HPV DNA test is a primary prevention method for cervical screening. This test detects the high risk or carcinogen HPV types by determining the DNA in the vagina or cervical cells. The tests are performed by a trained health worker by collecting a sample from the cervix using a swab or brush. The WHO recommended age for HPV DNA test is 30 years. However, in Namibia sexual activity begins in early teens and HIV prevalence is high, therefore the HPV DNA testing is initiated before the age of 30 years. The HPV DNA testing is highly sensitive but the specificity is low and to increase the specificity, a second test (VIA) can be performed according to the Namibian Cervical Cancer guidelines [13,55-57].

2.2.6 Management and treatment of Cervical Cancer

In Namibia, the Ministry of Health and Social Services (MoHSS) has implemented a new Cervical Cancer prevention guideline with the aim to reduce morbidity and mortality. It stipulates that women with pre-cancer can receive treatment from primary facilities while suspected or confirmed invasive cancer will be treated by medical specialists at hospitals to remove areas of pre-cancerous lesions. In Namibia, cryotherapy will be used for lesion when VIA is available and Large Loop Excision of the Transformation Zone (LLETZ) is performed by a specialist. There are several studies that highlight the treatment of pre-cancerous and cancer cells found in the cervix and treatment is very effective if commenced at an early stage[13,56 -58].

2.2.6.1 Cryotherapy

Cryotherapy eliminates pre-cancerous areas on the cervix by freezing them. It involves applying a high cooled metal disc to the cervix and freezing the abnormal areas. The procedure takes 15 minutes and is associated with mild discomfort.

According to the Namibian Cervical Cancer prevention guidelines, the eligibility criteria for cryotherapy are as follows:

- Lesion occupying less than 75% of the transformation zone
- Lesion is visible
- The cryotip can completely cover the lesion
- Lesion not suspicious for cancer
- No abnormal blood vessels are visible
- There are no polyps or scarring to prevent full contact between cervix and cryotip
- Client not pregnant
- The client does not have severe cervicitis

Post-procedure of cryotherapy in the cervix takes about a month to regenerate and during this time sexual intercourse must be avoided or a condom should be used [13,58].

2.2.6.2 Large Loop Excision of the Transformation Zone (LLETZ)

Loop Excision of the Transformation Zone (LLETZ) is the removal of abnormal areas from the cervix using a loop made of thin wire powered by an electrosurgical unit. The aim of LLETZ is to remove the lesions and the entire transformation zone by surgical excisional method. In cases where the lesion is not eligible for cryotherapy, LLETZ should be considered as an alternative treatment [13,56-58].

Post-LLETZ, the cervix takes about a month to regenerate and during this time sexual intercourse must be avoided or a condom should be used. Women will experience mild cramping and vaginal discharge for up to 1 month [45,58].

2.2.6.3 Combination treatment of invasive Cervical Cancer

Invasive Cervical Cancers are generally treated with surgery, radiotherapy and chemotherapy or a combination of two or three. However, radiotherapy is often needed for Cervical Cancer treatments. Radiotherapy is as effective as radical hysterectomy in the treatment of stage 1b Cervical Cancer. A study indicated that concurrent chemotherapy and radiotherapy are the treatments of choice for stages 2B–4A carcinoma of cervix and the chemotherapy schedule is weekly Cisplatin. Intra-uterine and intra-vaginal brachytherapy are an essential part of any radiotherapy regimen used to treat Cervical Cancer [59].

2.3. SUMMARY

Cervical Cancer remains a concern globally, as well as in Namibia where the disease is ranked as the second most frequent cancer of women in Namibia. Most women affected with the disease are in the prime of their lives, generally contributing to their families and to the social and economic development of their communities. However, studies indicate that due to limited availability of screening services globally and across Namibia, the disease may already be advanced by the time of diagnosis, which necessitates complicated treatment that can only be provided at referral hospitals far away from the women's homes. The availability of effective primary and secondary preventive screening and treatment programmes could lead to early detection of the disease and reduce its burden globally and in Namibia.

Factors such as HPV, cigarette smoking, use of oral contraceptives, multiple pregnancies and a positive family history of Cervical Cancer are but a few which have been repeatedly associated with Cervical Cancer. Risk factors for Cervical Cancer are well studied throughout the world; however, more studies are needed to be done in Namibia. Chapter 3 will focus on the research methodology used in the study.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

This chapter describes the research design used to meet the objectives of the study. A study design refers to the structural approach followed by the investigator to answer the research question. Epidemiological study designs have their strengths and limitations. The one used in this research was observational design: case-control type.

The design used included: the study population, sampling frame, sample size, research instrument, data collection and processing, data analysis and ethical considerations. The study aimed to assess the risk factors associated with Cervical Cancer amongst women attending health facilities in Windhoek, Khomas region.

3.2 RESEARCH DESIGN

The study design was quantitative unmatched Health Facility-based case-control study to determine the risk factors for Cervical Cancer, an analytical model. An analytical study aims to find the factors that predict or cause disease by examining associations rather than describing how many diseases there are. It also estimates the association between risk factors and the occurrence of the disease [60,61]. Therefore, the researcher chose a case control study because of its ability to determine the association between exposure (cases with the diseases) and controls (cases without the disease) to determine the outcome. The study relied on secondary data based on records of patients who are seen at the Oncology Centre and Health Facilities in Windhoek, Khomas Region.

3.3 RESEARCH METHODS

3.3.1 Research Setting

The study was conducted in Windhoek, the capital city of Namibia located in the central part of the country approximately 645 square kilometers area. There are more than six indigenous groups in Windhoek and other international groups, representing an ethnic cross-section of Namibia [62].

The region consists of one (1) district with many private facilities, two (2) main referral hospitals. Windhoek Central Hospital is the referral hospital for specialized cases. In addition, the region consists of one (1) health centre and ten (10) urban clinics, two (2) rural clinics and a hundred and ninety-nine (199) outreach points. All the clinics provide Pap smear services.

3.3.2 Research Population

A study population is defined as a group of individuals taken from the general population who share common characteristics, such as age, sex, or health condition. According to the 2011 Population and Housing Census, Windhoek has a population of 342 141 with annual growth rate of 3.5% with women constituting of 50%[64]. The Oncology Centre is the referral facility for all cancer patients in Namibia therefore, the study was conducted at this facility. All women diagnosed with Cervical Cancer treated and referred to the Oncology Centre in Windhoek during the study period (1 January 2016 to 30 June 2018) were participants if they met the criteria as cases. The control group were women screened for Cervical Cancer who had a negative Pap smear result at the same centre at health facilities in Windhoek during the study period.

3.4 SAMPLING AND SAMPLING FRAME

Sampling is defined as a statistical process of selecting a subset of the population from the target population available for study. Since the population of interest to the researcher may contain too many members (e.g. people) to study conveniently, samples of the population are drawn [14]. Simple random sampling methods were used to select and enrol participants into the study. These methods will be explained in the sections on sampling of cases and sampling of controls respectively.

Case definition:

Case: A case is defined as a "particular ailment, health disorder, or condition under investigation found in an individual or within a population or study group" [16]. In this study, cases were defined as women diagnosed with Cervical Cancer in the Oncology centre. The diagnosis was verified by reviewing their medical records before obtaining consent to conduct the interview.

Control: In a case control study, a control is defined as "person(s) in a group that is used for reference in comparison to a case group" [17]. In this study, control was defined as women screened for Cervical Cancer and tested negative but managed for other gynaecological conditions who were interviewed at the same centre and health facilities in Windhoek.

A simple random sampling method was used. A sampling unit is an individual and each individual in the population had an equal chance of being selected [1]. The researcher chose the simple random sampling method from a table of random numbers up to the desired sample size (201) to ensure that all women (cases and controls) had an equal chance of being selected for the study.

3.4.1 Sample size

The sample size was determined using EPI info version 7 Statcalc power for unmatched case control with the following specifications: Confidence level of 95%, power at 80% and 1:1 case control ratio, proportion of users of contraceptives in controls of 0.46 and odds of disease in those who reportedly used contraceptives increased by 13.4 in a previous study [10]. A sample size of 201 per group was indicated.

3.4.2 Inclusion criteria

Inclusion criteria are characteristics that the prospective subjects must have if they are to be included in the study sample [61]. The inclusion criteria used for this study were as follows:

- Women diagnosed with Cervical Cancer as cases and women without the disease as control with laboratory Pap smear results present

3.4.3 Exclusion criteria

Exclusion criteria are characteristics that disqualify prospective subjects from inclusion in the study [61]. The exclusion criteria used for this study:

- Negative Pap smear results
- Patient presented with other gynaecological problems outside the study period

3.5 RESEARCH DATA COLLECTION INSTRUMENT

A pilot tested standardized data collection tool (questionnaire) was utilized for data extraction. The fact that the sampling frame was constructed using a data collection tool assisted in classifying patients who were eligible for inclusion in the sampling frame. The questionnaire used was structured based on the WHO stepwise approach for non-communicable risk factors surveillance (steps) to interview controls. A list of

Cervical Cancer patients obtained from the cancer registry during the study period constituted the sampling frame. A similar process was carried out for the controls from a list of patients seen at health facilities Windhoek, Khomas region, Namibia. Section one determined the socio-demographic information; section two, the obstetric information.

3.6 DATA COLLECTION METHOD

A structured questionnaire was used to collect information through interviewing the participants (both cases and controls). The questionnaire was designed in English and translated into Afrikaans and other local languages by two native speakers. The researcher employed the services of two research assistants trained on how to complete the questionnaire. The researcher reviewed the data collected daily to ensure quality and comparability of data between research assistants.

3.6.1 Validity of the data collection instruments

Validity describes how accurate the instrument measured what it was supposed to measure to represent the concept in question [18]. It involves a process of data collection and analyses to determine the accuracy of the instrument.

3.6.1.1 Interview Questionnaire

An interview questionnaire is a written list of questions, plus space for answers to guide an observer, interviewer, researcher or investigator.

3.6.1.2 Face validity

The interview questionnaire was assessed by the Regional Family Chief Programme Officer to ensure that the questions met the objectives of the study. The questionnaire was pre-tested at Maxuilili Clinic on women with Cervical Cancer and women who tested negative after Cervical Cancer screening for relevance, sensitivity and

acceptability. The health facility for the pilot study was excluded from the study. The participating subjects from the pilot site used unique numbers in their green health passports as identification for exclusion from the official study. After the pilot study the questionnaire was edited accordingly.

3.6.2 Reliability of the data collection instrument

Reliability refers to the consistency of a measurement. The reliability of measurement is the degree to which the instrument produces equivalent results for repeated trials [19]. In this study, the researcher ensured that the data collection instrument was reliable.

Prior to the study, the questionnaire was tested and re-tested to minimize the data collection errors. The researcher interviewed women with Cervical Cancer and women who tested negative for Cervical Cancer from pilot sites. The researcher made comparisons if the same results were derived from the data collection tools.

3.7 DATA ANALYSIS

Data was analysed using EPI info 7 to generate proportions and frequencies. Results are presented in tables and graphs. Logistic regression was used to generate crude Odds Ratio (OR) and 95% Confidence Interval (CI) for each of the risk factors, while multivariate analysis for the significant variables was used to generate adjusted OR and 95% CI. The significant levels of P-value were set at <0.05.

3.8 ETHICAL CONSIDERATIONS

The study was carried out in compliance with and maintained the ethical principles, namely Autonomy, Beneficence, Maleficence and Justice, before and after the study. The study was commenced after approval from the University of Namibia Postgraduate Studies Committee and ethical clearance from the Health Research and Ethical Committee. Permission was also obtained from the Ministry of Health and

Social Services' Research and Ethics Committee (HREC) and from the Director of Khomas region. Prior to the commencement of the study, the Khomas Regional Health Directorate was informed. All enrolled study participants signed the written informed consent forms before participating in the study.

3.8.1 Autonomy

Participants were recruited in a non-coercive manner and the researcher ensured privacy through the allocation of a numerical identifier after consent. The questionnaire and consent forms were designed in English and translated into local languages by two native speakers. The participants were provided with informed consent forms and were given the choice to withdraw from the study at any given time. The purpose of the study and procedures thereof were explained to the participants and information obtained throughout the study was kept confidential and private. Data obtained from the study were kept in a lockable cabinet at the principal investigator's office under lock and key until the study was completed.

3.8.2 Confidentiality

The data collection tools made use of a registration number to protect the name of the study participant. A password-protected computer was used for data capturing and analysis.

3.8.3 Non-Maleficence

No study participant was exposed or subjected to physical or emotional harm.

3.8.4 Beneficence

It is the ethical responsibility to ensure that the study results were beneficial to the health needs of individuals who suffer from Cervical Cancer as well as the broad health

and development needs of the country. The study subjects had access to the relevant treatment for the condition under study.

3.8.5 Justice

All women in the Windhoek Khomas Regional Health District from different social, geographical and cultural backgrounds screened for Cervical Cancer were equally enrolled in the study until the sample size was obtained. The study was located at the Oncology centre and public health facilities in Windhoek, Khomas region.

3.9 SUMMARY

This chapter described how the study was conducted. It outlined the study design, study population, sample method and how the sample size was obtained. The data collection and analysis procedure were explained. The ethical considerations to ensure the validity and reliability were also discussed. The next chapter presents the main findings of the study.

CHAPTER 4

RESULTS OF THE STUDY

4.1 INTRODUCTION

This chapter presents the research findings based on the analysis of the data. The main findings of the study are risk factors associated with Cervical Cancer amongst women attending Oncology centre and health care facilities in Windhoek, Khomas region. The results are presented as descriptive and analytical format in tables and graph according to the objectives of the study.

The socio-demographic characteristics of the cases and controls are described in the form of frequencies, proportion and means as appropriate. A Chi-square test for difference was used to determine the statistical significance at 95% level of significance. Bivariate analysis was carried out using two by two tables to determine potential risk factors to obtain the odds ratio to evaluate the relationship between each factor (exposure) and Cervical Cancer (outcome). Multiple logistic regression was used for factors that were found to be significant in the bivariate analysis. It was used to determine the most significant risk factors and alleviate the effects of the confounders.

4.2 SOCIO-DEMOGRAPHIC AND MEDICAL CHARACTERISTICS OF CASES AND CONTROLS

The researcher interviewed 402 women at a ratio of 1:1 respectively from facilities in Windhoek. The cases were women diagnosed with Cervical Cancer treated and referred to the Oncology Centre in Windhoek during the study period (1 January 2016 to 30 June 2018) and the control group were women screened for Cervical Cancer who had negative Pap smear results at the health facilities in Windhoek during the study

period. Table 4.2.1 below presents the findings of this study on socio-demographic factors associated with Cervical Cancer.

Table 4.2.1 Socio-demographic characteristics of the study population

Characteristics	**Total N n=402**	**Cases n=201**	**Controls n=201**	**Chi square**	**P-value**
Age in years				0.75100	0.38616
30-39	76 (19%)	38 (19%)	38 (19%)		
40-49	147 (37%)	71 (35%)	76 (38%)		
50-59	132 (33%)	63 (31%)	69 (34%)		
60-69	47 (12%)	29 (14%)	18 (9%)		
Marital status				5.92900	*0.01
Married /Cohabitating	163 (41%)	93 (46%)	70 (35%)		
Single (separated, divorce and widow)	239 (59%)	108 (54%)	131 (65%)		
Place of residents				10.35047	*0.001
Urban	228 (57%)	98 (49%)	130 (65%)		
Rural	174 (43%)	103 (51%)	71 (35%)		

Educational status				11.25504	*0.001
No formal education	22 (5%)	15 (7%)	7 (3%)		
Primary education	68 (17%)	46 (23%)	22 (11%)		
Secondary education	256 (64%)	116 (58%)	140 (70%)		
Tertiary education	56 (14%)	24 (12%)	32 (16%)		
Employment status				1.14667	0.2
Employ in formal sector	110 (27%)	54 (27%)	56 (29%)		
Not formally employed	33 (8%)	9 (4%)	24 (12%)		
Self employed	46 (12%)	27 (13%)	19 (9%)		
Unemployed	213 (53%)	111 (56%)	102 (50%)		
Gravidity				6.67904	*0.001
Primigravida	83 (21%)	31 (15%)	52 (26%)		
Multigravida (>1 pregnancy)	319 (79%)	170 (85%)	149 (74%)		
Parity				7.61493	*0.001
Nulliparous/ at least one live birth)	89 (22%)	33 (16%)	56 (28%)		
Multipara (>2 or livebirth)	313 (78%)	168 (84%)	145 (72%)		

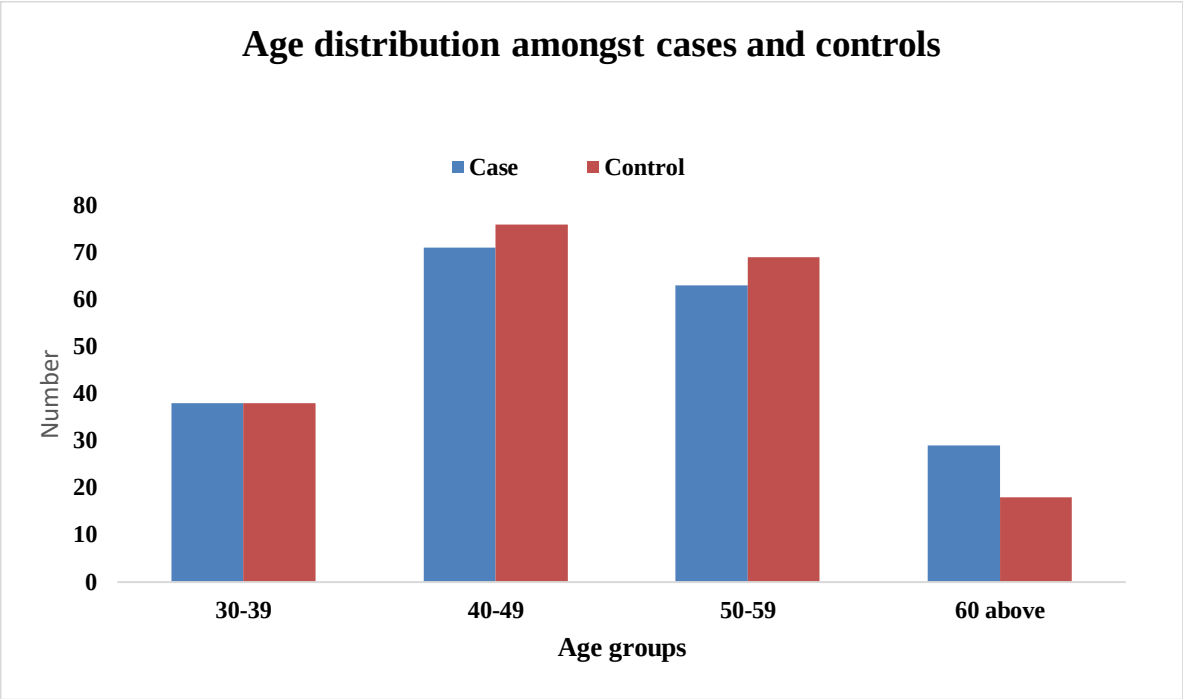

Figure 4.2.1: Age Distribution of Cases and Controls during study period

Figure 4.2.1 indicated that the majority, 71 (35%) of cases belonged to the 40-49 years age group whilst the least number of cases 29 (14%) belong to the 60-69 years age group. The same pattern was observed within the control group whereas 76 (38%) belong to 40-49 years age group and 18 (9%) to 60-69 years age group. The mean age amongst cases was 49±10.24 years (range 30-79 years) whereas in the control was 47±10.02 years (range 30-69 years). There was no statistical significance in the age distribution between cases and controls (p=0.39).

4.2.2 Place of Residence and Cervical Cancer

The majority of study participants 228 (57%) were from urban areas; cases 103 (51%) were mostly from rural areas compared to controls 70 (35%). The majority of controls were from urban areas 130 (65%). There was an association found between place of residence and Cervical Cancer (P= 0.001), indicated in Table 4.2.1.

4.2.3 Marital Status and Cervical Cancer

Figure 4.2.3 shows that the majority of the study population were single 239 (59%). Although amongst the cases 93 (46%) were married, 108 (54%) were single; in the control group, most of the study participants were single 131 (65%) and 70 (35%) were married. There was an association found between marital status and Cervical Cancer (p=0.01).

4.2.4 Employment Status and Cervical Cancer

More than half 213 (53%) of the study population were unemployed; cases 111 (56%) were more compared to the controls 102 (50%). Control study participants were mostly employed in the formal sector 56 (29%). Most cases were self-employed 27 (13%) compared to controls 19 (9%). There was no relationship between Cervical Cancer and employment status (p=0.2), as shown in Table 4.2.1.

4.2.5 Educational level and Cervical Cancer

Most of the study population had secondary education 256 (64%); the control group 140 (70%) compared to cases 116 (58%). A high proportion of cases 61 (30%) had primary and no formal education compared to controls 29 (14%). Thirty-two (16%) controls had tertiary education while cases were 24 (12%) whereas the control group were the highest 140 (70%) compared to 116 (58%) cases. The highest number of study participants with primary and no formal education was found amongst the cases with 61 (30%) compared to controls with 29 (14%). There was an association found between educational levels and Cervical Cancer (p= 0.001).

4.2.6 Gravidity and Cervical Cancer

A high proportion of the study population were multiparous 313 (78%) as shown in Figure 4.5.1 below. Nulliparity was more common amongst controls 56 (28%)

compared to cases 31 (15%). Gravidity status was associated with Cervical Cancer in this study, (p=0.001).

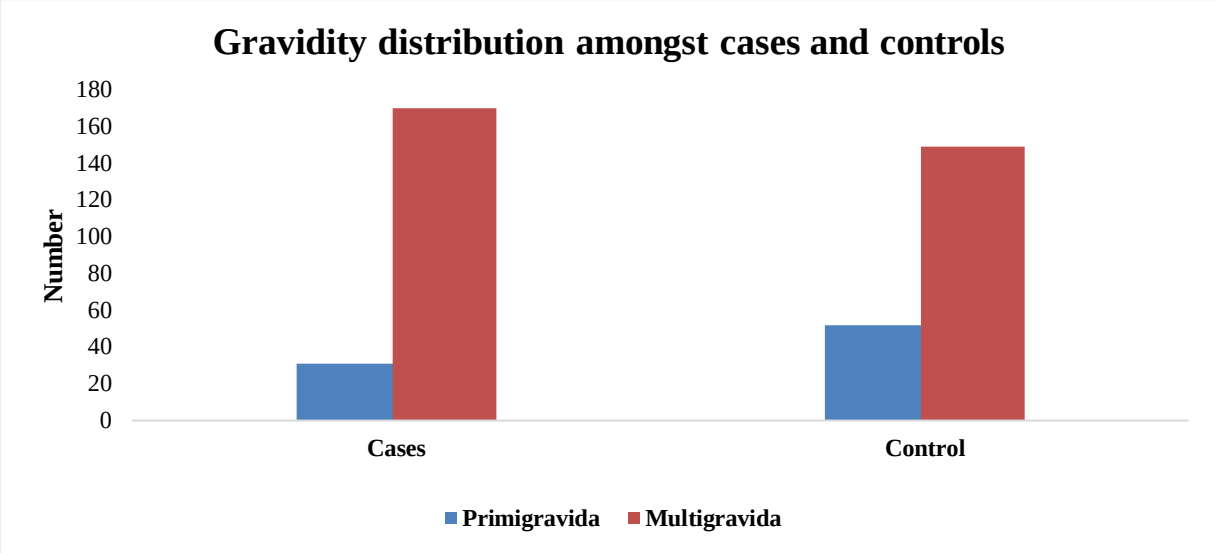

Figure 4.2.2 Gravidity distribution of cases and control during the study period (1 January 2016 – 30 June 2018)

4.3 BIVARIATE ANALYSIS OF POTENTIAL RISK FACTORS

Bivariate analysis was used to determine the significance and strength of association between the potential socio-demographic factors and the risk of developing Cervical Cancer. This initial analysis indicated which variables might be included based on the strength of association in the binary logistic regression model. A P-value of less than 0.05 was interpreted as statistical significance.

Table 4.3.1 Bivariate analysis of risk factors associated with cervical and their 95% Confidence Interval (CI)

Variable/Risk factor	Total	Case	Control	COR	95% CI	P value
Age ≥ 60 above						
Yes	46 (11%)	29 (14%)	18 (9%)	1.10	0.74-1.63	0.61
No	355 (89%)	172 (86%)	183 (91%)			
Married/Cohabitating						
Yes	163 (41%)	93 (46%)	70 (35%)	1.61	1.07-2.40	*0.01
No	239 (59%)	108 (54%)	131 (65%)			
Unemployment						
Yes	189 (47%)	72 (36%)	117 (58%)	2.49	1.66-3.73	*0.001
No	213 (53%)	129 (64%)	84 (42%)			
No secondary education						
Yes	90 (22%)	61 (30%)	29 (14%)	2.58	1.57-4.24	*0.001
No	312 (78%)	140 (70%)	172 (86%)			
Multigravida						
Yes	83 (21%)	31 (15%)	52 (26%)	1.99	1.16-3.14	*0.001
No	319 (79%)	170 (85%)	149 (74%)			
Residence Rural						
Yes	178 (44%)	114 (57%)	64 (32%)	2.80	1.86-4.21	*0.001
No	224 (56%)	87 (43%)	137 (68%)			
Knowledge on Cervical Cancer						
Yes	285 (71%)	136 (68%)	149 (74%)	0.15		
No	117 (29%)	65 (32%)	52 (26%)			

Any family history of Cervical Cancer						
Yes	140 (35%)	91 (45%)	49 (24%)	2.56	1.67-3.99	*0.001
No	26 2 (65%)	110 (55%)	152 (76%)			
Family history of Cervical Cancer						
Yes	67 (17%)	37 (18%)	30 (15%)	1.28	0.75-2.17	0.34
No	335 (83%)	164 (82%)	171 (85%)			
Age of first sexual intercourse <18 years						
Yes	137 (34%)	73 (36%)	64 (32%)	1.22	0.80-1.84	0.34
No	265 (66%)	128 (64%)	137 (68%)			
Life time partners (>2+)						
Yes	209 (52%)	92 (46%)	117 (58%)	1.65	1.11-2.44	*0.01
No	193 (48%)	109 (54%)	84 (42%)			
Contraceptive used						
Yes	247 (61%)	138 (69%)	109 (54%)	1.87	1.24-2.82	*0.001
No	154 (39%)	62 (31%)	92 (46%)			
Oral contraceptive use >5 years						
Yes	38 (9%)	16 (8%)	22 (11%)	1.72	0.96-3.10	0.06
No	28 (7%)	26 (13%0	2 (1%)			
HIV positive status						
Yes	103 (26%)	73 (36%)	30 (15%)	3.39	2.08-5.53	*0.001
No	278 (69%)	116 (58%)	162 (81%)			
Genital warts						
Yes	20 (5%)	15 (7%)	5 (3%)	2.62	0.99-6.89	*0.04
No	382 (95%)	186 (93%)	195 (97%)			

History of STI						
Yes	191 (48%)	103 (51%)	88 (44%)	0.33	0.90-1.98	0.14
No	211 (52%)	98 (49%)	113 (56%)			
Pap smear screening						
Yes	283 (70%)	128 (64%)	155 (77%)	0.51	0.33-0.79	*0.001
No	119 (30%)	73 (36%)	46 (23%)			
Smoking						
Yes	46 (11%)	30 (15%)	10 (8%)	2.02	1.06-3.	
No	356 (89%)	171 (85%)	185 (92%)			
Alcohol use						
Yes	107 (27%)	52 (26%)	55 (27%)	0.92	0.59-1.44	
No	295 (73%)	149 (74%)	146 (73%)			

Table 4.3.1 showed that in the bivariate analysis, marital status (OR=1.61) (1.07-2.40), unemployment (OR=2.49) (1.66-3.73), no secondary educational (OR=2.58) (1.57-4.24), multigravida (OR=1.99) (1.16-3.14) and rural placement (OR=2.80) (1.86-4.21) were significantly associated with Cervical Cancer with ($p < 0.05$).

The results also showed that study participants with a family history of cancer (OR:2.56) (1.67-3.99), contraceptive use (OR:1.87(1.24-2.82), positive HIV status (OR:3.39) (2.08-5.53), not attending Pap smear screening (OR:0.51 (0.33-0.79) life time partners >2+ (OR:1.81 (1.24-2.84), genital ulcers (OR:2.62 (0.99-6.59) were statistically significant ($p<0.05$). However, knowledge of Cervical Cancer was protective Crude odds ratios (COR's). Other risk factors such as age at first sexual intercourse <18 years, STI history, smoking, oral contraceptives used for longer than 5 years and alcohol used were not associated with Cervical Cancer ($p > 0.05$).

Table 4.4 Multivariate logistic regression analysis of risk factors for Cervical Cancer

Characteristics	AOR	95% CI	P-value
Family history cancer Yes No	2.55	1.64-3.95	*0.0004
Unemployment Yes No	2.56	0.26-059	*0.0001
Marital status Yes No	1.90	1.25-2.89	*0.003
Living in rural areas Yes No	2.77	1.26-4.21	*0.000002
Used of contraceptives u Yes No	1.64	1.08-2.49	*0.03
Lack of secondary education Yes No	2.49	1.50-4.13	*0.0005

Pap smear screening Yes No	1.92	0.33-0.82	*0.007

4.4.1 MULTIVARIATE ANALYSIS (LOGISTIC REGRESSION)

Table 4.4 shows the risk factors that were generated from the multivariate analysis. There were 11 risk factors from the bivariate analysis of which 8 were found to be associated with Cervical Cancer ($p<0.05$) in the multivariate analysis. The multivariate logistic regression analysis found that after adjusting for HIV positive status, the following variables were found to be significant risk factors of Cervical Cancer: family history of cancer (AOR:2.55; 95% CI, 1.64-3.95; p = 0.0004), unemployment (AOR: 0.39; 95% CI, 0.26-0.59; p = 0.0001), marital status (AOR: 1.90; 95% CI, 1.25-2.89;p=0.003), living in rural areas (AOR: 2.77; 95% CI, 1.26-4.21; p= 0.000002), use of contraceptive (AOR: 1.64; 95% CI, 1.08-2.49; p = 0.03), not obtain secondary education (AOR: 2.49: 95% CI, 1.50-4.13; p = 0.0005) and not attend Pap smear screening (AOR: 0.52; 95% CI, 0.33-0.82; p = 0.007).

4.5 SUMMARY

This chapter described the results of the study. The results highlighted the significant risk factors for Cervical Cancer among women attending Oncology centre and health facilities in Windhoek, Khomas region (n=402). Results are outlined in tables and graphs. The next chapter discusses the study findings in detail and its relation with other study findings.

CHAPTER 5

DISCUSSION

5.1 INTRODUCTION

In this chapter, the main findings are discussed. Comparisons of the findings of this study are made with published studies on risk factors associated with Cervical Cancer. The conclusions and recommendations are expressed in relation to the study objectives. Limitations experienced during this study are also described.

5.2 Discussions of the findings

5.2.1 Socio-demographic factors and medical characteristics

This unmatched case control study objective was to identify the risk factors associated with Cervical Cancer. This study demonstrated that age showed no statistical significance. However rural placement, unemployment, low educational levels and marital status were found to be associated as contributing risk factors for Cervical Cancer under socio demographic factors.

Women living in rural areas might be less able to access healthcare facilities and have limited exposure to urban marketing information. This could result in poorer health literacy, awareness and a greater likelihood of patients only presenting to a health centre once symptoms are considerably advanced. In the real-world women diagnosed with Cervical Cancer living in rural areas often need to move to urban regions to seek cancer treatment and follow-up in better equipped health care centres. The Oncology centre situated in Windhoek is the only equipped specialised facility in Namibia and serves as a referral centre for all the regions' cancer patients. A Kenyan study reported a similar finding that rural women are at increased risk of Cervical Cancer due to health

services co-factors such as poor-quality services, inadequate health workers, lack of screening programme [38].

Studies showed that the socio-economic status could have had a greater effect over the incidence of Cervical Cancer in some locations than in others especially when women in rural areas have little or no access to early detection and treatment [62]. A study in Mexico indicated that incidence of Cervical Cancer was higher in states with high marginalisation, where women have little or no access to early detection and treatment[63].

In this study more than half of the study respondents were single. The implication of being single could involve having more than one sexual partner which increases the likelihood of sexually transmitted infections (STI) such as HPV and Cervical Cancer. On the other hand, being married could provide a strong support system to attend to health needs. A study reported that married women had a higher recognition of Cervical Cancer risk factors than those who have never married [64].

Women with low educational level was a significant risk factor for Cervical Cancer in this present study as a high proportion of cases had no formal education or had no secondary education. A study in Mexico indicated that 69% of women who died from Cervical Cancer had no formal education compared to women with higher education [63]. The lack of education serves as a vicious circle limiting access of individuals to crucial information to prevent diseases, access to healthcare and the practice of individual health care rights [63]. Terán-Hernández et al (2016), opined that low levels of education are associated with increased frequency of riskier behaviours [63]. They suggested that improving education in young women or developing specific programs to improve access for women with no education or primary education could potentially

decrease Cervical Cancer mortality. The Mexican study previously alluded to, added that low socio-economic levels and no formal education were associated with increasing the probability of developing Cervical Cancer [62,63].

Unemployment was also found to be associated with Cervical Cancer. The current unemployment rate in the country is high, as indicated in the 2011 population census that 42% of employable Namibians are unemployed [64]. The latest Namibia labour force survey in 2016 indicated that the overall unemployment rate for Namibia is 34%. The unemployment rate was higher amongst females (38.3%) as compared to their male counterparts (29.8%); higher among rural dwellers (39.2%) than urban women (30.3%)[65]. The Mexican study indicated that unemployed women use health facilities less frequently or do not use them at all which could explain the low opportunity of timely prevention and detection of the illness [63].

5.2.2 Potential risk factors for Cervical Cancer

This objective of the study was to identify the risk factors for Cervical Cancer and the following were potential risk factors associated with Cervical Cancer: any family history of cancer, no Pap smear screening, contraceptives used and positive HIV status. These findings agree with many studies that these sociodemographic and medical factors are predictive factors in the incidence of the illness [37,39,62,63].

5.2.3 Associated Risk factors

HPV vaccine prevents the infection of different HPV types before exposure to the virus through sexual contact [53]. The majority of study participants were not aware or have never heard of HPV vaccine. As indicated in the literature review the lack of awareness about HPV vaccine is a hindrance in health service utilization[17,26].

Studies indicated that having a family history of cancer can increase the risk two to three times compared to those with no family history. However, some researchers suspect some of the familial tendency may be caused by an inherited condition that makes some women less able to fight off HPV infection compared with others [3,38]. There are risk factors that one can avoid like smoking and HPV infection by having one faithful life time partner and reduce risky sexual behaviour. Women with a history of cancer in their families are at risk and should go for medical check-up and Cervical Cancer screening regularly.

Not attending Pap smear screening for early detection of Cervical Cancer increased the risk to developed Cervical Cancer. According to literature reviewed, a Pap smear test detects abnormal cells before they turn into cancer cells rated from moderate to low sensitivity, detecting pre-cancer of grades Cin2 (moderate) and Cin 3 (severe) [51]. Currently, Pap smear is the most popular method because it is available at all public health facilities including ARV clinics. The results of this study showed that more controls went for Pap smears compared to cases.

Women with HIV positive status was associated with Cervical Cancer. Studies showed that women who were HIV positive often had HPV types that were more likely to persist (HPV 16,18) and were at increased risk of Cervical Cancer. It also indicated that HIV positive women developed more aggressive Cervical Cancer variants and resulted in deaths earlier than women who were HIV negative [53,62,63]. Another study indicated that a population with high HIV prevalence were more at risk of contracting HPV due to the congruent transmission patterns and their increased risk from immune compromise, thus they had greater risk of developing cancer. The current prevalence of HIV in Namibia was 12.6% among adults aged 15-64 years according to the Namibia population-based HIV impact assessment 2017 (NAMPHIA) [66]. In South

Africa, a large cohort on the HIV prevalence amongst adults is 18.9% indicated that HIV positive women had poorer survival rate than HIV negative Cervical Cancer patients [67]. A study in Nigeria where the risk factors for cervical pre-cancer and cancer amongst HIV positive women, reported 6% prevalence of cervical pre-cancer and cancer in HIV positive women. The result indicated an increased risk of cervical pre-cancer and cancer amongst HIV positive women in Nigeria [68].

Contraceptive use was found to be significantly associated with Cervical Cancer although the years of oral contraceptive use for longer than 5 years in the bivariate analysis was not found to be significant with ($P > 0.05$). Some studies indicated that hormonal influence of oral contraceptives increased the expression of HPV genes in the cervix thereby facilitating HPV persistence [34]. Similar results on long term use of oral contraceptives were supported by these studies [11,35-36].

Multiple pregnancies in many studies are significantly associated with Cervical Cancer as illustrated in the literature review by studies conducted in of 25 epidemiological studies UK and a study conducted in Kenya [38,39]. The study showed no statistically significant association between Cervical Cancer and multiple pregnancies.

However, the multiple logistic regression which was meant to determine the most significant factors and alleviate the effects of potential confounders did not found any association between Cervical Cancer and multiple pregnancies, smoking, life time partner (>2+), genital warts, alcohol use and history of STI. Although previous studies found that covariates such as multiple pregnancies, smoking, life time partner (>2+), genital warts and alcohol are significant predictors of Cervical Cancer [28,29-31,39] this study found them to be insignificant.

5.3 CONCLUSION

In conclusion, various Cervical Cancer risk factors were identified in the study. The independent risk factors for Cervical Cancer among women attending the Oncology and Health Facilities in Windhoek, Khomas region are rural placements, unemployment, no secondary education, marital status, HIV positive status, not attending Pap smear screening and the use of contraceptives. Awareness campaigns about Cervical Cancer symptoms, risk factors, promotion about prompt help seeking and information about the new screening and treatment programmes of Cervical Cancer are crucial.

5.4 STUDY LIMITATIONS

The study was limited by the following factors

- Due to seasonal peak most of the region stopped with referrals of patients to Windhoek, Khomas region and most patients' follow-up dates were scheduled for January. Although the Oncology centre and wards functioned normally, fewer cases were seen. Therefore, cases were selected as they came to the facilities, but controls were selected randomly as indicated in the sampling process
- Incomplete records of cases such as patients' weight, height which were not documented cause limitations to the study.

5.5 RECOMMENDATIONS

- Seeing that single women are more at risk of getting Cervical Cancer, the Ministry of Health and Social Services could start with the introduction of HPV vaccine in government facilities for girls 9-13 years before they initiate sexual activities.

- To conduct community awareness and health education to women on the importance of cervical screening that might lead to early detection of precancerous lesions.
- Ministry of Health and Social Services to rollout Visual Inspection with Ascetic Acid (VIA) screening and cryotherapy primary treatment to all health facilities especially rural facilities to ensure women with precancerous lesions received treatment before it progresses into invasive cancer.
- To liaise with the Ministry of Education and non-governmental organisations to provide literacy classes to educate women about risk factors of Cervical Cancer and make women understand that family history of cancer can increase the risk two to three times higher than those with no family history therefore to come more frequently for Pap smear and VIA screenings.
- Ministry of Health and Social services should ensure that all ARV clinics especially those with high prevalence of HIV infection patients should provide Pap smear and
- Establish a proper database for women diagnosed with Cervical Cancer in health facilities of the Ministry of Health the same as used by the Cancer Association for population-based research studies.
- It is suggested that Ministry of Health and Social services should avail resources such as mobile clinics to promote Cervical Cancer screening which aims to detect cancer at an earlier stage as well as provide these services to women at hard to reach areas.
- Health workers in facilities and community health workers should be equipped with knowledge through training to conduct health education and create

awareness on the risk factors, prevention, signs and symptoms and where to seek treatment of Cervical Cancer in the community.

- The prevalence of Cervical Cancer as one of the preventative cancers can be reduced if all the State health facilities as well as Private hospitals promote and provide screening and treatment to the general population.

5.5 SUMMARY

This chapter presented the discussions of the findings of the study in line with its objectives. The study revealed that sociodemographic factors such as unemployment, living in rural areas, family history of cancer, positive HIV status, women not attending Pap smears, use of contraceptives were strongly associated with Cervical Cancer. These findings could assist the Ministry of Health in Khomas region to implement preventative strategies which should target the identified risk factors. The chapter also discussed the conclusions, recommendations and limitations of the study.

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APPENDICES

Appendix A: Participant information sheet and consent form

Participant information

My name is Elmarie Eiman a 2nd year MScAE student in the Public Health Department of Faculty of Health Sciences, University of Namibia, Windhoek. I am conducting research on risk factors associated with Cervical Cancer amongst women attending the Oncology Centre and health facilities in Windhoek, Khomas Region as part of the Master of Science (Applied Field Epidemiology) degree requirements. You are being asked to participate in this study because you fulfil the criteria as a patient attending this centre for Cervical Cancer screening or care.

Purpose of study: To identify the risk factors of Cervical Cancer and determine the socio-demographic, medical characteristics of patients with Cervical Cancer attending Oncology Centre and health facilities in Windhoek Khomas Region. This research project will be conducted under the supervision of Prof. A. Rukewe and Dr. Q. Wessels

Information will be gathered through two steps of data collection:

- **Step 1:** Interview questions
- **Step 2:** Review medical record of height, weight and BMI

We will now describe what is involved in this study in more detail. You may ask any questions you have. We will ask you to sign a consent form.

Step 1 of the survey will involve the interviewer asking you some questions about you:

- Age
- Marital status
- Educational status
- Religion
- Employment and income
- Medical aid
- Smoking and alcohol use
- Involvement in sports

Step 2 of the study will involve reviewing medical record passport to obtain the following information:

- Height
- Weight
- BMI

Timeframe: It is estimated that step 1 and 2 of the study will take approximately 30 minutes. **Community benefits:** The results of this study will assist the Ministry of Health and Social Services (MoHSS) to provide wide primary prevention strategies that could assist in programme planning and development

Your rights: The understated are your right: -

- Decline to take part in this study
- Withdraw your consent at any time

- Decline to answer any questions in the interview that you do not wish to answer

Confidentiality: Your responses will remain confidential and anonymous. Your name will not be used in any report of the study.

Results: The study results will be made available to the Ministry of Health and Social Services and for scientific publications.

Ethical approval: This study has received ethical approval from the Research ethics review committee of the MoHSS and the University of Namibia (UNAM).

CONSENT FORM

Dear Participant

Simple random selection: You have been randomly selected to be part of this survey and this is why we would like to interview you. This survey is conducted by a trainee field epidemiologist of the MoHSS and UNAM and will be carried out by professional interviewers from MoHSS.

Confidentiality: The information you provide is totally confidential and will not be disclosed to anyone. It will only be used for research purposes. Your name, address, and other personal information will not be recorded on the instrument. A code will be used for the questionnaire with your answers without identifying you.

Voluntary participation: Your participation is voluntary and you can withdraw from the survey after having agreed to participate. You are free to refuse to answer any question that is asked in the questionnaire. If you have any questions about this survey you may ask me or contact me at +264 81 268 9193 or eimanelmarie@yahoo.com

Consent to participate: Signing this consent indicates that you understand what will be expected of you and are willing to participate in this survey.

Read by: Participant	Interviewer
Agreed	Refused

Signatures

I hereby provide INFORMED CONSENT to take part in Steps 1 and 2 to determine the risk factors for Cervical Cancer. For participants under 21 years old, a parent or guardian must also sign this form.

Participant ID: _____ Sign: _____

Parent/Guardian: _____ Sign: _____

Statement by the researcher/person taking consent

I/the participant has accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands. I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily. A copy of this consent form has been provided to the participant.

Name of Researcher/person taking the consent: _____

Signature of Researcher /person taking the consent: _____

Date: _____ (Day/month/year)

Appendix B: Research questionnaire

Cervical Cancer study questionnaire assessing Risk Factors associated with Cervical Cancer in Windhoek Khomas region, Namibia January 2016 to 30 June 2018

Research Questionnaire

Questionnaire Number 3 digits:

Date of interview _____

Interviewer's name_____

Health Facility: _____

Case/ Control _____

Section A: Socio-demographic information

1. How old are you now (in years)? _____

2. How would you describe yourself?

African (1) Caucasian (2) Asian (3) Mixed (4)

3. What is your marital status? (Tick only one) Single (1) Married (2)

Separated (3) Divorced (4) Widow (5) Cohabitating (6)

4. What is your educational level (Tick only one)

- ☐ No formal education at all (1)
- ☐ Primary education (1- 7 grades) (2)
- ☐ Secondary education (8-12 grades) (3)
- ☐ Tertiary (above grade 12) (4)

5. Employment Status (Tick only one)

- ☐ Employed in formal sector (1)
- ☐ Not formally employed (2)
- ☐ Self-employed (3)
- ☐ Unemployed (4)

6. Where are you living? (Tick only one) Urban (1) Rural (2)

7. Do you have medical insurance scheme?

Yes (1) No (2)

Section B: Gynaecological /Obstetric history (Write or Tick)

7. Do you have children?

Yes (1) No (2)

7.1 Gravida (how many pregnancies have you had?) _____

7.2 Parity (How many deliveries have you had?) _____

7.3 Have you ever delivered all your children in the Hospital?

Yes (1) No (2)

7.4 History of home delivery?

Yes (1) No (2)

C: Risks factors for Cervical Cancer (Please tick only one)

8. Have you ever received HPV vaccination?

Yes (1) No (2)

9. Have you ever heard of Cervical Cancer?

Yes (1) No (2)

10. Any family history of cancer?

Yes (1) No (2)

10.1. Did anyone in your family contract Cervical Cancer?

Yes (1) No (2)

10.2. If yes, specify

Mother (1) Grandmother (2) Sister (3) Aunt (4)

Cousins (5) Extended family members others specify_____

11. At which age did you have the first sexual intercourse? _____

11.1 How many life time sexual partners do you have? _____

11.2 Did your sexual partner have other sexual partners?

Yes (1) No (2) I'm not sure (3)

12. Do you use contraceptives?

Yes (1) No (2)

12.1. Oral pill (1)

Injectable (2)

IUCD (3)

12.2 How long did you use oral contraceptives?

Less than a year (1)

1-3 years (2)

3-5 years (3)

Longer than 5 years (4)

13. BMI

Weight

Height

14. HIV status

Positive (1)

Negative (2)

Unknown (3)

14.1 If positive are you on ARV treatment?

Yes (1) No (2)

15. Have you had any history of STI?

Yes (1) No (2)

15.1 If yes, how was it treated?

Self-medication

Doctor-treated

16. Have you had genital warts before?

Yes (1) No (2)

17. Have you ever been screened for Cervical Cancer (Pap smear test) before?

Yes (1) No (2)

18. Do you smoke?

Yes (1) No (2)

19. How long have you been smoking?

☐ Less than 5 years

☐ More than five years

20. If yes, how many packets per day?

☐ Less than 1pack

☐ 1 pack or more

21. Do you drink alcohol?

Yes (1) No (2)

Appendix C: Permission letter from UNAM

Appendix D: Ethical clearance certificate

Appendix E: Permission letter of Ministry of Health and Social Services

Appendix F: Letters from Central Hospital and Khomas Regional Health Directors