Risk Factors Associated with the Presence of Cervical Lesions in Women Attending a Family Planning Clinic in Harare Zimbabwe: A Cross-Sectional Study

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DECLARATION

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Any sources that I have used or quoted have been cited and referenced.

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Date: December 2022

Signed:  …….

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ABSTRACT

Background: Cervical cancer is the fourth most common cancer affecting women worldwide. It is the second most common malignancy in Sub-Saharan countries such as Zimbabwe. Various risk factors are associated with cervical cancer. Data on cervical cancer incidence and prevalence in Zimbabwe is collected through the Zimbabwe National Cancer Registry. However, data on socio-demographic and sexual behavioural risk factors associated with cervical cancer in the Zimbabwean context is limited. Papanicolaou (Pap) smears, when given as part of routine primary care have shown to decrease the incidence of cervical cancer but so far, no study has been done in Zimbabwe to characterise women that are accessing Pap smear testing, the outcomes of these Pap smears, and the risk factors associated with cervical cancer outcomes in Zimbabwean women.

Aim: This study aimed to determine the prevalence of different types of squamous intraepithelial lesions (SIL) and of invasive cervical cancer detected through Pap smear and risk factors associated with SIL among the Zimbabwean women who accessed Pap smear testing at the Zimbabwe National Family Planning Clinic (ZNFPC).

Methodology: This was an observational cross-sectional study enrolling 161 women aged between 18-65 years who were screened for SIL and invasive cervical cancer using a Pap smear method at ZNFPC. Women were selected using a convenience sampling method and an interviewer-administered questionnaire was used to collect socio-demographic, sexual behavioural, and sexually transmitted infections data. All these data were captured using an Excel spreadsheet and analysed using IBM SPSS (version 26) statistical package.

Results: One hundred and sixty-one women participated in the study. The prevalence of SIL in our cohort was 19.3%; with 11.8% of these women presenting with low-grade squamous intraepithelial lesions (LSIL) whilst 7.5% showed high-grade squamous intraepithelial lesions (HSIL). The researcher did not find any cases of invasive cervical cancer. The only significant associations found were between the positive SIL outcome and the type of contraceptive used (adjusted OR=0.180, 95% CI:0.011-0.155, p=0.023) as well as the educational level of the participants (adjusted OR=0.162, 95% CI: 0.003-0.223, p= 0.045).

Conclusion: This study showed a high prevalence of SIL in our cohort. Moreover, those participants who were not using any form of contraceptives and those with high levels of education were more likely to present with SIL. The results of this study emphasise the need for continued research into the understanding of the risk factors associated with SIL . Furthermore, the results will highlight the need to adopt targeted interventions directed at preventing and combating cervical cancer in Zimbabwe.

KEYWORDS

Cervical Cancer

Squamous Intraepithelial Lesions (SILs)

High-grade Squamous Intraepithelial Lesions (HSIL)

Low-grade Squamous Intraepithelial Lesions (LSIL)

Precancerous Lesions

Women

Pap smear

Screening

Risk Factors,

Human Papilloma Virus (HPV)

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LIST OF ABBREVIATIONS

COC	Combined Oral Contraceptive
HIC	High Income Countries
HPV	Human Papilloma Virus
HSIL	High-grade Squamous Intraepithelial Lesions
ICC	Invasive Cervical Cancer
LIC	Low-Income Countries
LMIC	Low- and Middle-Income Countries
LSIL	Low-grade Squamous Intraepithelial Lesions
SIL	Squamous Intraepithelial Lesions
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
VIAC	Visual Inspection with Acetic acid and Cervicography
WHO	World Health Organization

DEFINITIONS FOR THIS STUDY

Cervical cancer: A malignant tumour of the cervix, the lowermost part of the uterus.

Early sexual debut: Having had your first sexual encounter before the age of 16, which is the legal age of consent in Zimbabwe.

Multiple sexual partners: Having had more than one sexual partner in your lifetime.

Papanicolaou (Pap) smear test: A procedure in which a small brush is used to gently remove cells from the surface of the cervix and the area around it so that they can be checked under a microscope for cervical cancer or cell changes that may lead to cervical cancer. A Pap smear may also help find other conditions, such as infections or inflammation. It is usually done at the same time as a pelvic exam.

Precancerous lesions: Abnormal tissue that is associated with an increased risk of developing *cancer.*

Squamous Intraepithelial Lesions: Abnormal growth of squamous cells on the surface of the cervix. These lesions are pre-cancers, which means they are not cancer but have the potential to become cancer and spread to other tissues.

CHAPTER ONE: INTRODUCTION

1.1 Background

According to the World Health Organization (WHO, 2019), cancer was the second leading cause of death worldwide, with the Global Cancer Statistics (GLOBOCAN) of 2020 showing that there were over 19 million new cancer cases and almost 10 million deaths globally (Sung *et al.*, 2021). Cervical cancer, which is cancer that develops in a woman's cervix (an organ that connects the uterus to the vagina), is the fourth most common cancer affecting women worldwide (WHO, 2019; Barrow *et al.*, 2020). It is one of the most commonly diagnosed cancers and a leading cause of cancer deaths in women after breast cancer, with 604 000 new cases and 342 000 deaths recorded in 2020 (Sung *et al.*, 2021). This is a notable increase from data captured in 2018 which showed 570 000 new cases and 311 000 deaths (WHO, 2019; Zhang *et al.*, 2021). Ninety percent of cervical cancer cases and 80-85% of cervical cancer deaths occur in low and middle-income countries (LMICs) (Ali-Risasi *et al.*, 2015; WHO, 2020). Similarly, in the WHOs Global Strategy for Elimination of Cervical Cancer (WHO, 2020) document, it is outlined that cervical cancer incidence and mortality are two to three times as high in the LMICs compared to high-income countries (HICs). This has been attributed to various socio-economic and cultural factors such as poverty, availability of and access to health care and screening services, lack of knowledge and education around cervical cancer, as well as early marriage and sexual risk behaviours (Zhang *et al.*, 2021). Like most LMICs, Sub-Saharan Africa (SSA) has a high burden of cervical cancer, with cervical cancer being the second most common cancer within the region and the main contributor to cancer incidence and mortality among women (World Health Organization, 2011; Sung *et al.*, 2021). Eight out of ten cases of cervical cancer occur in SSA countries, with the highest burden being in the Southern Africa, where eSwatini has the highest incidence, then Malawi followed by Zimbabwe having the highest mortality rates (Kuguyo *et al.*, 2017; Bray *et al.*, 2018; Gabaza *et al.*, 2019).

Zimbabwe has a high prevalence of cervical cancer, with Barrow *et al* (2020) stating that cervical cancer accounts for one third of all cancers in the population. Previous estimates recorded in 2016 corroborate this fact, with Gabaza, Chonzi & Chadambuka et al (2019) showing that 33% of cancer cases reported in Zimbabwean women were cervical cancers, with these accounting for 12% of all cancer deaths. On the other hand, according to Kuguyo *et al* (2017), the prevalence of cervical cancer in Zimbabwe is 19%, with cervical cancer being the leading cause of cancer deaths in women aged 15-44 years. The highest recorded annual mortality rate due to cervical cancer in Zimbabwe is 64% (Kuguyo *et al.*, 2017). Bruni *et al* (2019) highlighted that 3 186 new cervical cancer cases are diagnosed annually, with the annual crude incident rate being 36.7 per 100 000, a number that has since increased to 39.2 per 100 000 women in 2020 (WHO,

2021). This makes cervical cancer the most common cancer affecting women in Zimbabwe. Barrow *et al* (2020) reported 2 151 deaths per year that are attributed to cervical cancer in Zimbabwe, mostly within the 60-64 year age group, making cervical cancer the leading cause of cancer mortality in older adult women in Zimbabwe (ICO, 2021). Despite differing data regarding the prevalence and mortality rate of cervical cancer in the Zimbabwean population, the obviously high burden of cervical cancer makes cervical cancer prevention, screening, and early treatment a public health priority.

The WHO recommends secondary prevention measures in the form of screening and treatment of precancerous lesions to reduce mortality caused by cervical cancer (WHO, 2019). As a result of this, the WHO published comprehensive guidelines and strategies to be employed for secondary prevention, including screening of women between the ages of 30-49 years using Papanicolaou smear test (Pap smear) and visual inspection with acetic acid cervicography (VIAC) test, to detect abnormal cytological changes or dysplasia in cervical cells (National Cancer Institute, no date; WHO, 2014, 2020; Kuguyo *et al.*, 2017). Dysplasia of cervical cells, which is thought to be found in 1 to 5% of the general population, results in the development of squamous intraepithelial lesions (SIL), which over time may lead to the development of cervical cancer (Nkfusai *et al.*, 2019). Bruni *et al* (2019) emphasise that Pap smears are particularly effective for detecting these changes, with results indicating either no abnormal cell, the presence of mild dysplasia resulting in the formation of low-grade squamous intraepithelial lesions (LSIL) or the presence of moderate or severe dysplasia resulting in high-grade squamous intraepithelial lesions (HSIL) on the surface of the cervix (National Cancer Institute, no date; ICO, 2021). ICO (2021) also suggests that early detection of precancerous lesions tends to result in their successful treatment. It also prevents the possibility of precancerous lesions developing to cervical cancers and their subsequent spreading into other cervical tissues, thus causing invasive cervical cancer (ICC). However, based on the 2017 WHO report, only 26% of the population in low-income countries (LICs), Zimbabwe included, have access to pathology and Pap smear services in the public sector (WHO, 2019)**.** Lack of access to screening facilities results in decreased screening, late disease presentation and poor diagnosis and treatment of cervical cancer (Kuguyo *et al.*, 2017; Barrow *et al.*, 2020). These precursors lead to increased burden of cervical cancer in Zimbabwe, resulting in various public health implications.

Various risk factors have been associated with cervical cancer. Observed differences in incidence and mortality from cervical cancer in HICs compared to LICs have been attributed to various socio-economic and cultural factors that have also resulted in differing exposures to these risk factors (Ali-Risasi, Verdonck & Padlko, 2015). Human Papilloma Virus (HPV), a sexually transmitted infection (STI), is the biggest and most documented risk factor for the development of precancerous SIL on the surface of the cervix, that

can result in the development of cervical cancer (National Cancer Institute, no date; WHO, 2020). Particularly, the presence of high-risk HPV subtypes, particularly subtype 16 and 18 in cervical tissue, increases the chances of abnormal cervical cytology progressing to cervical cancer by 95% (Kuguyo *et al.*, 2017; WHO, 2019). It is, however, important to note that, HPV infection is a necessary but not sufficient cause of cervical cancer. Moreover, not all HPV positive patients develop cervical cancer (Sung *et al.*, 2021). It is, therefore, important to investigate the association between cervical cancer and its afore-mentioned determinants, especially in LICs. Other documented risk factors include sexual history, tobacco smoking, HIV/AIDS infections, other sexually transmitted infections other than HPV infection, long-term use of oral contraceptives, parity, age at first pregnancy and socio-economic status (American Cancer Society, 2020; Sung *et al.*, 2021) . However, data on cervical cancer prevalence and its afore-mentioned determinants in the Zimbabwean context is limited.

1.2 Problem Statement

There is sparse information on cervical cancer prevalence and its associated risk factors in SSA countries(Ali-Risasi *et al.*, 2015) . With the exception of studies conducted in countries like Nigeria, Rwanda and the Democratic Republic Congo (Ali-Risasi, Verdonck & Padlko, 2015; Durowade, Osagbemi & Salaudeen, 2012; Makuza, Nsanzimana & Muhimpundu, 2015), there is a dearth of studies in Africa and Southern Africa specifically, especially in Zimbabwe, that describe the association between SIL and various socio-demographic and behavioural factors associated with cervical cancer lesions. Pap smears, when offered as part of routine primary care or as part of routine national screening programmes have shown to decrease the incidence of cervical cancer in several HICs such as the United Kingdom (UK) and Finland (Kuguyo *et al.*, 2017; WHO, 2020; Zhang *et al.*, 2021). In the United State (US), where cervical cancer was once the leading cause of death in women, the implementation of regular Pap smears has resulted in a decrease in the incidence and mortality rate of cervical cancer patients due to early detection of precancerous lesions (Nkfusai *et al.*, 2019). However, due to limited resources, inadequate infrastructures, and lack of skilled cytopathologists, LICs like Zimbabwe have been unable to implement Pap smear programmes on a national level, despite Pap smears' increased reliability and efficacy to detect cervical cancer when compared to the VIAC test. In Zimbabwe, Pap smears are offered in private and selected public health facilities at a cost, with the VIAC test being favoured in most facilities due to its ease of set up, overlooking the variability in its sensitivity and how heavily user dependant it is (Gabaza *et al.*, 2019; WHO, 2020). Gabaza *et al*

(2019) conducted a study with the aim of characterising women accessing VIAC and their outcomes. However, to my knowledge, no study has been done in Zimbabwe, to characterise women that are accessing

Pap smear testing, the outcomes of these Pap smears and the factors associated with cervical cancer outcomes in women.

1.3 Aim

The aim of this study is to determine the prevalence of different types of SIL detected through Pap smears, the prevalence of invasive cervical cancer and the risk factors associated with the burden of squamous intraepithelial lesions among the Zimbabwean women who accessed Pap smear testing at ZNFPC between June and November 2021.

1.4 Objectives

The specific objectives for this study were to:

1. Determine the prevalence of LSIL, HSIL and invasive cervical cancer among women accessing Pap smear tests at a ZNFPC.
2. Determine the socio-demographic characteristics, sexual behaviours and sexually transmitted infections (that is, HIV and STI statuses) among women accessing Pap smear tests at a ZNFPC.
3. Determine the association between the presence of SIL and various socio-demographic characteristics, sexual behaviours and sexually transmitted infections among women accessing Pap smear test at a ZNFP clinic.

1.5 Study Rationale

This study was conducted to outline the prevalence and the extent of various SIL that could result in the development of cervical cancer in Zimbabwean women who were receiving Pap smears at ZNFPC. The study also aimed to highlight the potential burden of cervical cancer among Zimbabwean women and to show the associations between precancerous lesions and the Zimbabwean women's socio-demographic characteristics, sexual behaviours, and sexually transmitted infections. Such data is not readily available in Zimbabwe and hence the burden of disease study such as the current one was done to add to the existing body of knowledge on this topic, and to inform Zimbabwean Public Health policies. The study also meant to provide baseline data for future research on the current topic.

This study was done in accordance with the Zimbabwe National Health Strategy (2016-2020), which launched a national programme aimed at promoting screening and early detection of cervical cancer. The study also fulfilled the WHO global strategy to eliminate cervical cancer, which aims to screen 70% of women aged between 35 and 45 years for cervical cancer, using a high-performance test. Prevalence data

generated from the current study partly highlighted the population groups that require immediate response from policymakers and health managers, with regards to the allocation of health services and resources for maximum impact. This is especially important in a resource-limited setting such as Zimbabwe, where there are constraints in terms of health information systems, health infrastructure and resources which need to be used prudently. This study characterised those women currently accessing Pap smears, and it also highlighted the risk factors associated with different cytological abnormalities. The outcomes of the current study highlighted the need to scale-up other secondary prevention interventions such as HPV DNA testing, HPV vaccination as well as the nationwide cervical cancer screening programme targeted at women who could be at risk of cervical cancer but may be asymptomatic. This is especially important as it may improve the current poor prognosis of women who present with cervical cancer at the Zimbabwean health services, especially those who usually present to the clinic when cancer is at its advanced stage.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Considering the ever-increasing burden and mortality rate due to cervical cancer globally, regionally and in Zimbabwe as highlighted above, and initiatives that have been taken by the WHO, Zimbabwe Ministry of Health and Child Care (Zimbabwe Ministry of Health and Child Care, 2013; WHO, 2020) , through their Nationa, it has become imperative to determine risk factors that may affect the development of SIL. This literature review explored the current available evidence for the current burden of disease of cervical cancer and its associated risk factors. This review highlighted the continued relevance of this topic and the need for continued research if we are to attain the goal of " … a world where cervical cancer is eliminated as a public health problem …" (WHO, 2020: 7).

2.2 Search Strategy

To find existing evidence on cervical squamous intraepithelial lesions and associated risk factors, a literature search was performed using Google and Google Scholar primarily. These searches eventually led to articles being found on various platforms such as PubMed, PLOS, BioMed Central and Science Direct to name a few. The initial search was conducted in July 2020, and the last search was conducted in April 2022. Terms used in this search included various combinations of the following key terms within the global context as well as in Sub-Saharan Africa, Southern Africa, and Zimbabwe:

- *Disease outcome:* "Cervical cancer" OR "SIL" OR "HSIL" OR "LSIL" OR "Squamous intraepithelial lesions prevalence" OR "precancerous lesions" OR "abnormal cervical lesions"
- *Population:* "Women" OR "burden of disease"
- *Independent variable:* "Risk factors" OR "HPV infection" OR "Human Papillomavirus"
- Procedure: "Pap smears" OR "screening"

The operator AND was used in different combinations of key words during the search and no filters were used. Moreover, grey literature (in the form of country reports on the topic) were captured through hand search of popular websites such as WHO, American Cancer Association, International Agency for Research on Cancer, and specific government departments in SSA and Zimbabwe.

2.3 Literature Captured

In total, twenty-four documents were found to be relevant to the current research topic as they spoke on the prevalence and incidence of cervical cancer and SIL globally, within SSA, Southern Africa and Zimbabwe, as well as the risk factors that were associated with the development of cervical cancer and SIL. Seven of these were reports that provided statistics across multiple countries, thirteen were articles that documented outcomes of observational studies that occurred in Greece (Parthenis *et al.*, 2018), Thailand (Saibua Chichareon, Rolando Herrero, Nubia Mun˜oz, F. Xavier Bosch, Jacobs, Judith Deacon, Mercedes Santamaria and Chris J. L. M. Meijer, 1998), Indonesia (Ashar *et al.*, 2020), Cameroon (Nkfusai *et al.*, 2019), Democratic Republic of Congo (Ali-Risasi *et al.*, 2015), Ethiopia (Teame *et al.*, 2018; Tsehay & Afework, 2020; Beyene *et al.*, 2021; Kasa *et al.*, 2021), Nigeria (Durowade *et al.*, 2012), Rwanda (Makuza *et al.*, 2015), South Africa (Fonn *et al.*, 2002) and Tanzania (Obure *et al.*, 2009). The remaining four articles highlighted multicentre studies that occurred across multiple continents (Moreno, Bosch, Muñoz, Meijer, Shah, Walboomers and Franceschi, 2002; Munoz *et al.*, 2002; Louie *et al.*, 2009; Liu *et al.*, 2015).

2.3.1 Reports

Of the seven reports, two gave an overview of the global incidence, prevalence and mortality rate of cervical cancers (Arbyn *et al.*, 2020; Sung *et al.*, 2021), one reported on associated cancer risk factors (American Cancer Society, 2020) and four highlighted the association between cervical cancer and HPV infection (Bosch and de Sanjosé, 2003; De Vuyst *et al.*, 2013; Chin'Ombe *et al.*, 2014; ICO, 2021). These reports allowed me to get a deeper understanding around the global and regional burden of cervical cancer and SIL and how the epidemiology of the disease has changed over time.

2.3.2 Observational articles

There were fourteen observational articles captured which answered similar research questions as the one answered in the current mini thesis, thereby providing relevant evidence-based arguments around the topic. In addition, most of these studies were conducted in SSA, hence they seemed relevant and acted as guides to the current study setting.

Eight of the studies were cross-sectional studies whilst six were case control studies. Of the cross-sectional studies, three focused on the prevalence and various risk factors associated with cervical cancer and cervical cancer lesions in three African countries (Durowade *et al.*, 2012; Ali-Risasi *et al.*, 2015; Makuza *et al.*, 2015). Two studies aimed to determine the prevalence of cervical cancer in South Africa and Cameroon (Fonn *et al.*, 2002; Nkfusai *et al.*, 2019), whilst one study explored the prevalence and severity of SIL in Tanzania (Obure *et al.*, 2009). One study explored the role that early sexual debut and high parity

played in the development of SIL (Ashar *et al.*, 2020) and the last one explored the association between STI, HPV and SIL in a Greek cohort (Parthenis *et al.*, 2018).

Of the case control studies, three studies examined various risk factors of cervical cancer in a Thailand and Ethiopian cohort (Saibua Chichareon, Rolando Herrero, Nubia Mun˜oz, F. Xavier Bosch, Jacobs, Judith Deacon, Mercedes Santamaria and Chris J. L. M. Meijer, 1998; Teame *et al.*, 2018; Beyene *et al.*, 2021). Two studies explored the role that specific risk factors played in the development of precancerous lesions, namely age of sexual debut and first pregnancy, parity and previous HPV infection (Munoz *et al.*, 2002; Louie *et al.*, 2009). One study aimed to determine the role that oral contraceptive played in the development of cervical cancer (Moreno *et al.*, 2002).

2.3.3 Systematic reviews and meta-analysis

Included in the 14 articles reviewed were systematic reviews and meta-analyses documents. These were included in the current review as they were efficient sources of information that summarised data and work that had been done globally around the current research topic over a specified period. One review assessed the prevalence of SIL in Ethiopia and how this changed over time (Kasa *et al.*, 2021), while another review also done in Ethiopia looked at the prevalence of SIL and determinants of precancerous lesions in Ethiopia (Tsehay and Afework, 2020). The last meta-analysis was conducted to determine the role that having multiple sexual partners played in the development of cervical cancer (Liu *et al.*, 2015).

2.4 Literature Review Findings

The reviewed literature highlighted several factors related to the prevalence of cervical cancer.

2.4.1 Burden of disease of cervical cancer

Burden of disease studies provide information on areas and populations that require response from policymakers and health managers (SOPH, 2019). As illustrated by SOPH (2019), such studies give health managers information required to plan and allocate health care services and resources for maximum impact. These studies also aid health managers in assessing the impact of the programmes and services currently running, in this case, the Pap smear programme. Prevalence studies help assess the programme's coverage, who is accessing the services and the effectiveness of the service over time as seen by changes or the lack thereof in the prevalence of the disease (SOPH, 2019). The WHO conducted a study to assess the global burden of cervical cancer, describing existing patterns of the disease and its associated mortality rate across 185 countries (Arbyn *et al.*, 2020). The outcomes of this study showed that 84% of cervical cancer cases and 88% of related deaths occurred in low resource countries, with the highest incidence found in SSA

countries, particularly in eSwatini, Malawi, Zambia, Zimbabwe, Tanzania, Burundi, Uganda, Lesotho and South Africa (Arbyn *et al.*, 2020). Recent data obtained confirms a generally high prevalence of cancerous lesions in SSA. In 2020, the International Agency for Research on Cancer examined the global cancer burden using estimates on cancer incidence and mortality at a global level, as well as how these differ across different geographical regions (Sung *et al.*, 2021). This report, commonly referred to as GLOBOCAN estimates, showed an increase in cervical cancer incidence and mortality globally, with the highest incidence and mortality being seen in SSA, with rates being highest in Eastern, Southern and Middle Africa, specifically in Gambia, Kenya, Malawi, the Seychelles, South Africa, Uganda and Zimbabwe (Sung *et al.*, 2021).

The prevalence of cervical lesions varies across African states, with Nkfusai *et al* (2019) attributing such differences to differing availability of cervical cancer screening programmes and differing access to care and treatment once a diagnosis has been made. Ali-Risasi *et al* (2015) conducted a prevalence study to determine the prevalence of precancerous cervical lesions in adult women in the Democratic Republic of Congo, as well as associated socio-demographic and behavioural characteristics of the women being tested for cervical cancer. Of the 1 018 participants, 76 women were diagnosed with LSIL or higher (LSIL, HSIL or ICC), resulting in an overall prevalence of 7.5%, with the prevalence in HIV positive women being 31% (Ali-Risasi *et al.,* 2015). A study conducted in South Africa, aimed at describing the age specific prevalence rates of cervical cancer in 468 women, showed that the prevalence of LSIL was 2.42%, that of HSIL was 1.9% and that of invasive cancer was 0.47% (Fonn *et al.*, 2002). In comparison, a recent meta-analysis conducted in Ethiopia, to determine the prevalence of precancerous lesion, showed a significantly higher prevalence of SIL as compared to the previous two studies mentioned above, with results showing a pooled prevalence of 15.16%, with the report showing a steady increase in prevalence between 1992 and 2019 (Kasa *et al.*, 2021). Other studies done in Nigeria, Tanzania and Malawi have shown prevalence data ranging between 4% to 10% of cancerous lesions, with numbers going as high as 16% in countries such as Uganda (Obure *et al.*, 2009; Durowade *et al.*, 2012; Ali-Risasi *et al.*, 2015). These studies all show the variability in the prevalence of precancerous intraepithelial lesions across SSA, but also emphasise the high prevalence of SIL within the region.

2.4.2 Cervical cancer risk factors

It is well established that cervical cancer has an infection related etiology with HPV infection(Sung *et al.*, 2021). Various studies have shown that 95-100% of cervical cancer specimens had HPV DNA (Bosch & de Sanjosé, 2003). Globally, HPV subtype 16 and 18 contribute to 16-32% LSIL and 41-67% of HSIL (ICO, 2021). Chichareon *et al* (1998) in a case-control study aimed at investigating the association between invasive cervical cancer and HPV infection in Thailand, showed that 95% of women with carcinoma had HPV infection (Saibua Chichareon, Rolando Herrero, Nubia Mun˜oz, F. Xavier Bosch, Jacobs, Judith Deacon, Mercedes Santamaria and Chris J. L. M. Meijer, 1998).The trend is similar in SSA where studies have shown a high prevalence of HPV subtype 16 and 18 in cases of invasive cervical cancer (De Vuyst *et al.*, 2013). In Zimbabwe, persistent infection with HPV is the major risk factor of cervical cancer (Chin'Ombe *et al.*, 2014). Chin'Ombe *et al* (2014) outlined various studies conducted in Zimbabwe that showed high HPV prevalence that ranged from 63% to 97% in women diagnosed with cervical cancer. ICO (2021) reported an HPV prevalence of 22.7% and 18.2% in low-grade and high-grade lesions respectively, specifically in Zimbabwe.

However, as mentioned before, HPV infection is a necessary but not sufficient cause of cervical cancer, and not all HPV positive patients develop cervical cancer (ICO, 2021; Sung *et al.*, 2021). Despite several studies that have shown an undeniable causal role that HPV infection plays in the development of cervical cancer there are other risk factors that are known to be associated with cervical cancer incidence and prevalence as they increase exposure to HPV infection (Bosch *et al.*, 2002). For instance, sexual history such as history of sexual transmitted infection including HIV, early sexual debut, early age of first marriage, age of first pregnancy, parity and having multiple sexual partners are risk factors for cervical cancer (American Cancer Society, 2020).

2.4.2.1 History of sexually transmitted infection

Various STIs such as genital chlamydia and HIV have been found to be co-prevalent with HPV and are thought to be associated with the presence of SIL (Parthenis *et al.*, 2018). A history of sexually transmitted infection has been associated with the occurrence of SIL with Tsehay and Afework (2020) showing that women who had a history STI were 6.22 times more at risk of developing precancerous lesions.

2.4.2.2 Multiple sex partners

Having multiple sexual partners, which is defined as having had more than one sexual partner in your lifetime has been shown to increase the likelihood of developing SIL. A meta-analysis by Liu *et al.* (2015)

showed that having multiple sexual partners was a risk factor for cervical cancer even after controlling for HPV infection (Liu *et al.*, 2015). Ali-Risasi *et al.* (2015) corroborated this finding, showing that having more than three sexual partners was associated with the development of LSIL or greater lesions. This association was substantiated by a study conducted in Nigeria that showed that early sexual debut and number of sexual partners were predictors and risk factors of cervical cancer development (Durowade, Osagbemi & Salaudeen, 2012). A systematic review and meta-analysis conducted by Tsehay and Afework (2020) aimed at determining the prevalence and determinants of precancerous lesions in women in Ethiopia found that women who had multiple sexual partners were 2.67 times more likely to develop precancerous cervical lesions than women who had only one lifetime sexual partner. Similarly, a study conducted in Tanzania by Obure *et al.* (2009) showed that women with multiple sexual partners had higher rates of precancerous lesions than women who had one lifetime partner. The risk of having multiple sexual partners includes women having male partners who have two or more other partners, with studies showing that this increases the risk of developing precancerous lesions (Teame *et al.*, 2018; Beyene *et al.*, 2021).

2.4.2.3 Early sexual debut

Early sexual debut has been associated with increased risk of HPV acquisition and in turn the development of ICC. Early sexual debut can result in early marriage and early childbearing. Evidence suggests that both these factors are associated with cervical cancer, especially in women who had their first pregnancy when they were younger than 20 years old (Louie *et al.*, 2009; American Cancer Society, 2020). A pooled analysis of case control studies on ICC from eight developing countries showed that women whose first sexual debut was 16 years and below were 2.4 times more at risk of developing ICC than women whose sexual debut was above 21 year (Louie *et al.*, 2009). This data is also corroborated by Makuza, Nsanzimana and Muhimpundu (2015) who showed that the risk of developing cervical cancer lesions in a Rwandan cohort was higher in women who had their sexual debt before the age of 20 years. A case control study conducted by Beyene *et al.* (2021) in Ethiopia, to identify the risk factors of precancerous lesions in women, found that women who had their sexual debut before the age of 20 years were 2.39 times more likely to develop precancerous lesion.

2.4.2.4 Parity

Multi-parity is a risk factor of cervical cancer, as it is thought to result in increased exposure to HPV virus due to increased sexual activity, hormonal changes and suppressed immune system experienced during pregnancy (American Cancer Society, 2020). This is especially true in women who have high parity, defined as having more than 4 children (Ashar *et al.*, 2020). A pooled analysis to assess the influence of parity on cervical cancer in HPV positive women showed an association between the number of full-term

pregnancies and risk of cervical cancer (Munoz *et al.*, 2002). Munoz *et al.* (2002) also showed that the risk of cervical cancer increased with the number of full-term pregnancies.

2.4.2.5 Duration and use of combined oral contraception

Various studies have shown an association between use of hormonal contraceptives and the incidence of cervical cancer, specifically the combined oral contraceptive (COC). Ashar *et al.* (2020) for instance, highlights from work conducted by Green, (2007) , that the duration of use of the COC, that is, use for more than 10 years, increases the risk of cervical cancer from 7.3 to 8.3 per 1000 population in LMICs. In a study designed to assess the association between long-term use of oral contraception and cervical cancer, Moreno, Bosch and Munoz (2002) found that long-term contraceptive use, that is, use for five years or longer was associated with a three-fold increase of risk of cervical cancer.

2.5 Summary of literature review

To summarise the literature presented in this chapter, although there is an estimated burden of cervical cancer in Zimbabwe of 19% (Kuguyo *et al.*, 2017), to our knowledge, recent data on the prevalence of SIL and cervical cancer and their determinants in the Zimbabwe is sparse and unavailable. As seen in the literature above, globally, there has been an increase in the prevalence of cervical cancer, with the highest prevalence of precancerous lesions being found in SSA. As highlighted above, the prevalence of SIL and cervical cancer differ across different countries globally and among different African nations and as such, prevalence studies such as the one this researcher conducted are useful in bridging the existing research gap in Zimbabwe. Finally, as shown in the afore-presented literature, there is an undeniable and well documented association between the development of precancerous lesions and HPV infections. However, other risk factors, namely history of sexual transmitted infection including HIV, early sexual debut, parity, duration, and use of oral contraceptives and having multiple sexual partners play a significant role in the development of precancerous lesions as they increase exposure to HPV infection. However, the extent that these factors play in the development of precancerous lesions in the Zimbabwean population, to our knowledge has not been documented. Hence the current study provides such data, that will inform the refining, development, implementation, and expansion of cervical cancer prevention programmes aimed at curbing cervical cancer incidences and the associated deaths.

CHAPTER 3: METHODOLOGY

3.1 Introduction

The following chapter describes the methodology used in conducting this study. I start by describing the research design and setting. This is followed by a description of the study population and the sampling method used. The data collection process, tools and procedures used are described. Lastly, is the description of how statistical analysis was conducted, as well as ethical considerations for this research.

3.2 Study Design

The researcher utilised a cross-sectional study design which allows researchers to estimate the prevalence and burden of SIL over a period of time (Sedgwick, 2014). This design also enabled the researcher to investigate multiple exposures and their association with the SIL, enabling the formulation of an objective view on the possible relationship between SIL and any socio-demographic or behavioural factors (Sedgwick, 2014; SOPH, 2019). Also, the cross-sectional nature of the current study made it easy and quick to collect data, since the data was collected at one point in time, with no participant follow up required. This was especially useful during the COVID-19 pandemic, where COVID restrictions and lockdown regulations made it difficult to access and enrol participants in clinical setting, as well as follow them up over a period of time. As there was no follow up period, there was no loss to follow up either (Sedgwick, 2014). The design and lack of a follow up period allowed the researcher to enrol many participants at minimal cost compared to other study designs, making the research design relatively inexpensive.

3.3 Study Setting

Zimbabwe is a low-income country (LIC) in Southern Africa and has a population of about 16.53 million people. Harare is the capital city, with a population of approximately 1.5 million people. According to the International Agency for Research on Cancer, in 2020 Zimbabwe had 3043 new cervical cancer cases with an age standardized incidence rate of cervical cancer is 86.1 per 100 000 (Bray F *et al.*, 2017). This makes cervical cancer the most common cancer affecting women in Zimbabwe (Bruni, Bero,Serrano & Mena, 2019). In Harare for instance, 26.6% of cervical cancer cases in 2015 occurred amongst black women (Chokunonga *et al.*, 2018) . The VIAC method of screening for cervical cancer was adopted in 2012 and is offered at public health facilities free of charge. Pap smears on the other hand, are offered at private and specified public health facilities at a cost (Gabaza *et al.*, 2019).

The current study was conducted at ZNFPC, which is located in Harare. This clinic provides health care services to Harare's densely populated South-Western suburbs and peri-urban settlements, and it falls under the Ministry of Health and Child Care. The clinic provides family planning and sexual reproductive health services including the screening of cervical cancer using the Pap smear method for approximately 10 000 adults and adolescents each year (Zimbabwe National Family Planning Council, 2022) Women attending the clinic usually come voluntarily seeking services offered by ZNFPC or are referred to the clinic from other clinics and hospitals in and around Harare. The ZNFPC is one of the few public facilities that offers Pap smears to the public. As such, it sees over 100 women a month from within and outside the city of Harare. Suspected cancer patients are referred to specialist care for biopsy and eventual treatment by a consultant gynaecologist.

3.4 Study Population

Women from in and around Harare metropolitan area who sought out Pap smear services at ZNFPC between June and October 2021 were enrolled. The population included women who were born women and would therefore have a cervix. The women were required to have been sexually active at least once as cervical cancer is primarily considered a sexually transmitted disease.. Women enrolled into the study had to be 18 years and above as the legal age of majority in Zimbabwe is 18 years. .The study included women between the ages of 18-65 years, as various cancer organisation currently recommend routine screening for cervical cancer every three years from the ages of 21-65 years (Kuguyo *et al.*, 2017; White, Shoemaker & Benard, 2017). . Women meeting the inclusion criteria highlighted below were eligible for study participation.

Inclusion criteria: Women were included in the study if they were born as women, report ever having vaginal sexual intercourse at least once in their lifetime and aged within 18-65 years. The women also had to have their Pap smear results available after testing.

Exclusion criteria: The study excluded women not born females, who were younger than 18 years or older than 65 years and did not have their Pap smear results available after testing for any reason.

3.5 Sampling Strategy

Convenience sampling was used in this study. Participants who reported to ZNFPC, requiring a Pap smear where informed about the study and asked verbally by the clinic nurse if they were willing to participate. Women who were willing to participate in the current study gave a written consent, and those who met the inclusion criteria were enrolled into the current study (Sedgwick, 2013). If a potential candidate refused

participation, the next available candidate was asked to participate until the required sample size was reached. Sampling method was sensitive to the restrictions imposed by the Zimbabwe Health Ministry and Child Care, due to the COVID-19 pandemic that restricted movement of people in the community. The only movements allowed were to procure food and seek healthcare services. Therefore, random probability sampling would have been difficult to conduct as there was no large population or sampling frame to sample from. As such, the primary researcher had access to the ZNFPC and its patients only, as she worked at the facility, making this sampling method the easiest way to access participants under the current global pandemic.

3.5.1 Sample size calculation

The formula highlighted by Pourhoseingholi, Vahedi and Rahimzadeh (2013) was used to calculate sample size:

For instance, $n=Z^2\ P(1-P)/d^2$ was used*:* Where n= sample size, Z=level of confidence. 95% level of confidence which corresponds to 1.96 will be used, P=prevalence of cervical cancer in similar studies and d= effect size. The prevalence of cervical cancer was 7.5% based on the study by (Gabaza *et al.*, 2019), while an effect size of 5% was used.

Therefore, n = 1.96 x 1.96 x 0.075(1-0.075)/0.05 x 0.05

=3.8416 x 0.075(0.925)/0.0025

= 0.2665/0.0025

= 106.6

Because the prevalence of cervical cancer lesions is generally low in communities even though the study was conducted in a high-risk group, where sometimes the participants investigated may not have positive outcomes for SILs, a larger sample size (N=157 women) was proposed, with 5% catering for nonresponse. As such, 165 women were recruited to participate in the study

3.6 Data Collection and Procedures

The following procedures and steps were followed during data collection:

3.6.1 Socio-demographic and sexual behavioural variables

Socio-demographic, sexual behavioural and sexual transmitted disease variables were collected using a face-to-face interviewer administered structured questionnaire (See Appendix 1). The interviewers were trained clinic nurses, whom the participant was going to receive their Pap smear from. The clinic nurses received protocol training on the aims and objectives of the research, as well as on how to administer the questionnaire.The questionnaire could be administered in English or Shona, the local languages, based on the participant's choice.. The questions elicited the women's socio-demographic information including the age, marital status, parity, highest level of education attained, income earning capacity and whether the women ever smoked cigarettes. The questionnaire then went on to elicit information about the women's sexual behaviours and sexually transmitted infections, including their HIV status, their sexually transmitted infections (STIs), contraceptives used, and length of time on those contraceptives, the number of lifetime sexual partners the women had, as well as the age of their sexual debut.

This questionnaire was used for data collection as it was regarded as the efficient way of eliciting information regarding possible exposures and determinants of cervical cancer, especially in the observational studies such as this (Nieuwenhuijsen, 2005). The questionnaire was short (that is, one page), with structured straightforward questions to prevent participant fatigue and ensure a high response and question completion rate. Using a trained clinic nurse to administer the questionnaire face-to-face, allowed the participant to ask for clarity if there was something they did not understand. The questionnaire was pretested on eight participants (5% of that total sample size) to ensure the reliability and validity of the questionnaire (Nieuwenhuijsen, 2005). The clinic nurses were well versed in the subject manner as they were responsible for conducting the Pap smears and other reproductive health services on a day-to-day basis..

3.6.2 Cytology / Pap smear test

Cytology results were generated from a sample collected from a Pap smear. To collect a sample, a speculum was inserted into the vagina, to hold the walls of the vagina open, allowing the clinic nurse to see the cervix clearly. Cervical cells were collected from the cervix using the cytology brush and spatula. The sample was fixed onto a glass slide and sent to the cytology lab for analysis by a pathologist. The Pap smear cervical samples collected were examined by the pathologist to determine if there were any cervical cell abnormalities. Results from the Pap smear were classified as:

Normal: where there were no abnormal cells identified at the surface of the cervix.

Low-grade cervical lesion (LSIL): where there were changes in the size, shape, and number of squamous cells. Precancerous cells are present but are years away from becoming cancer (ICO, 2021)

High-grade cervical lesions (HSIL): where there was a large number of distinct precancerous cells on the surface of the cervix that potentially may become cancerous and invade the tissues of the cervix or showed evidence of cervical cancer (ICO, 2021) .

Invasive cervical cancer (ICC): where precancerous cells had invaded the basement membrane of the cervix and the woman is considered to have cervical cancer (ICO, 2021).

Pap smear results were recorded by the pathologist in the patient records and the information was transcribed from the patient record onto Appendix 2 by the clinic nurse.

3.7 Data Analysis

Raw data on socio-demographic, sexual behavioural, sexually transmitted infections and cervical cytology were collected and categorised using an Excel (2021) spreadsheet (see the data capturing tool as Appendix 3). Data were exported to IBM SPSS statistical package (version 26) for analyses. Descriptive statistical analysis highlighting ranges, frequencies, prevalence's / percentages of socio-demographic and sexual behavioural characteristics were conducted to describe the population. Data on cervical cytology were analysed to determine the overall prevalence of abnormal cytology and the prevalence of each grade of lesions. Data are, therefore, presented in tables and figures. A Chi-square test was conducted to determine if there were significant differences between groups. Binomial logistic regression and linear regression were employed to determine the associations between dependent variables (presence of SIL) and independent variables (socio-demographic characteristics, behavioural factors and health statuses). P-values that are < 0.05 and confidence intervals that do not overlap are, therefore, used to show significant relationships / associations.

3.8 Outcome Validity

To ensure the correct power of the sample, a sample size calculation was conducted, and an adequate sample of women was enrolled to take part in the study (HealthKnowledge, 2020). Participants in the current study were chosen according to a distinct inclusion and exclusion criteria from a well-defined population, to prevent selection bias. To increase the validity of the study, the questionnaire was administered by trained clinic nurses who were health care professionals, knowledgeable and well versed on the current research topic. In addition, the questionnaire was pretested on a subsample of participants (N=8) that were of similar characteristics as those in the current research, to make sure that the questions

were reader friendly, easy to understand and accurate in capturing the information relevant to the current study.

3.9 Reliability

To ensure reliability, a standardised questionnaire was used as our data collection tool to ensure that the data were collected in the same manner for each participant. All clinic nurses were trained to use the protocol and data collection tools, to ensure that there would not be any variability in the way the data was collected between participants. The researcher conducted data verification on all complete questionnaires and cytology lab results, checking for errors thus also ensuring reliability (Nieuwenhuijsen, 2005).

3.10 Ethical Considerations

Before the study could commence the proposal was submitted to the University of the Western Cape (UWC)'s higher degrees office for project registration and to seek approval to conduct the study. Moreover, ethics approval to conduct the study was obtained from the UWC's Biomedical Research Ethics Committee (BMREC) on the 21st of January 2021 (Ref Number: BM20/10/18) (See Appendix 4). Permission to conduct the research at ZNFPC was received from the ZNFPC Ethics Committee on 16 March 2021 (Ref Number: Q7/7/21/661) (Appendix 5) and the Medicines Research Council of Zimbabwe (MRCZ) on 07 June 2021, upon submission of application forms to conduct the study (Ref Number: MRCZ/B/2119) (Appendix 6). Delays in receiving research approval and beginning enrolment were experienced due to the COVID-19 pandemic restrictions that resulted in national shutdowns of research related services.

Patients approached to participate in the study were informed that participation was completely voluntary, and that refusal of participation would not affect the clinical care they would receive at ZNFPC. Patients were informed that they could refuse to participate in the study at any point in the research process without consequences. Participants were not reimbursed for participation in the study and only those who gave written informed consent were enrolled into the study. Participants received a detailed information sheet with detailed information on what the study was about, and how the data collected would be used, as well as contact details of the investigator in their language of choice (for example, English or Shona). Participants were encouraged to ask questions before signing the consent forms.

To ensure the confidentiality of the participants, participants were assigned participant identification numbers, thus maintaining their anonymity. However, a link log, linking the participant identification number with their particulars was created and stored in a separate file from participant records. The participant records, that is, the questionnaire and Pap smear results were stored in participant binders in a

locked cabinet in the researcher's office where access is restricted to the researcher. The consent forms and link log were stored in separate binders and drawers, away from other study material in the researcher's office. Electronic data were stored on the researcher's laptop and files that were password protected. Data generated from this research will be kept for five years after which electronic files will be deleted and paper-based information will be shredded. Results from the research will be shared with the UWC School of Public Health, MRCZ and the ZNFPC Ethics Committee and if seen fit, will be used in a publication, to add to the existing body of knowledge regarding cervical cancer and its risk factors, therefore, upholding the principle of beneficence. In this case, no personal identifications will be divulged to maintain the total confidentiality of the participants.

CHAPTER 4: RESULTS

4.1 Introduction

The current chapter presents the study findings. The chapter begins by describing the socio-demographic characteristics, the sexual behaviours and sexually transmitted infections of women who received Pap smears at ZNFPC. In this chapter, the women's Pap smear outcomes as well as the prevalence of different grades of SIL are also described. Emphasis is also put on presenting the association between various socio-demographic characteristics of the women, their sexual behaviours, sexually transmitted infections and the subsequent Pap smear outcomes.

4.2 Socio-demographic Characteristics of Participants

In total, 165 participants were interviewed, however, only 161 fitted the study selection criteria. Four women were ineligible as they were older than 65 years, as various cancer organisation currently recommend routine screening for cervical cancer, every three years from the ages of 21-65 years (Kuguyo *et al.*, 2017; White, Shoemaker & Benard, 2017).

Table 4.1: Socio-demographic characteristics of women who received Pap smears at ZNFPC Harare

VARIABLE	FREQUENCY(n)	PERCENT (%)
Age in Years		
21-30	31	19.3
31-40	44	27.3
41-50	50	31.1
51-60	22	13.6
61-65	14	8.7
Marital Status		
Married	126	78.3
Unmarried	35	21.7
Educational Level		

Primary	30	18.6
Secondary	109	67.7
College	22	13.7
Cigarettes Smoking		
Yes	0	0
No	161	100
Income Earning		
Yes	73	45.3
No	88	54.7
Parity		
0 children	18	11.2
1-3 children	85	52.8
>3 children	58	36
Type of Contraceptive		
No contraceptive	82	50.9
COC	44	27.3
Other	35	21.8
Time on Contraceptive(years)		
4 years and below	41	25.5
5 years and above	38	23.6
Never	82	50.9

*COC-Combined Oral Contraceptive

**Other-Jadelle implant, Depo provera injectable, IUCD device, Male and female condoms, Tubal ligation

As shown in Table 4.1, of the 161 women that received Pap smears, the highest proportion of women (31.1%), were within the age group 41 and 50 years, followed by 27.3% within the age group 31 to 40 years. The majority of women were married (78.3%) and had secondary school education (67.7%). None of the women in the current study reported ever smoking a cigarette in their lifetime. More than half of the women (54.7%) reported that they did not have any form of income. As also highlighted in Table 4.1, the majority of women (52.8% and 50.9%) had between 1-3 children and had never used any form of contraception, respectively. Of the women who used contraceptives, 27.3% were on combined oral contraceptives that are composed of levonorgestrel and ethinylestradiol tablets and 23.6% had been on their contraceptive method for more than five years, respectively.

4.3 Sexual Behaviours and Sexually Transmitted Infections of the Participants

Table 4.2 below shows the sexual behaviours and sexually transmitted infections among the women enrolled in the current research. Most women (94.4%) had their first sexual experience when they were 16 years and above, with only 5.6% reporting early sexual debut (that is, having their first intercourse before the age of 16 years). Among those women who reported early sexual debut, one woman reported having sexual debut at the age of 7 years due to sexual assault (data not shown). Still on Table 4.2, 91.9% of women reported having had between 1-3 sexual partners in their lifetime. Of those who reported that they had >3 sexual partners in their lifetime (that is, 8.9%), one participant reported having had eleven partners in her lifetime (data not shown).

Table 4.2 below also shows that 13.0% and 27.3% of the women reported that they were HIV positive at the time and have had an STI before respectively. In this table, it is also shown that most women (96.9%) knew their HIV status with only 3.1% reporting that they did not know their status.

Table 4.2: Sexual behaviours and sexual health status of women who received Pap smears at ZNFPC Harare

VARIABLE	FREQUENCY(n)	PERCENTAGE (%)
Age of Sexual Debut in years		

<16	9	5.6
≥16	152	94.4
Number of Sex Partners		
<3	148	91.9
>3	13	8.9
HIV Status		
Negative	135	83.9
Positive	21	13
Unknown	5	3.1
STI Status		
Never had	117	72.7
Ever had	44	27.3

Figure 4.1 below shows the frequency of different STIs as reported by women in this study. As shown below, the most reported STI was Gonorrhoea (12.4%), with 6.8% of women being unaware of the type of STI they had been diagnosed with.

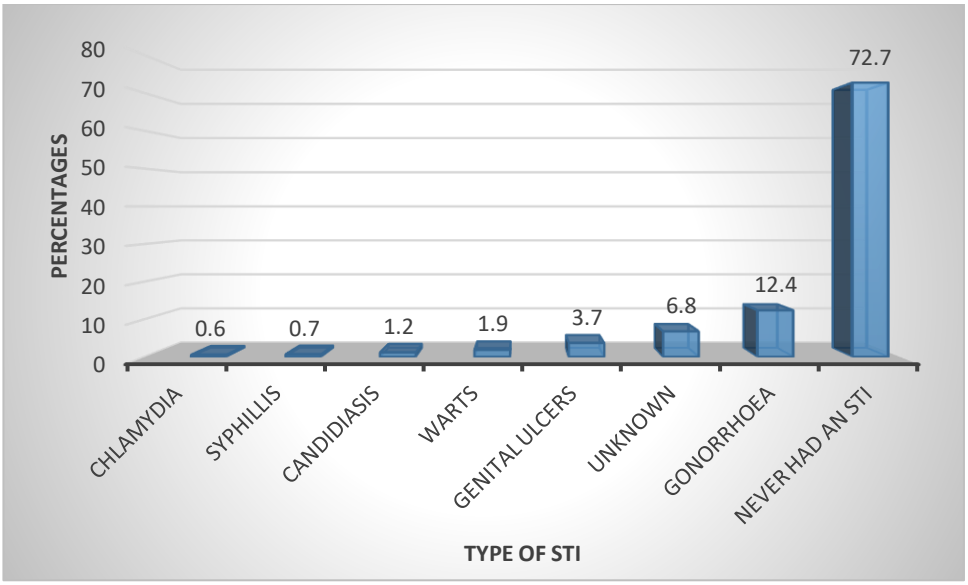

Figure 4.1: Percentage of women reporting different STI

4.4 Prevalence of Squamous Intraepithelial Lesions (SIL)

Table 4.3 below shows the prevalence of SIL found in the current study.

Table 4.3: Prevalence of squamous intraepithelial lesions in women who received Pap smears at ZNFPC Harare

PAP SMEAR RESULTS	FREQUENCY(n)	PERCENTAGE (%)
Normal	130	80.7
LSIL	19	11.8
HSIL	12	7.5

*LSIL-Low grade squamous intraepithelial lesion

**HSIL-High grade squamous intraepithelial lesion

Of the 161 women enrolled in the current study, 80.7% presented with normal Pap smear outcomes, while 19.3% presented with abnormal cytology results, showing the presence of SIL. Of the women with abnormal cytology results, 11.8% showed LSIL while 7.5% showed HSIL. However, based on the outcomes observed, none of the women's outcomes showed the presence of ICC.

4.5 Association between Socio-demographic, Sexual Behavioural Characteristics, and Health Status with Pap Smear Results (normal versus abnormal)

Table 4.4 below shows the outcomes of normal versus abnormal Pap smear group differences by socio-demographic, sexual behaviours and sexually transmitted infections.

Table 4.4: Chi-square test to determine Pap smear outcome by socio-demographic characteristics, sexual behaviours, and sexual health status

VARIABLE	PAP SMEAR OUTCOME		
	Normal n(%)	**Abnormal n(%)**	**p-value**
Age in years			
21-30	25 (80.6)	6 (19.4)	
31-40	36 (81.8)	8 (18.2)	
41-50	41 (82.0)	9 (18.0)	0.563
51-60	19 (86.4)	3 (13.6)	
61-65	9 (64.3)	5 (35.7)	
Marital status			
Married	104 (82.5)	22 (17.5)	0.237
Unmarried	26 (73.3)	9 (25.7)	
Education			
Primary	28 (93.3)	2 (6.7)	
Secondary	86 (78.9)	23 (21.1)	0.122
College/University	16 (72.7)	6 (27.3)	
Earning Income			
Yes	60 (82.2)	13 (17.8)	0.672
No	70 (79.5)	18 (20.5)	
Age of sexual debut			
<16	7 (77.8)	2 (22.2)	0.816

≥16	123 (80.9)	29 (19.1)	
Number of sex partners			
1-3 partners	121 (81.8)	27 (18.2)	0.272
>3	9 (69.2)	4 (30.8)	
Multi-parity			
0 children	15 (83.3)	3 (16.7)	
1-3 children	68 (80.0)	17 (20.0)	0.992
>3 children	47 (81.0)	11 (19.0)	
Contraceptive			
COC	39 (88.6)	5 (11.4)	
Other	31 (88.6)	4 (11.4)	0.046
None	60 (73.2)	22 (26.8)	
Time on contraceptive			
1-4 years	36 (87.8)	5 (12.2)	
5 years and above	33 (89.2)	4 (10.8)	0.055
Never	61 (73.5)	22 (26.5)	
HIV Status			
Negative	109 (80.7)	26 (19.3)	
Positive	17 (81.0)	4 (19.0)	0.999
Unknown	4 (80.0)	1 (20.0)	
Ever had STI			
Yes	35 (79.5)	9 (20.5)	0.813
No	95 (81.2)	22 (18.8)	

*COC-Combined Oral Contraceptive

**Other-Jadelle implant, Depo provera injectable, IUCD device, Male and female condoms, Tubal ligation

Based on the outcomes presented in Table 4.4 above, most women who were screened for SIL had normal Pap smear results when comparing by socio-demographic, behavioural and health status groups. There were no significant differences between women with normal Pap smear results compared to women with abnormal Pap smear results. The only significant difference observed was with contraceptives use, where more women who had never been on any contraceptive method (26.8%) were more likely to have abnormal Pap smear results, showing the presence of SIL, compared to women who had been on COC or any other form of contraceptive. This difference was also significant (χ^2= 6.167, df=2, p= 0.046). It is also important to note that, the time of being on contraceptive also produced a p-value that was tending to significance (p=0.055).

Table 4.5 below shows the outcomes of LSIL versus HSIL by socio-demographic characteristics, sexual behaviours, and sexually transmitted infections. In total, this study had 31 (19.3%) women who presented with SIL. Of these women, 19 (11.8%) had LSIL and 12 (7.5%) had HSIL. Similarly, there were no significant difference between SIL groups found by socio-demographic characteristics, sexual behaviours and sexually transmitted disease outcomes. In this case all the p-values were > 0.05.

Table 4.5: Chi-square test to determine Low-grade Squamous Intraepithelial Lesions versus High-grade Squamous Intraepithelial Lesion by socio-demographic characteristics, sexual behaviours and health outcomes

VARIABLE	PAP SMEAR OUTCOME-SIL RESULTS ONLY		
	LSIL n(%)	**HSIL n(%)**	**p-value**
Age in years			
21-30	6 (19.4)	0 (0.0)	
31-40	6 (13.6)	2 (4.5)	
41-50	5 (10.0)	4 (8.0)	0.062
51-60	1 (4.5)	2 (9.1)	
61-65	1 (7.1)	4 (28.6)	
Marital status			
Married	13 (10.3)	9 (7.1)	0.5
Unmarried	6 (17.1)	3 (8.6)	

Education			
Primary	1 (3.3)	1 (3.3)	
Secondary	13 (11.9)	10 (9.2)	0.183
College/University	5 (22.7)	1 (4.5)	
Earning Income			
Yes	10 (13.7)	3 (4.1)	0.294
No	9 (10.2)	9 (10.2)	
Age of sexual debut			
<16	2 (22.2)	0 (0.00	0.45
≥16	17 (11.2)	12 (7.9)	
Number of sex partners			
1-3 partners	15 (10.1)	12 (8.1)	0.061
>3	4 (30.8)	0 (0.0)	
Multi-parity			
0 children	3 (16.7)	0 (0.0)	
1-3 children	10 (11.8)	7 (8.2)	0.735
>3 children	6 (10.3)	5 (8.6)	
Contraceptive			
COC	3 (6.8)	2 (4.5)	
Other	4 (11.4)	0 (0.0)	0.083
None	12 (14.6)	10 (12.2)	
HIV Status			
Negative	17 (12.6)	9 (6.7)	
Positive	2 (9.5)	2 (9.5	0.728

Unknown	0 (0.00	1 (20.0)	
Ever had STI			
Yes	8 (18.2)	1 (2.3)	0.118
No	11 (9.4)	11 (9.4)	

*LSIL-Low grade squamous intraepithelial lesion

**HSIL-High grade squamous intraepithelial lesion

***COC-Combined Oral Contraceptive

****Other-Jadelle implant, Depo provera injectable, IUCD device, Male and female condoms, Tubal ligation

4.5.2 Binary logistic regression analysis to show the risk of developing abnormal Pap smear outcomes

Based on Table 4.6 below, we found no significant association between the presence of SIL and most of the socio-demographic characteristics, sexual behaviours and sexually transmitted infections both before and after adjusting for the confounding effects of HIV and STI statuses. In this case, all the p-values were greater than 0.05. The exception was observed with contraceptive use. In this case, women who were not on any form of contraceptives were 2.932 times more likely to present with SIL when compared to their counterparts who were on COC. However, this association only tended to significance after adjusting for HIV status and ever having an STI, [OR = 2.860, 95% CI: (0.999-8.184), p=0.052 and adjusted OR=2.932, 95% CI: (1.017-8.451), p=0.05].

Table 4.6: Binary logistic regression analysis to determine the risk of developing abnormal cervical cytology / Pap smear outcomes

VARIABLE	**ABNORMAL PAPSMEAR OUTCOME**			
	Odds Ratio 95% CI	**p-value**	**Adjusted Odds Ratio 95% CI**	**p-value**
Age in years				
21-30	Ref			
31-40	0.926 (0.286-2.998)		0.936 (0.286-3.060)	
41-50	0.915 (0.291-2.878)	0.59	0.935 (0.287-3.048)	0.597

51-60	0.658 (0.146-2.975)		0.671 (0.145-3115)	
61-65	2.315 (0.565-9.484)		2.345 (0565-9.735	
Marital status				
Married	Ref			
Unmarried	1.636 (0.674-3.971)	0.276	1.696 (0.661-4.351)	0.272
Education				
Primary	Ref			
Secondary	3.744 (0.830-16.899)	0.156	3.791 (0.834-17.233)	0.142
College/University	5.250 (0.946-29.147)		5.721 (0.993-32.966)	
Earning Income				
Yes	Ref			
No	1.187 (0.537-2.621)	0.672	1.199 (0.538-2.763	0.657
Age of sexual debut				
<16	1.212 (0.239-6.140)	0.816	1.180 (0.221-6.314)	0.846
≥16	Ref			
Number of sex partners				
1-3 partners	Ref			
>3	1.992 (0.571-6.948)	0.28	1.984 (0.563-6.989)	0.286
Multi-parity				
0 children	Ref			
1-3 children	1.250 (0.324-4.816)	0.946	1.248 (0.323-4.820)	0.947
>3 children	1.170 (0.288-4.758)		1.165 (0.286-4.752)	
Type of Contraceptive				

COC	Ref			
Other	1.006 (0.249-4.068)	0.053	1.020 (0.251-4.141)	0.05
None	2.860 (0.999-8.184)		2.932 (1.017-8.451)	

*COC-Combined Oral Contraceptive

**Other-Jadelle implant, Depo provera injectable, IUCD device, Male and female condoms, Tubal ligation

4.5.3 Linear regression analysis to determine the risk of developing abnormal cervical cytology / Pap smear outcomes

Table 4.7 below shows linear regression to determine unadjusted and adjusted association between abnormal Pap smear results and all the other study variables after controlling for HIV status and ever having an STI.

Most of the associations for SIL and socio-demographic characteristics, sexual behaviours and sexually transmitted infections did not reach statistical significance with p-values being greater than 0.05. However, a significant association was observed between the SIL outcome, and the type of contraceptives used, [OR= 0.179, CI (0.011-0.154), p=0.023, AOR (adjusted for HIV) = 0.180, CI (0.011-0.155], p= 0.023 and AOR (adjusted for STI) = 0.181, CI (0.012-0.156), p= 0.023].

An association was also found between SIL and educational level, that tended to significance after adjusting for the confounding effect of HIV infection [that is, OR= 0.154, CI (0.0000-0.218), p=0.051, AOR (adjusted for HIV) = 0.157, CI (0.000-0.218), p= 0.050]. However, it became significant after removing confounding effect of STI infection (that is, AOR (adjusted for STI) = 0.162, CI (0.003-0.223), p= 0.045] in this group of women.

Table 4.7: Linear regression to determine unadjusted and adjusted association between abnormal cervical cytology results and all the other study variables

VARIABLE	**ABNORMAL PAP SMEAR OUTCOME**			
	Odds Ratio 95% CI	**p-valu**	**AOR 95% CI**	**p-value**
Age in years				

	0.05 (-0.035-0.069)	0.527	0.051 (-0.036-0.069) 0.054 (-0.035-0.071)	0.529 0.507
Marital status	-0.086 (-0.0232-0.067)	0.276	-0.087 (-0.233-0.067) -0.087 (-0.238-0.072)	0.277 0.291
Education	0.154 (0.000-0.218)	0.051	0.157 (0.000-0.218) 0.162 (0.003-0.223)	0.05 0.045
Earning Income	-0.033 (-0.150-0.098)	0.674	-0.033 (-0.151-0.098) -0.034 (-0.153-0.098)	0.676 0.669
Age of sexual debut	-0.018 (-0.300-0.237)	0.818	-0.018 (-0.302-0.238) -0.015 (-0.303-0.251)	0.817 0.854
Number of sex partners	0.087 (-0.101-0.351)	0.275	0.087 (-0.101-0.353) 0.086 (-0.104-0.353)	0.275 0.282
Multi-parity	0.007 (-0.092-0.101)	0.926	0.007 (-0.092-0.101) 0.007 (-0.0093-0.101)	0.926 0.935

Type of Contraceptive				
	0.179 (0.011-0.154)	0.023	0.180 (0.011-0.155) 0.181 (0.012-0.156)	0.023 0.023

*COC-Combined Oral Contraceptive

**Other-Jadelle implant, Depo provera injectable, IUCD device, Male and female condoms, Tubal ligation

4.6 Summary of Results

In summary, the findings showed that out of the 161 women enrolled into the study, 19.3% had SIL. 11.8% of these women presenting with LSIL whilst 7.5% presented with HSIL. In this study no cases of invasive cervical cancer were found. Finally, the researcher only managed to observe that those women who were not on any form of contraceptive and those with a higher educational level were more likely to develop SIL.

CHAPTER 5: DISCUSSION

5.1 Introduction

The current study aimed to determine the prevalence of SIL and invasive cervical cancer and their associated risk factors, among them being the socio-demographic characteristics, sexual behaviours and sexually transmitted infections among women accessing Pap smear tests at a ZNFPC.

Notable findings were that most women receiving Pap smears were within the ages 31-50 years, married, had between 1-3 children, and had secondary education or higher. Most women reported that they did not have a source of income and were not on any form of contraception. Of those on contraceptives, the majority were on the COC composed of levonorgestrel and ethinylestradiol tablets, and these contraceptive group differences were found to be significant (p=0.046). There were no cases of women who reported that they ever smoked cigarettes.

Regarding sexual behaviours and sexually transmitted infections, the majority of the women reported that they engaged in sexual intercourse later in life (that is, when they were 16 years or older) and they had less than three lifetime sexual partners. Only 13.0% of the women reported that they were HIV positive and 27.3% reported that they had had an STIs before. However, these group differences were not significant with both p-values for HIV and STI status being >0.05.

Finally, in the current study, the researcher found a high prevalence of SIL (19.3%) amongst women receiving Pap smears, with a higher prevalence of LSIL (11.8%) than HSIL (7.5%). However, there were no significant group differences observed in this case. None of the women presented with invasive cervical cancer outcomes.

Overall, the researcher found no associations between the presence of SIL and the women's socio-demographic characteristics, sexual behaviours, and sexually transmitted infections. However, there was a weak and negative association between the presence of SIL and education level but only after removing the confounding effects of STI status (AOR= 0.162, CI [0.003-0.223], p= 0.045). Similar negative associations were observed between SIL status and no use of a contraceptives, before and after removing the confounding effects of STI and HIV status (OR= 0.179, CI [0.011-0.154], p=0.023, AOR (adjusted for HIV) = 0.180, CI [0.011-0.155], p= 0.023, AOR (adjusted for STIs) = 0.181, CI [0.012-0.156], p= 0.023).

5.2 Research Participation by Socio-demography

Of note is that in our study, like in other studies conducted in other African countries such as the Democratic Republic of Congo, Ethiopia, Tanzania, Rwanda and Nigeria, the majority of women who presented to the health care centres for cervical cancer screening were older women, that is, 31 years and above, married, had 1-3 children, as well as did not smoke or had minimal use of cigarettes (Obure *et al.*, 2009; Durowade *et al.*, 2012; Ali-Risasi *et al.*, 2015; Makuza *et al.*, 2015; Teame *et al.*, 2018; Beyene *et al.*, 2021).

The prevalence of contraceptive use differed in this study's cohort compared to other studies conducted in Ethiopia, where more than half of the women who were receiving cervical cancer screening in these studies reported use of a contraceptive method (Teame *et al.*, 2018; Beyene *et al.*, 2021). In this study, just over half of the women reported never having used any form of contraceptive. This could be attributed to the age of women that reported for Pap smears as Fonn *et al.* (2002), in their study found that contraceptive use amongst women receiving Pap smears was higher in clinics that screened younger women compared to clinics that screened older women, such as the women that we screened in our study. However, of those who did report contraceptive use, the type of contraceptives used in the study conducted in Ethiopia differed from the types used in this study's cohort. As reported by Teame *et al.* (2018), in their study, the use of injectable contraception was the most prevalent, followed by use of the oral contraceptive pill. In the current study on the other hand, COC were most prevalent and then other contraceptives.

Most women in the current study had a secondary education or higher (81.4%) which differs from studies conducted in Rwanda and Tanzania where the majority of women who receive cervical cancer screening services at health centres, either VIAC or Pap smears have a primary school level education as their highest education level attained (Obure *et al.*, 2009; Makuza *et al.*, 2015). For instance, in their Tanzanian cohort, Obure *et al.* (2009) showed that 72.2% of women who screened for SIL had a primary school level education, whilst in Rwanda, Makuza *et al.* (2015) in their study had 81.9% of the women who were screened for cervical cancer at health centres, having a primary school level education or no education at all. Results for the current study are similar to those found by Rosyda, Santoso and Yunitasari (2019) in their systematic review that aimed to determine if educational level affected women's participation in cervical cancer screening services. Rosyda, Santoso and Yunitasari (2019) found that women with a higher education level, such as that seen in the researcher's cohort, were more likely to seek out cervical cancer screening services. The author attributed this to higher health literacy and access to information regarding cervical cancer and its risk factors (Rosyda, Santoso and Yunitasari, 2019). This may result in increased

screening in women in these demographics and increased prevalence of SIL in women with a high educational level, as seen in the results of the current study.

5.3 Research Participation by Sexual Behaviour and Sexual Health Status

Of interest with respect to women's sexual behaviour is that, like in most LMIC studies (Durowade *et al.*, 2012; Ali-Risasi *et al.*, 2015; Makuza *et al.*, 2015; Beyene *et al.*, 2021), women participating in this research tended to engage in sex later in life and had 1-3 lifetime sexual partners.

The prevalence of HIV seems to vary across different LMICs. For instance, in the study conducted by Obure *et al.* (2009), the HIV prevalence of women receiving cervical cancer screening was 44%, whereas Makuza *et al.* (2015) and Beyene *et al.* (2021) found the HIV prevalence in Rwanda and Ethiopia to be 10% and 13.3 % respectively. In this study, the researcher found an HIV prevalence of 13%, which is similar to the prevalence reported in the current Zimbabwe Demographic Health Survey of 13.8% among women in Zimbabwe (Zimbabwe Demographic Health Survey, 2016).

5.4 Prevalence of SIL

The prevalence of SIL (19.3%) observed in the current study seems to be high compared to the outcomes of the studies conducted in Burkina-Faso, Nigeria, South Africa, Malawi and Kenya, where observed prevalence outcomes for SIL range from 4% to10% (Ali-Risasi *et al.*, 2015). In fact, according to existing evidence, the prevalence of SIL among women vary across the African continent. For instance, previous studies conducted in the Democratic Republic of Congo, South Africa and Rwanda showed the prevalence of SIL were within the 2% to 5% range (Fonn *et al.*, 2002; Ali-Risasi *et al.*, 2015; Makuza *et al.*, 2015). Moreover, a small study that recruited 60 sexually active women between the ages of 17-60 years, that was conducted in Cameroon, showed the prevalence of SIL to be 3.33% (Nkfusai *et al.*, 2019). Studies conducted in Ethiopia, Tanzania and Uganda, on the other hand, showed higher prevalence of SIL that ranged from 14% to 17% (Obure *et al.*, 2009; Tsehay & Afework, 2020). Moreover, a recent systematic review and meta-analysis conducted to determine the prevalence of precancerous lesions in Ethiopia resulted in a pooled prevalence of precancerous lesions of 15.16% (Kasa *et al.*, 2021). This was still below the prevalence observed in the current study.

Variation in the prevalence of precancerous lesions across countries could be attributed to varying existence and access to screening programmes, differing management or treatment options, as well as differing sexual and cultural practices that may increase a woman's risk of developing SIL (Nkfusai *et al.*, 2019; Tsehay & Afework, 2020). However, this study's findings are congruent with other studies and reports, showing a

generally high prevalence of SIL within the region, and in Zimbabwe. Kuguyo *et al.* (2017) for instance, in their study reported the prevalence of cervical cancer in Zimbabwe to be 19%. These researchers attributed such a high prevalence to women presenting late at health centres due to lack of screening, testing, and treatment facilities (Kuguyo *et al.*, 2017). The high prevalence of SIL shown in the current study and supporting literature highlight the potential of SIL progressing to invasive cervical cancer in Zimbabwean women.

We found no evidence of invasive cervical cancer in our study. This could be attributed to the high prevalence of LSIL, which have a low risk to none of developing to a cervical cancer, and has a high probability of resolving on it own within 18 to 24 months(John Hopkins Medicine, no date; Cleveland Clinic, 2021). However, the presence of HSIL, which are considered precancerous emphasises the need for policies directed at improving screening services, such as Pap smears, for this disease in Zimbabwe.

5.5 Risk Factors of SIL

Several risk factors have been found to related to the prevalence of SIL.

5.5.1 Age

In the current study, the prevalence of SIL was the highest in the age group 61-65years, although this association was not significant. This is in accordance to previous literature that have shown that the likelihood of precancerous lesions increases with age (Teame *et al.*, 2018; Beyene *et al.*, 2021). Teame *et al.* (2018) postulate that this could be attributed to women in this age group having been exposed for longer periods of time to the HPV virus or due to the slow progression of development of SIL. I would also add that this reflects the age group that has never been exposed to the HPV vaccine, which was only introduced in Zimbabwe in 2018.

5.5.2 Marital status and multiple sexual partners

Although not significant, the presence of SIL was more likely in women who were unmarried or those who have had more than three sexual partners. These results are supported by previous studies conducted, with Obure *et al.* (2009), whom in their study that looked at the prevalence and severity of SILs in Tanzania, found that cervical SIL were more likely in unmarried women compared to their married counterparts. This outcome was attributed to the likelihood that single women had multiple sexual partners, a factor that has been associated with increased prevalence of SIL (Obure *et al.*, 2009). As seen in the current study, having

had more than three sexual partners increases the odds of developing SIL by 1.984 times, despite the result not being significant even after adjusting for HIV and STI status. Similar results have been reported in multiple studies conducted within the region (Makuza *et al.*, 2015; Teame *et al.*, 2018; Tsehay & Afework, 2020; Beyene *et al.*, 2021). A recent cross-sectional survey conducted in Indonesia, to determine the relationship between different socio-demographic characteristics and the risk of developing precancerous lesions, found that women who had more than one sexual partner in their lifetime were more likely to develop precancerous lesions (Ashar *et al.*, 2020). This has been attributed to the fact that women who have had multiple sexual partners are more likely to be exposed to the HPV virus, which is a known risk factor of SIL (Teame *et al.*, 2018; Ashar *et al.*, 2020; Beyene *et al.*, 2021).

5.5.3 Educational level

In the current study, the researcher found an association between educational level and the presence of SIL, but only after removing the confounding effects of STI status. In fact, based on the logistic regression conducted, the odds of developing SIL in the current study increased with an increase in educational levels, with women who had attained a university or college education being more likely to have SIL compared to those with a secondary and primary education. These findings are in total contrast to the existing literature that suggests that having tertiary education results in reduced risk of developing abnormal cervical lesions (Hamoonga *et al.*, 2017). In their study, Hamoonga *et al.* (2017) aimed to determine the prevalence of abnormal cervical cytology and its association with educational levels attained by women in Zambia. They found that the risk of developing SIL decreased with an increase in educational level, with having a tertiary education offering the highest protective effect when compared to having no formal education. Rosyda, Santoso and Yunitasari (2019) corroborate Hamoonga *et al.* (2017) findings, also highlighting that women with tertiary education have higher health literacy and therefore, are more likely to seek and understand health information regarding cervical cancer. Moreover, the authors argue that being more educated equates to people securing jobs that improve their socio-economic statuses, and resources that improves access to Pap smear tests and other sexual health related programmes that are costly. These assumptions are corroborated by Barrow *et al.* (2020) who found that women with a higher education were more likely to have ever heard about cervical cancer. In addition, Murfin *et al.* (2020) in their study found that, having a higher level of education resulted in increased uptake of cervical cancer screening programmes. Therefore, increased prevalence of SIL with increase in educational levels in this study's cohort, could be attributed to the increased health literacy and access to Pap smear services that come with increased education in women. An increase in educational levels results in women becoming more aware of the risks and dangers of cervical cancer and are empowered to seek out and access screening services, resulting in a higher prevalence in this group.

5.5.4 Type of contraception used

Based on the logistic regression analysis, some indication could be seen that the odds of developing SIL could be almost three times more likely in women that are not on any form of contraception compared to women on COC, even though this relationship only tended to significance. When the researcher conducted linear regression analysis, the relationship improved and became significant, such that those women on COC were less likely to present with SIL, compared to their counterparts who were either not on any form of contraceptives, or those who were on other contraceptives. This significant difference remained, even after removing the confounding effects of HIV and STI statuses. The varying relationship between the use of oral contraceptives and its association with SIL has been documented in many studies in the last two decades. Chih *et al.* (2014) have shown that the prolonged use of COC for over five years is protective against the development of SIL. Moreover, a case-control study conducted in American Indian women showed that women who had been using COC had decreased risk of developing SIL (Schiff *et al.*, 2000). According to Chih *et al.* (2014), this relationship could be attributable to the protective effect that oestrogen, found in COC, has on the cervical mucosal immune system. In fact, literature suggests that oestrogen thickens the cervical mucus, thereby preventing the penetration and subsequent acquisition of HPV infection that results in the development of SIL (Schiff *et al.*, 2000).

The current study outcomes, which show increased odds of acquiring SIL when not on contraceptives or when you use other contraceptives other than COC, are corroborated by outcomes in other international literature. For instance, a study conducted in the Netherlands to determine the association between the type of contraceptives and the development of SIL showed that the use of Intra Uterine Devices (IUDs) was associated with an increase in risk of developing SIL (Loopik *et al.*, 2020). Furthermore, Schiff *et al.* (2000) found that the use of IUDs and depo medroxyprogesterone was associated with increased risk of the development of SIL. A similar study conducted in Jamaican women to determine if there was an association between use of hormonal contraception and development of SIL, found that use of depo medroxyprogesterone increased the odds of developing SIL by 2.43 times (McFarlane-Anderson *et al.*, 2008). The current study, therefore, adds to this growing body of literature around the possible association between other contraceptives, other than oral hormonal contraceptives and their association with the development of SIL.

5.6 Limitations

This study has several limitations. Firstly, the study used convenience sampling method to recruit participants, making the results not generalizable to the entire Zimbabwean population, but to the sub-

sample of Zimbabweans with similar characteristics. The study relied on participants providing their personal information and history over their lifetime, which could result in recall bias. The lack of stronger association between the variables could be attributed to the small sample size, although this was a powered sample that used the previous prevalence for similar studies conducted in SSA. In this study, the researcher did not test for current HPV infection. However, the researcher found out that STI infection acted as a confounder that mediated the association between education level and risk of developing SIL. Therefore, the lack of stronger association between variables could be attributed to the confounding effect of STI infections in general and HPV infection specifically. Lastly, with regards to type of contraceptives, the study's analysis was focused on the use of COC versus other contraceptive methods, including non-users. This type of categorisation makes interpretation of the results difficult and would require further investigation into the potential association between individual contraceptive methods and development of abnormal cervical cytology. Finally, due to time constraints, the current study did not investigate the association of other risk factors for SIL, such as the cultural practices that have been shown to be important risk factors in other African countries.

5.7 Concluding Remarks

Cervical cancer remains a public health concern as seen by the high prevalence of SIL in this study's population. Various risk factors are attributed to the development of precancerous lesions, with my study finding a significant association between non-use of any contraceptive method and attaining a higher level of education being associated with the development of SIL. The implications of the findings to public health policy in Zimbabwe are highlighted below in my recommendations, with a need to increase cervical cancer screening options and services as well as continued research around the association between contraception, educational level and SIL.

CHAPTER 6: RECOMMENDATIONS

6.1 HPV DNA Testing

In this study, the researcher did not test HPV infection and therefore, HPV infection may have acted as a confounder that may have resulted in the lack of a significant association being found between cytology results and socio-demographic and sexual behavioural risk factors. This was due to the inability to test for HPV infection at ZNFPC, where the study was conducted. It is, therefore, recommended that high risk HPV DNA tests be employed as a primary screening test for cervical cancer in Zimbabwe, according to the guidelines by the WHO (World Health Organization, 2021). Traditionally, Pap smears have been used to screen women for cervical cancer and according to World Health Organization (2021), this has resulted in a fivefold decrease in cervical cancer deaths. However, this method requires trained experts to collect and process the cytology samples, as well as access to colposcopy facilities in order to confirm the positive cytology results and provide appropriate treatment (World Health Organization, 2021). Such human resources and infrastructures may not be readily available in low resource settings like Zimbabwe.

HPV DNA testing would be an objective measure of cervical cancer risk in an individual, as it identifies HPV infection in women, including infection by HPV 16 and HPTV 18, which are the common genotypes that cause cervical cancer. Samples can either be collected by the health care provider or self-collected, making the test easy in resource limited settings as they do not require any expertise training unlike Pap smears (World Health Organization, 2021). Furthermore, evidence shows that self-testing might increase uptake of cervical cancer screening, resulting in early detection and treatment of SIL. This testing method also does not have challenges of quality assurance as compared to the VIA method (World Health Organization, 2021). Easy access of the testing method due to ease of use and low cost will allow the screening of cervical cancer to be scalable to every health care facility in the country, allowing the health sector to screen more women and meet the targets of no cases of cervical cancer by 2030.

6.2 Nationwide Screening for Cervical Cancer

As reported previously, the researcher found a high prevalence of SIL in the current study, and as such, continued efforts in nationwide screening for cervical cancer through a widespread, community-based screening programme that is decentralised, far reaching and not just located in Harare is recommended. Gabaza *et al.* (2019) noted that the 10 to 20 year gap between the development of SIL and its potential progression to invasive cervical cancer is "… an opportunity to screen, detect and treat the disease before its progression to cancer …" (Gabaza *et al.*, 2019: 1). The scale up of population based screening services, such as Pap smear screening being offered in more government primary health care clinics within the

community, will allow women that might otherwise not know that they might have SIL or might not have the resources to seek out such services, to receive access to this essential service, aiding in the prevention of the development of cervical cancer (Durowade *et al.*, 2012). Upscaling of screening services would also allow for repeated screening of women every 3 to 5 years as recommended, resulting in early detection and treatment of disease(Sung *et al.*, 2021). As highlighted by Durowade *et al.* (2012), increased screening will also enable the continuous collection of up to date and relevant data on the burden of cervical cancer within Zimbabwe.

6.3 HPV Vaccination

As part of the national programme, it is also recommended that the Government of Zimbabwe accelerate its HPV vaccination programme to reduce the prevalence of SIL in the nation. In May 2018, Zimbabwe introduced HPV vaccination into the national immunization programme, targeting girls between 10-14 years (LaMontagne *et al.*, 2022). According to the study conducted by LaMontagne *et al.* (2022), 90% of the girls between 10-14 years had received at least one dose of the HPV vaccine in three districts in Zimbabwe. This success has been attributed to school-based HPV vaccination programmes, that have increased access to the vaccine to the school going demography. Maintaining an annual schedule for school-based HPV vaccination would result in a decrease in the prevalence of SIL and cervical cancer cases as seen in countries like Finland and Australia, who have attributed their low prevalence of cervical cancer to high vaccination rates (Zhang *et al.*, 2021).

6.4 Research

Lastly, further research into the role that contraceptives play in the development of SIL, especially with respect to different types of contraceptives used and their association with cervical cancer incidence is highly encouraged. There is a need for continued research on the role that education plays in the development of SIL as well as other drivers and risk factors that may be associated with the development of abnormal cervical lesions such as cultural related sexual practices and norms. This can be done using more rigorous research methods with results being incorporated into public health messaging and policies, resulting in a comprehensive approach to the fight against cervical cancer.

6.5 Conclusion

The researcher commends the Ministry of Health of Zimbabwe for its continued efforts in its fight against cervical cancer through its various programs. We do however recommend expanding these efforts with the use of HPV DNA testing as a primary screening test for cervical cancer due to its scalability in resource limited setting. The researcher is also recommending continued and expanded nationwide community-

based screening programmes using the Papsmear test as repeated cytology testing as a gold standard has resulted in reduced cervical cancer incidence in many developed countries. School-based HPV vaccination programmes for early testing, detection and treatment of squamous intraepithelial should also be implemented. Lastly, we recommend continued research into risk factors that result in the increased prevalence of cervical cancer, with such research resulting in the development of evidence based public health programmes and policies.

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APPENDICES

Appendix 1: Socio-demographic and Behavioural Questionnaire Data Collection Tool

SOCIODEMOGRAPHIC AND BEHAVIOURAL QUESTIONNAIRE

Aim: To collect socio-demographic and sexual behavioural data of women accessing Pap smears at ZNFPC

PTID:……. **DATE**:……
. …

DEMOGRAPHICS

Please tick appropriate response

Date of birth	……
Age	……
Are you currently married?	Yes No
What is the highest level of education?	No schooling Primary school Secondary school College or University
How many cigarettes do you smoke in a day?	….....
How many children have you given birth to alive?	….....
Do you earn an income on your own?	Yes No

BEHAVIOURAL ASSESSMENT

What is your HIV status?	Positive Negative Unknown
Have you ever had an sexually transmitted infection (STI)?	Yes No
If the answer above is Yes…do you know which one you had?	Name of STI: …… …
How many sex partners have you had in your life?	….....
At what age did you start having sex?	….....
What contraceptive/family planning method are you currently using?	….....
How long have you been using the contraceptive you currently are on?	….....

Aim: Kuunganidza ruzivo rezvevakadzi vanouya kunoongororwa nePapsmear SHONA											
PTID:											
DEMOGRAPHICS											
Zuva rekuzvarwa											
Makore											
Makarorwa here?					Yes						
					No						
Makasvikira papi pachikoro?					No schooling						
					Primary school						
					Secondary school						
					College or University						
Munobhema mudzanga mingani pazuva?											
Mune vana vanganani?											
Mari yamunowana, muozvishandira here?					Yes						
					No						
BEHAVIOURAL ASSESSMENT											
Munoziva here mamiriro enyu panyaya dzeHIV?					Postive						
					Negative						
					Unknown						
Makamboita here chirwere chepabonde?					Yes						
					No						
Kana makamboita chirwere chepabonde, munoziva here kuti makaita chipi chacho?										Name of STI:	
Muhupenyu hwenyu wese, makasangana nevarume vangani pabonde											
Makatanga kuita zvebonde mune makore mangani?											
Munoshandisa chii kudzivirira nhumbu?											
Pane zvamurikushandisa kudzivirira nhumbu, mazvishandisa kwenguva yakareba sei?											

Appendix 2: Cytology Results Data Collection Tool

Cytology Results
Participant ID:
Date:
Instructions: Tick corresponding Pap smear result

	Yes	No
Normal		
LSIL		
HSIL		
ICC		

Appendix 3: Excel Data Collection Tool

	Appendix: Variables for Socio Demographic and Sexual Behaviour											
Patient code	**Age (in years)**	**Marital status (Y/N)**	**Education Level (0-No schooling/1-primary/2-secondary/3-college or university**	**No of cigarettes smoked in a day**	**No of live births**	**Income earning (Y/N)**	**HIV status (+/-/unknown)**	**Ever had STI (Y/N)**	**Type of STI (1-Trichomonas/2-Gonorrhoea/3-Chlamydia/4-Unknown)**	**No of sex partners**	**Age of sexual debut**	**Contr (1-OC Other**

Appendix 3: Excel Data Collection Tool

Variables for Socio-demographic and Sexual Behaviour

Patient code	
Age (in years)	
Marital status (Y/N)	
Education level (0-No schooling/1-primary/2-secondary/3-college or university	
No of cigarettes smoked in a day	
No of live births	
Income earning (Y/N)	
HIV Status (+/-/unknown)	
Ever had STI (Y/N)	
Type of STI (1-Trichomonas/2-Gonorrhoea/3-Chlamydia/4-Unknown)	
No of sex partners	
Age of sexual debut	
Contraceptive (1-OC/2-Other)	
Length of time on current contraceptive	
Pap smear result (Normal/LSIL/HSIL/ICC)	

Appendix 4: UWC's Biomedical Research Ethics Committee (BMREC) Approval

UNIVERSITY *of the* WESTERN CAPE

60 YEARS *of hope, action & knowledge*

21 January 2021

Ms K Hlahla
School of Public Health
Faculty of Community and Health Sciences

Ethics Reference Number: BM20/10/18

Project Title: Risk factors associated with the presence of cervical lesions in Women attending a Family Planning Clinic in Harare Zimbabwe: A Cross Sectional Study

Approval Period: 21 January 2021 – 21 January 2024

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

Permission to conduct the study must be submitted to BMREC for record-keeping.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

Director: Research Development
University of the Western Cape
Private Bag X 17
Bellville 7535
Republic of South Africa
Tel: +27 21 959 4111
Email: research-ethics@uwc.ac.za

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE

Appendix 5: ZNFPC Ethics Committee Approval

ZIMBABWE NATIONAL FAMILY PLANNING COUNCIL
Family Planning: It's Your Choice

ZIMBABWE NATIONAL FAMILY PLANNING COUNCIL

HEADQUARTERS AND SPILHAUS CENTRE
No 1 Swiss Way, Harare Hospital Grounds
P.O. Box ST220
Southerton
Harare, Zimbabwe

Tel: (04) 668459
662789
E-mail: ed@znfpc.org.zw
Website: www.znfpc.org.zw

Your Ref .....

Our Ref... **Q7/7/21/661**

16 March 2021

The Principal Investigator
University of the Western Cape
Faculty of Community and Health Sciences
School of Public Health
SOUTH AFRICA

Dear Kudzai Hlahla

RE: Project Title: Risk factors associated with the presence of cervical lesions in Women attending a Family Planning Clinic in Harare Zimbabwe: A Cross Sectional Study

Reference is made to your letter dated 11 February 2021 requesting for permission to conduct an observational study for your mini thesis in Public Health.

Please, be advised that permission has been granted for you to conduct an observational study for your study entitled: **Project Title: Risk factors associated with the presence of cervical lesions in Women attending a Family Planning Clinic in Harare Zimbabwe: A Cross Sectional Study.**

The condition is that the results should be shared with ZNFPC.

Yours faithfully

DR M. MURWIRA

EXECUTIVE DIRECTOR

Appendix 6: Medicines Research Council of Zimbabwe (MRCZ) Approval

Telephone: 08644073772/791193
E-mail: mrcz@mrcz.org.zw
Website: http://www.mrcz.org.zw

Medical Research Council of Zimbabwe
Josiah Tongogara / Mazowe Street
P. O. Box CY 573
Causeway
Harare

APPROVAL

MRCZ/B/2119

08 June, 2021

Kudzai Hlahla
34 Teviotdale Road
Vainona
Harare

RE: - Risk factors associated with the presence of cervical lesions in women attending a family planning clinic in Harare Zimbabwe: A Cross Sectional Study

Thank you for the application for review of Research Activity that you submitted to the Medical Research Council of Zimbabwe (MRCZ). Please be advised that the Medical Research Council of Zimbabwe has **reviewed** and **approved** your application to conduct the above titled study.

This approval is based on the review and approval of the following documents that were submitted to MRCZ for review: -

1. Full protocol
2. Informed Consent Form (English and Shona)
3. Data collection tool

- **APPROVAL NUMBER** : **MRCZ/B/2119**

This number should be used on all correspondence, consent forms and documents as appropriate.

- **TYPE OF MEETING** : **Expedited**
- **APPROVAL DATE** : **07 June, 2021**
- **EXPIRATION DATE** : **06 June, 2022**

After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ offices should be submitted three months before the expiration date for continuing review.

- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ Offices or website.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices or website.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (0242) 791193, 0864407377203 or by e-mail on mrcz@mrcz.org.zw

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.
- In addition to this approval, all clinical trials involving drugs, devices and biologics (including other studies focusing on registered drugs) require approval of Medicines Control Authority of Zimbabwe (MCAZ) before commencement

Yours Faithfully

.....

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
2021 -06- 07
APPROVED
P.O. BOX ... HARARE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH