PREVALENCE OF CERVICAL INTRAEPITHELIAL NEOPLASIA AMONG WOMEN WHO SCREEN VIA/VILI POSITIVE:ARE WE OVERTREATING WITH SCREEN AND TREAT APPROACH?

Dissertation presented in part fulfillment of Master of Medicine in Obstetrics and Gynaecology

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DECLARATION

I declare that the study "**Prevalence of cervical intraepithelial neoplasia among women who screen VIA/VILI positive:Are we overtreating with screen and treat?"** is my own work. All resources and materials I have used or quoted have been indicated and acknowledged by means of reference. I further declare that this dissertation has not been submitted for the award of any other degree or to any other university or institution.

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DEDICATION

I dedicate this book to my father David, my mother Mary, my dear wife Judy and my sons Henry and Nathan for their unwavering support and prayers throughout the journey.

You prop me up to stand tall.

CERTIFICATE OF AUTHENTICITY

This is to certify that this dissertation is the original work of Dr. Oduor J. Michael, Master of Medicine student in the Department of Obstetrics and Gynaecology, School of Medicine, University of Nairobi, Registration number H58/74807/2014. The study was carried at Kenyatta National Hospital under the supervision of the Department of Obstetrics and Gynaecology, School of Medicine, College of Health Sciences, University of Nairobi. It has not been presented to any other university for award of degree.

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May God bless you.

ABBREVIATIONS

CIN …… Cervical Intraepithelial Neoplasia

HIV …… Human Immunodeficiency Virus

HPV…… Human Papilloma Virus

VIA……. Visual Inspection with Acetic acid

VILI…… Visual Inspection with Lugol's Iodine

LEEP…….. Loop Electrosurgical Excision Procedure

WHO……... World Health Organization

IARC…….. International Agency for Research on Cancer

LSIL…… Low grade Squamous Intraepithelial Lesion

HSIL…… High grade Squamous Intraepithelial Lesion

KNH…… Kenyatta National Hospital

UON…… University of Nairobi

RH…… Reproductive Health

DEFINITIONS

Cervical intraepithelial neoplasia is the abnormal growth of the cells of the uterine cervix usually starting at the transformation zone that have the potential to develop into cancer. The development of these abnormal growth has been linked to certain types of human papilloma viruses

Cervical cancer screening tests are tests used to identify women with possible presence of cancer or precancer lesions of the cervix that is yet to be diagnosed in the absence of clinical symptoms.

Loop electrosurgical excision procedure is the surgical removal of the transformation zone together with the ectocervix using an electrosurgical wire loop with the aim of excising the entire premalignant lesion.

Cryotherapy refers to the use of freezing and re-thawing process to destroy both benign and malignant cells in the treatment of premalignant lesions of the cervix

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ABSTRACT

Background: Effective screening for premalignant cervical lesions remains a challenge in sub Saharan Africa including Kenya. This is due to inadequate infrastructure, skilled personnel and cost required for pap smear and HPV DNA screening programs. This has led to late diagnosis of invasive cancer with attendant high morbidity and mortality. The screen and treat strategy using visual methods like visual inspection with acetic acid and visual inspection with lugol's iodine (VIA/VILI) has been recommended by WHO in such settings to reduce cost and loss to follow up. However, no local evaluation of the VIA/VILI screened positive congruence to colposcopy biopsy and histology has been done. This is needed to estimate possible overtreatment since guidelines for similar strategy using pap smear sets overtreatment level at less than 10%

Broad objective: To determine the proportion of women with abnormal histology findings following a positive VIA/VILI screen at Kenyatta National Hospital between January 2012 and December 2016 and to determine the histological classification.

Methodology

***Study design*:** This was a cross-sectional study in which records of 425 women who underwent colposcopy guided biopsy and histology at Kenyatta National Hospital after positive VIA/VILI screening were reviewed and agreement between the screening results and biopsy histology results assessed.

Study setting: This was a hospital-basedstudy conducted at the Kenyatta National Hospital reproductive health clinic 66.

Study population: Women with positive VIA/VILI screening results who underwent colposcopy guided biopsy and histology at KNH between 2012 and 2016 and had histology results available in the files.

Sample size: Records of 425 patients were used for the study.

Data collection: Data was collected using a standard data abstraction form.

Data analysis*:* Data was analyzed using SPSS version 21.0 for statistical analysis. Categorical data was summarized into percentages and continuous variables into means. The proportion of women with CIN was presented as a percentage with 95% confidence interval. CIN classification of the true positives was presented as percentages. Associations between the CIN and clinical characteristics was done using chi square test of associations.

Results: Out of 492 patients screened, 425 were included in the analysis. About half (53.4%) of the women had abnormal histology findings that is CIN I, CIN II, CIN III or microinvasive disease. Those with CIN II and above were 34.8%. Patients with HIV infection were found to be more likely to have CIN II and above compared to the non-infected.

Conclusion: This study shows low congruence between VIA/VILI screening and presence of CIN II and above indicating possible overtreatment of 65% using screen and treat approach. Guidelines to minimize levels of overtreatment should be developed before implementing the screen and treat strategy using VIA/VILI.

INTRODUCTION

Cancer of the cervix remains the leading cause of cancer deaths among women in sub-Saharan Africa including Kenya. Often the diagnosis is made in late stage of the disease due to low uptake cervical cancer screening. Effective screening and timely treatment of premalignant cervical lesions reduces the morbidity and mortality from invasive cancer of the cervix(1,2).

Cervical intraepithelial neoplasia (CIN) is a histological diagnosis that describes the pre-malignant lesions of the cervix(3).This diagnosis provides an opportunity for treatment before development of invasive diseasesince cancer of the cervix has a long natural history of 10-15 years(1,4). However, this may be shorter in HIV infected patient(5).Screening for cervical pre-cancer lesions can be done using either Pap smear, visual inspection with acetic(VIA), visual inspection with lugol's iodine (VILI) and Human Papilloma Virus (HPV) DNA testing(6). In robust screening programs, the pap smear and HPV DNA testing are commonly used. However, in resource limited settings their uptake remain low due to poor health service infrastructure, inadequate personnel, inadequate laboratory facilities and high cost to the patient among others(7).Due to these limitations, resource limited settings including Kenya have adopted the visual screening methods –VIA/VILI.

VIA involves inspection of the cervix with the naked eye after application of 3 to 5% acetic acid. Areas with high number of undifferentiated cells will appear acetowhite thus reported as positive. For VILI, the cervix is applied with lugol's iodine and again inspected with the naked eye. Pre-cancerous cells usually have less glycogen thus do not take up the iodine and so will appear as saffron yellow and reported as positive(7).

Diagnosis involves histological evaluation of tissue biopsy usually colposcopic guided biopsy.Based on the degree of dysplasia then the lesion can be graded as CIN I, CIN II, CIN III or microinvasive disease.

Treatment modalities include cryotherapy, loop electrosurgical procedure(LEEP) or cone biopsy. At Kenyatta National Hospital, cryotherapy is not routinely used. Patients with CIN II and above are either managed through LEEP and where not feasible then cone biopsy is considered.Those with CIN I or normal histology findings

Thisapproach of screening, diagnosis and treatment is described as the three step approach and poses the challenges of increased number of clinic visits, high cost to patients, loss to follow up and long waiting period before definitive treatment is offered.

In resource poor settings such as Kenya, the World Health Organization (WHO) has recommended the screen and treat approach using the visual screening methodsto reduce cost and loss to follow up(8). This involves presumptive treatment of all patients who have a positive screening results before definitive diagnosis is made.

The screen and treat approach has been successfully implemented using the pap smear based screening. However, the main concern has been the possible overtreatment of premalignant lesions. This has led to guidelines on what should be acceptable levels of overtreatment. The National Health Service Cervical Screening Program (NHSCSP), 2010 guidelines sets the overtreatment at less than 10%. A Systematic review has showed that this is achievable with minimal overtreatment(9). However, no evaluation of the VIA/VILI screened positive congruence to colposcopy biopsy and histology has been done.

LITERATURE REVIEW

Globally, there is minimal data on the actual prevalence of CIN. Different regions have reported varying levels of prevalence depending on availability of robust national screening program. In the United states, Henry Henk et al estimated the prevalence at about 0.28% in 2004(10). A retrospective survey in Turkey estimated the prevalence if pre-malignant lesions at 1.7%. This was noted to be relatively lower than the rate in other European countries partly due to lack of population based screening programs(11). The combined prevalence for both low grade and high grade lesions across China is estimated at about 2.7% while a cross-sectional study at Kenyatta National Hospital in 2003 estimated the prevalence at about 13. 4%(12,13). However, the burden of invasive cancer of the cervix still remains relatively high in developing countries including Kenya. In sub-Saharan Africa, it is the leading cause of cancer deaths while Kenya records 4,802 new cases annually and a 75 years old cumulative risk of 4.4%(14,15).

The history of CIN lesions can take any of the three pathways. Thus, there can be regression, persistence or progression. Regression describes the return of the cervical epithelium to its normal cytological appearance. Persistent lesions generally do not get more atypia during subsequent evaluation while progression means there is increased atypia or development of overt malignancy. The probability of either pathway depends on the degree of atypia or CIN grade. Majority of CIN I lesions generally regress. It is estimated that 49 – 60% of CIN I will regress. About 30 – 40% of the CIN I will persist at 6 months whereas about 10% progress to CIN III. Just about 1% will progress to invasive cancer. For CIN II, the percentage that progress to a higher grade lesion is higher. About 20% will progress to CIN III with 5% further progressing to invasive cancer. About 40% of patients with CIN II will regress to normal or persist. For CIN III,

the progression to invasive cancer is 12 -20%. About 50% persist while only about 30% regress(16,17).

Over the years, effective screening programs have helped reduce the incidence and mortality associated with cancer of the cervix. Between 1965 and 1982, the mortality from cancer of the cervix in Iceland fell by 80% following a nationwide screening program. In the same period Finland and Sweden also reported 50% and 34% reduction in cervical cancer mortalities following implementation of national screening programs. Denmark that only had 40% coverage of screening also reported 25% reduction in mortalities. The United States recorded 50% decline in cervical cancer mortalities between 1975 and 2008 due to the screening program(2,18). For maximum reduction of incidence of cervical cancer and reduction in mortality due to the same, effective screening and treatment program targeting 100% coverage of the women is critical. In set up where the screening programs are not well established, it is estimated that even a single screening in a lifetime at age 35 years can reduce the risk of invasive disease by between 25 – 36%(19).

Traditionally, the cytology based pap smear has been used as the gold standard in screening for cancer of the cervix. Recently, use of HPV DNA testing has been recommended as the preferred screening modality. In resource poor settings, visual inspection with acetic acid and lugol's iodine (VIA/VILI) has been recommended by WHO as an alternative to the Pap smear. The sensitivity and specificity of VIA/VILI is generally comparable to that of the pap smear in picking out the premalignant lesions. VIA/VILI has been noted to have slightly higher sensitivity but lower specificity compared to the pap smear. Most cross-sectional studies reported the sensitivity of VIA/VILI between 60% - 90% compared to pap smear 50% - 60%. The specificity for VIA/VILI was 71% - 94% compared to pap smear at 93% - 100%(20–23). Following studies

by the International Agency for Research on Cancer (IARC), a number of countries such as Nepal and Bangladesh have also incorporated VIA/VILI in their national screening programs (24). Because of the ease of VIA/VILI and the relatively low cost, many countries employ the opportunistic screening strategy. For instance in Kenya, women who come for other reproductive health services end up benefiting from screening for cancer of the cervix(7).

The current screening protocol in Kenyatta National Hospital involves the threestep approach thus: VIA/VILI then colposcopy guided biopsy and histology followed by LEEP depending on the histology results. The three step approach described as screen, diagnose and treat approach, has a number of challenges including high number of clinic visits and the attendant cost to the patients. This leads to higher incidence of loss to follow up. To address this, WHO has recommended the screen and treat approach in resource limited settings(8). This is thought to reduce the number of clinic visits and cost to the patient thus reducing loss to follow up. A systematic review by Ebisch et al supports this approach with cytology based screening(9). The screen and treat approach in our protocol would involve screening with VIA/VILI followed by LEEP. This has the potential to reduce the number of clinic visits, reduce the loss to follow up, shorten the time period between screening and treatment(19,25,26). However, the risk of overtreatment in implementing this strategy using VIA/VILI remains less studied as this is largely used in the developing countries without robust screening programs.

JUSTIFICATION

The uptake of VIA/VILI screening is increasing in Kenya due to lack of access to pap smear. The World Health Organization has recommended the screen and treat approach using the visual screening methods in resource limited settings such as Kenya. This is aimed at reducing cost and loss to follow up.

The main concern of this approach has been the potential of overtreatment. In setups where the screen and treat approach has been implemented using cytology based screening such as the pap smear, systematic reviews have shown acceptable levels of overtreatment of less than 10%.

To the best of our knowledge, no study has been done in Kenya to evaluate the level of overtreatment when screen and treat is implemented using the visual screening methods. This study will therefore offer an opportunity to have a baseline assessment of possible overtreatment using the screen and treat approach. It will inform policy at Kenyatta National Hospital whether to implement the screen and treat or continue with screen, diagnose and treat approach.

CONCEPTUAL FRAMEWORK

Narrative

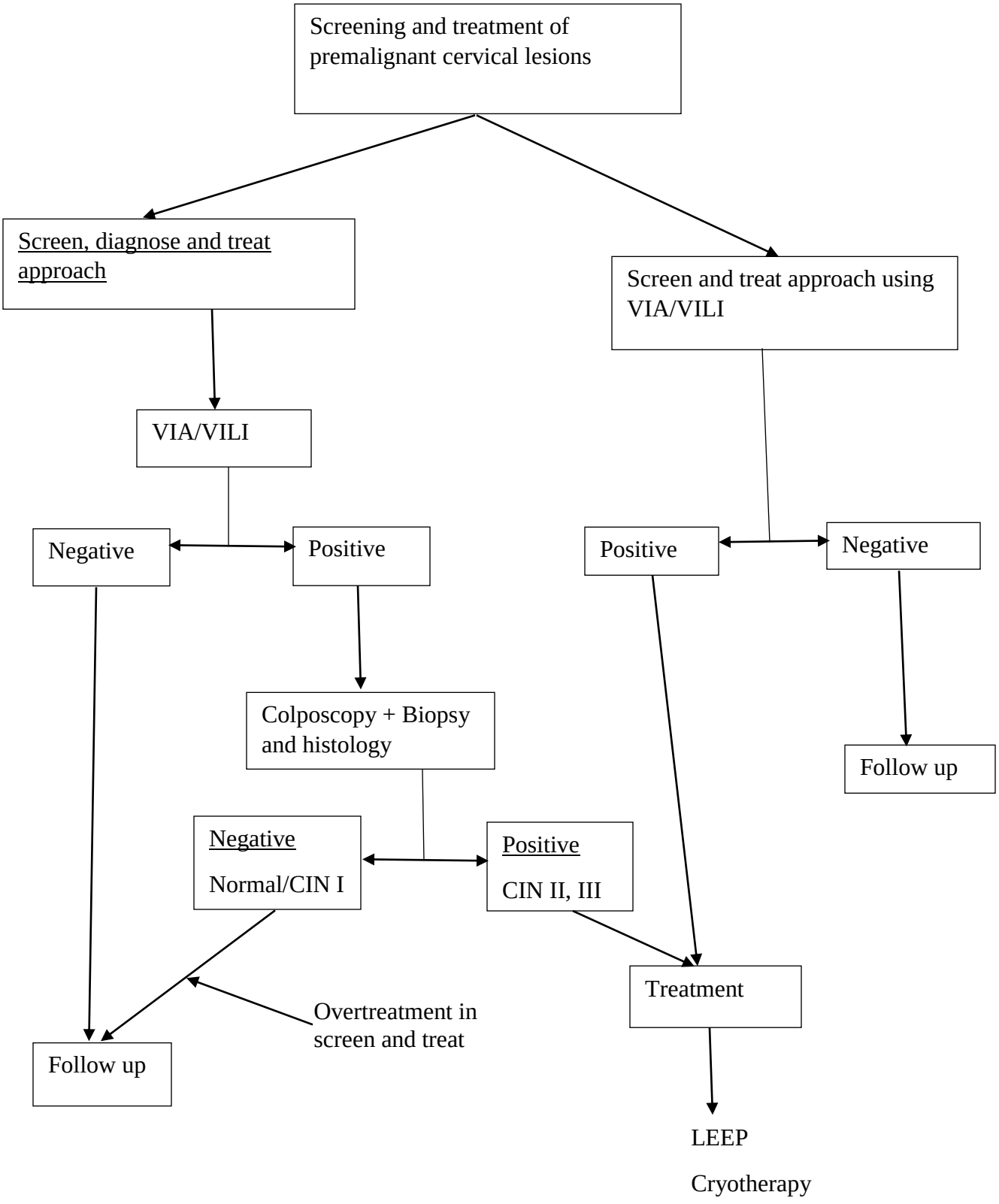
Cancer of the cervix is still a leading cause of cancer mortality among women worldwide. Most of this burden is borne by the developing countries including Kenya. Over the years, research has demonstrated that screening of women leads to discovery of premalignant lesions that when treated appropriately, reduces the incidence of cervical cancer thus reducing mortality.

In Kenya, screening for cancer of the cervix is increasingly being done using VIA/VILI. This is influenced by cost, availability of trained personnel and laboratory infrastructure. Women who screen positive on VIA/VILI are then offered cryotherapy or LEEP in the screen and treat approach. However, at Kenyatta National Hospital women who screen positive on VIA/VILI undergo colposcopy guided biopsy to get a histological diagnosis before treatment is offered. For most premalignant lesions, the women undergo LEEP and further follow up after treatment. This forms the screen, diagnose and treat approach. The challenges associated with this include loss to follow up, high number of clinic visits and increased cost to patients.

To address these challenges, the screen and treat approach has been recommended by WHO. This involves offering treatment to all those who screen positive before definitive diagnosis. The approach is envisaged to reduce the number of clinic visits and reduce loss to follow up.

However, there is concern of possible overtreatment where women who would have had negative histology results following biopsy all end up getting treatment. This concern has led to guidelines being set of what should be acceptable level of overtreatment.

Schematic


Screening and treatment of premalignant cervical lesions
Screen, diagnose and treat approach
Screen and treat approach using VIA/VILI
VIA/VILI
Negative
Positive
Positive
Negative
Colposcopy + Biopsy and histology
Follow up
Negative
Normal/CIN I
Positive
CIN II, III
Treatment
Overtreatment in screen and treat
Follow up
LEEP
Cryotherapy

Research question

What is the prevalence of cervical intraepithelial neoplasia among women who underwent colposcopy guided histology following a positive VIA/VILI screen at Kenyatta National Hospital between 2012 and 2016?

Broad objective

To determine the prevalence of cervical intraepithelial neoplasia among women who underwent colposcopy guided histology following a positive VIA/VILI screen at KNH between 2012 and 2016.

Specific objectives

Among women who undergo colposcopy guided histology following a positive VIA/VILI screen in KNH between 2012 and 2016:

1. To determine the sociodemographic and clinical characteristics.
2. To determine the proportion with positive histology findings.
3. To determine the CIN classification of those with positive histology findings.

METHODOLOGY

Study design

This was a cross - sectional study in which records of 425 women who underwent colposcopic biopsy and histology at Kenyatta National Hospital between January 2012 and December 2016 after positive VIA/VILI screening were reviewed.

Study setting

The study was conducted at the Kenyatta National Hospital reproductive health clinic 66. The clinic offers specialized reproductive health services including cancer of the cervix screening, colposcopy and treatment of premalignant lesions using LEEP. The clinic serves as the referral center for most facilities within Nairobi that have no access to colposcopy and LEEP services. It conducts about 10 – 12 colposcopy and 3 - 5 LEEP procedures per week. These procedures are conducted by different colposcopists at the facility. The histology is conducted at the University of Nairobi histology laboratory.

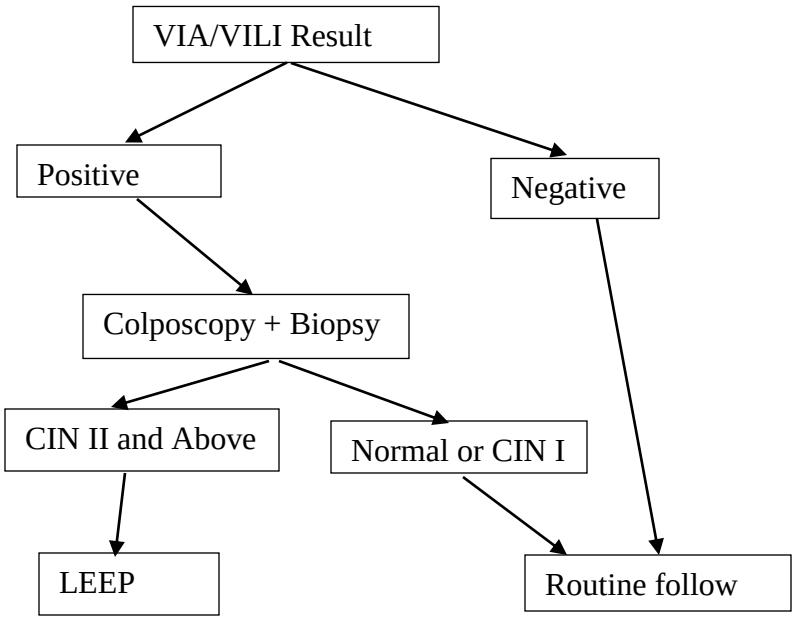


Figure 1. Kenyatta National Hospital screening and treatment flowchart for premalignant cervical lesions using VIA/VILI screening

Study population:
The study population were women aged 15 years and above who were seen at KNH clinic 66 between January 2012 and December 2016 following cervical cancer screening using VIA/VILI

Inclusion criteria

i. Women with positive VIA/VILI screening results who underwent colposcopy guided biopsy and histology with results available in the patient's file.

Exclusion criteria

i. Women with macroscopic invasive disease.
ii. Women with history of previous treatment of premalignant lesions eg. LEEP, cryotherapy
iii. Women who have undergone hysterectomy

Sample Size
We used Fisher's formula thus $\boldsymbol{n = \frac{Z^2 \times p\,(1-p)}{d^2}}$

Where

n – The required sample size

Z – Standard normal at 95% CI = 1.96

p – Proportion of VIA/VILI positive patients with positive colposcopy results = 50% (Albert et al.)(21).

d – The precision error for estimating the proportion = 5%

n = 384

There was an additional 10% to cater for files with missing data. Thus total sample size needed was 384 + 38.4 = 423

This study sampled **425** patients to estimate the proportion of positive colposcopy guided histology results within 5% level of significance.

Sampling Procedure

We used a convenient sampling procedure. A list of all registered patients who tested positive for VIA/VILI test between January 2012 and December 2016 and underwent colposcopy guided biopsy and histology was drawn. We then used the list to retrieve the patients' files. The files for the eligible patients with complete information were retrieved consecutively until the desired sample size was achieved.

Data Variables

Independent variables

Positive VIA/VILI screening results

Dependent variables

The outcome variables of interest include the number of patients whose histology results were positive for CIN and the CIN classification.

Data Collection

Data was collected using a standardized data abstraction form. This was done by the help of two research assistants. The research assistants were medical officers recruited from Kenyatta National Hospital. Theyunderwent training on the use the questionnaire before the commencement of data collection. Data on both exposure and outcome variable of interest was retrieved from patients' files. During the research period the patients' files and records obtained

from them were kept under lock and key and were only accessible to the principal investigator. The files were then handed back to the hospital central records department.

Data Management

All the collected data were de-identified and anonymized. Data was entered into a Microsoft excel database with inbuilt consistency and validation checks. It was cleaned and stored in a password protected external storage device [USB] with data being accessible to the principle investigator and supervisors.

Data Analysis

Data was analyzed using SPSS version 21.0 for statistical analysis. Categorical data was summarized into percentages and continuous variables into means. The proportion of women with CIN was presented as a percentage with 95% confidence interval. CIN classification of the true positives was presented as percentages. Associations between the CIN and clinical characteristics was done using chi square test of associations.

Ethical Considerations

Ethics approval was sought from the Kenyatta National Hospital - University of Nairobi Ethics and Research committee. Administrative permission was sought from the Department of Obstetrics and Gynaecology of The University of Nairobi and the hospital administration through the Assistant Director for reproductive health's office.

No consent was required as this was a retrospective study using patients' records

Confidentiality was maintained in handling the study records. The records were assigned serial numbers and all identifiers to the patient omitted in the study records. These records were only used for research purposes and accessed by the principal investigator and the supervisorsInformation sharing – important findings from the study will be made available to

policy makers at the Ministry of Health, Kenyatta National Hospital Management and the Department of Obstetrics and Gynaecology, University of Nairobi.

Study limitation

The main limitation was possible inter observer variability in reporting of VIA/VILI, colposcopy guided biopsy and histology evaluation.

The study was not able to assess the sensitivity and specificity of VIA/VILI since the records of those who screened negative were not available.

However, since about 50% of the patients were referred from peripheral facilities the findings of this study are generalizable to our setting.

RESULTS

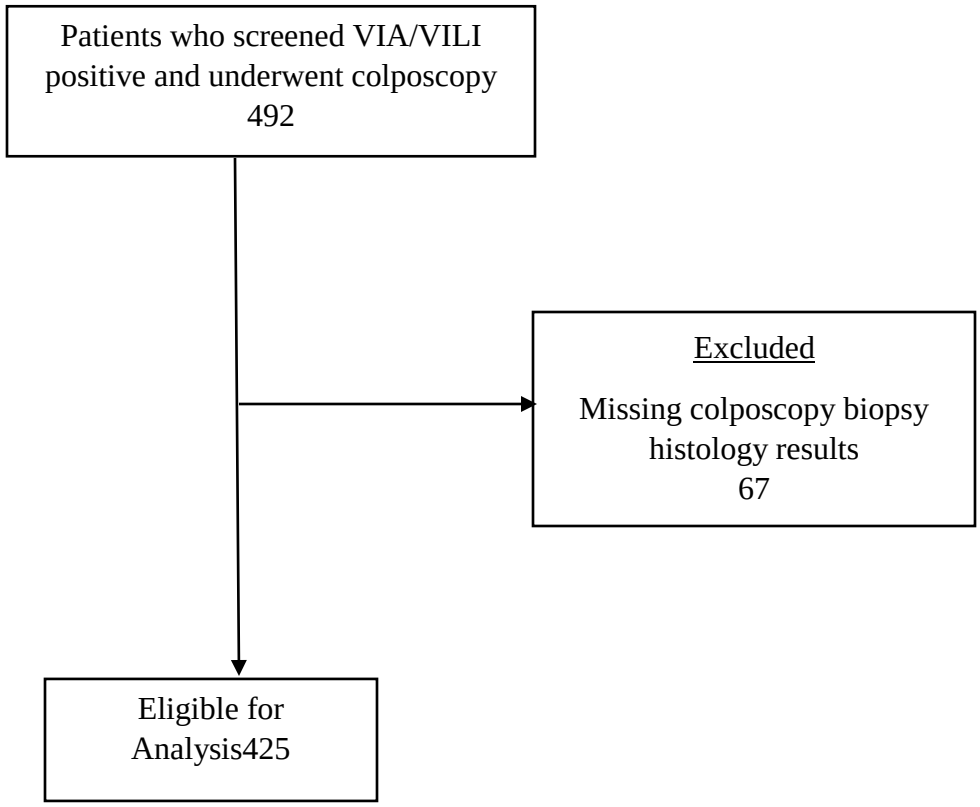


Figure2.Eligibility flowchart for women who screened VIA/VILI positive and underwent colposcopy and biopsy at Kenyatta National Hospital between 2012 and 2016.

As shown in figure 1, a total of 492 of all the patients who underwent colposcopy following a positive VIA/VILI screening results during the study period were considered for analysis.After assessment of the records, sixty seven were missing the histology results thus excluded from the study. The remaining 425 met the inclusion criteria and were included in the analysis.

Table 1: Sociodemographic characteristics of patients who screened VIA/VILI positive and underwent colposcopic biopsy and histology at Kenyatta National Hospital, 2012 – 2016

	Frequency (%)	Mean
Age		
≤ 20 years	7 (1.6)	
21 – 30 years	90 (21.2)	38.6
31 – 40 years	166 (39.1)	
41 – 50 years	120 (28.2)	
51 – 60 years	33 (7.8)	
> 60 years	9 (2.1)	
Marital Status		
Single	105 (24.7)	
Married	271 (63.8)	
Separated	11 (2.6)	
Divorced	2 (0.5)	
Unknown	36 (8.5)	
Parity		
Nulliparous	24 (5.6)	
Primipara	65 (15.3)	
Multiparous	336 (79.1)	
Level of Education		
None	7 (1.6)	
Primary	130 (30.6)	
Secondary	106 (24.9)	
College	78 (18.4)	
Unknown	104 (24.5)	

In table 1 above, the mean age of women undergoing colposcopy was 38.6 years with 67.3% being between 31 and 50 years. Majority of the women were married accounting for 63.8%. About 3.1% of the women were previously married and were currently either separated or divorced. Over 79% were multiparous and had some formal education.

Table 2: Association between siciodemographic characteristics and CIN among patients who screened VIA/VILI positive and underwent colposcopic biopsy and histology at Kenyatta National

Hospital, 2012 – 2016

	N = 425			
Variable	Abnormal*	Negative for CIN	OR (95% CI)	P value
Age				
≤ 20	4 (57.1)	3 (42.9)	1.0	
21 – 30	43 (47.8)	47 (52.2)	1.1 (0.2-10.5)	0.633
31 – 40	87 (52.4)	79 (47.6)	1.4 (0.2-8.5)	0.806
41 – 50	74 (61.7)	46 (38.3)	2.0 (0.1-5.9)	0.811
51 – 60	15 (45.5)	18 (54.5)	1.0 (0.2-12.5)	0.574
> 60	4 (44.4)	5 (55.6)	1.7 (0.2-18.8)	0.614
Parity				
Nulliparous	13 (54.2)	11 (45.8)	1.0 (0.4-2.3)	0.977
Primipara	33 (50.8)	32 (49.2)	0.9 (0.5-1.5)	0.647
Multiparous	181 (53.9)	155 (46.1)	1.0	
Marital Status				
Unknown	20 (55.6)	16 (44.4)	1.0	
Single	57 (54.3)	48 (45.7)	1.0 (0.4-2.0)	0.895
Married	6 (54.5)	5 (45.5)	1.0 (0.4-1.8)	0.953
Separated	142 (52.4)	129 (47.6)	0.9 (0.4-1.8)	0.722
Divorced	2 (100.0)	0	-	0.999
Level of Education				
Unknown	47 (45.2)	57 (54.8)	0.7 (0.4-1.3)	0.248
None	63 (59.4)	43 (40.6)	1.3 (0.7-2.3)	0.449
Primary	73 (56.2)	57 (43.8)	1.1 (0.6-1.9)	0.746
Secondary	2 (28.6)	5 (71.4)	0.3 (0.1-1.9)	0.217
College	42 (53.8)	36 (46.2)	1.0	

***Abnormal - CIN I, CIN II, CIN III and microinvasive disease**

From table 2 above, none of the sociodemographic characteristics had significant association with development CIN. In the level of education, those with secondary school education and the women whose level of education were unknown were noted to have lower risk of developing CIN

Table 3: Clinical characteristics of patients who screened VIA/VILI positive and underwent colposcopic biopsy and histology at Kenyatta National Hospital, 2012 – 2016

	N = 425			
Variable	Abnormal*	Negative for CIN	OR (95% CI)	P value
HIV serostatus				
Unknown	22 (44.9)	27 (55.1)	1.0 (0.5-1.8)	0.990
Positive	97 (71.3)	39 (28.7)	3.0 (1.9-4.8)	<0.001
Negative	108 (45.0)	132 (55.0)	1.0	
Patient on HAART				
Yes	94 (72.9)	35 (27.1)	2.7 (0.2-44.1)	0.489
Unknown	2 (40.0)	3 (60.0)	0.7 (0-18.1)	0.810
No	1 (50.0)	1 (50.0)	1.0	
Currently on FP				
Yes	93 (52.5)	84 (47.5)	1.0 (0.7-1.5)]	0.964
Unknown	24 (55.8)	19 (44.2)	1.1 (0.6-2.2)	0.720
No	95 (52.8)	85 (47.2)	1.0	

***Abnormal - CIN I, CIN II, CIN III and microinvasive disease**

In table 3 above, HIV infection was noted to have significant association with intraepithelial lesions and microinvasive disease OR 3.095% CI (1.9-4.8), P(<0.001). Of the HIV positive, 94.6% were on HAART. However, the HIV treatment status had no significant effect on the risk of developing CIN.Family planning use was not associated with risk of CIN.

Table 4: Histology findings of patients who screened VIA/VILI positive and underwent colposcopic biopsy and histology at Kenyatta National Hospital, 2012 – 2017

	Frequency (%)
Normal and CIN I	277(65.2)
Negative for intraepithelial lesion or malignancy	198 (46.6)
CIN I	79 (18.6)
CIN II and Above	148(34.8)
CIN II	82 (19.3)
CIN III	48 (11.3)
Microinvasive Disease	18 (4.2)

In table 4 above, among women who had positive VIA/VILI screening results 46.6% had normal histology results. Abnormal histology findings(CIN I, CIN II, CIN III or microinvasive disease) was noted in 53.4%. Of these 18.6% had CIN I while only 34.8% had CIN II and above.

Table 5. CIN classification according to age and HIV serostatus among women who screened VIA/VILI positive and underwent colposcopic biopsy and histology at Kenyatta National Hospital, 2012 – 2016

	Colposcopy Histology Results					
Characteristic	Normal	CIN I	CIN II	CIN III	Microinvasive Disease	P -value
Age group						
≤ 20	3 (42.9)	2 (28.6)	2 (28.6)	0	0	0.404
21 – 30	47 (52.2)	14 (15.6)	18 (20.0)	9 (10.0)	2 (2.2)	
31 – 40	79 (47.6)	25 (15.1)	29 (17.5)	21 (12.7)	12 (7.2)	
41 – 50	46 (38.3)	33 (27.5)	26 (21.7)	12 (10.0)	3 (2.5)	
51 – 60	18 (54.5)	3 (9.1)	6 (18.2)	5 (15.2)	1 (3.0)	
> 60	5 (55.6)	2 (22.2)	1 (11.1)	1 (11.1)	0	
HIV serostatus						
Negative	132 (55.0)	38 (15.8)	38 (15.8)	22 (9.2)	10 (4.2)	
Positive	389 (28.7)	30 (22.1)	37 (27.2)	22 (16.2)	8 (5.9)	<0.001
Unknown	27 (55.1)	11 (22.4	7 (14.3)	4 (8.2)	0	

Patients with HIV infection were noted to be likely to have a higher degree of intraepithelial neoplasia. In this group, the proportion of those with CIN II and above was higher at 49.2% compared to the general population at 34.8%. The age of the patient did not significantly affect the distribution of the CIN lesions. Table 5.

DISCUSSION

Although uptake of screening for cancer of the cervix is very low(3.2%), the average age of women attending screening is 38.6(27). A single screen at this age can reduce the lifetime risk of invasive disease by 25% - 36%(18). However, this falls short of the national guidelines that recommends routine screening from 25 years(28). Therefore, more effort to encourage early routine screening in the general population is needed.

The proportion of women with abnormal histology following a positive VIA/VILI screening results was 53.4% while those with CIN II and above was 34.8% as shown in table 4.These findings are comparable to findings in other studies that reported proportion of CIN II and above of between 20% and 38%(29–31). This low congruence between VIA/VILI positive screening results and presence of CIN could be due to lack of standardized training in reporting VIA/VILI screening results. For instance Amidu et al found variability of 13% and 16% on the sensitivity of VIA and VILI respectively between nurses and physicians with the physicians having better performance(32). It is possible that some patients with conditions such as ectropion and cervicitis could have been reported as positive screening results.

This lowagreement between the screening results and presence of CIN II and above poses a great challenge in using VIA/VILI to implement the screen and treat strategy.This study estimates possible overtreatment at 65% in programs implementing the screen and treat strategy using VIA/VILI.

Microinvasive disease accounted for 4.2% of our study population. Therefore, if the screen and treat strategy were to be implemented with VIA/VILI, this population would be at risk of undertreatment. A study in Busia Kenya reported a similar rate of 3%, however, their population was of between ages 30 to 39(30). Our study found that HIV infected patients were more likely

to have higher grade CIN lesions and microinvasive disease possibly increasing the risk of under treatment in this subgroup in set ups using VIA/VILI to screen and treat.

Although VIA/VILI screening can be used as an alternative to the pap smear due to its comparable sensitivity and specificity in a set up without robust routine screening, the recommendation of treating all those who test positive on this screening modality becomes challenging to implement in our set up given that up to 65% of these patients would require just routine follow up screening without definitive treatment. This situation poses a dilemma to program managers as the limited resources available end up being channeled to treating patients who do not need the treatment instead of increasing access to screening for the whole population. When screen and treat is implemented using pap smear screening, the proportion of patients with CIN II and above is 77.1%. However, if this is restricted to patients with HSIL on screening, the proportion is 92.2% thus overtreatment is estimated at 7.8%(33)This is within the National Health service Cervical Screening Program (NHSCSP), 2010 guidelines recommendation of less than 10%.

Among the HIV infected patients, 94.6% were on HAART. This underscores the achievements of the government policy to have 90% of those who are HIV positive on treatment. However, the treatment status does not eliminate the increased risk of developing CIN and subsequent invasive disease in women who are HIV infected.

CONCLUSION

Our study shows possible overtreatment of up to 65% using the screen and treat approach with VIA/VILI due to the low congruence between VIA/VILI positive screening results and presence of CIN II and above.

RECOMMENDATIONS

1. We recommend the screen, diagnose and treat approach while screening with VIA/VILI in our set up
2. More research and development of guidelines on how to minimize overtreatment before the screen and treat approach is implemented with VIA/VILI.

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APPENDIX

Appendix 1: Data Abstraction Form

Serial No._____

Probability of CIN among women who screen VIA/VILI positive and undergo colposcopy guided histology at KNH using colposcopy guided histology as gold standard

Bio data

Age _____ Parity _____+ _____

Marital Status:

Single ☐ Married ☐ Separated ☐ Divorced ☐ Unknown ☐

Level of Education:

None ☐ Primary ☐ Secondary ☐ College ☐ Unknown ☐

Clinical Data

HIV Serostatus: Unknown ☐ Negative ☐ Positive ☐

If HIV positive, is patient on HAART Yes ☐ No ☐ Unknown ☐

Family Planning Use:

Current: Yes ☐ No ☐

If yes, Method _____ Unknown ☐

Previous: Yes ☐ No ☐

If yes, Method _____ Unknown ☐

Screening results

VIA Negative ☐ Positive ☐ Suspicious for cancer ☐ Date ____/____/____

VILI Negative ☐ Positive ☐ Suspicious for cancer ☐ Date ____/____/____

Facility where VIA/VILI done: Kenyatta National Hospital ☐ Other facility ☐

Colposcopy examination

Entire squamocolumnar junction seen: Yes ☐ No ☐

Endocervical curettage (ECC) done: Yes ☐ No ☐

Colposcopy visual findings:

Colour: No lesion ☐ Leukoplakia ☐ Pale-white ☐ Bright-white ☐ Dull-white ☐

Borders: Faint, indistinct, geographic ☐ Smooth, straight outlines ☐ Internal borders ☐

Rolled or peeled edges ☐

Vessels: No vessel ☐ Branching normal ☐ Fine punctation ☐ Coarse punctation ☐

Fine Mosaic ☐ Coarse Mosaic ☐ Atypical Vessels ☐

Size: 1 quadrant ☐ 2 quadrants ☐ 3 quadrants ☐ 4 quadrants ☐

Colposcopy Histology results

Normal ☐ CINI ☐ CIN II ☐ CINIII ☐ Microinvasive disease ☐

Date ____/____/____

ECC results

Not done ☐ Normal ☐ CINI ☐ CIN II ☐ CINIII ☐