Risk Factors for Cervical Precancer Lesions among Women Attending Cervical Cancer Screening Clinics in Harare, 2013

By

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Abstract

Background: Cervical cancer is the most common cancer in women in Zimbabwe. Preliminary analysis of the prevalence of precancer lesions of the cervix in Harare City revealed that the prevalence is around 7%. This is relatively high compared to those in the southern African region (3%). If the burden of the cervical cancer is to be reduced then risk factors for the precancer cervical lesions (precursor to cancer) for women in Harare have to be established. ***Methods:*** A total of 180 women who were attending Visual Inspection with Acetic acid and Cervicography (VIAC) clinics in Harare were enrolled in a case control study. A case was a woman 18 and above years with histologically confirmed cervical dysplasia. Data on demographic characteristics and risk factors for precancer lesions of the cervix were obtained with consent and these were then compared between the cases and controls. ***Results:*** The significant risk factors were having more than one sexual partner (OR=1.9; 1.21-3.72), being HIV positive (OR 8.4; 4.17-17.09), early sexual debut (<15years) (OR=3.4; 1.18-9.8), a previous history of any form of STI (OR= 3.06; CI= 1.64-5.69) and being single (OR=2.30; 1.12-6.56). HIV infection was found to have an effect modification for the association of sexually transmitted infections (STIs) and precancer lesions. History of genital warts appeared to have the strongest association (OR=4.29; CI= 1.37-13.40) with precancer lesion compared to other forms of STIs. ***Conclusion:*** The association of precancer lesions and HIV, STIs suggest that there is need to reduce the prevalence of HIV and STIs if the prevalence of the cervical precancer lesions is to be reduced. To achieve this strengthening health education on use of barrier methods to prevent STIs and HIV is required and there is need for integration of HIV services with cervical cancer screening for early detection in these women at higher risk.

Key words: Harare, Cervical precancer lesions, risk factors, HIV, STIs

DECLARATION

I certify that this dissertation is my original work and submitted for the Master in Public Health Programme. It has not been submitted in part or in full to any university and/or any publication.

Student:

Signature_____Date_____

Michael Vere

I, having supervised and read this dissertation, am satisfied that this is the original work of the author in whose name it is being presented. I confirm that the work has been completed satisfactorily for presentation in the examination.

Academic Supervisor:

Signature_____Date_____

Dr. G. Shambira

Chairman:

Signature_____Date_____

Professor S. Rusakaniko

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List of Acronyms

1. CIN : cervical intraepithelial lesion
2. LSIL, HSIL: *low* grade and *high* grade *squamous intraepithelial lesion*.
3. HPV: human papilloma virus
4. HIV: Human immunodeficiency virus
5. WHO: World Health Organisation
6. HAART: Highly Active Antiretroviral therapy
7. VIAC: Visual inspection of the cervix with acetic and cervicography
8. LEEP: Loop electrosurgical excision procedure
9. ART: antiretroviral therapy.
10. OICs: Opportunistic Infectious Conditions clinics
11. ZDHS: Zimbabwe Demographic Health Survey
12. WIDH: Wilkins Infectious Disease Hospital

Chapter 1

1.1 Introduction

Cervical precancer lesions are the precursor cells to cervical cancer and although not all of the precancer lesions develop in to cancer, all the cervical cancers pass through this premalignant stage which can be detected through screening. Cervical precancer lesions are found on the uterine cervix.

The uterine cervix is covered by two kinds of cells, which line the surfaces of many organs and body systems which are squamous cells and glandular cells. Squamous cells are cells that are flat, thin found in the outer layer of the cervix that opens into the vagina (ectocervix) Glandular cells or columnar cells are cells which are column-shaped cells that produce cervical mucus and are found in the cervical canal (endocervix).
The area where squamous and glandular cells meet is called the transformation zone. It is also called the squamocolumnar junction. This is the area where the precancer lesions of the cervix develop. It has been established that this vulnerable to infections such as HPV that are implicated in the development of cervical precancerous lesions[1]. The cervical precancer lesion s are classified using two different systems which help in grading the severity of the lesions.

There is the WHO guidelines which classify these precancer lesions as cervical intraepithelial neoplasia 1, 2 and 3(CIN1, CIN2 and CIN 3) where CIN 3 is the worst form of neoplastic change while CIN1 is the least. The Bethseda system classifies these precancer lesions as low grade and high grade squamous intraepithelial lesion (LSIL, HSIL). Most cervical cancers (80 to 90 percent) are squamous cell cancers. Adenocarcinoma (glandular) is the second most common type of cervical cancer, accounting for the remaining 10 to 20 percent of cases. Adenocarcinoma develops from the glands that produce mucus in the

endocervix. While less common than squamous cell carcinoma, the incidence of adenocarcinoma is on the rise, particularly in younger women[1]

Some precancer lesions of the cervix develop into cervical cancer. It is the second most common malignancy in women worldwide, and it remains a leading cause of cancer-related death for women in developing countries. Cancer of the cervix tends to occur during midlife. Half of the women diagnosed with the disease are between 35 and 55 years of age. It rarely affects women under age 20, and approximately 20 percent of diagnoses are made in women older than 65.

Estimates of worldwide and regional cancer incidence and mortality published by the World Health Organization in the GLOBOCAN 2012 report showed that the numbers for cervical cancer would continue to climb, especially in developing countries. The estimated annual incidence worldwide is now more than 528,000 and the mortality more than 266,000. About 75% of women in industrialized countries have been screened for cervical cancer in the previous five years, compared to less than 5% in developing countries[2].

The main risk factor for developing cervical cancer is the sexually transmitted human papilloma virus (HPV) that infects the cervix. Other risk factors for developing cervical cancer include becoming sexually active at a young age; having many sexual partners, or having a sexual partner that has had many sexual partners and smoking. An immune system weakened from taking drugs following a transplant, or having a disease such as AIDS. The use of birth control pills for a long period of time and giving birth to many children has also been associated.

HIV-positive women have a higher prevalence and incidence of cervical precancerous lesions than HIV negative women. HIV-positive women have a 2-fold to 4-fold greater rate of HPV infection than HIV-negative women. The prevalence of HPV among HIV-positive women is

associated strongly with CD4 counts and HIV viral load. Highly active antiretroviral therapy (HAART) has been shown to decrease HIV viral loads, increase CD4 cell counts, and decrease most opportunistic infections. Since the introduction of HAART there has been a decline in certain malignancies in HIV-infected individuals. However, studies on the impact of HAART on the natural history of cervical squamous intraepithelial lesions (SILs) have produced inconsistent results. In HIV-infected women, there is an increased risk of HPV infection and squamous intraepithelial lesions (SIL), the precursor of cervical cancer. There is still limited evidence for understanding the natural history and epidemiology of HPV-induced cervical cancer in HIV-infected women.

Cervical cytology has proved to be one of the most successful examples of cancer screening and has resulted in significant decreases in incidence and mortality from invasive cervical cancer in regions in which comprehensive programs have been instituted. The Pap smear has been the backbone of cervical cancer screening programs in North America over the past five decades; however, recent advances, including liquid-based cytology, HPV typing, and direct visualization techniques (VIAC), are proposed to address the inherent weaknesses of cytologic screening in women who are screened. Cervical cancer is preventable through screening. Visual inspection of the cervix with acetic acid and cervicography (VIAC) is one method that is cheap and suitable for mass screening. Widespread screening will lead to a significant decrease in the mortality of cervical cancer the second most common female malignancy worldwide. Another means of preventing this disease involves HPV vaccines but these are expensive and not yet being used on a wide scale. Cervical cytological examination (Pap smear) is also a method used but its more expensive.

Visual inspection of the cervix with acetic acid and cervicography (VIAC) is the screening method that has been implemented in the city of Harare.

There are treatment options for precancerous cervical lesion if one is detected. Loop electrosurgical procedure is when an electrically charged wire is used to excise abnormal cells from the cervix. Cryotherapy is freezing the abnormal cells with a cold probe using nitrogen oxide and the frozen cells then die and shed of gradually from the cervix thereby removing the precancer cells of the cervix. Laser treatment is when the precancerous cervical lesion is destroyed using a beam of laser light. Conization/cone biopsy is when cone-shaped piece of tissue containing the precancerous area of the cervix is surgically removed and sent for histology[3].

1.2Problem statement

The prevalence of precancer lesions in Harare among the approximately 4000 women that had been screened was high (7%, see table 1 below) compared to other regions on the African continent. In a study in South Africa in 10 geographically defined areas the prevalence of precancerous lesions was 3.72%. In a multicentre study in West Africa the prevalence of precancer lesions was 1.9 %. Thus the prevalence in the Harare population is higher. Studies on prevalence and risk factors for cervical cancer have been done elsewhere and factors such as early sexual debut, human papilloma virus infection have been cited. Locally, studies of risk factors for cervical precancer lesions have not been done in recent years. Table below shows the VIAC positivity rate among the women screened.

Table 1: VIAC Positivity Rate, Harare (*First Quarter Report Maternal and Child Health, Harare city, 2013)*[4]

VIAC Result	Frequency	Percent
Negative	3711	92.1%
Positive	282	7%
Total	4026	100.0%

The table below shows the proportions of the various levels of cervical dysplasia among the women who managed to have cervical biopsy done since the cervical cancer screening program began.

Table 2: Cervical Biopsy Results, Harare, 2012-13(*First Quarter Report Maternal and Child Health, Harare city 2013)*[4]

Lesion	**Proportion (n=89)**
CIN I	21% (19)
CIN II	25% (22)
CIN III	34% (30)
Carcinoma	10% (9)
Others (pyogenic granulomata, haemorrhagic corpus luteum cysts, inflammation)	10% (9)

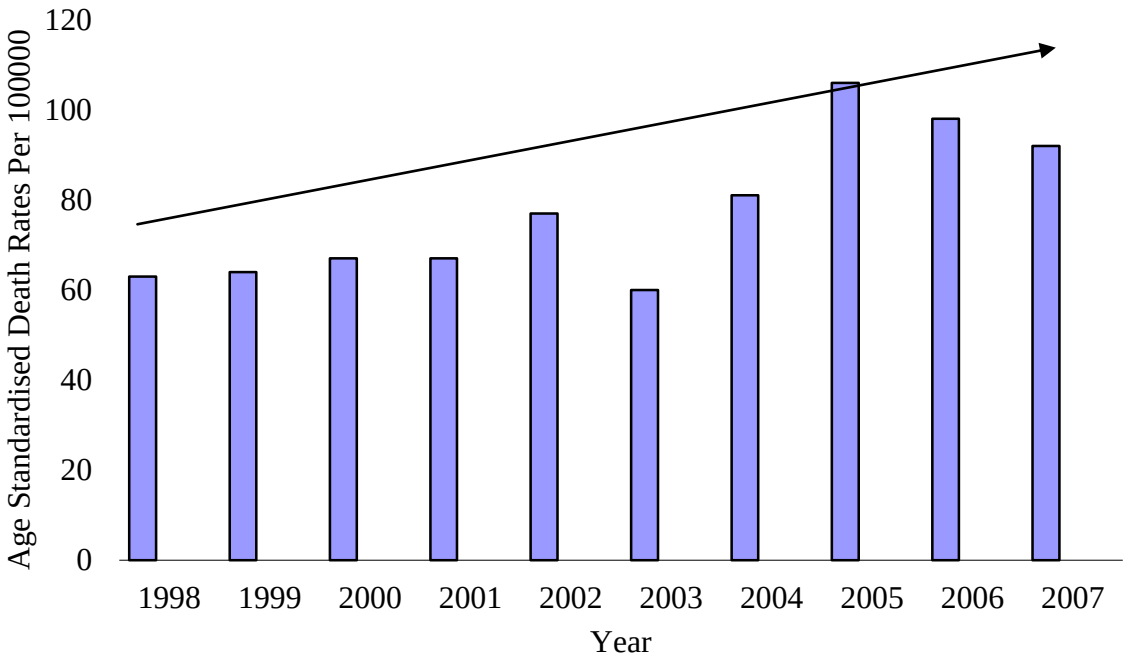
Only a proportion of those with a positive VIAC result went on to have biopsy. The proportion of histologically confirmed cervical precancer lesions among those who had a positive VIAC result and managed to have biopsy for the period 2011-2013 (table 2) was 80% and when this percentage is combined with invasive cancer lesions it becomes 90%.

Justification

Cervical cancer is the number one malignancy in women in Zimbabwe. Zimbabwe has got one of the world's highest age standardized death rates (ASR) from cervical invasive cancer, e.g. 67 per 100 000 people in Harare and since 1997 the rates have been going up as shown in the graph below. An insight into the major risk factors may be important if we are to control the disease.

The figure below shows the Age Standardised Death Rates (ASR) from Cervical Cancer.

Figure 1: Zimbabwe's Growing Cervical Cancer Burden, 2009[5]



Research question

1. What are the risk factors for cervical precancer lesions?

Objectives

Broad objective

To determine factors associated with precancer lesions among patients attending VIAC clinics in the city of Harare.

Specific objectives

1. To determine the socio-demographic characteristics of women with precancer lesions in Harare, 2013.
2. To compare the HIV and reported sexual history of women with precancer lesions of the cervix and women without in Harare, 2013.

3. To compare the history of STIs and gynaecological history of women with precancer lesions of the cervix and women without in Harare, 2013.

Chapter 2

Literature review

There have been several studies on the risk factors for precancer cervical lesions and HPV virus has been implicated as causal agent to cervical dsykariosis (precancer cells). However there are other factors that have also been implicated.

It was found in a study by Muñoz N, Franceschi S, Bosetti C et al[6] that there was a direct association between the number of parity and precancer cervical lesion risk: the odds ratio for seven full-term pregnancies or more was OR=3.8 compared with nulliparous women, and OR= 2.3 compared with women who had one or two full-term pregnancies.

In a study by Luchters, Vanden Broeck et al[7] in Kenya it was concluded that the prevalence of precancer lesions among HIV-infected sex workers was four times the prevalence in the HIV negative women. HPV 16 and HPV 18 were associated with cervical precancer lesions in this study, however other high-risk HPV serotypes were also found. It was also concluded that HIV-infected sex workers were likely contribute disproportionately to HPV transmission and thus posing risk for cervical precancer lesions. Existing efforts to prevent HIV and HPV transmission were concluded to be inadequate. In another study, out of the total of 715 women that were screened for cervical cancer in a study in Kenya by Memiah, Mbuthia and Kiiru et al[8] the median age of the participants was 40 years (range 18–69 years). It was also found that prevalence of precancerous lesions (CINI, CINII, CIN III) was approximately 27%. Controlling for other variables in logistic regression analysis, not being on ART was found to be independently associated with the risk of cervical precancer lesions and those not on ART were 2.21 times more likely to have the cervical precancer lesions than those on ART. In a related retrospective cohort study in South Africa by Zeier, Botha and van der

Merwe et al[9] to compare outcomes of HIV positive participants on ART and those not it was found that for the HIV group, antiretroviral therapy that was started before the first low grade squamous intraepithelial lesion (LSIL) was associated with decreased risk for progression compared with no antiretroviral therapy (RR = 0.66, 95%). It was also found that antiretroviral therapy also improved clearance when corrected for excision treatment and age (RR = 1.71).

According to a similar study by Khan MJ, Castle PE, Lorincz AT et al[10], on the elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 it was found that those with HPV 16 had a higher risk(18%) of progressing to CIN III or worse than those with HPV 18 (13%). Though this study showed the importance of distinguishing the HPV serotypes we did not distinguish the different HPV serotypes in this current study.

Findings from the study by Bosch, Muñoz, and de Sanjosé et al[11] suggested that some cases of HPV infection were undetected or that other sexually transmitted factors contribute to the causation of cervical precancer lesions. Early age at first intercourse and early age at first birth were found to be independently associated with an increased risk of cervical precancer lesions. Low educational level was also a risk factor and the number of sex partners was a surrogate for HPV infection. Smoking and parity after age 24 were weakly and inconsistently associated with the risk of cervical precancer lesions. Previous screening and ever having undergone a Caesarean section were protective factors. A cohort study[12] of 2040 HIV-negative women in Zimbabwe and South Africa, revealed that testing positive for STI at enrolment was associated with incidence of cervical precancer lesions. Other associated factors were greater than 3 live births, more than one lifetime partner and inconsistent use of condoms. Testing positive for an STI may mean one has been exposed to oncogenic HPV

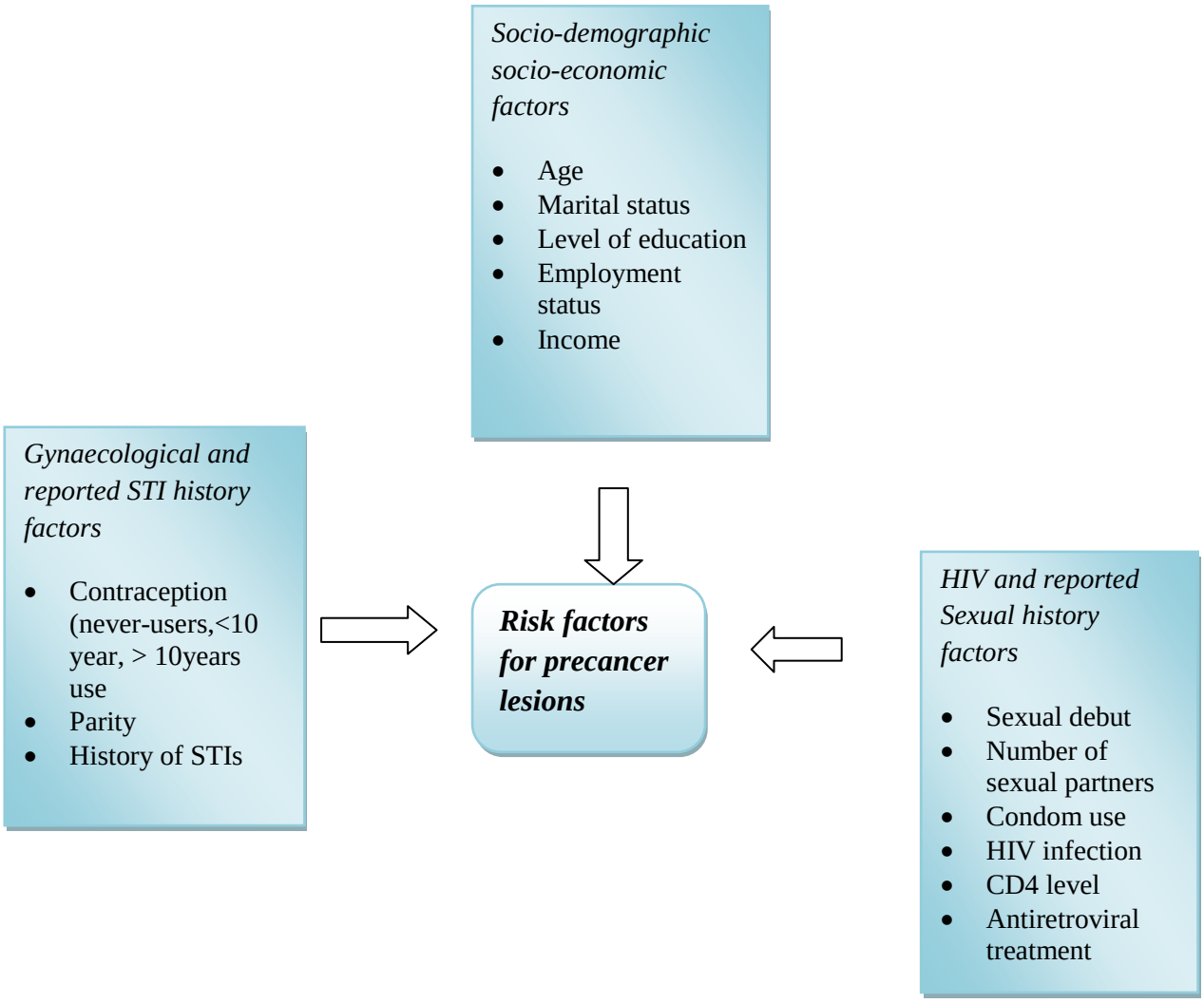
infection. In a similar study by Comino, Borrego and Garcia et al in the CLEOPATRA study[13] on risk factors for precancer in Spain found out that a lifetime number of two or more sexual partners, young age (18–25 years), a history of genital warts, and unmarried status were the strongest independent risk factors for HPV infection of any type. Living in an urban community, country of birth other than Spain, low level of education, and current smoking status were also independent risk factors for HPV infection. A weak inverse association between condom use and HPV infection was observed. Unlike monogamous women, women with two or more lifetime sexual partners showed a lower risk of infection if their current partner was circumcised and a higher risk of infection if they were current smokers.

Long-term use of oral contraceptives could be a cofactor that increases risk of cervical carcinoma by up to four-fold in women who are positive for cervical HPV DNA according to a study in Spain by Moreno, Bosch and Muñoz et al[14]. However they concluded that in the absence of worldwide information about HPV status, extra effort should be made to include long-term users of oral contraceptives in cervical screening programmes.

A study by Kjaer SK, Frederiksen K, Munk C and Iftner T[15] in Denmark on the long-term absolute risk of cervical intraepithelial neoplasia grade 3 or worse following human papillomavirus infection showed that the estimated probability of developing CIN grade 3 (CIN3) or worse within 12 years of follow-up was 26.7% and the estimated absolute risk for CIN3 or cancer within 12 years of the second examination among women who were HPV16 DNA positive at both examinations was 47.4%.

The figure below outlines the framework for the description of risk factors for cervical precancer lesions.

Figure 2: Logical Framework for Describing Risk Factors for Cervical Precancer Lesions



The risk factors for cervical cancer were grouped in the categories given in the figure above.

Chapter 3

3.1Research methods

3.2Study Design**:**

We conducted an unmatched case control study.

Study setting:

The study was conducted in Harare city health centres offering VIAC in Harare namely Wilkins Infectious Disease Hospital (WIDH), Highfield Polyclinic, Mbare Polyclinic.

Study population

The study population were women age 18 and above and were residing in Harare regardless of duration.

Inclusion and exclusion criteria

- ***Inclusion criteria***: We included women 18years and above that were Harare residents regardless of duration and had agreed to participate in this study. Participants were recruited regardless of their HIV status CD4+ cell counts or current ART status.
- ***Exclusion criteria*****:** We excluded women who have had hysterectomy, those who have had a previous diagnosis of cervical cancer or those currently with cancer. We also excluded pregnant women, women who reported that they had not yet engaged in sexual activity and those who were below the age of 18.

Study participants

3.2.1Case definition

- ***Case:*** A case was a woman resident in Harare for any duration, aged 18 years and above who was attending VIAC clinic. The woman must have had a VIAC positive result and had histological evidence of precancerous cervical cells on biopsy.

- ***Control:*** A control was a woman resident in Harare, aged 18years and above who was attending VIAC clinic and had a negative result (*no aceto-white lesion on cervix after staining with acetic acid).*

NB*:* A positive VIAC means that there are aceto-white lesions on the cervix after staining with acetic acid and precancerous lesions have this property.

3.3Data collection and analysis

Data were collected using an interviewer administered questionnaire which was composed of 33 questions. This questionnaire had questions pertaining to demographic characteristics and the risk factors of developing precancerous lesions of the cervix *(see appendix).* This data were then entered into epi-info version 7 for analysis. Descriptive statistics (proportions) were used to characterise some of the variables. Odds ratios (OR), 95% Confidence intervals and two tailed p-values were calculated. The variables that were found to be significant with a p-value of less than 0.05 on unadjusted analysis were included in the multivariate logistic regression analysis together with those with p-value less than 0.25. Logistic regression analysis was done using STATA 10.

HIV testing and counselling was routinely offered to all study participants. Those found to be HIV positive had CD4 counts done after consenting.

3.4Sample size calculation

Stat cal in epi-info 7 was used to calculate sample size and the following assumptions were made

- 95% level of confidence
- 80% power
- Use of oral contraception had an odds ratio of 3 for the development of precancer lesions of the cervix (James V, Lacey Jr et al)[16] 'Oral Contraceptives as Risk Factors for Cervical Adenocarcinomas and Squamous Cell Carcinomas

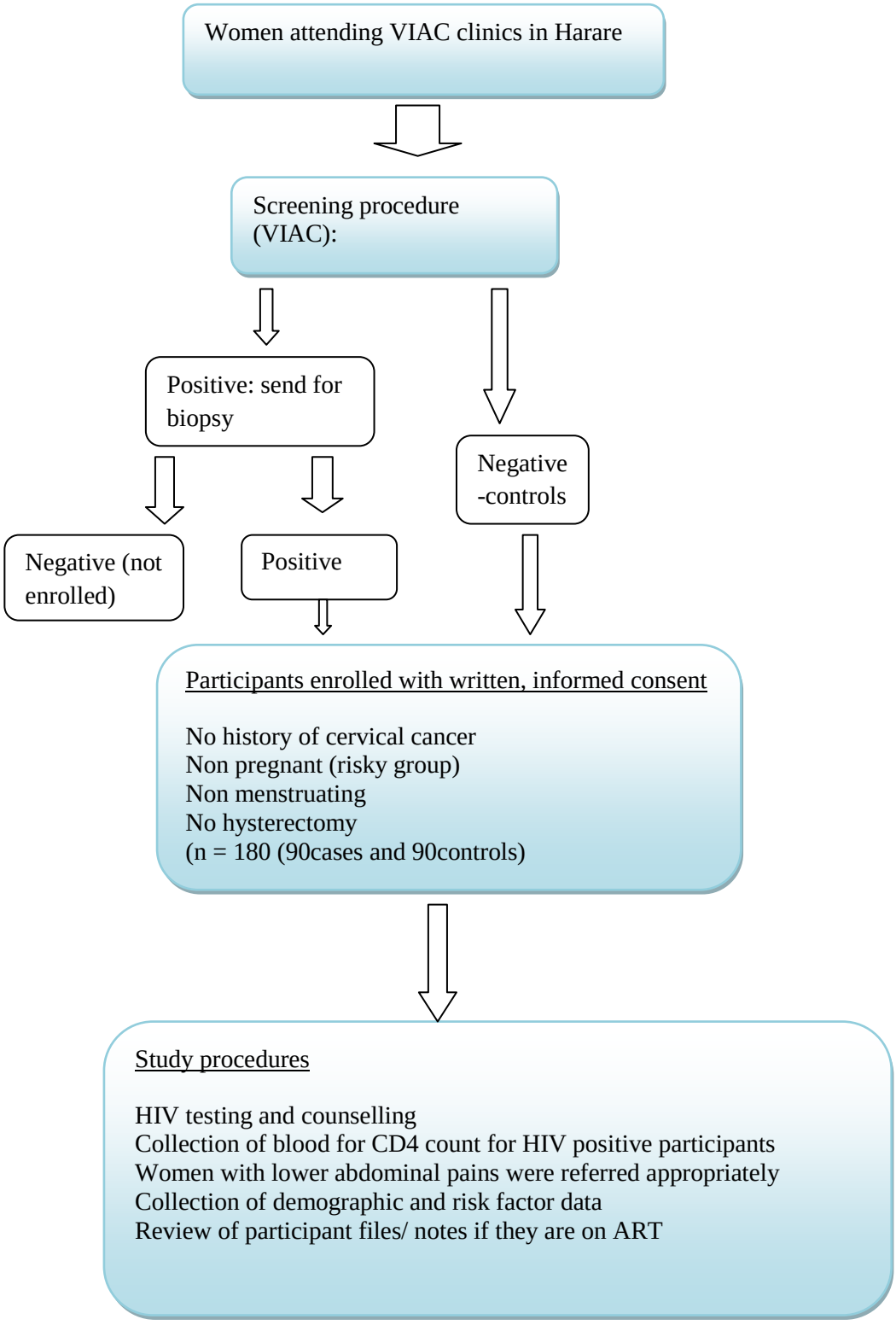
The minimum sample size calculated was 75 cases and 75 controls and allowing for 20 % non response rate[16], the required sample size was 90 cases and 90 controls.

Sampling

Because of the small number of women proceeding to having cervical biopsy, cases were consecutively selected as they were confirmed histologically after biopsy until the sample size of 90 was reached. The controls were selected systematically from the list of 3070 controls. The list of controls was obtained from the combined list of the VIAC negative women from the three health centres offering VIAC (WIDH, Highfields Polyclinic, Mbare polyclinic). A sampling interval of 20 was used after dividing 3070 by 180. The first control was selected randomly by the lottery method from the first 20 numbers on the list.

The figure below shows the enrolment procedures.

Figure 3: Study enrolment, Procedures



Women with histologically confirmed cervical dysplasia were enrolled. Women with lower abdominal pain and were referred to outpatients for management.

Ethical considerations and permission to conduct the study

Permission to conduct this study

Permission to conduct the study was sought from Health Studies Office, Director of health services, District Medical officer responsible for the VIAC program and Medical Research Council of Zimbabwe.

Ethical considerations

The purpose of the study was clearly explained to the study participants. An explanation was given that there are no costs, injuries and risks anticipated in this study and that participation was voluntary and they may decide against participation during the interview even if they had initially consented. We also gave the participant information on who to contact in case there are queries about the research or about their rights regarding participation in the study. After all this had been done then a written consent was sought from all study participants. Women who had lower abdominal pains were referred appropriately. Those with precancerous lesions had Loop electrosurgical excision procedure (LEEP) done to remove the precancerous lesion. Follow-up is being done monthly to check on the outcomes of those who had LEEP. Confidentiality was maintained throughout the study and no names were captured on the questionnaires.

Chapter 4

Results

A total of 180 women were interviewed.

Demographic characteristics of cases and controls

The results of the statistical analysis of age were presented on a different table from the other demographic characteristics because of the differences in the type of analysis used. The following table *(table3)* shows the age group distributions of the study participants.

Table 3: Age Group Distributions of Cases and Controls, Harare, 2013

Variable	Category	Case n=90(%)	Controls n=90(%)	Chi-square, p-value
Age group	16-25	13(14)	18(18)	3.1, 0.67
	26-35	27(30)	20(24)	
	36-45	30(34)	28(31)	
	46-55	12(13)	10(11)	
	56-65	5(6)	9(10)	
	>65	3(3)	5(6)	

Median age for cases= 36.5years (Q1=31.0, Q2=43.5)

Median age for controls= 39 years (Q1=30.0, Q=45.5)

As the table above shows, the majority of the participants were in the age groups 26-45 (65% in this age group for cases and 56% for controls). There were no significant differences in the age groups between cases and controls *(chi-square p-value of 0.67).* The median age for cases

was 36.5years (Q_1=31; Q_3=43, 5) and for controls was 38years (Q_1= 30; Q_3=45,5). The following table *(table 4)* is showing the other demographic characteristics of cases and controls.

Table 4: Demographic Characteristics of cases and controls, Harare, 2013

Variable	Category	Case n=90(%)	Controls n=90(%)	OR	CI
Employment	Employed	34(37)	43(48)	0.64	0.67-4.89
	Unemployed	56(62)	46(52)		
Education	Primary	28(36)	16(19)	2.39	1.31-6.17
	Secondary	49(64)	67(81)		
Income level	<500	74(82)	64(71)	1.88	0.86-4.28
	>500	16(18)	26(29)		
Marital status	Single	32(36)	19(20)	2.30	1.76-8.19
	Married	58(64)	71(80)		

There were no significant differences in the employment status and the average monthly income between the cases and controls. There was however a statistically significant difference in the marital status and level were controls were 2.30 times more likely to be married than controls and cases were 2.39 times more likely to have reached primary school level than secondary.

The following table shows HIV and reported sexual history factors associated with cervical precancer lesions.

Table 4: HIV and Sexual History Factors Associated with Cervical Precancer Lesions, Harare, 2013

Variable	Category	Case n(%)	Control n(%)	OR	CI	p-value
HIV status	Positive	31(36)	71(70)	8.40	4.17-17.09	0.00
	Negative	55(64)	15(30)			
Base line CD4	<350	37(69)	11(69)	1	0.30-0.29	1
	>350	17(31)	5(31)			
ART	On ART	17(31)	7(47)	0.53	0.16-1.68	0.36
	Not on ART	37(69)	8(53)			
Age of sexual debut	</=15years	15(17)	5(6)	3.4	1.18-9.80	0.02
	>15years	75(83)	85(94)			
Sexual partners	1partner	37(47)	26(29)	1.90	1.21-3.72	0.03
	2 or more	48(53)	64(71)			
Condom use	Sometimes	26(29)	10(11)	3.25	1.26-7.23	0.00
	never	64(71)	80(89)			

There was a statistically significant association between HIV status and cervical precancerous lesions of the cervix. Those who were HIV positive were 8.4 times (OR=8.4, CI= [4.17-17.09]) more likely to have precancer lesions of the cervix than those who were HIV negative, among those interviewed. However there was no difference in the risk of cervical precancer lesions between those who had CD4 count below 350 and those with CD4 count above 350. ART was protective (OR=0.53) but this association was not statistically significant (CI= [0.16-1.68]). There was no statistically significant association between the duration on ART and the risk of precancer lesions

Those who had sexual debut before the age of 15 were 3.4 times more likely to have cervical precancer lesions and this was statistically significant (p=0.02). The median age of sexual debut for cases was 18(Q_1= 16.5; Q_2=20.5) and for controls was 19(Q_1=18.5; Q_2=21.5).

Having more than one lifetime sexual partner was a significant risk factor (OR=1.9; p-value=0.03). We compared those with parity of 4 and below and those with 5 or more and we found that there was no statistically significant association between parity and the risk of cervical precancer lesions (OR=1.45; CI= 0.17-2.97).

Always using a condom was found to be associated with increased risk of cervical precancer lesions compared to never (OR=3.25; CI= 1.27-7.23).

The following table shows some of the factors associated with cervical precancer lesions studied (gynaecological and STIs).

Table 5: Factors Associated (Gynaecological and STIs) with Cervical Precancer Lesions, Harare, 2013

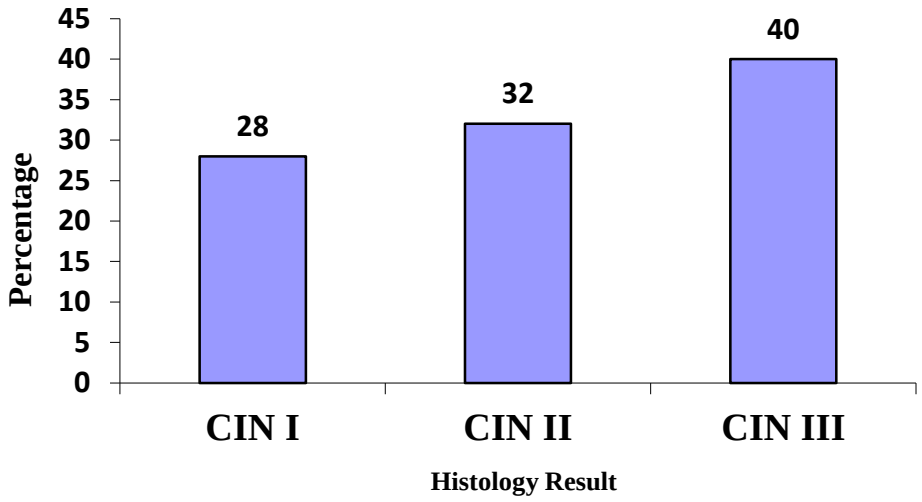
Variable	category	Case n(%)	Control n(%)	OR	CI	p-value
Parity	</=4	73(81)	65(75)	1.45	0.71-2.97	0.37
	>4	17(19)	22(25)			
Ever had an STI	Yes	49(54)	25(28)	3.06	1.64-5.69	0.00
	no	41(46)	64(72)			
Ever had genital warts	Yes	18(22)	4(6)	4.29	1.37-13.40	0.01
	No	63(78)	60(94)			
Ever used OC	always	66(72)	69(75)	0.84	0.45-1.76	0.34
	Sometimes	24(28)	21(25)			
Duration of OC use	</=10years	37(55)	34(48)	1.34	0.97-3.40	0.08
	>10 years	30(45)	37(52)			

The history of suffering from STIs was significantly associated with the development of cervical precancer cells with those with this exposure having 3.06 times the risk of precancer lesions than those not exposed**.** The association of genital warts and cervical precancer

lesions was stronger (OR=4,29) and this was also statistically significant. There was no statistically significant association of contraceptive use and the risk of cervical precancer lesions.

The graph below shows the proportion of each CIN grades of histologically confirmed CIN among the cases.

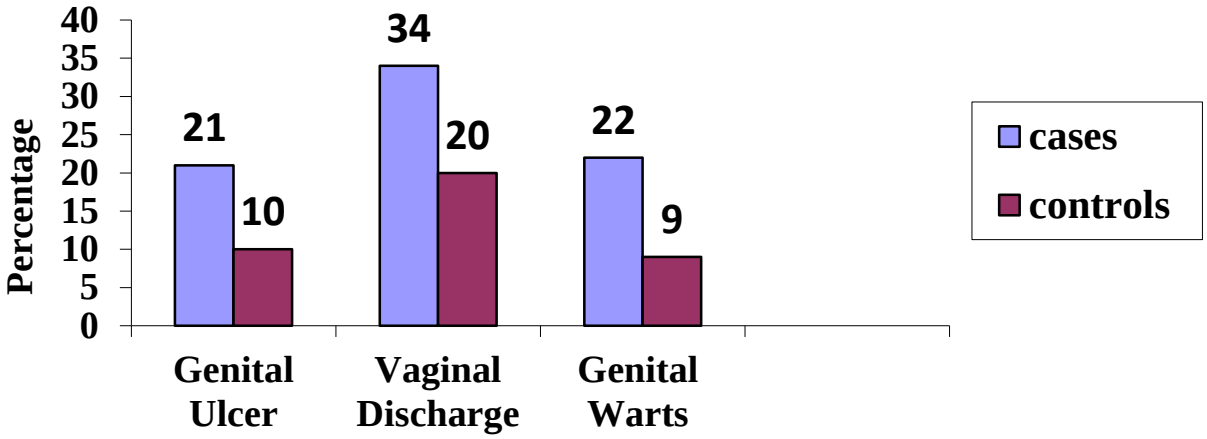
Figure 4: Histology Results for the cases and controls, Harare, 2013



Amongst the ninety histologically confirmed cervical precancer cases CIN III contributed the most with forty percent whilst the least was CIN I with twenty eight percent.

The following graph shows the various STIs that the cases and controls had a history of suffering from.

Fig. 5 Distribution of the various STIs among cases and controls, Harare, 2013



The history of STIs was higher among cases than controls. Vaginal discharge was the commonest STI among both cases and controls while genital warts and genital ulcer were the least among controls and cases respectively.

Shown below is the association of cervical precancer lesions with the various types of STIs.

Table 6: Association of cervical precancer lesions with various STIs, Harare, 2013

STI		Cases	Controls	OR	CI
Genital ulcer	No	71(79)	81(90)	2.40	1.02-5.65
	Yes	19(21)	9(10)		
Vaginal discharge	No	59(66)	72(80)	2.10	1.08-4.17
	Yes	31(34)	72(80)		
Genital warts	No	18(22)	4(6)	4.29	1.37-13.40
	Yes	63(78)	60(94)		

All forms of STIs were associated with the development of cervical precancer lesions and this was statistically significant. Having suffered genital warts implied more risk (OR=4.29; CI= 1.37-13.40) than the other forms of STIs and this was statistically significant.

Stratified analysis

We did stratified analysis to find out the effect of HIV status on the risk of cervical precancer lesions among those with a history of STIs and the following table (*Table 7)* shows the risk of cervical precancer lesions among those who were HIV negative.

Table 7: Risk of precancer lesions among those HIV negative

Variable	**Category**	**Case**	**Control**	**OR**	**CI**
Ever had STI	Yes	12(39)	19(27)	1.73	0.71-4.22
	No	19(61)	52(73)		

Shown below *(table 8)* is the association of STIs and cervical precancer lesions among those who are HIV positive.

Table 8: Risk of precancer lesions among those HIV positive

Variable	**Category**	**Case**	**Control**	**OR**	**CI**
Ever had STI	Yes	35(64)	6(35)	3.2	1.03-10.00
	No	20(36)	11(65)		

Crude odds ratio for the association between STIs and cervical precancer lesion is 3.06 (1.64-5.69) *see table 5*. When stratified by HIV status, the chi-square for interaction of the 2 stratum specific odds ratio for the association of STIs and cervical precancer lesions is 5.49 with p-value of 0.02, thus there is a statistically significant difference in the odds ratio by stratum. The crude OR lies between the stratum specific OR. Thus there was effect modification.

We therefore conclude that the risk of cervical precancer lesions among those with STIs was positively modified by the HIV status. The risk of precancer lesions among those with a history of STIs was only statistically significant when one was HIV positive as well. Presented in *table 9* below are the independent risk factors for cervical precancer lesions.

Table 9: Independent Risk factors associated with Precancer lesions after logistic regression, Harare, 2013

Variable	Category	Adj. OR	p-value
Q2level of educ.	None (dummy variable)		
	Primary	0.38	0.04
	Secondary	0.12	0.02
Any STIs	No (dummy variable)		
	Yes	3.10	0.00
Q20sex debut	</=15years (dummy variable)		
	21-25years	0.21	0.04
Q30HIVresults	Negative(dummy variable)		
	Positive	10.62	0.00
Q23sex partners	One partner		
	>5partners	0.23	0.02

Adjusting for other variables, in logistic regression, the level of education (primary and secondary) was protective compared to not going to school at all. A history of STIs remained a risk factors (Adj OR=3.10; p-value=0.02) as compared to not having any STIs. Sexual debut between 21-25years was protective compared to that before 15 years after adjusting for other variables (Adj OR= 0.21; p-value=0.04). Being HIV positive remained a significant risk factor after adjusting for other variables (Adj OR= 10.62; p-value=0.00). Having more than 5 sexual partners was found to be protective compared to having one sexual partner.

Chapter 5

5.1Discussion

This case-control study was conducted at health institutions HIV care is also provided. Thus, the sources of referrals to these VIAC clinics include these HIV care centres. This might have contributed to the high HIV prevalence (39%) found in this study compared to the Zimbabwe national prevalence of 13.1% (ZDHS, 2012)[17].

The association of HIV and cervical precancer lesions found in this study is consistent with findings in literature[6, 8]. These studies have found that the prevalence of CIN is higher in HIV positive women than HIV negative women. In the WIHS[17] study in Europe cervical cytological findings were abnormal in 38% of the HIV positive and 16% of the HIV negative. In Southern Europe, several studies[24,25,29,30] have also reported an increased risk of cervical dysplasia among HIV positive compared to HIV negative women. The mechanism by which HIV increases the risk is not well understood but this finding has obvious public health implications of the need to integrate cervical cancer screening with HIV services which is not yet common practice in Zimbabwe.

Currently, Zimbabwean guidelines state that it is not cost effective to screen those who are less than 25 years of age for precancer lesions if they are HIV negative. We found in this study that there was higher risk of cervical precancer lesions (OR=4.33; CI= 2.12-6.17) among those who are HIV positive below the age of 26years *(see table 5above)* than those who were HIV negative. However, from these study findings it is difficult to conclude that there is no need for screening those below 25years because of the relatively small sample size, the higher prevalence of HIV in this study compared to the general population and the fact that this was not a cross sectional study which will be able to measure prevalence/disease

of burden. A cohort study would be able to measure incidence and relative risk and thus better characterise the risk than a case-control study which is more prone to selection bias. ART was protective however this association was not statistically significant *(see table 4 above).* This might have been because of the smaller sample size and the nature of the study design. A cohort study would be more informative regarding the protective effect of ART as was found in a cohort study in South Africa[14] where ART was found to a significant protective effect on the progression of CIN. In a French cohort study[23], the prevalence of CIN reduced from 69% to 53% after a mean of 5months of ART (p=0.04) which shows that ART was protective. This calls for the need for integration of cancer screening and HIV services so that as many women as possible are screened for cervical cancer.

The finding that there no significant association of the risk of precancer lesions with level of CD4 is contrary to findings in Zambia[6] and other studies[20,21,22]. It was found in the Zambian study that those with lower CD4 counts were at higher risk of cervical dysplasia. This contradictory finding may be as a result of the relatively smaller sample size of this study (180) compared to theirs (715) and the lower cut off CD4 count used in the Zambian study (200) compared with the one we used (350) . The reason for using a higher CD4 count (350) cut off in this study was that the Zimbabwe national guidelines on ART already recommend initiating ART at CD4count of 350 and so any recommendations from the study would have to also take into account this new cut off point.

With the high HIV prevalence in Zimbabwe (13.1%-ZDHS, 2012), access to VIAC clinics should be made universal so that precancer lesions of the cervix can be detected early in most of the women in Zimbabwe. Integration of precancer cervical screening in OICs may go a long way to reduce the cervical cancer morbidity and mortality in Zimbabwe and this should be made an established practice.

Consistent use of condoms was found to be a risk factor for precancer lesions. This seemingly paradoxical finding maybe because those women who consistently use condoms may perceive their partners as high-risk for STIs as compared with those who never use condoms thus these high risk partners might have already exposed them to oncogenic HPV infection.

The high risk for precancer lesion of the cervix posed by a history of STIs in this study is consistent with findings in literaturel[12, 19] were STI was a predictor of incident of cervical precancer lesions. Even genital ulcers and vaginal discharge syndrome was found to be associated with risk of cervical precancer lesions however, having suffered from genital warts had the strongest association with precancer lesions of the cervix as shown in *table 6*. This stronger association may be because of the association human papilloma virus with both genital warts and precancer lesions of the cervix as found in literature[5]. The association of STIs other than genital warts with precancer lesions of the cervix needs further evaluation. In view of the increase in STIs in Harare (Annual Report, Harare City, 2011&12), the use of barrier methods to prevent STIs should be highlighted and emphasised in health education campaigns in Harare.

Early sexual debut (<15years) was significantly associated with the risk of cervical precancer lesions compared with late (>15years) onset of sexual activity. This is consistent with literature[18,19]. Early onset of sexual activity may result in more risk because of the longer duration of possible risk of exposure to oncogenic HPV infection thereby predisposing the women to cervical precancer lesions. Behavioural change is required to address such issues as early sexual debut. Since 25% of cases had sexual debut before 16 years, which is school going age, health education in schools on consistent use of condoms if early sexual debut occurs is important.

A number of studies have found (oral contraception) OC users at increased risk of precancer lesions of the cervix,[20, 21] after prolonged use (>10years). In this study however we did not find statistically significant association between precancer lesions and pronged use of oral contraception. This could be explained by the difference in study design used here compared to the above mentioned which were cohort studies where they were able to measure incident cases for those taking oral contraception and compare with those not taking oral contraception. Moreover we relied on reported use and thus there might be recall bias. However these studies were not able to eliminate the potential effect of concomitant HPV infection.

Having more than one lifetime sexual partner posed risk of precancer cervical lesions because of the potential of exposure to oncogenic HPV viruses. Perhaps fewer partners mean fewer previous infections with genital HPV which is assumed to cause precancer lesions of the cervix. This concurs with findings in literature[18,19]. On logistic regression, however the association of 2-5 partners with precancer lesions was not statistically significant *(see appendix 2/table 9)*. Those with more than 5 partners were protected (Adj OR=0.23: p-value=0.02). This seems not biologically plausible but this might be because those with 5 or more partners protect themselves from STIs (because perceived risk of STIs) compared to those who have one partner or fewer partners because of perceived safety from STIs.

Parity has been found to be associated with precancer in literature[7], however in this study it was not found to be associated. This disparity maybe as a result of the smaller sample size compared to the study quoted above.

Seventy seven percent of the participants were earning less than 500 US dollars per month and also seventy seven percent were unemployed. This is a general reflection of the low level income and high unemployment for most Zimbabweans contributing to the low socio-

economic status. Those with lower income were at a greater risk of precancer lesions of the cervix however this association was not statistically significant (p-value=0.08). Lower level of education (primary and never) was associated with higher risk compared to higher levels. Literature on precancer lesions of the cervix associates low socio-economic status with increased risk of these lesions[9, 10] and this may partly explain high burden of cervical cancer in Zimbabwe and Sub-Saharan Africa. Improving the socio-economic wellbeing of the country is long term solution to fighting the cervical cancer burden. Medium to short term solutions like vaccinations and screening for cervical precancer lesions are more appropriate.

Being single was found to be significantly associated with the risk of cervical precancer lesions. This might be explained by the risky sexual behaviours that might be associated with people who do not have partners (widowed, never married, and separated) which might put them at risk of HPV infection thus predisposing them to precancer lesions of the cervix.

High grade dysplasia cervical dysplasia (CIN III) contributed the most (40%). This finding is contrary to findings in India[17] that showed CIN III was the least contributor to precancerous lesions, however the Indian study was a cross sectional study. Purposive sampling of cases which was done because of the limited number of histologically confirmed cervical dysplasia might have introduced selection bias which might have contributed to the difference in findings.

5.2Conclusion

The risk factors found in this study concur with findings from literature. The significant risk factors associated with cervical precancer lesions were low socio-economic status (low education), being HIV positive, history of any form of STI, more than one sexual partner and early (before 15 years) sexual debut. HIV status positively modified the risk of cervical precancer lesions among those with STIs. The association of HIV and STIs with cervical

precancer lesions found suggests the need to reduce the prevalence of these conditions. To achieve this strengthening health education on use of barrier methods to prevent STIs and HIV is required.

Recommendations

1. We recommend to the Chief Health Promotion Officer to strengthen health education on barrier methods to prevent STIs and educate girls on the risk of cervical cancer posed by early sexual debut and having multiple sexual partners.

2. We recommend to the HIV program manager to ensure that HIV positive women are screened for cervical precancer lesions in Harare.

Limitations

1. This study was conducted at health institutions where HIV care is also provided, thus, the sources of referrals to the study sites include these HIV care centres. This might have contributed to the high HIV prevalence (39%) found might overestimate the association of HIV and cervical precancer lesions.
2. While we verified history of STIs with records in 63 % of participants, we relied on reported history of STIs in 37% the participants and this might affect the accuracy of some of the findings on STIs.
3. Cases in this study were hospital/clinic based and these may have differences with population based cases in with regards to risk factor profile for cervical precancer lesions.

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APPENDIX 1: DATA COLLECTION TOOL

Data collection tool

Questionnaire for the participants (cases and controls)

How are you? My name is Michael Vere. I am a public health officer from the University of Zimbabwe. I am carrying out a study on the factors associated with precancer lesions in Harare. The purpose of the research is to identify factors that may put you at risk of having precancer cervical cancer which can lead to cervical cancer. If the factors are identified they will assist in coming up with effective prevention and control strategies.

Your participation in the study is voluntary and you are allowed to decline participation and all the information I will collect from you will be kept confidential and your name will not be recorded on this form.

Consent

I have understood the information and I am willing to participate in the study.

Participant's signature---------- Date----------

CASE [ ] CONTROL [ ]

Part 1:Demographic characteristics

1. What is your age? (years completed).....
2. What is your level of education?

   a) primary b)secondary c) tertiary d) none

3. What is your marital status?

   a)married b) divorced c) widowed d)cohabitating e) single

4. What is your average monthly income? ($US)

   a) <500 b) 500-2000 c) >2000

5. What is your current employment status?

   a) informally employed b) formally employed c) unemployed d) other

6. What is your religion?

   a) Apostolic b) Pentecostal c) Anglican d) Catholic e) other

Part 2: Risk factors for precancer lesions

7. Do you use oral contraception to prevent pregnancy?

   a) always b) sometimes c) never

8. If always or sometimes, for how long have you been using oral contraception?

   a) <5years b) >5years

9. Do you have children a. Yes b. No
10. How many children have you had or pregnancies beyond 7 months? Specify.....

    a) </=4children c)>4children

11. Have you had a sexually transmitted infection in your life time?

a) Yes b) no c) don't know

12. If yes, how many times?.....times a) never b) <3times c) >3times

13. Have you had a sexually transmitted infection in the past 3 months?

a) yes b) no

14. If yes what form of STI? *Select all that apply*

a) ulcer b) vaginal discharge c) Genital warts d) other

15. Have you had genital warts yourself?

a) yes b) no

16. Have you ever been screened for cervical cancer before ?

a) Yes b) no

17. If yes, when were you screened?

a) in the past 3 years b) more than 3 years ago

18. Which method was used?

a) pap smear b) VIAC

19. What was the result of that screening test?

a) positive b) negative

Part 3

20. How old were you when you first had sex?

a. </=15years b.16- 20 years c. 21-25 d. >26 years

21. How many sexual partners have you had in the past 3 months? Specify.....

a. none b. 1 c. 2-5 d. >5 e. Don't know

22. How many sexual partners have you had in the past 12 months?

a. none b. 1 c. 2-5 d. >5 e. Don't know

23. How many sexual partners have you had in your life time? Specify.....

a) one b) more than one but less than 5 c) more than 5

24. Do you use condoms whenever you are having sex?

a) always b)sometimes c) never d) I abstain

25. Did you use a condom the last time you had sex ?

a) yes b) no c) don't remember

26. Has your partner had STIs in the past 12 months?

a)yes b) no

27. Is your male partner circumcised?

a) Yes b) no

28. If yes, when was the circumcision?

a) before marriage b) after marriage

Part 4

29. Have you been tested for HIV before?

a) yes b) no

30. What was the result?

a) positive b) negative c) unknown

31. If positive what is the baseline of CD4 cell count? Specify .....

a) <350 b) >350

32. Are you on Antiretroviral therapy(ART)?

a) yes b) no

33. If yes, how long have you been on ART? Specify .....months

a) < 36 months b) > 36months

Thank you .....

APPENDIX 2: LOGISTIC REGRESSION OUTPUT

Logistic regression Output

```
  Number of obs   =       180
                                LR chi2(15)     =      70.30
                                Prob > chi2     =     0.0000
Log likelihood = -86.841554                     Pseudo R2       =     0.2881

------------------------------------------------------------------------------
             casestatus |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
------------------------+-----------------------------------------------------------------
       q2levelofeducation |
                      1  |  -.9586662   .4806283    -1.99   0.046     -1.90068    -.016652
                      2  |  -2.141475   .9268934    -2.31   0.021    -3.958153   -.3247975
                      3  |   .2878963   .7734523     0.37   0.710    -1.228042    1.803835
                         |
        q3rmaritalstatus |
                      1  |   1.132861   1.073151     1.06   0.291    -.9704758    3.236198
                      2  |   1.366977   .9099917     1.50   0.133    -.4165745    3.150528
                      3  |    -1.0149   .5783812    -1.75   0.079    -2.148506    .1187068
                         |
           anystislife |   1.128816   .4149536     2.72   0.007     .3155219     1.94211
                         |
         q4levelofincome |
                      1  |   .4764941   .5207908     0.91   0.360     -.544237    1.497225
                      2  |    .19399   1.127512     0.17   0.863    -2.015892    2.403872
                         |
          q20firsthadsex |
                      1  |  -1.572361   .7678423    -2.05   0.041    -3.077304    -.067418
                      2  |  -.9375831   .7101456    -1.32   0.187    -2.329443    .4542767
                      3  |          0  (empty)
                         |
           q30hivresult |
                      1  |   2.369559   .4894332     4.84   0.000     1.410288    3.328831
                      2  |   2.365113   1.581812     1.50   0.135    -.7351819    5.465408
                         |
q23sexualpartnerslifetime |
                      1  |   .5798817    .500659     1.16   0.247    -.4013919    1.561155
                      2  |   -1.48094    .662044    -2.24   0.025    -2.778523   -.1833579
                         |
                   _cons |   .3238308   .7765219     0.42   0.677    -1.198124    1.845786
```

APPENDIX 3: SHONA QUESTIONNAIRE

Gwaro remibvunzo yemaCases nemaControls

Makadinini henyu? Ini ndinonzi Michael Vere. Ndiri mudzizi wekuUniversity yeZimbabwe. Ndirikuita tsvakiridzo yekuda kuona kuti chii chinikonzeresa gomarara rechibereko muvanhu vemuHarare. Kana izvi zvikawanikwa zvino gona kuti vazveutano va kwanise kudziidzisa vanhu nezvekudzivirirwa kwegomarara rechibereko.

Makasunuguka kuramba zvenyu kuva mumwe vavanhu vatichabvunza mibvunzo maererano netsvkiridzo iyi. Asi mukabvuma zvenyu, zvatichakurukura zvachachengetedzwa zvakananaka zveketi hapana anozozviziva kunze kwangu nemi. Zita renyu harisikuzonyorwa pamagwaro aya.

Ndingapfuurira mberi here?

- Hongu
- Kwete

Zvikonzero zvekuramba

- Handina nguva
- Handisikuda chete
- Zvimwe _____

Signature ---------- Zuva ----------

Case [ ] **Control [ ]**

Chikamu chokutanga

1. Mune makore mangani ? ----------
2. Makagumira gwaro ripi kuchikoro
   - Handina kuenda kuchikoro
   - Primary
   - Secondary
   - Tertiary
3. Makaroorwa here?
   - Ndakaroorwa
   - Takarambana
   - Ndakafirwa
   - Tiri kubika mapapoto
   - Handisati ndawanika
4. Munowana mari yekawanda sei pamwedzi?

   a. <500 b. 500-2000 c. >2000
5. Munoshanda here?

   a) Ndinozvishandira b) ndinoenda kubasa c) handishande

   d) zvimwe.....
6. Munopinda chitendero chipi?

   a) Apostolic b) Pentecostal c) Anglican d) Catholic

   e) zvimwe.....

Chikamu chechipiri

7. Munoshandisa mapiritsi ekudzivirira pamuviri here

a. hongu b. Kwete

8. Kana iri hongu, maveneguva yakadii muchishandisa mapiritsi aya?

a. <5 years b. > 5 years

9. Mune vana here

a. Hongu b. kwete

10. Kana iri hongu ,mune vana vangani?

a. </ =4 b. >4

11. Makamborwara nechirwere chepabonde here?

a. Hongu b. Kwete

12. Kana iri hongu kanagani?

a. handina b. < 3times c. 3-5times d. > 5times

13. Mumwedzi mitatu yapfuura makamborwara nechirwere chepabonde here?

a. hong b. Kwete

14. Kana iri hongu chipi chacho chirwere?

a. ronda b. Discharge c. Zvimwe.....

15. Makamboita mawarts here kunhenge dzenyu?

a. hongu b. Kwete

16. Makambotariswa muromo wechibereko here maererano ne chirwere chegomarara?

a. hongu b. Kwete

17. Kana iri hongu iriini pamakatariswa?

a. mukati memakore maviri apfuura b. Patopfuura makore maviri

18. Makaongororwa nenzira ipi yacho?

a. pap smear b. VIAC

19. Zvii zvakabuda pamakaongororwa

a. muromo wechibereko waive wakanaka b. Ndakanzi pangangoita gomarara rechibereko

Chikamu chechitatu

20. Makatanga kuita zvepabonde muine makaore mangani?

a. </=15years b.16- 20 years c. 21-25 d. >26 years

21. Makasangana nevarume vangani mumwedzi mitatu yapfuura ?

a. handina b. 1 c. 2-5 d. >5 e. Handichazivi

22. Makasangana nevarume vangani mugore rapfuura ?

a. hanadina wandakasangana naye b. 1 c. 2-5 d. >5 e. Handichzivi

23. Makasangana nevarume vangani muupenyu hwenyu hwese?

a. hanadina wandakasangana naye b. 1 c. 2-5 d. >5 e. Handichzivi

24. Munoshandisa macondoms here kanamuchirarwa nemurume nguva dzose?

a. nguva dzose b. Dzimwe nguva c. handotombomashandise

25. Makashandisa comdom here pamakapedzisira kusangana nemurume?

a. hongu b. Kwete c. Handichazivi

26. Murume wenyu akimbo ita chirwere chepabonde here mugore rapfuura?

a. hongu b. Kwete

27. Murume wenyu aka checheudzwa here?

a. hongu b. Kwete

28. Kana iri hongu riini?

a. tisati taroorana b. Tatoroorana

Chikamu chechina

29. Makamboongororwa cherwere cheHIV here?

a. hongu b. Kwete

30. Zvakabuda muongororo iyi zveive zvakamira sei?

a. ndakabatwa HIV b. Handina kubatwa HIV c. Handina kupiwa zvakabuda

31. Kana makabatwa HIV ,CD4 yaive yakasvika papi?

a) <350 b) >350

32. Kana yaive <350 muri kunwa maARV here?

a. hongu b. Kwete

33. Kana iri hogu, mavaneguva yakadini muchinwa maARVs?

a) handipfuuri makore matatu b) > ndapfuura makore matatu

.....MAZVITA.....

APPENDIX 4: SHONA CONSENT

TSAMBA YECHITENDERANO

Kutanga

Musoro weTsvakiridzo: Ongororo yezvinokonzera Gomarara remuromo wechibereko muguta reHarare, 2013.

Muongorori: Michael Vere [MBchB (UZ)]

Foni: 0772 288 097 or 04 708039

e-mail: vere.michael@yahoo.com

Zvamunofanirwa kuziva musati mapinda mutsvakiridzo iyoyi:

- ✓ Tsambs yechitenderano iyi inobatsira kuti muve neruzivo rwune udzamu pamusoro pe tsvakiridzo
- ✓ Hamumanikidzwe kupinda muongororo iyi
- ✓ Hapana mari yamichpiwa nekupinda muongororo iyi
- ✓ Tsvakiridzo iyi iri kuitwa kuti tigoziva zvimwe zvangokonzera gomarara rechibereko
- ✓ Munobvumirwa kuramba kuenderera mberi netsvakiridzo iyi nyangwe mavapakati payo
- ✓ Hapana zvakashata zvinoitika nyangwe mukaramba kupinda tsvakiridzo iyi.
- ✓ Bvunzayi mibvunzo yamunoda musati mapinda mutsvakiridzo iyi

Chinangwa chetsvakiridzo iyi

Murikukumbirwa kuti mupinde mutsvakiridzo ine musoro unoti: Ongororo yezvinokonzera Gomarara remuromo wechiberekomuvakadzi vemuguta reHarare, 2013. Tino tarisira kuwana zvinokenzera gomarara remuromo wechibereko kana tapedza ongororo iyi.

Zvatichange tichiita muongororo iyi

Tichakubvunzayi mibvunzo inokwana makumi matatu nemitatu maererano nezvetsvakiridzo iyi. Tinotarisira kuta maminitsi gumi nemashanu pamibvunzo iyoyi. Muchazokumbirwawo kuongororwa ropa renyu maererano nechirwere cheHIV. Kana mukawanikwa muine chirwere che HIV muchazoongororwa masoja emumuviri kuti akawanda sei.

Kupinda kwenyu mutsvakiridzo

Zvakakosha kuti muzive kuti kupinda kwenyu mutsvakiridzo iyi kuda kwenyu uye hamumanikidzwe. Mukaramba zvenyu hapana chakashata chinoitika kwamuri uye munobvumirwa kuuya kumakiriniki ezvegomarara rechibereko nyangwe marimba kupinda mutsvakiridzo iyi.

Kuvimbika kweongororo

Patsvakiridzo iyoyi hapana patinonyora zita renyu. Zvichabuda muongororo iyi kuti tichazviturirawo kuHarare City Health Department neUniversity yeZimbabwe. Chinagwa chekutaurirana newamwe ndechekuti vanhu vamuguta reHarare vagobatsirikawo nezvinenge zvabuda muongororo iyi.

Kushungurudzika

Hapana kushungurudzika kwatinotarisira mutsvakiridzo iyi. Tichakutorayi ropa pachigunwe kuti tiongorore chirwere cheHIV. Uwandu hweropa iri hwakafanana neuwandu hwedonnhwe remvura. Tichatora zveropa paruoko rwenyu rekutarisa masoja emumuviri menyu kuti

akawnda sei kana mabatwa chirwere cheHIV. Uwandu hweropa irir hwakafanana netii sipunu imwe chete.

Zvakanakira kuvamuongororo iyi

Hapana mari kana zvimwe zvinhu zvamunopihwa mutsvakiridzo iyi asi kuvamo kwenyu mutsvakiridzo iyi kunobatsira kuti imi mugoziva zvakawanda maererano negomarara rechibereko.

Mumwe muripo

Hapana mari dzamunotarisirwa kubhadhara kuti muvemuongororo iyi.

Mibvunzo

Kana paine mibvunzo yamuinayo makasununguka kuibvunza.

Kubvuma kwenyu

Mave pachidanho chekuti munyore kuti munoda kupinda here mutsvakiridzo kana kuti hamudi. Kana mukasaina apa zvinoreva kuti manzwisisa zviri muchitenderano chino uye mapindirana nazvo kuti munoda kuva mutsvakiridzo iyi.

_____ _____

Zita remupinduri (nyorai zvinooneka) Zuva

Runyoro rwechibvumirano rwemupinduri	Nguva

Muchapihwawo imwe tsamba yechitenderano yamuchanochengeta

Kana mune mibvunzo isina kupindurwa nemuongorori zvichisanganisira mibvunzo pamusoro peongororo ino, kodzero dzenyu kana mibvunzo yakanangana nekubatwa kwamaitwa muongororo ino, kana kusabatwa zvakanaka kwamunenge maitwa makasununguka kufonera boka reMedical Research Council of Zimbabwe panhamba dzerunhare dzinoti: 04-791792 kana 04-791193.

APPENDIX 5: ENGLISH CONSENT FORM

Introduction

Topic: Predictors of cervical precancer lesions among women attending Visual Inspection of cervix with Acetic acid and Cervicography in Harare city, 2013

Principal investigator: Michael Vere [MBchB (UZ)]

Phone number: 0772 288 097 or 04 774141/2

***What you should know before you consent*:**

- ✓ This consent is meant for you to familiarise yourself with the purpose, risks, and benefits of this research study.
- ✓ Participation in this study is voluntary
- ✓ There is no monetary benefit for participating in this study.
- ✓ The aim of this research is to gain knowledge on probable causes of cervical precancer lesions in Harare and this will help you and other women.
- ✓ You are allowed to decline participation in this study now and even during the interview if you feel that you are no longer comfortable with continuing.
- ✓ There is no penalty for refusing participation.
- ✓ Please review this consent form carefully.
- ✓ Ask any questions before you make a decision.

Purpose

You are being asked to participate in a study on: Predictors of cervical precancer lesions among women attending Visual Inspection of cervix with Acetic acid and Cervicography (VIAC) in Harare city, 2013. The aim of the study is to come up with the possible factors that are associated with the development of cervical precancer lesions in Harare.

Procedures and Duration

We are going to be conducting interviewer administered interviews. During the interview we are going to ask you a set of 33 questions and this is expected to take at most 15 minutes of

your time. You are allowed not to answer some of the questions if you are not comfortable with answering them.

We will be offering you HIV testing and counselling. HIV testing will not mandatory so you are allowed to opt out after you have been offered. Those who are found to be HIV positive will have CD4 count (measures the capacity of your body to fight diseases) done at the VIAC clinic and if it's low to warrant treatment with HIV.

Voluntary Participation

It's important for you to know that participation in this study is voluntary and that refusal to participate does not have any negative consequences on you. You will still have access to Harare city VIAC services now and in future. You are allowed to decline participation even when you are in the middle of the interview.

Confidentiality

We will not include your name on the questionnaire if you agree to participate in this study. Results of this study will be shared with Harare City Health Department and the University of Zimbabwe. The purpose of the sharing is for the Harare community to benefit as well from our findings.

Risks

This study is not expected to cause any physical risk. We are going to collect blood for HIV testing on your thump (one drop) and for CD4 if found positive (one teaspoon of blood).

Benefits

We do not promise that you will receive monetary or material benefits from this study. However your participation in this study may be a chance for you to know more about the risk factors for cervical cancer which is the number one cancer in women in Zimbabwe.

Additional Costs

There will be no additional costs to you for your participation in this study.

Answers to Questions

Ask any questions with regards to this study that you on areas that you don't clearly comprehend.

Authorization

You are making a decision whether or not to participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

Name of Research Participant (please print)	*Date*
Signature of Participant or legally authorized representative	*Time*

You will be given a copy of this consent form to keep

If you have any questions concerning this study or concerns beyond those answered by the investigator, including questions about the research, your rights as a research subject or research-related injuries, or if you feel that you have been treated unfairly and would like to talk to someone other than the researcher, please feel free to contact the Medical Research Council of Zimbabwe on telephone 04-791792 or 04-791193.