“INTEROBSERVER VARIABILITY OF VISUAL INSPECTION METHODS BETWEEN PHYSICIAN AND NURSE FOR CERVICAL CANCER SCREENING: A CROSS SECTIONAL STUDY”

REG.NO. BJ0110001

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

MASTER OF SURGERY

in

OBSTETRICS AND GYNAECOLOGY

**DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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ENDORSEMENT

This is to certify that the dissertation entitled **"INTEROBSERVER VARIABILITY OF VISUAL INSPECTION METHODS BETWEEN PHYSICIAN AND NURSE FOR CERVICAL CANCER SCREENING: A CROSS SECTIONAL STUDY"** is a bonafide research work done by **CANDIDATE REG NO. BJ0110001**.

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LIST OF ABBREVIATIONS USED

AAR	= Age Adjusted Incidence Rate
ACCP	= Alliance for Cervical Cancer Prevention
ACS	= American Cancer Society
AGC	= Atypical glandular cells
AIS	= Adenocarcinoma in situ
ASC	= Atypical Squamous Cells
ASCUS	= Atypical Squamous Cells of Undetermined Significance
CDC	= Centers for Disease Control and Prevention
CIN	= Cervical Intraepithelial Neoplasia
CT	= Computed Topography
Cx	= Cervix
DVI	= Direct Visual Inspection
FIGO	= Federation Internationale de Gynecologie et d'Obstetrique
HBCR	= Hospital Based Cancer Registries
HIV	= Human Immunodeficiency Virus
HPV	= Human Papilloma Virus
HPV-DNA	= Human Papilloma Virus- Deoxyribonucleic acid
HSIL	= High grade Squamous Intra epithelial Lesion
IARC	= International Agency for Research on Cancer
IMB	= Inter Menstrual Bleeding
K	= Kappa
LEEP	= Loop Electrosurgical Excision Procedure
LSIL	= Low grade Squamous Intra epithelial Lesion
MRI	= Magnetic Resonance Imaging
NCRP	= National Cancer Registry Programme

NPV = Negative Predictive Value

OCP = Oral Contraceptive Pills

PAP = Papanicolaou

PBCR = Population Based Cancer Registries

PCB = Post Coital Bleeding

PET = Positron-Emission Tomography

PMB = Post Menopausal Bleeding

PPV = Positive Predictive Value

RCI = Reid Colposcopic Index

SEA = South East Asia

U.S FDA = United States Food and Drug Administration

USPSTF = United States Preventive Services Task Force

VIA = Visual Inspection with Acetic acid

VIAM = Visual Inspection with Magnification

VILI = Visual Inspection with Lugol's Iodine

WDPV = White Discharge per Vagina

ABSTRACT

Objective: To evaluate and compare predictive value of visual inspection methods and assess the concordance of results between physician and nurse for cervical cancer screening as compared to colposcopy and histopathology.

Study design: Cross sectional study

Study place: Colposcopy Clinic at Gynaecology Outpatient department (OPD), K.L.E. University Teaching Hospital, Belgaum

Source of data: All sexually active women from age 20 to 50 years attending Colposcopy Clinic with complaints of persistent vaginal discharge, inter menstrual bleeding, post coital bleeding, suspicious looking cervix and positive screen test.

Study interventions: VIA and VILI by both physician and nurse and the findings were interpreted independently. This was followed by colposcopy done by a gynaecologist blinded to the results of VIA and VILI and directed biopsy was taken if indicated. Negative colposcopy and histopathology were considered as the reference standard. Test positivity was defined by histopathology report of cervical intraepithelial neoplasia 2 (CIN 2) and above.

Results: VIA by doctor had a higher sensitivity (100% versus 88.23%) and higher specificity (57.5% versus 56.2%) when compared with the nurse. There was almost perfect agreement between their VIA findings (kappa=0.83). VILI findings of doctor had a sensitivity and specificity of 82.3% and 59.65% respectively, while nurse had a sensitivity of 76.47% and specificity of 58.36%.

There was almost perfect agreement (kappa=0.87) between VILI by the doctor and nurse.

Conclusion: Visual inspection can be performed reliably by trained nurses and doctors and is an effective screening option in low resource settings. Intensive training and periodic reinforcement sessions are needed so as to reduce the false positive results.

Keywords:

Cervical cancer; Colposcopy; Paramedical worker; Visual inspection with acetic acid; Visual inspection with Lugol’s Iodine,

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Chapter 1

Introduction

INTRODUCTION

Cervical cancer is an important public health problem that deserves urgent attention. It is an important area of action for any cancer control programme because of the burden of disease, and the potential for effective prevention via screening.

Cervical cancer is the second most common cancer among women worldwide, with an estimated 529,409 new cases and 274,883 deaths in 2008.[1] About 86% of the cases occur in developing countries, representing 13% of female cancers. Worldwide, mortality rates of cervical cancer are substantially lower than incidence with a ratio of mortality to incidence of 52%.[1] Majority of cases are squamous cell carcinoma and adenocarcinomas are less common.

India has a population of 366.58 million women ages 15 years and older who are at risk of developing cervical cancer. Current estimates indicate that every year 132,000 women are diagnosed with cervical cancer and 74,000 die from the disease hence, every 7th minute a woman dies due to cervical cancer.[2]

Cervical cancer ranks as the 1st most frequent cancer among women in India, and the 1st most frequent cancer among women between 15 and 44 years of age.[1]

This condition affects not only the health and lives of women, but also their children, families, and their community. This extended impact is often undervalued when setting health priorities and requires greater consideration by policy makers.[3]

Unlike many other cancers, cervical cancer is mostly preventable. Because of the slow progression of cervical precancer to cervical cancer, there is a window of upto ten years or more to detect and treat precancerous lesions and prevent their progression to invasive cancer.[3]

Cancer of the cervix can be prevented in two ways: (1) preventing initial Human Papilloma Virus (HPV) infection through vaccination and (2) screening for precancerous lesions and providing early treatment to prevent progression to cancer.[4] HPV vaccination is costly and affordable only by the affluent.

While high quality cytology, screening may not be feasible for wide scale implementation in developing countries because of lack of necessary infrastructure, quality control and poor sensitivity of cytology, alternative screening modalities such as visual screening techniques and HPV-DNA can be explored.

Routine cytological screening of women has resulted in a dramatic decline in cervical cancer deaths over the past four decades in wealthier countries.

A key reason for continuing high mortality in the developing world is the shortage of efficient, high-quality precancer screening and treatment programs in those regions. Most developing countries lack the infrastructure and trained personnel needed to replicate the cytology-based, multi-visit approach used in wealthier countries to detect precancerous lesion i.e, pap smears followed by colposcopy and biopsy.[5]

The challenges and failure in implementing cervical cytology screening in poor resource settings has resulted into exploring alternative methods for down staging of the cervical cancer during last decade. Some of these methods are:

Single visit approach using Visual Inspection of Cervix with Acetic Acid (VIA), Visual Inspection of Cervix with Lugol's Iodine (VILI), Self collected samples for cytology and Human Papilloma Virus (HPV)-DNA testing, education and counselling, Increasing coverage by camp approach, Low cost HPV tests, HPV vaccines.[2]

VIA and VILI are two modifications of a direct visual assessment of the cervix, different only in regard to the solutions applied to enhance the cervical lesions. They are based on the ability of the trained healthcare workers to detect acetowhite areas or yellow non-iodine uptake areas in the cervical transformation zone.

A range of personnel including doctors, nurses, midwives and paramedical health workers can be rapidly trained to perform VIA and VILI in short courses of 5–10 days duration.[7]

A wide range of teaching materials is now available for VIA training courses, making VIA particularly attractive as a screening test in low-resource settings. The ability to utilize mid-level providers is important as it extends accessibility to cervical cancer screening in regions where physician time and resources are scarce.[4]

Cervical cancer prevention services include counselling, a screening test (with or without a diagnostic test), and precancer treatment for women who test positive. These services can be provided at various levels of health facilities by a wide range of health personnel. Programs can implement a health facility-based (static) approach, a mobile (outreach) approach, or combine the two approaches.[3]

In addition, a well functioning referral network is essential to ensure continuity of care for women needing additional diagnostics and treatment. Trained community health workers/volunteers can be engaged to build and maintain links with the community to encourage women to utilize the service, to track women who need to be treated and followed up, and to provide community-based palliative care.[3]

As a result of ACCP experience in providing training to nurses and doctors in these techniques, it is now widely agreed that training should be competency based, combining both didactic and hands-on approaches.[6]

In this study, we evaluate the feasibility of training and implementing visual inspection methods by nurse by assessing concordance of result between physicians and nurses.

Chapter 2

Objectives

OBJECTIVES

The objective of the study was to evaluate and compare test performance of visual inspection methods by doctor and nurse for cervical cancer screening.

Chapter 3

Review of Literature

REVIEW OF LITERATURE

Epidemiology

Frequency

Worldwide

World Health Organization reported that, cancer of the cervix is the second most common cancer in women worldwide, with about 500000 new cases and 250000 deaths each year. Almost 80% of cases occur in low-income countries, where cervical cancer is the second most common cancer in women. Virtually all cervical cancer cases (99%) are linked to genital infection with human papillomavirus (HPV), which is the most common viral infection of the reproductive tract.[10]

Globocan 2008 reports that, cervical cancer is the third most common cancer in women, and the seventh overall, with an estimated 530 000 new cases in 2008. More than 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers.[11]

Overall, the mortality: incidence ratio is 52%, and cervical cancer is responsible for 275 000 deaths in 2008, about 88% of which occur in developing countries: 53 000 in Africa, 31 700 in Latin America and the Caribbean, and 159 800 in Asia.[11]

Cervical Cancer Incidence and Mortality Worldwide in 2008 Summary[11]

Estimated numbers (thousands)	Cases	Deaths
World	530	275
More developed regions	76	32
Less developed regions	453	242
WHO Africa region (AFRO)	75	50
WHO Americas region (PAHO)	80	36
WHO East Mediterranean region (EMRO)	18	11
WHO Europe region (EURO)	61	28
WHO South-East Asia region (SEARO)	188	102
WHO Western Pacific region (WPRO)	105	46
IARC membership (22 countries)	193	96
United States of America	11	3
China	75	33
India	134	72
European Union (EU-27)	31	13

The frequency varies considerably between developed and developing countries, however: Cervical cancer is the second most common cancer in developing countries, but only the tenth most common in developed countries. Similarly, cervical cancer is the second most common cause of cancer-related

deaths in women in developing countries but is not even among the top 10 causes in developed countries.[12]

The American Cancer Society (ACS) estimates that in the United States, 12,170 new cases of cervical cancer will be diagnosed in 2012.[14] Internationally, more than 500,000 new cases are diagnosed each year; rates vary widely, ranging from an annual incidence of 4.5 cases per 100,000 in Western Asia to 34.5 per 100,000 women in Eastern Africa.[15] In industrialized countries with well-established cytology screening programs, the incidence of cervical cancer ranges from 4 to 10 per 100,000 women.

The incidence of CIN 2/3 disease in the US is about 150 per 100,000 women, with the peak incidence around 800 per 100,000 women in the 25-29 year age group. The incidence of abnormal cytology screens for all ages is an order of magnitude larger, at 7800 per 100,000 women.[16]

The annual age-specific assessments of cervical cancer in 187 countries from 1980 to 2010 show that global cervical cancer incidence increased from 378,000 cases per year in 1980 to 454,000 cases per year in 2010 (annual rate of increase, 0.6%). Cervical cancer death rates have been decreasing, but the disease still accounted for 200,000 deaths in 2010; in developing countries, 46,000 of these women were aged 15-49 years, and 109,000 were aged 50 years or older.[17]

An estimated 12,170 cases of invasive cervical cancer are expected to be diagnosed in 2012. Incidence rates have declined over most of the past several decades in both white and African American women. Since 2004, rates have

decreased by 2.1% per year in women younger than 50 years of age and by 3.1% per year in women 50 and older.[16]

An estimated 4,220 deaths from cervical cancer are expected in 2012. Mortality rates declined rapidly in past decades, due to prevention and early detection as a result of screening with the Pap test, but have slowed in recent years. From 2004 to 2008, rates decreased by 2.6% per year in African American women and were stable in white women.[16]

South East Asia Region

The SEA Regional Office presented an information paper on cervical cancer and its prevention in the South-East Asia Region during 2008. There are 1.3 million estimated cases of cancers resulting in 850,000 cancer deaths each year, which accounts for 9 percent of deaths from all causes. The most recent estimates for cervical cancer, from Globocan 2002, estimated 177,402 cases of cervical cancer with 96,091 deaths every year.[17]

Indian scenario

The Indian Council of Medical Research initiated a network of cancer registries under the National Cancer Registry Programme (NCRP) in 1981 and data collection commenced in these registries from January 1982. The results on incidence rates provided by the Population Based Cancer Registries (PBCRs) have shown the variation in patterns of cancer in general and that of cancer cervix in particular. Cancer of the cervix has been the most important cancer in women in India, over past two decades. All the urban Population Based Cancer Registries

at Bangalore, Bhopal, Chennai, Delhi and Mumbai have shown a statistically significant decrease in incidence rates of this site of cancer. Since over 70% of the Indian population resides in the rural areas, cancer cervix still constitutes the number one cancer. Based on the data of the PBCRs, the estimated number of new cancers during 2007 in India was 90,708.[18]

In the hospital based cancer registries (HBCRs), cancer of the cervix is the leading site of cancer in Bangalore and Chennai, the second leading site in Mumbai and Thiruvananthapuram and the third leading site in Dibrugarh. This site of cancer constitutes between 11.4 (Thiruvananthapuram) to 30.7% (Chennai) of all cancers in women in these five HBCRs. The rise in the occurrence of cancer was at the later age in Thiruvananthapuram as compared to the other four HBCRs. Over 63 to 89% of all cervical cancers had regional disease at the time of presentation. Around 40% of all cervical cancer patients in Bangalore, Chennai and Mumbai did not receive treatment at the Reporting Institution despite having had a diagnosis of cervical cancer.[18]

Rank, relative proportion (%) of all cancer in females, crude (CR) and age adjusted (AAR) incidence rates per 100,000 person for cancer of the cervix in the population based cancer registries (PBCRs) under the National Cancer Registry Programme of India[18]

PBCRs	Rank	%	CR	AAR
Bangalore	2	15.7	14.3	18.8
Barshi	1	37	20.0	22.8
Bhopal	2	17.9	12.0	17.7
Chennai	2	18.5	20.3	22.3
Delhi	2	14.9	12.3	17.4
Mumbai	2	13.2	11.5	13.4
Ahmedabad	2	18.6	6.9	7.9
Kolkata	2	15.7	13.2	12.3
Dibrugarh District	5	6.6	3.8	5.1
Kamrup Urban district	2	14.4	12.8	17.3
Sichar town	1	20.6	10.6	12.1
Imphal west district	1	15.9	17.2	20.5
Mizoram state	3	13.5	13.7	17.4
Aizwal district	1	15.0	20.6	25.4
Mizoram state excl Aizwal	2	12.0	9.8	12.6
Sikkim state	1	11.1	6.9	10.9

Based on 2004-2005 data for Bangalore, Barshi, Bhopal, Chennai, Delhi, Mumbai, Ahmedabad 2005 data for Kolkata and 2005 – 2006 data for Dibrugarh district, Kamrup Urban District, Silchar Town, Imphal West District, Mizoram State Aizwal District, Mizoram State Excl. Aizwal. Sikkim[18]

Age-related demographics

The Centers for Disease Control and Prevention (CDC) surveillance of screening-detected cancers (colon and rectum, breast, and cervix) in the United States from 2004 to 2006 reported that the incidence of late-stage cervical cancer was highest among women aged 50-79 years.[19] However, cervical cancer may be diagnosed in any woman of reproductive age.

Indeed, rates of cervical adenocarcinoma have been increasing in women under 40 years of age.[20] These cases are less easily detected with Pap test screening, and survivorship is low because cases tend to be detected at a late stage. Moreover, the HPV types causing adenocarcinoma are different from the types causing squamous carcinoma. HPV 16, which is a stronger carcinogen than other HPV types, has been found more frequently in younger women than in older ones.[21,22]

Race-related demographics

Racial variation in cervical cancer rates per 100,000 women in the United States, according to Surveillance Epidemiology and End Results (SEER) data from 2005-2009, was as follows:

- Hispanic - 11.8
- African American - 9.8
- American Indian/Alaska Native - 8.1
- White - 8.0
- Asian/Pacific Islander - 7.2

Except for Asian/Pacific Islanders, women of other races have higher mortality from cervical cancers than their white counterparts in the United States do.[23] Death rates from cervical cancer have been highest among African Americans; however, death rates in African-American women decreased by 2.6% per year from 2004 to 2008 while remaining stable in white women.[13]

Causes

With rare exceptions, cervical cancer results from genital infection with HPV, which is a known human carcinogen.[24-27] Although HPV infections can be transmitted via nonsexual routes, the majority result from sexual contact.

More than 120 different types of the human papillomavirus (HPV) have been isolated; of these types infect the epithelial lining of the anogenital tract and other mucosal areas. In the majority of individuals, HPV infections are transient and asymptomatic with most new infections resolving within 2 years. Epidemiological data from the U.S. National Health and Nutrition Examination Survey determined that the prevalence of HPV infection in a representative sample of women was highest in those aged 20–24 years (44.8%). HPV infection has been firmly established as the primary cause of cervical cancer. It is not clearly understood why HPV infections resolve in certain individuals and result in cervical intraepithelial neoplasias in others, but several factors are thought to play a role; including individual susceptibility, immune status and nutrition, endogenous and exogenous hormones, tobacco smoking, parity, co-infection with other sexually transmitted agents such as HIV, herpes simplex virus type 2 and Chlamydia trachomatis as well as viral characteristics such as HPV type,

concomitant infection with other types, viral load, HPV variant and viral integration. Worldwide, pooled data from case–control studies indicated that HPV DNA could be detected in 99.7% of women with histologically confirmed squamous cell cervical cancer compared with 13.4% of control women. Both HPV infection and cervical cancer are associated with a substantial economic burden.[28]

Worldwide, the plethora of HPV types causing cervical cancer varies from one country to another, however, over 70%, in any given country, are caused by only 2 types, HPV16 and HPV 18.[28]

The progression from HPV infection to cervical cancer occurs over a series of 4 steps: HPV transmission, acute HPV infection, persistent HPV infection leading to precancerous changes, and invasive cancer. More than 40 HPV types can infect the cervix, and researchers continue to refine the importance of various high-risk HPV types. Human papillomavirus types 16 and 18 are responsible for approximately 70% of cervical cancer cases. As a result, tests have been developed to detect HPV in the clinical setting. The U.S. Food and Drug Administration has approved multiple HPV tests for specific uses in cervical cancer screening or follow-up, and additional tests are awaiting approval.[28]

Risk factors

Infection with, and persistence of, HPV are not only associated with age. The risk for HPV acquisition markedly increases with the number of lifetime sexual partners. Co-infection with other sexually transmitted agents, such as

Chlamydia trachomatis and herpes simplex virus, may be associated with risk for HPV infection. Co-infection with HIV may impair the ability of the immune system to control HPV infections. Additional risk factors for cervical cancer include history of smoking, younger age at first intercourse and at first pregnancy, high parity, and long-term use of oral contraceptives. Women previously treated for any CIN has two to three fold increased risk for future cervical cancer, but may not have an increased risk for death from cervical cancer.[28]

HIV infection is associated with a five fold increase in the risk of cervical cancer, presumably because of an impaired immune response to HPV infection.[29]

Signs and symptoms

Early cervical cancer is generally asymptomatic. Symptoms of advanced cervical carcinoma are inter menstrual bleeding, heavier menstrual flow, post menopausal bleeding, postcoital bleeding, foul smelling excessive blood stained discharge per vagina , pelvic pain and low back ache. Patients with advanced cancer will present with signs of advanced disease, such as cachexia, haematuria, pedal oedema, blood stained stool and fistulae formation resulting in urinary and rectal incontinence.[15]

Natural history and progression of cervical cancer

A clear understanding of the natural history of cervical cancer is a key to planning and implementing a rationale screening program. Cervical carcinogenesis model includes 3 steps: HPV infection, progression to high grade

preinvasive lesion and invasion. Most infections (95%) including those with cytologic abnormalities, resolves spontaneously, returning to HPV DNA negativity, often with seropositivity. The direct precursor to cervical cancer is high grade squamous intra epithelial lesions (HSIL) which can progress to cervical cancer over a period of up to 10 years. Most low grade squamous intra epithelial lesions (LSIL) regress especially, incidental cases in younger women below 35 yr of age. Prevalent cases are less likely to regress. Thus, the natural history suggests that the screening initially should focus on women at the higher risk of precancerous lesion-women in their 30's and 40. Cervical cancer most often develops in women after age of 40 and peaks around age 50. Precursor lesions remains detectable up to 10 years before cancer develop, with a peak SIL rate at about 35 years.[30]

Natural history model and clinical data suggest that cervical cancer generally develops slowly from precursors. Therefore, screening can take place infrequently and still have a significant impact on morbidity and mortality. Screening every three years has almost as great an impact (91%) as screening every year (93%) reduction in incidence. Even screening every 10 years can have a significant impact (64%) on incidence. Screening emphasis, then, should be on coverage rather on frequency.[30]

The different screening modalities have been cytology or Pap smear, visual inspection with acetic acid (VIA) or Lugol's Iodine (VILI) and high risk human papilloma virus (HPV) screening.[31]

Diagnosis

Complete evaluation starts with screening with visual inspection methods or Papanicolaou (Pap) testing. Positive results should prompt colposcopy and biopsies with further workup of cervical intraepithelial neoplasia (CIN), including excisional procedures. If pathologic evaluation after loop electrosurgical excision or conization suggests invasive cancer with positive margins, the patient should be referred to a gynecologic oncologist. Patients with suspicious or grossly abnormal cervical lesions on physical examination should undergo biopsy regardless of the cytologic findings.

Once the diagnosis is established, a complete blood count, renal and hepatic function tests, chest x ray and imaging studies should be performed for to look for abnormalities for any possible metastasis.

Cystoscopy and proctoscopy should be performed in patients with a bulky primary tumor to help rule out local invasion of the bladder and the colon. Barium enema studies can be used to evaluate extrinsic rectal compression from the cervical mass.

More complex radiologic imaging studies can be used to guide the choice of therapeutic options as well as for staging. These may include computed tomography (CT), magnetic resonance imaging (MRI), and positron-emission tomography (PET).[15]

Papanicolaou Testing

For many years, the Pap test has been the standard method for cervical cancer screening. Retrospective data have shown that screening with a Pap test reduces the incidence of cervical cancer by 60-90% and the death rate by 90%.[15]

Because of false negatives, the best that a Pap test can do is to reduce the incidence of cervical cancer to 2-3 per 100,000 women. False-negative tests mostly result from sampling error, which can be reduced by ensuring that adequate material is taken from both the endocervical canal and the ectocervix. Smears without endocervical or metaplastic cells should be repeated.[15]

The limitations of the conventional Pap test include limited sensitivity (51%) and a significant proportion of inadequate specimens. In addition, accurate interpretation of conventional Pap tests is often compromised by the presence of artifacts (blood, mucus, obscuring inflammation, scant cellular material, or air-drying artifact).[15]

Newer liquid-based Pap test technologies have become available. In a randomized, controlled trial from the Netherlands that compared liquid-based and conventional cervical cytology, liquid-based cytology reduced the proportion of unsatisfactory specimens from 1.1% to 0.3% and eliminated obscuring blood, poor fixation, cytolysis, and insufficient spreading of cells as causes of unsatisfactory results.[32]

With liquid-based cytology, however, older women (primarily those 55-60 years of age) were more likely to have a sample called unsatisfactory.

Nevertheless, 18-month follow-up showed that women with unsatisfactory results by either method were not at higher risk for cervical abnormalities.[32]

ThinPrep Papanicolaou test

Test samples for the ThinPrep Pap test are collected the same way as those for the conventional Pap test. However, the specimen is placed in a preservative solution rather than on a slide. An automated processor prepares the sample and makes a uniform slide for review. Mucus and blood are removed in the process. The ThinPrep Papanicolaou test was approved in 1996 by the US Food and Drug Administration (FDA) as an alternative to the traditional conventional smear.[15]

Human Papillomavirus Testing

The Hybrid Capture II assay for HPV was approved by the FDA in 2003 as a new approach for cervical cancer. This test is useful for interpreting equivocal results from a Pap test. If a woman has a Pap test result showing ASCUS but a subsequent HPV test is negative, she can be rescreened with Pap testing in 3 years; if the HPV test is positive, then additional workup with a colposcopy is indicated.

The ACS guidelines favor using HPV testing with cytology in women aged 30 years and older. If both tests are negative, then the next Pap test can be delayed for 5 years.[15]

Imaging Studies for Metastasis

A routine chest radiograph is obtained to help rule out pulmonary metastasis. Chest radiography may be considered optional for disease that is stage IB1 or lower.[33]

A CT scan of the abdomen and pelvis is performed to look for metastasis in the liver, lymph nodes, or other organs and to help rule out hydronephrosis or hydroureter. MRI or positron-emission tomography (PET) scanning is an alternative to CT scanning; in fact, PET scanning is now recommended for patients with stage IB2 disease or higher.[33]

Magnetic resonance whole-body diffusion-weighted imaging scanning has been used to distinguish uterine cervical carcinoma from normal uterine cervix. This technique can also differentiate metastatic nodes from benign nodes.[34]

Surgical Staging

Clinical staging protocols can fail to demonstrate pelvic and aortic lymph node involvement in 20-50% and 6-30% of patients, respectively. For that reason, surgical staging sometimes is recommended. Pretreatment surgical staging is the most accurate method of determining the extent of disease.

However, there is little evidence to suggest that routine surgical staging yields any significant improvement in overall survival. Therefore, the decision whether to perform pretreatment surgical staging should be made on an

individual basis after a thorough nonsurgical workup, including fine-needle aspiration of lymph nodes, has failed to demonstrate metastatic disease.[15]

Histologic Findings

Precancerous lesions of the cervix usually are detected via a Pap test. The Pap test classification system has evolved over the years. Standardized Pap test reporting emerged from a 1988 workshop sponsored by the National Cancer Institute. Currently, cervical cytology results are reported according to the 2001 Bethesda System.[35]

2001 Bethesda System for reporting cervical cytologic diagnoses[35]

Specimen adequacy may be the single most important quality assurance component of the system. Specimen classifications are as follows:

- Satisfactory for evaluation (note presence/absence of endocervical/ transformation zone component)
- Unsatisfactory for evaluation (specify reason)
- Specimen rejected/not processed (specify reason)
- Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

General categorization (optional) is as follows:

- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality
- Other

Possible interpretations or results are as follows:

- Negative for intraepithelial lesion or malignancy
- Observed organisms (*Trichomonas, Candida*, bacteria) and cellular changes consistent with herpes simplex virus are reported
- Reporting other nonneoplastic findings (inflammation and atrophy) is optional
- Epithelial cell abnormalities
- Squamous cell
- Atypical squamous cells (ASC)
- ASCUS
- ASC where a high-grade squamous intraepithelial lesion (HSIL) cannot be excluded (ASC-H)
- Low-grade squamous intraepithelial lesion (LSIL)
- Encompassing HPV, mild dysplasia, and CIN 1
- HSIL
- Encompassing moderate and severe dysplasia, carcinoma in situ, CIN 2, and CIN 3
- Squamous cell carcinoma
- Glandular cell
- Atypical glandular cells (AGC) (specify endocervical, endometrial, or not otherwise specified)
- AGC favoring neoplastic (specify endocervical or not otherwise specified)
- Endocervical adenocarcinoma in situ (AIS)

- Adenocarcinoma
- Other (list not comprehensive)
- Endometrial cells in a woman aged 40 years or older

Automated review and ancillary testing are included as appropriate. Educational notes and suggestions are optional. The histology of cervical malignancy is predominantly that of squamous cell carcinoma, which represents approximately 80% of cases, with adenocarcinomas representing almost 20%. Less common histologies include small cell carcinoma, melanoma, and lymphoma.

Screening Recommendations

The American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology have issued joint guidelines for cervical cancer screening.[36] In addition, the US Preventive Services Task Force (USPSTF) has issued updated 2012 guidelines whose recommendations are consistent with those of these other groups.[37]

Screening recommendations for specific patient age groups are as follows:[36,37]

- < 21 years – No screening recommended
- 21-29 years – Cytology (Pap smear) alone every 3 years
- 30-65 years – Human papillomavirus (HPV) and cytology cotesting every 5 years (preferred) or cytology alone every 3 years (acceptable)

- > 65 years – No screening recommended if adequate prior screening has been negative and high risk is not present

The USPSTF cautions that positive screening results are more likely with HPV-based strategies than with cytology alone and that some women may have persistently positive HPV results and require prolonged surveillance with additional frequent testing. Similarly, women who would otherwise be advised to end screening at age 65 years on the basis of previously normal cytology results may undergo continued testing because of positive HPV test results.[37]

Current US guidelines advise against using HPV testing to screen for cervical cancer in women younger than 30 years; the ACS advice it for screening in women 30-65 years of age, HPV testing alone is not currently recommended for most clinical settings in the US.[37]

Women who have had a total hysterectomy may stop undergoing cervical cancer screening. Exceptions are as follows:

- Women who had a hysterectomy without removal of the cervix
- Women who have had a CIN grade 2 or 3 lesion treated in the past 20 years
- Women who have had cervical carcinoma at any time

Women in whom co-testing shows a negative Pap smear but a positive HPV test should have 12-month follow-up co-testing. Women with atypical squamous cells of undetermined significance (ASCUS) on Pap smear but a

negative HPV test can be rescreened with cotesting in 5 years or with cytology alone in 3 years.[36]

World Health Organization (1992) recommended that in low resource settings, the aim should be to screen every woman once in her lifetime-at 40 years. Frequency of screening should be increased to 'once every 10 years' and then 'once every 5 years' for women 35-55 years of age. The frequency could be increased based on resources.[38]

Resource constraint has been a major hurdle in organizing screening programs. It has been estimated that in India, even with a major effort to expand cytology services, it will not be possible to screen even one-fourth of the population once in a lifetime in the near future. In most developing countries, there has been no success to develop a high quality cytology service. In Mexico, for instance, the low quality of cytology services has been a major barrier. The false negative rate for Pap smear in Mexican cytology centers was as high as 54%. In Colombia, a shortage of cytotechnicians has been a key barrier (PATH 2000).[39]

In addition to high false negative rate of Pap tests, deficiencies in trained personnel, adequate cytology laboratories and infrastructure has been a challenge in implementing cervical cytology for mass screening. Therefore, there is a need to look at alternate practicable options for developing countries.

Visual approaches to screening

In developed countries cervical cytologic screening of every women is part of National Health policy. In India, due to other more rampant problems of reproductive health including population control, cytological screening for cervical cancer and its precancerous lesions is not being focused. Thus, alternative tests can be offered to every woman for detecting cervical precancerous lesions before invasive cancer develops. It involves 3 different approaches: Visual inspection of cervix with acetic acid (VIA), visual inspection with magnification (VIAM), and visual inspection after application of Lugol's iodine (VILI).[40]

VIA

It involves swabbing the cervix with 3-5% acetic acid (Vinegar). After 30-90 seconds, a transient reaction occurs due to osmotic dehydration of dysplastic cells, which accentuate the optically dense chromatin to aceto white areas. VIA is a simple and inexpensive low technology test that does not require a laboratory infrastructure and providers can be trained in 1 to 2 wk. Consumables required are cheap and universally available. The test results are available immediately, enabling further investigation/treatment to be performed in the same session. This avoids recall of women for procedure, resulting in logistic advantages, better compliance and cost savings.[41]

The sensitivity of VIA for high grade lesions and invasive cancer ranged from 70.9-82.6% and specificity from 64.1 to 86.5% in cross sectional studies in Zimbabwe, China and India.[42-44] VIA has a higher sensitivity but lower

specificity than that of cytology.[45] Lower specificity of VIA implies a higher number of women requiring additional investigation and treatment. It remains to be seen whether specificity can be improved by further developments in test definitions and training strategies

Lesions viewed by VIA vary in their size, whiteness, opacity and margins. Unlike cytology, where different grades of severity are stated as ASCUS, LSIL, HSIL, invasive cancer, VIA is recorded as positive, negative, inadequate or doubtful. Acetowhitening may be due to many causes other than dysplastic epithelium. To implement appropriate medical protocols, health care providers must carefully consider the features of a lesions. Thus feasibility of VIA based screening is dependent on training and monitoring.[45]

Concerns have been expressed about reproducibility and quality control of VIA in field conditions.[46] It has been shown in the Barshi trial that the test positivity of VIA declined from 17% at the beginning of the project to 10% by the middle of the project, after a brief period of retraining. A VIA based screening programme may be more readily integrated into primary care health service in developing countries. Model based simulations of cost effectiveness indicate that cervical cancer screening strategies that incorporate VIA and eliminate colposcopy may be attractive alternatives to cytology.[46]

While in a cluster randomized trial in Dindigual involving over 49,000 women, VIA intervention showed reduction in both incidence and mortality by 25 and 35% respectively in seven years after one round of screening,[47] a similar

trial in Barshi, Osmanabad district, failed to show any reduction in mortality.[48] However, the reasons for these discordant results are not known.

Visual inspection with magnification (VIAM):

VIAM is the visualization of cervix under low magnification after application of acetic acid. It is not yet known whether use of magnification offer a significant advantage over VIA. Studies[45,49] have shown VIAM was not superior to VIA, even there was some loss of specificity.

Magnification did not give any improvement in detection rate of high-grade dysplasia or cancers over the use of VIA in studies from South Africa[50] and from Kolkatta.[49]

Visual inspection after application of Lugol's (VILI)

VILI is the visualization of cervix after application of Lugol's iodine. VILI is considered positive, if yellow iodine non uptake areas are visualized closed to the squamo columnar junction or if the entire cervix or a growth on the cervix turned yellow. Among the visual test assessed, VILI seems to be particularly promising, detecting 75% of all cases of HSIL compared with VIA and VIAM which detected less than two third of cases. The pooled sensitivity of VILI 91.8% (range 76-97.3%) has been shown to be higher compared to those of VIA (76.9%) and VIAM (64.2%).[50,51] The other advantage cited for VILI is that the yellow colour changes associated with a positive VILI test result could be recognized with much greater ease by trained health workers compared with the aceto white lesions associated with VIA. The major disadvantage of VILI is the

low specificity of the test. One of the difficulties with VILI is that staining effects persist for 30-45 min and diagnostic procedure such as colposcopy after VILI must be delayed for this period of time, if it is to be administered on the same day.[31]

Advantage of visual techniques has been very high negative predictive value more than 99%. A woman negative by VIA/VILI, need not further undergo any investigation. These women may, however be advised to undergo a VIA or VILI after a minimum interval of three years. Only 10-15% women who are test positive with visual techniques require further evaluation. These characteristics make them ideal alternative tools for primary screening.[31]

The application of acetic acid improves the recognition of lesions. Different criteria have been used by various groups of workers for recognition of lesions. A study categorized the appearance of the cervix on direct visual inspection with acetic acid (DVI) into five types: suspicious lesion, definite lesion, non-confluent scattered lesion, ill-defined lesion and no lesion.[52] When any lesion was considered DVI positive, the sensitivity of the test for detection of high-grade lesion was 70% and specificity 79.3%, whereas when only definite lesions were considered the benchmark for positivity, the sensitivity for detection of high-grade lesions fell to 58.3% but specificity increased to 83.5%.[53]

Visual inspection with acetic acid as a screening test in the prevention of cervical cancer has been extensively evaluated for its accuracy for more than a decade. The Government of India and World Health Organization have recommended VIA as primary screening test to be performed by trained nurses

and health workers at the primary health care level (Government of India & World Health Organization, 2006).[54]

Several variables have been identified which affect the performance of VIA like the light source used, presence of inflammation and standardized training. However, limited information is available regarding the difference in the test performance between paramedical workers and physicians. The feasibility of introducing low resource methods for cervical cancer screening by training paramedical workers in visual inspection has been the subject of debate for over a decade.[53]

VIA and VILI have several screening advantages - minimal requirement of infrastructure and equipment, immediate result, preliminary screening of high risk cases for referral and, not the least, it can be performed by nursing sisters and trained paramedical workers. Several studies indicate that VIA has an ability nearly equivalent to or better than that of cervical cytology to detect cervical cancer precursors.[53]

The main problem of VIA and VILI is the subjective nature of the tests. There are different criteria for defining positivity. Proper training of paramedical staff and even doctors is required if one is to use stringent criteria such as those devised by the International Agency for Research on Cancer (IARC), but these are more specific.[55]

On the other hand, using less stringent criteria where any white lesion would be considered positive increases the sensitivity of the test.[52]

This is important in rural settings if the test is expected to be performed by paramedical workers and the aim is to minimize the false negatives. But often this is accompanied by unacceptably high rates of false positivity and less positive predictive values. A large number of women labelled positive will require subsequent referral, which will again be a problem in a low resource setting. In India, even doctors in primary or community health centres may need to rely on these visual inspection techniques for primary screening because of lack of available facilities for cytology and colposcopy.[53]

A few studies have compared the performance of doctors and paramedical workers. A study found overall 89.6% agreement between the findings of a paramedical worker and a gynaecologist in a hospital-based study on clinical downstaging of cancer cervix.[56]

Another study found good concordance between the findings of the paramedical worker and the gynaecologist both with lesser and greater strictness of criteria, using unaided visual inspection of the cervix in the general population.[57]

Given the large number of women who are eligible for testing in India and other developing countries, the logistics of training and appointing personnel to carry out visual inspection on all women are also daunting. A pilot study to explore the performance of these tests when applied to women who are at higher risk for cervical cancer reported that, even in this setting the results are in accord with other studies, where visual inspection of the cervix after application of acetic acid is associated with a high sensitivity but low specificity and positive

predictive values for high grades of CIN and invasive cancer.[58,59] VILI results had lesser diagnostic accuracy when compared with VIA in case of the doctor, but for the nurse both VIA and VILI had similar test performance. Since VILI was performed after VIA by the same person, the results of VILI could be biased by the VIA results.[53]

On contrary, a recent study[60] to provide an updated estimation of the accuracy of visual inspection with acetic acid (VIA) in detecting true disease reported that, screening for precancerous and cancerous cervical lesions using VIA is a simple, low-cost, and efficient alternative to cytologic testing in low-resource areas. Study reported an 80% sensitivity (range, 79%-82%) and a 92% specificity (range, 91%-92%) for VIA. Study region, capacity of screener, or size of the study population did not modify VIA accuracy. The positive predictive value was 10% (range, 9%-10%).

A similar study[54] in our institute conducted during 2009 reported better sensitivity and specificity by physician as compared to that of the nurse. The characteristics of the study population and the criteria used to categorize VIA test results of the present study were similar to a study done in India in 2003. However the sensitivity of VIA by nurse (100%) was found to be better than that by physician (88%) but the specificity by physician (63%) was superior to that by nurse (53%) in their study. These findings were contradictory to the findings by another study in 2006 where test characteristics of VIA done by both physician and nurse were in the same range as mentioned in various studies.

Another study[61] from Africa in a primary health care setting reported the sensitivity by physician and nurse as 71% and 55% and specificity as 71% and 65% respectively, but the sensitivity by nurse and physician were significantly lower.

In the Osmanabad trial[48] authors concluded that a single HPV testing resulted in 50% reduction in incidence and mortality for cervical cancer while VIA and cytology had no effect.

A contradictory outcome was noted in a randomized control trial[47] in Dindigul district in South India where it was found that there was a reduction in cervical cancer incidence and mortality by 25% and 35 % respectively with a single visit VIA followed by cryotherapy done by mid level providers.

Chapter 4

Methodology

METHODOLOGY

The present study was conducted in the department of obstetrics and gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study design

The study design was a cross sectional study.

Duration of study

This cross sectional study was conducted from December 2010 to July 2012.

Source of data and materials

All sexually active women from age 20 to 50 years attending Colposcopy Clinic with complaints suggestive of cervical cancer at Colposcopy Clinic in Gynaecology outpatient department (OPD), KLE Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a University Teaching Hospital attached to Jawaharlal Nehru Medical College were included in the study.

Sample size: 250.

$$n = \frac{Z\alpha^2 p_0(1-p_0)}{d^2 (1-p_e)^2}$$

Z_α- value of Z for 95% confidence is 1.96.

p_0- proportion of agreement. p_o=80/100=0.8

p_e- proportion of agreement by chance.p_e=49.82/100=0.4982

d- confidence interval .d=0.1

$$n = \frac{(1.96)^2 \times 0.8 \times 0.2}{(0.1)^2 \ (1-0.4982)^2} = 244.1 \approx 250$$

The eligible pool will be 288, that is, 80% of the average of the women who have undergone colposcopy in the last three years. Assuming that 10% of the women might refuse to consent, 252 of the women are likely to be eligible for the study, enabling us to meet our sample size of 250.

Inclusion criteria

All sexually active women from age 20 to 50 years attending Colposcopy Clinic with complaints of:

- Intermenstrual bleeding.
- Post coital bleeding.
- Persistent vaginal discharge.
- Suspicious looking cervix.
- Positive screening test.

Exclusion criteria:

- Prior hysterectomy.
- Pregnancy.
- Obvious growth on cervix.

Procedure

In this study, physicians were the post graduate students of department of obstetrics and gynaecology and nurses were those posted in outpatient department of obstetrics and gynaecology.

In the preliminary phase of the study, the nurses and physicians received training for a period of 3 to 4 days, on anatomy and pathophysiology of cervix, review of images and videos of normal and abnormal cervices followed by hands on clinical examination. They were taught to categorize the VIA and VILI results as positive and negative based on the IARC criteria.

Method of collection of data:

Ethical clearance

The ethical clearance was obtained from Review Board of Jawaharlal Nehru Medical College, Belgaum. (Letter No. MDC/PG/ dated 8.10.2010).

Screening and Enrolment

All women between age group 20-50 years visiting colposcopy clinic were screened for eligibility based on selection criteria. Informed consent was obtained at the time of enrolment into the study from the eligible women. The investigator obtained a signature or left hand thumb impression from the consented subject. Adequate time was provided for describing the study and describing the risks and benefits of participation in the study. No undue pressure was placed on the patient to enrol in the study. It was further explained that lack

of participation will not affect the usual and anticipated standard of care. The women were enrolled in the study only after taking their signature or left hand thumb impression on informed consent form (Annexure I). After having obtained the consent, a proforma was filled which contained the general information of the patient, chief complaints if they had any, menstrual history, obstetric history and a thorough physical examination was done. Patient was then placed in lithotomy position after voiding urine. Under all aseptic precautions, Cusco's speculum was inserted. Cervix was visualized for any gross pathological features and SCJ. After visualizing SCJ, cervix was cleaned with normal saline. VIA and VILI were performed both by physician and nurse. VIA was done by applying 5% freshly prepared acetic acid on the cervix and interpreted after 1 minute using 100 watt bulb. VILI was done by applying Lugol's iodine on the cervix. VIA and VILI were interpreted both by physician and nurse.

Observations were recorded independently by both physician and nurse without disclosing their findings to each other. Number, size, location and extension of the lesions into the endocervix were noted. Gynaecologist who was blinded to the results of VIA and VILI performed colposcopy. Biopsy was taken from abnormal areas. Negative colposcopy and histopathology were considered as the reference standard. Test positivity was defined by histopathology report of cervical intraepithelial neoplasia 2 (CIN 2) and above. Patients were advised follow up after 1 week to collect the histopathological report and if report showed pre cancerous lesions, surgical procedures like cryotherapy or Loop electrosurgical excision procedure (LEEP) or hysterectomy were advised depending on the histopathological report.

Screening intervention procedures

Visual inspection with acetic acid (VIA)

A trained physician performed the VIA. VIA was done by applying freshly prepared 5% acetic acid on the cervix using cotton swab. The cervix was visualised under the illumination of 100 watt bulb and the result was interpreted at the end of 1 minute as positive and negative as per the IARC criteria (chart 1).

Visual inspection with Lugol's iodine (VILI):

VILI was performed after VIA by applying Lugol's iodine on the cervix and interpretation of results done as per the IARC criteria (chart 2).

Colposcopy

Colposcopy was done by a gynaecologist who was blinded to the result of VIA and VILI. It was performed using normal saline, green filter, acetic acid and Lugol's iodine. Findings were recorded and Modified Reid Colposcopic Index (MRCI) (chart 3) was assigned as per the findings.

Colposcopy guided cervical punch biopsy

Where colposcopy revealed a precancerous lesion, a cervical punch biopsy was performed using a punch biopsy forceps.

Other treatment / surgical procedure

Women with histological confirmed lesion of CIN 2 and above were counselled to undergo either Cryotherapy or Loop electrosurgical excision procedure (LEEP) or hysterectomy following appropriate evaluation.

Chart 1. IARC Criteria for interpretation of VIA[56]

VIA negative (-)

VIA screening is reported as negative in the case of any of the following observations:

- No acetowhite lesions are observed on the cervix.
- Polyps protrude from the cervix with bluish-white acetowhite areas.
- Nabothian cysts appear as button-like areas, as whitish acne or pimples.
- Dot-like areas are present in the endocervix, which are due to grapelike columnar epithelium staining with acetic acid.
- There are shiny, pinkish-white, cloudywhite, bluish-white, faint patchy or doubtful lesions with ill-defined, indefinite margins, blending with the rest of the cervix.
- Angular, irregular, digitating acetowhite lesions, resembling geographical regions, distant (detached) from the squamocolumnar junction (satellite lesions).
- Faint line-like or ill-defined aceto whitening is seen at the squamocolumnar junction.
- Streak-like acetowhitening is visible in the columnar epithelium.

- There are ill-defined, patchy, pale, discontinuous, scattered acetowhite areas

VIA positive (+)

The VIA test outcome is reported as positive in any of the following situations:

- There are distinct, well-defined, dense (opaque, dull- or oyster-white) acetowhite areas with regular or irregular margins, close to or abutting the squamocolumnar junction in the transformation zone or close to the external os if the squamocolumnar junction is not visible.
- Strikingly dense acetowhite areas are seen in the columnar epithelium.
- The entire cervix becomes densely white after the application of acetic acid.
- Condyloma and leukoplakia occur close to the squamocolumnar junction, turning intensely white after application of acetic acid.

VIA positive, invasive cancer

The test outcome is scored as invasive cancer when;

- There is a clinically visible ulceroproliferative growth on the cervix that turns densely white after application of acetic acid and bleeds on touch.

Chart 2. IARC Criteria for interpretation of VILI[56]

VILI negative (-)

VILI screening is reported as negative in the case of any of the following observations after iodine application:

- A normal cervix; the squamous epithelium turns mahogany brown or black and the columnar epithelium does not change colour.
- Patchy, indistinct, ill-defined, colourless or partially brown areas are seen.
- Pale areas of no or partial iodine uptake are present on polyps.
- A leopard-skin appearance is associated with *T. vaginalis* infection.
- Pepper-like non-iodine uptake areas are seen in the squamous epithelium, far away from the squamocolumnar junction.
- Satellite, thin, yellow, non-iodine uptake areas with angular, or digitating margins, resembling geographical areas, are seen far away from the squamocolumnar junction.

VILI positive (+)

- The outcome is scored as positive if dense, thick, bright, mustard-yellow or saffron yellow iodine non-uptake areas are seen in the transformation zone, close to or abutting the squamocolumnar junction or close to the os if the squamocolumnar junction is not seen or when the entire cervix turns densely yellow.

VILI positive, invasive cancer:

- Invasive cancer is reported when a frank, nodular, irregular, ulceroproliferative growth is visible on the cervix which turns densely yellow on application of iodine.

Modified Reid Colposcopic Index (RCI)[56]

A. Color:

Zero point if:

- Low intensity aceto whitening (not completely opaque).
- Indistinct acetowhitening.
- Transparent /translucent acetowhitening.
- Acetowhitening beyond the margin of the transformation zone.
- Pure snow white colour with intense surface shine.

One point if:

- Intermediate shade-grey/white colour and shiny surface.

Two points if:

- Dull, opaque, oyster white; grey.

B. Lesion margin and surface configuration.

Zero point if:

- Microcondylomatous/ micropapillary contour.
- Flat lesions with indistinct/features or finely scalloped margins.
- Angular, jagged lesions.
- Satellite lesions beyond the margin of the transformation zone.

One point if:

- Regular shaped symmetrical lesions with smooth, straight outlines.

Two points if:

- Rolled, peeling edges.
- Internal demarcations between areas of differing colposcopic appearances central area of high-grade change and peripheral area of low grade change.

Vessels:

Zero point if:

- Fine/ uniform caliber vessels- closely and uniformly placed.
- Poorly formed patterns of fine punctuation and/or mosaic vessels.
- Beyond the margin of the transformation zone.
- Fine vessels within microcondylomatous or micropapillary lesions.

One point if:

- Absent vessels.

Two points if:

- Well defined coarse punctuation or mosaic.
- Sharply demarcated and randomly and widely placed.

C. Iodine staining.

Zero point if:

- Positive iodine uptake giving mahogany brown colour.
- Negative uptake of insignificant lesion,i.e.,yellow staining by a lesion scoring three points or less on the first three criteria.

- Areas beyond the margin of the transformation zone, conspicuous on colposcopy, evident as iodine negative areas.

  One point if:

- Partial iodine uptake- variegated, specked appearance.

  Two points if:

- Negative iodine uptake of significant lesion, i.e., yellow staining by a lesion already scoring four points or more on the first three criteria.

Colposcopic prediction of histological diagnosis using RCI[56]

RCI (Overall score)	**Histology**
0-2	Likely to be CIN 1
3-4	Overlapping lesion: likely to be CIN 1 or CIN 2
5-8	Likely to be CIN 2-3

Biopsy report[56]

Biopsy result were categorised as Chronic cervicitis, CIN1, CIN 2, CIN 3 and invasive carcinoma of cervix**.**

Instruments and reagents:

1. Examination table with stirrups.
2. A pair of gloves.
3. Cusco's bivalve self retaining speculum of various sizes.
4. Sim's speculum
5. Anterior vaginal wall retractor.

6. Vulsellum.
7. Colposcope- Dr. Camscope video colposcope.
8. Punch biopsy forceps.
9. Sponge holding forceps.
10. Cotton swabs and gauze pieces.
11. Specimen container.
12. Reagents- Normal saline, 5% acetic acid and Lugol's iodine.
13. Formalin.

Preparation of 5% acetic acid:

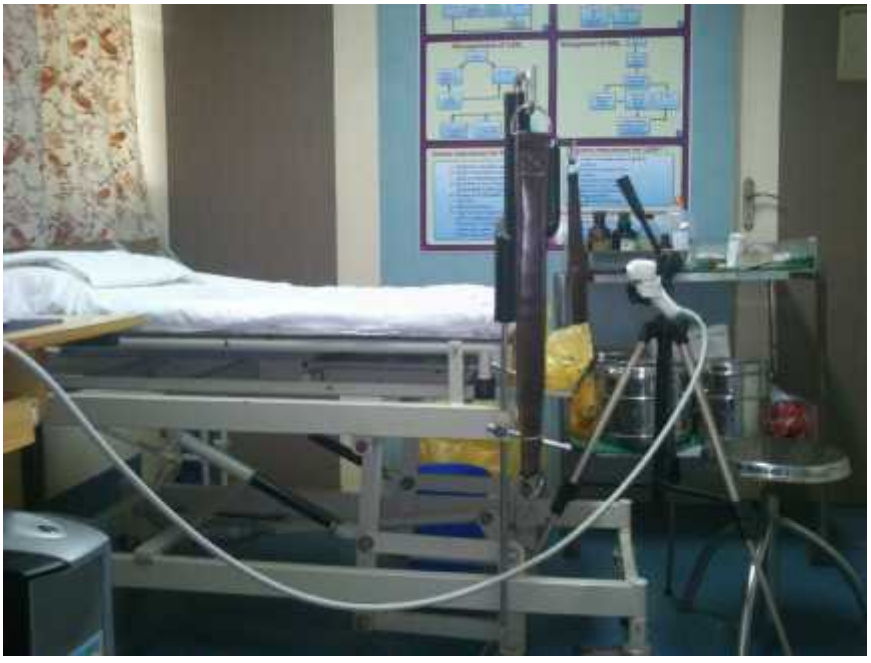
Ingredients	**Quantity**
1. Glacial acetic acid	5 ml
2. Distilled water	95 ml

Preparation: Carefully add 5 ml of Glacial acetic acid into 95 ml of distilled water and mix thoroughly.

Storage: Freshly prepared acetic acid was used for the study and the remaining solution was discarded at the end of the day.

Label: 5% diluted acetic acid.

Photograph 1. Instrument trolley



Photograph 2. Colposcopy clinic

Statistical analysis

Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV) and the 95% confidence intervals (95% CI) were calculated using standard formulae with CIN 2 or above as disease threshold for each test by both nurse and physician. The tests accuracy was calculated separately for nurse and physician and the characteristics of VIA and VILI between nurse and physician were compared using chi-square test. Concordance of both the tests between the physician and nurse will be determined by kappa statistics.

$$1.\ \text{Sensitivity} = \frac{\text{True positive}}{\text{True positive + False negative}} \times 100$$

$$2.\ \text{Specificity} = \frac{\text{True Negative}}{\text{True positive + True negative}} \times 100$$

$$3.\ \text{Positive predictive value} = \frac{\text{True Positive}}{\text{True positive + False positive}} \times 100$$

$$4.\ \text{Negative predictive value} = \frac{\text{True Negative}}{\text{True Negative + False negative}} \times 100$$

Landis and Koch criteria for agreement on kappa statistics.

Kappa	Agreement
<0.0	poor
0.0 – 0.20	slight
0.21 – 0.60	moderate
0.61 – 0.80	substantial
0.81 – 1.00	almost perfect

Chapter 5

Results

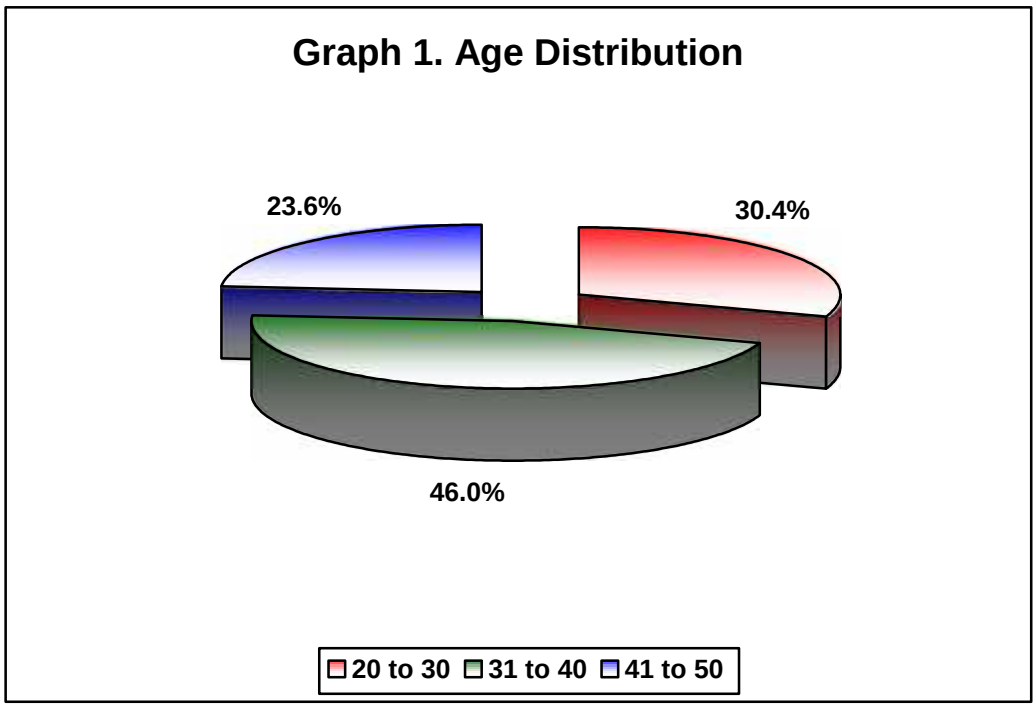
RESULTS

The present one year cross-sectional study was conducted at Colposcopy Clinic, Outpatient department, Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from December 2010 to July 2012. A total of 250 women were studied.

The data obtained was coded and entered into Microsoft excel spread sheet. The analysis was done and results were interpreted as below.

Table 1. Age distribution

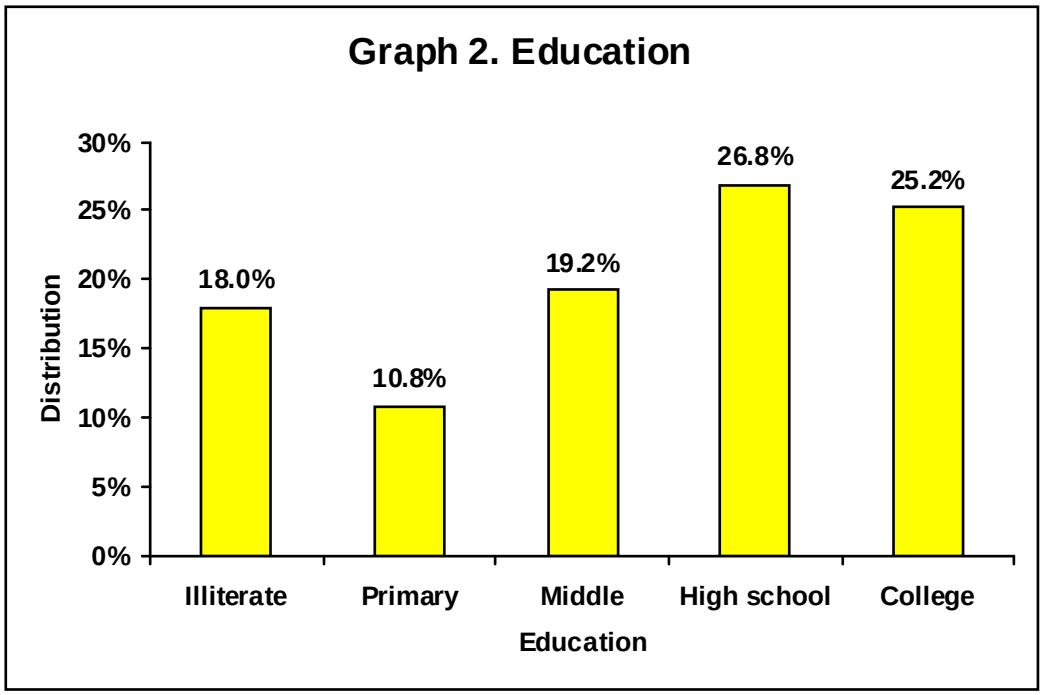
Age group	Number	Percentage
20 – 30	76	30.4
31 – 40	115	46.0
41 – 50	59	23.6
Total	**250**	**100**



In this study most (46%) women were aged between 31 to 40 years followed by 30.4% between 20 to 30 years and 23.6% women had age between 41 to 50 years.

Table 2. Education

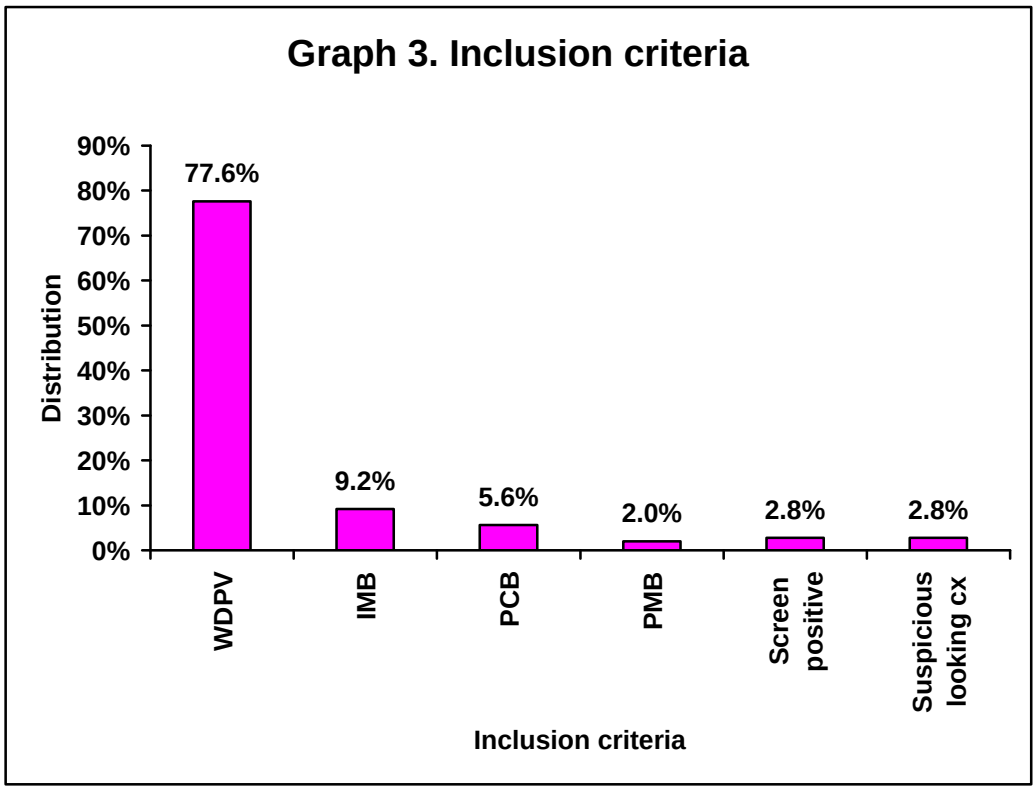
Education	Number	Percentage
Illiterate	45	18.0
Primary	27	10.8
Middle	48	19.2
High school	67	26.8
College	63	25.2
Total	**250**	**100**



In the present study 26.8% of women had completed high school education, 25.2% studied up to college, 19.2% had middle school education and 10.8% had primary education. However 18% of women were illiterates.

Table 3. Inclusion criteria

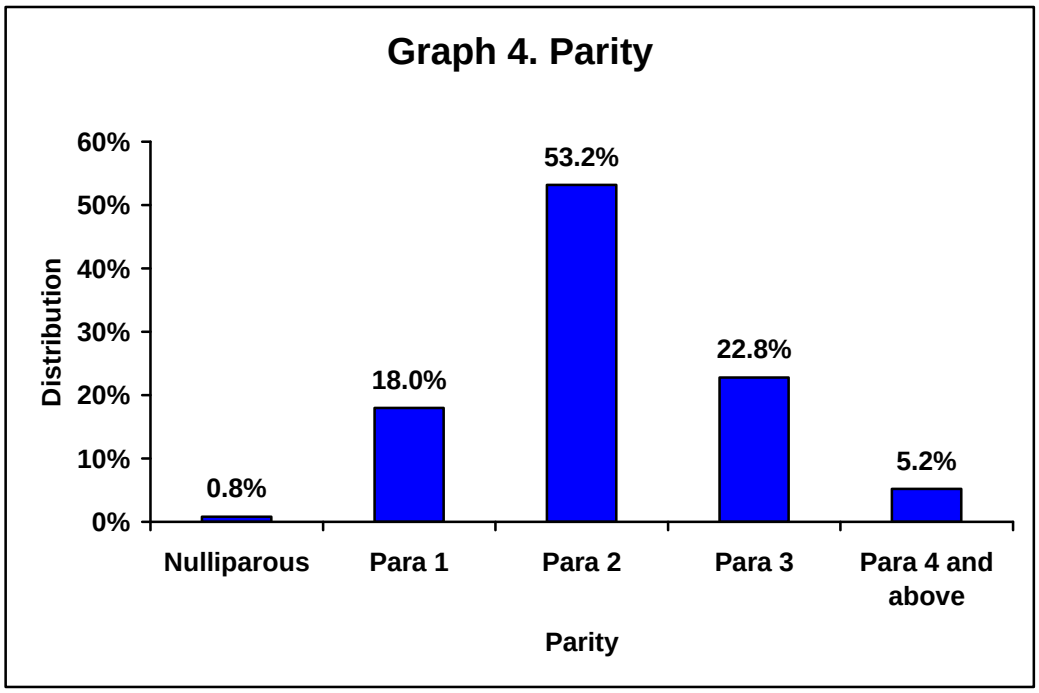
Inclusion criteria	Number	Percentage
White discharge per vagina	194	77.6
Inter menstrual bleeding	23	9.2
Post coital bleeding	14	5.6
Post menopausal bleeding	5	2.0
Screen positive	7	2.8
Suspicious looking cervix	7	2.8
Total	**250**	**100**



In this study WDPV was the commonest (77.6%) complaint with which patients presented with.

Table 4. Parity

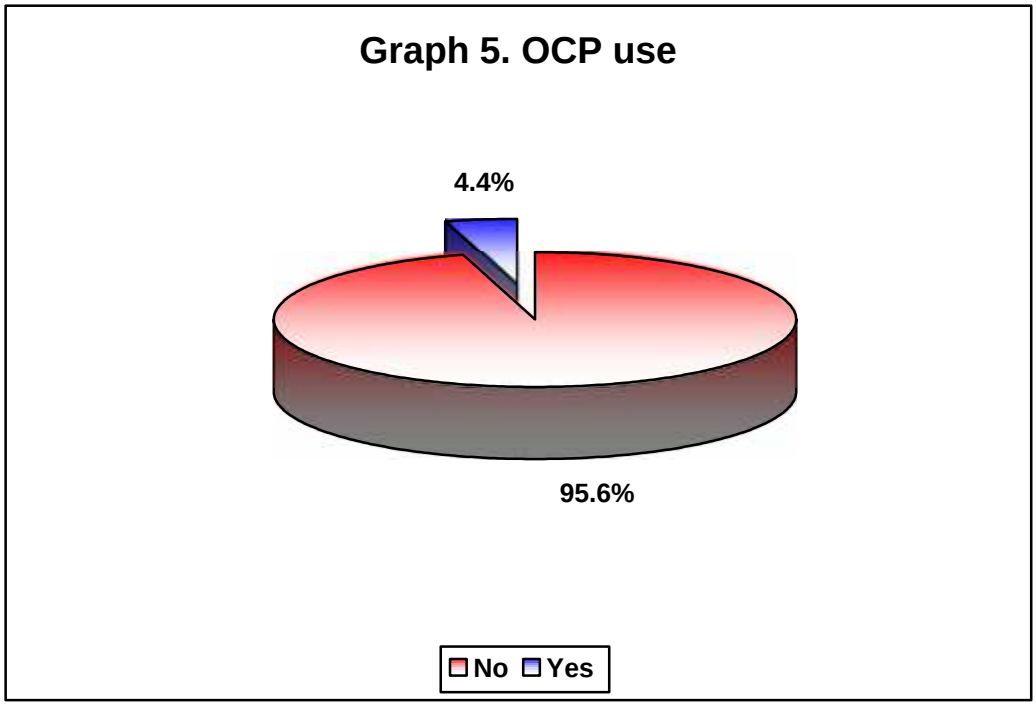
Parity	Number	Percentage
Nulliparous	2	0.8
Para 1	45	18.0
Para 2	133	53.2
Para 3	57	22.8
Para 4 and above	13	5.2
Total	**250**	**100**



In this study 53.2% women were para 2, 22.8% were para 3 and 18% were para 4. Para 4 and above was recorded in 5.2% patient and 0.8% were nulliparous.

Table 5. Use of oral contraceptives

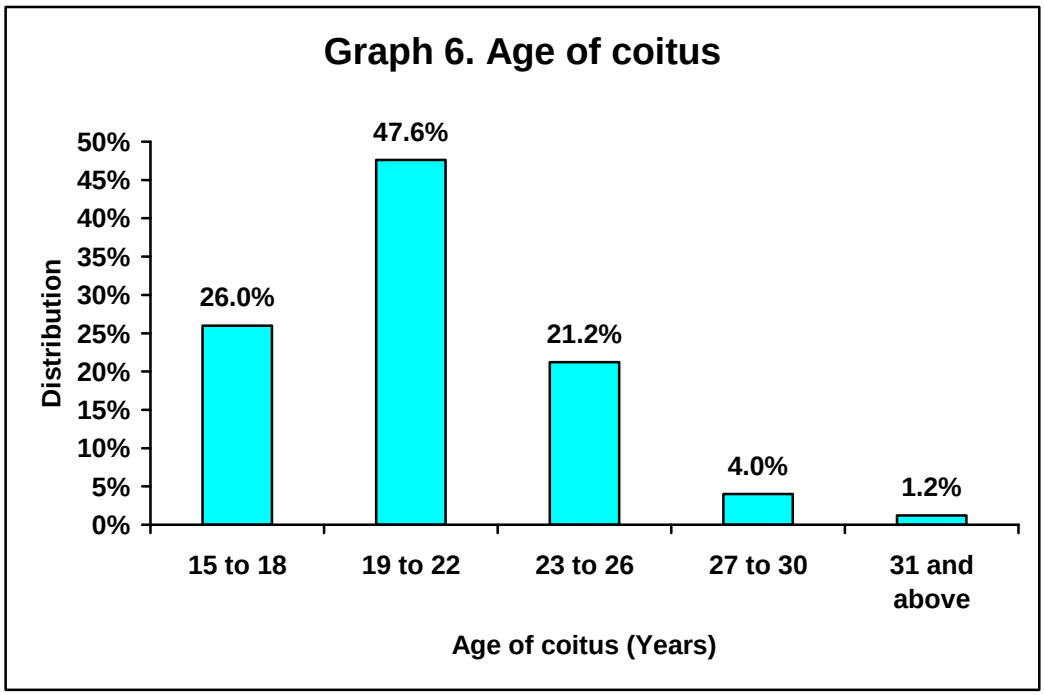
Contraceptive use	Number	Percentage
No	239	95.6
Yes	11	4.4
Total	**250**	**100**



In the present study the use of oral contraceptives was noted among 4.4% women.

Table 6. Age of coitus

Age of coitus (Years)	Number	Percentage
15 – 18	65	26.0
19 – 22	119	47.6
23 – 26	53	21.2
27 – 30	10	4.0
31 and above	3	1.2
Total	**250**	**100**



In the present study 47.6% had age of coitus between 19 to 22 and 26.0% had at 15 to 18 years.

Table 7. Multiple sex partner

Multiple sex partner	Number	Percentage
No	244	97.6
Yes	6	2.4
Total	**250**	**100**

The history of multiple sex partners was present among 2.4% women.

Table 8. History of tobacco chewing

Tobacco chewing	Number	Percentage
No	250	100
Yes	0	0
Total	**250**	**100**

None of the women present with past and current history of tobacco chewing.

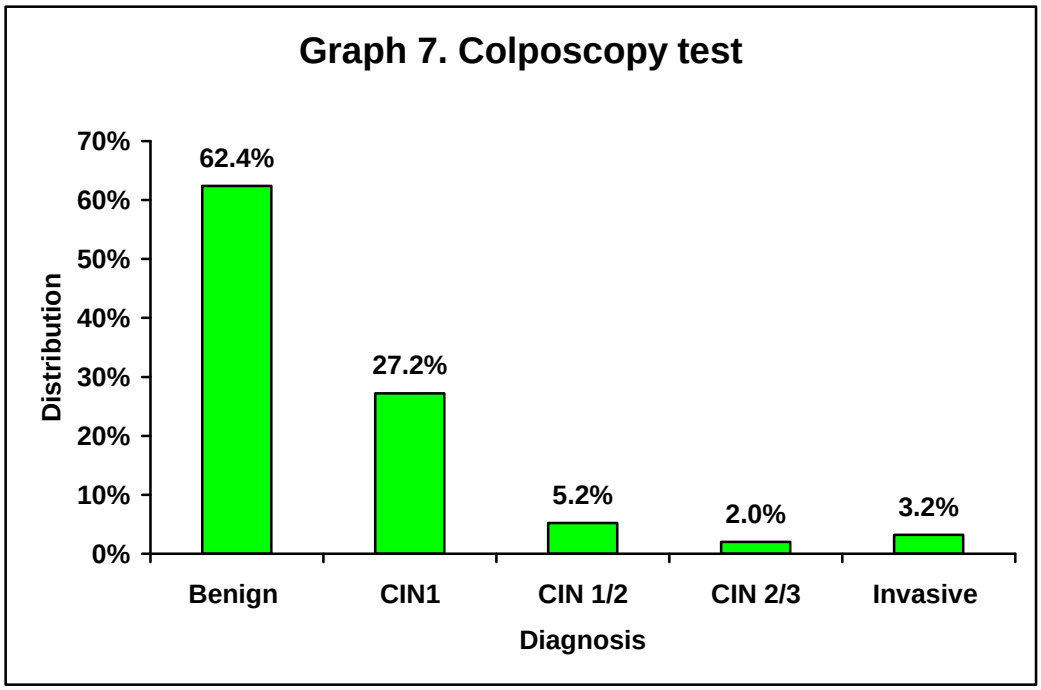
Table 9. HIV Infection

HIV infection	Number	Percentage
No	246	98.4
Yes	4	1.6
Total	**250**	**100**

In this study HIV infection was present among 1.6% of the women.

Table 10. Colposcopy test

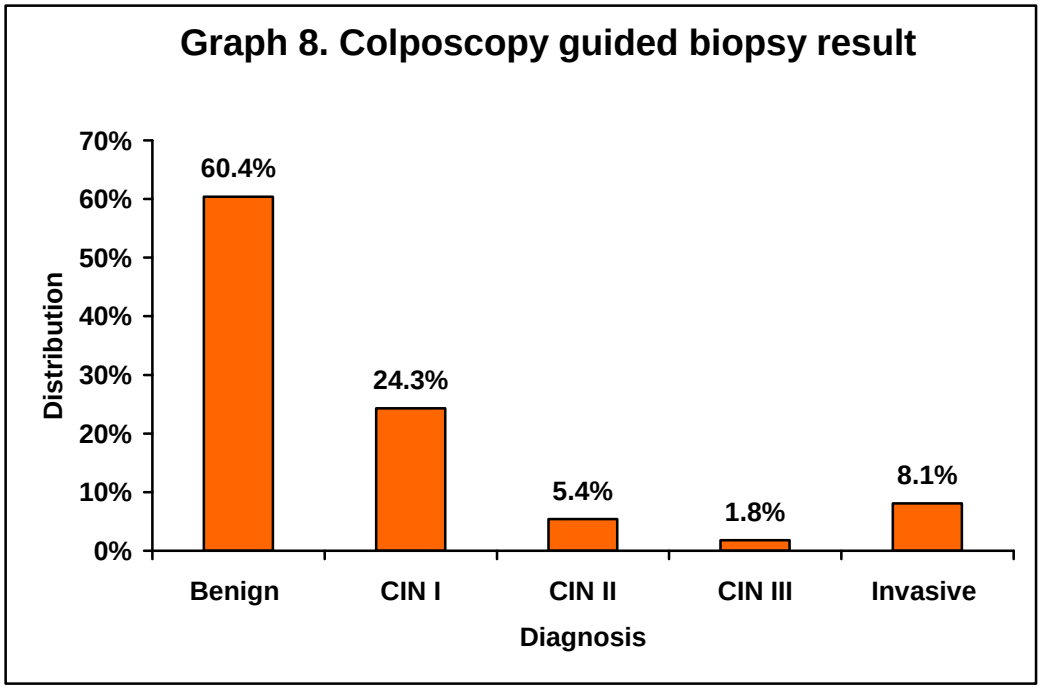
Diagnosis	Number	Percentage
Benign	156	62.4
CIN 1	68	27.2
CIN 1/2	13	5.2
CIN 2/3	5	2.0
Invasive	8	3.2
Total	**250**	**100**



In the present study the colposcopic findings revealed benign lesions among 62.2%, CIN1 in 27.2%, CIN 1/2 in 5.2%, CIN 2/3 in 2% and invasive among 3.2%.

Table 11. Colposcopy guided biopsy result

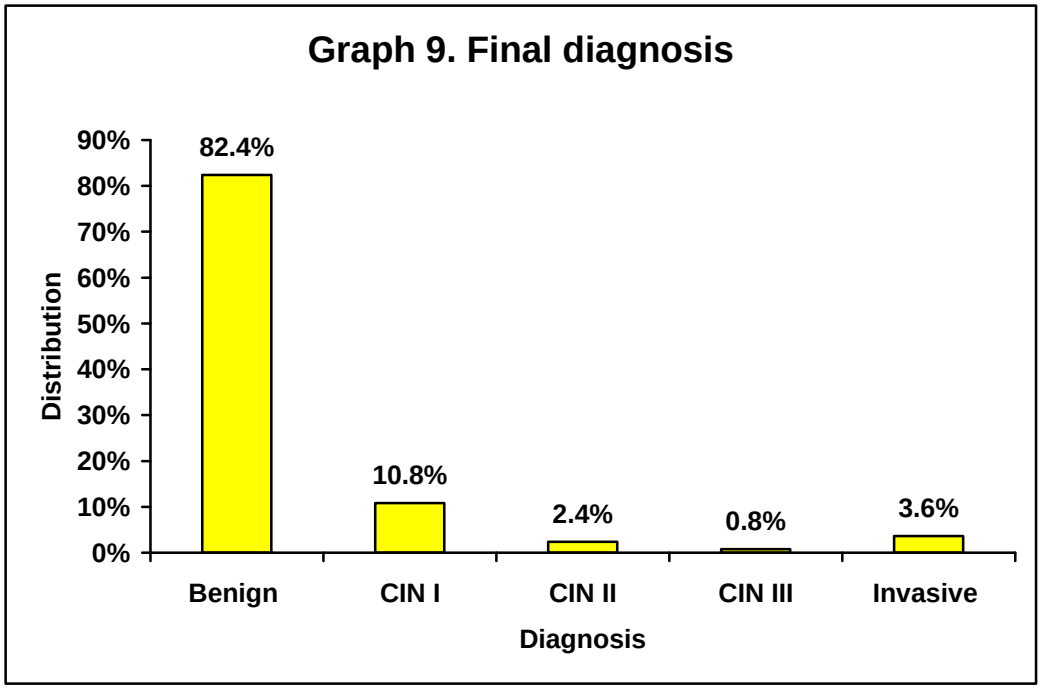
Final diagnosis	Number	Percentage
Benign	67	60.4
CIN 1	27	24.3
CIN II	6	5.4
CIN III	2	1.8
Invasive	9	8.1
Total	**111**	**100**



Colposcopy guided biopsy was taken in 111 cases. 60.4% cases had benign lesions, 24.3% had CIN I, 5.4% had CIN II, 1.8% had CIN III and Invasive carcinoma was diagnosed in 8.1% cases.

Table 12. Final diagnosis

Final diagnosis	Number	Percentage
Benign	206	82.4
CIN 1	27	10.8
CIN II	6	2.4
CIN III	2	0.8
Invasive	9	3.6
Total	**250**	**100**

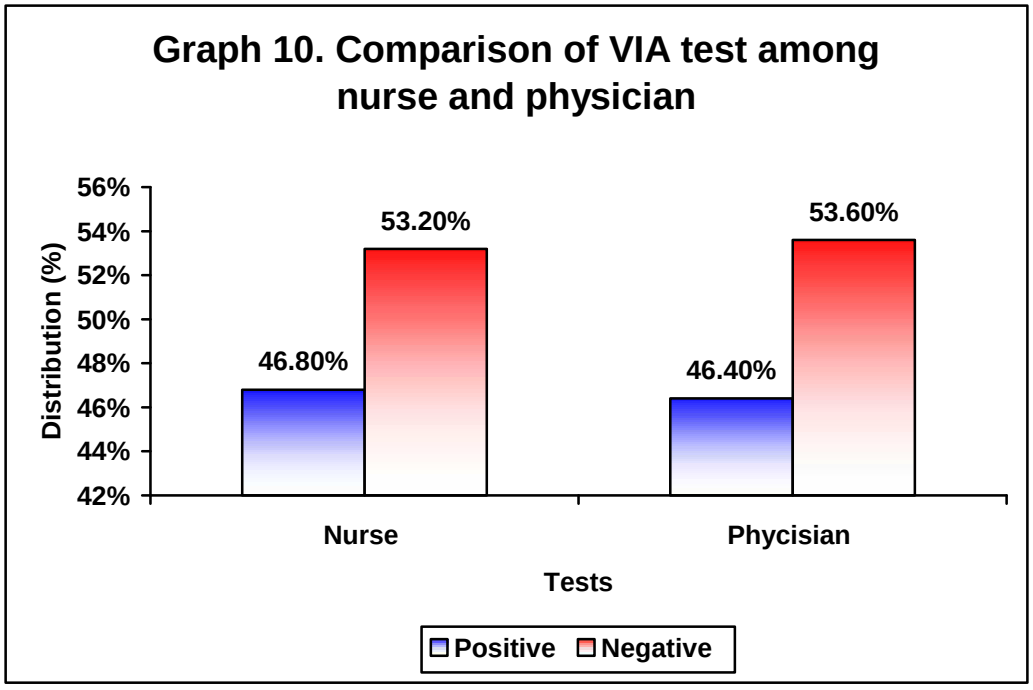


The final diagnosis was confirmed in 82.4% as benign, 10.8% as CIN I, 2.4% as CIN II, 0.8% as CIN III and 3.6% as invasive.

Table 13. Comparison of VIA test among nurse and physician

VIA by Nurse	Physician				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	106	91.4	11	8.3	117	**46.8**
Negative	10	8.6	123	91.7	133	**53.2**
Total	**116**	**46.4**	**134**	**53.6**	**250**	**100.0**

k = 0.831 (Almost perfect agreement) **p < 0.001**

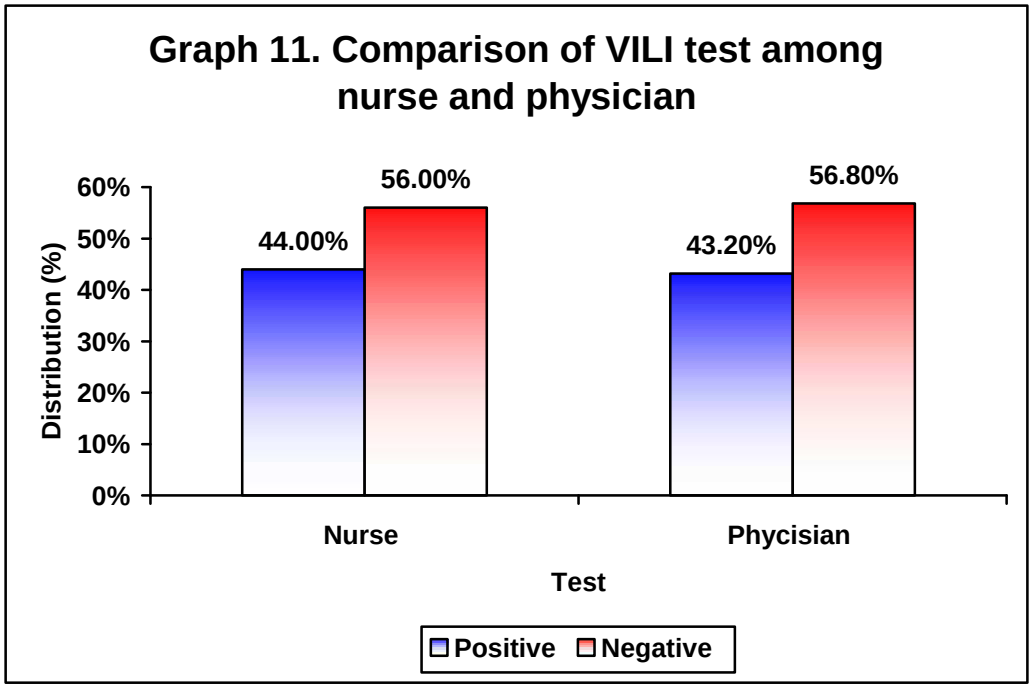


In the present study, VIA positive both by physician and nurse was present in 106 cases (91.4%). There was almost perfect agreement between the two (k=0.831).

Table 14. Comparison of VILI test among nurse and physician

VILI by Nurse	Physician				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	101	93.5	9	6.4	110	**44.0**
Negative	7	6.5	133	93.6	140	**56.0**
Total	**108**	**43.2**	**142**	**56.8**	**250**	**100.0**

k = 0.870 (Almost perfect agreement) **p < 0.001**

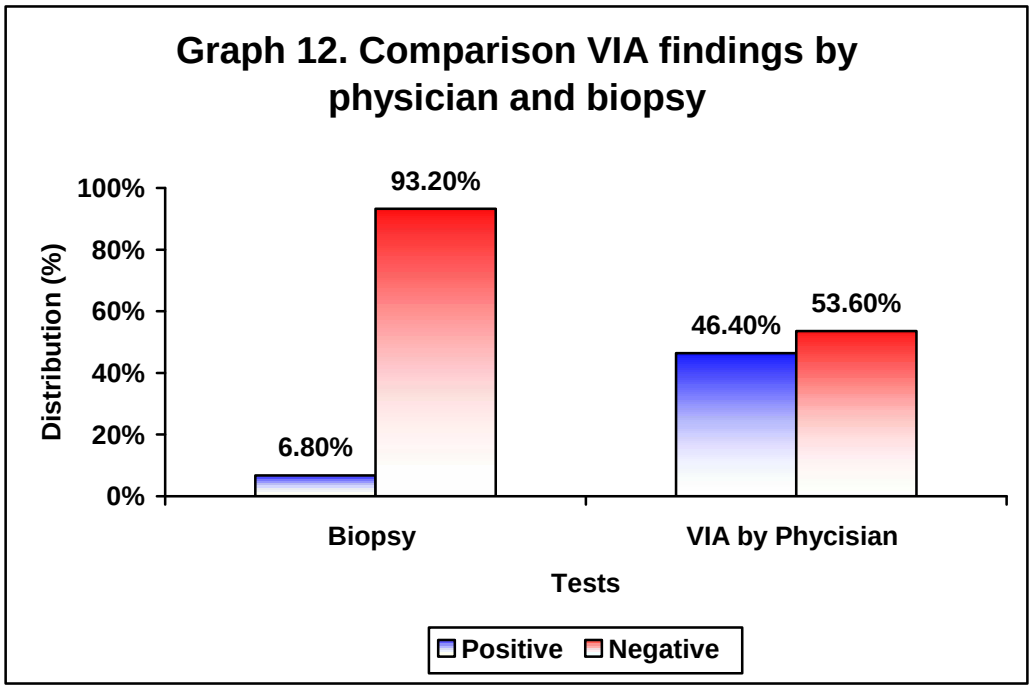


In this study during VILI, 101 cases (93.5%) were positive by both nurse and physician with almost perfect agreement between the two (k=0.87).

Table 15. Comparison VIA findings by Physician and Biopsy

VIA by physician	Biopsy findings				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	17	100	99	42.5	116	**46.4**
Negative	0	0	134	57.5	134	**53.6**
Total	**17**	**6.8**	**233**	**93.2**	**250**	**100.00**

k = 0.187 **p < 0.001**

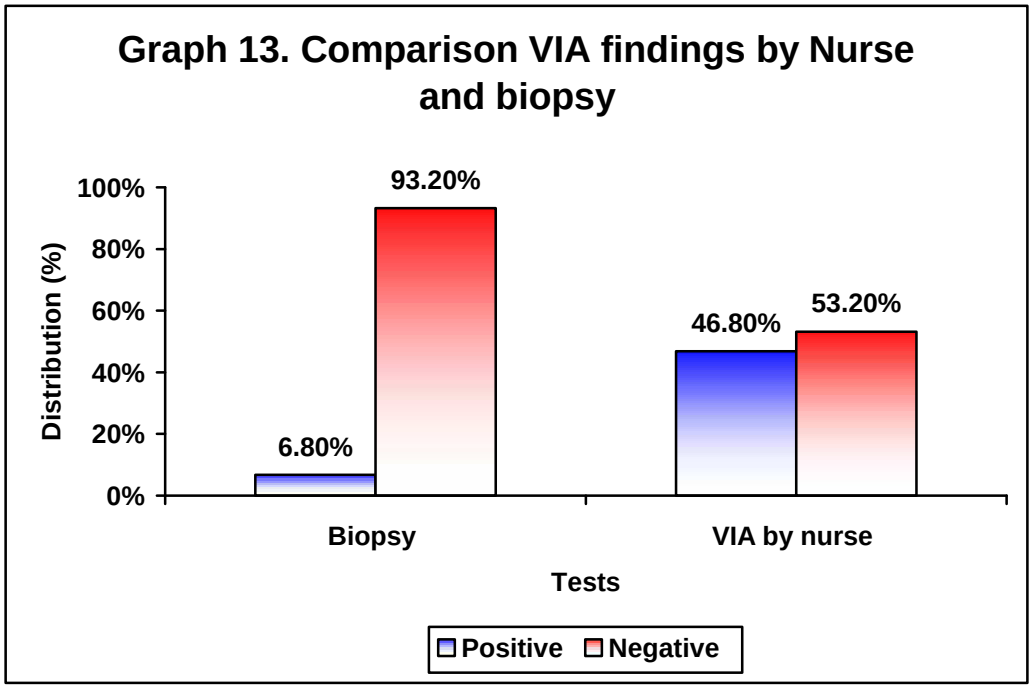


In the present study biopsy result revealed 6.8% positive cases compared to 46.4% as predicted by physician.

Table 16. Comparison VIA findings by Nurse and Biopsy

VIA by nurse	Disease				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	15	88.3	102	43.7	117	**46.8**
Negative	2	11.7	131	56.3.	133	**53.2**
Total	**17**	**6.8**	**233**	**93.2**	**250**	**100.0**

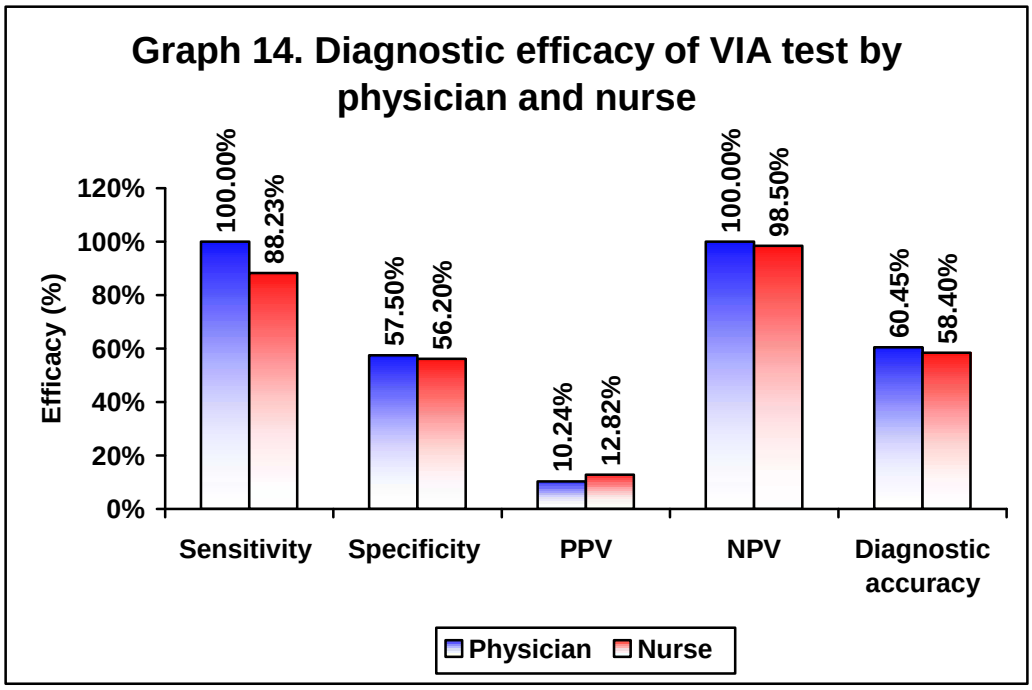
k = 0.107 **p < 0.001**



In the present study, biopsy result revealed positive in 6.8% cases compared to 46.8% as predicted by nurse.

Table 17. Diagnostic efficacy of VIA test by physician and nurse

Diagnostic efficacy	Physician	Nurse
Sensitivity	100.00%	88.23%
Specificity	57.5%	56.2%
Positive predictive value	10.24%	12.82%
Negative predictive value	100.00%	98.5%
Diagnostic accuracy	**60.45%**	**58.4%**

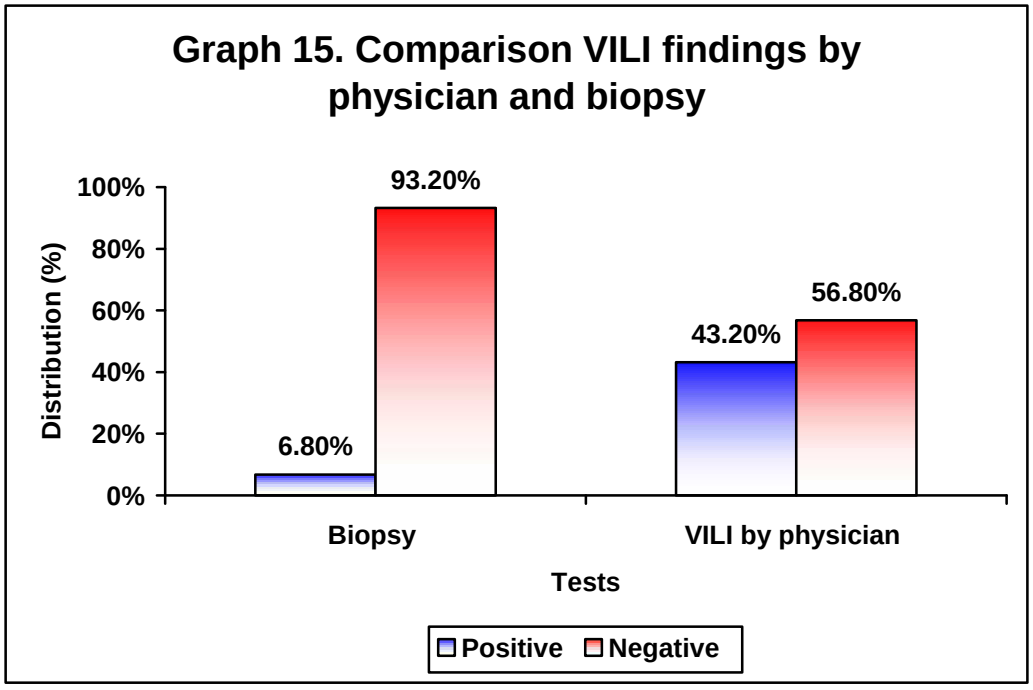


In this study, the overall diagnostic accuracy of VIA with CIN 2 and above as disease threshold was 60.45% by physician and 58.4% when performed by nurse.

Table 18. Comparison VILI findings by physician and biopsy

VILI by physician	Disease				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	14	82.4	94	40.3	108	**43.2**
Negative	3	17.6	139	59.7	142	**56.8**
Total	**17**	**6.8**	**233**	**93.2**	**250**	**100.00**

k= 0.095 **p = 0.001**

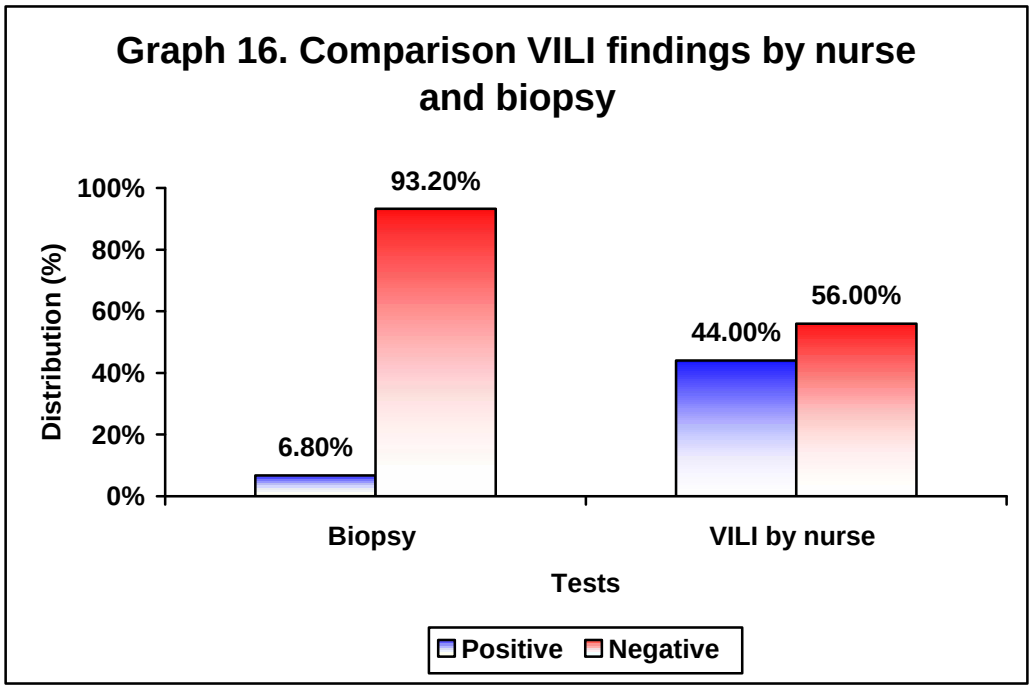


In the present study, biopsy result revealed positive cases in 6.8% compared to 43.2% as predicted by physician.

Table 19. Comparison VILI findings by Nurse and Biopsy

VILI by nurse	Disease				Total	
	Positive		Negative			
	Number	Percent	Number	Percent	Number	Percent
Positive	13	76.5	95	41.6	110	**44.0**
Negative	4	23.5	136	58.4	140	**56.0**
Total	**17**	**6.8**	**233**	**93.2**	**250**	**100.0**

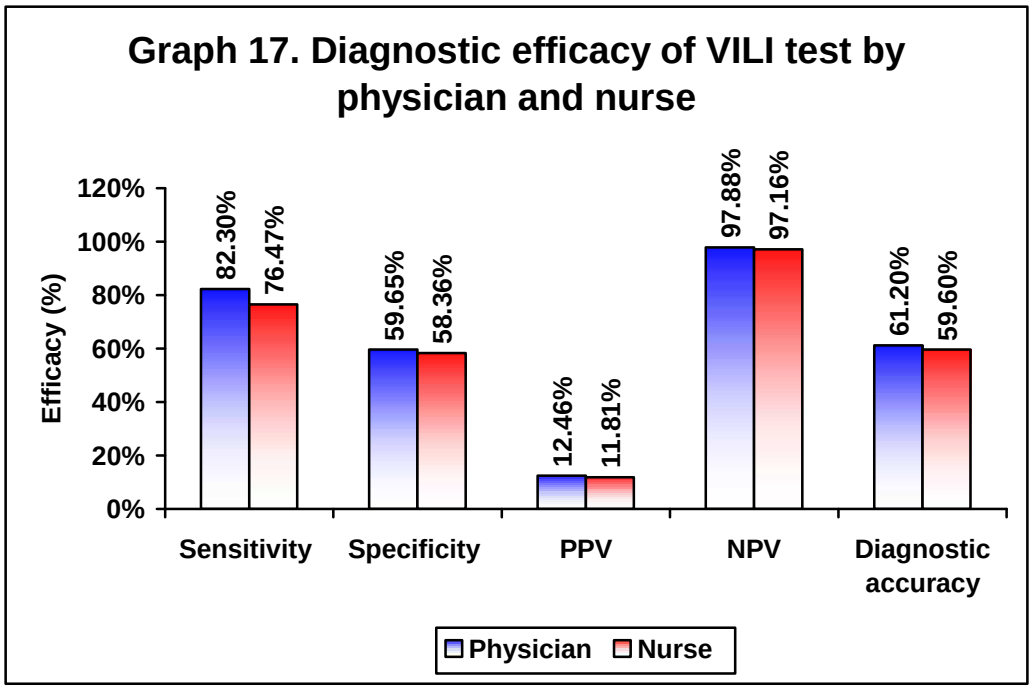
k= 0.080 **p = 0.005**



In this study biopsy result revealed 6.8% positive cases compared to 44% that were predicted by nurse.

Table 20. Diagnostic efficacy of VILI test by Physician and Nurse

Diagnostic efficacy	Physician	Nurse
Sensitivity	82.3%	76.47%
Specificity	59.65%	58.36%
Positive predictive value	12.46%	11.81%
Negative predictive value	97.88%	97.16%
Diagnostic accuracy	**61.20%**	**59.60%**



In this study the overall diagnostic accuracy of VILI with CIN 2 and above as disease threshold was 61.20% with physician and 59.60% when performed by nurse.

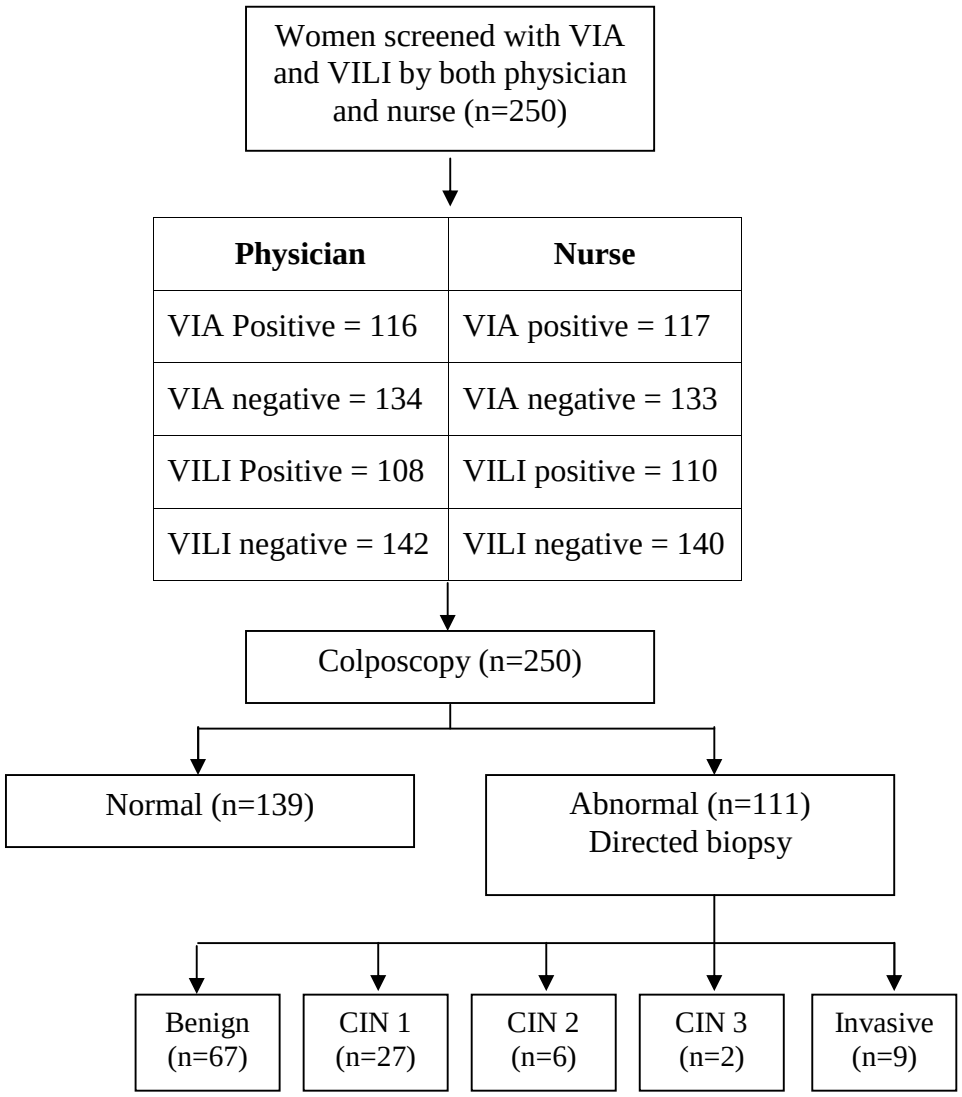
Chapter 6

Discussion

DISCUSSION

The present study was carried out in select population who were referred to colposcopy clinic to explore the test performance of VIA and VILI by physician and nurse and to evaluate the feasibility and efficacy of training the physician and nurse in interpreting VIA and VILI results. Before the commencement of the study, both physicians and nurses received training.

Women Screened By VIA and VILI by Physician and Nurse



We evaluated 250 women who fulfilled the eligibility criteria and provided informed consent. Maximum number of women was in the age group of 31-40 years (46%) with mean age of 35.5 years. In terms of parity majority of the women were para 2 (53.2%). The common presenting complaint was persistent white discharge per vaginum seen in 77.6% , followed by inter menstrual bleeding in 9.2%, post coital bleeding in 5.6%, suspicious looking cervix and screen positive in 2.8% each and post menopausal bleeding in 2%.

Few studies have been conducted using different criteria for interpreting the result of VIA. In this study, we interpreted the result using the criteria described by IARC, which were stringent than those described by Denny et al.[52]

The test characteristics of the study population and the criteria used to categorize VIA and VILI results of the present study were similar to a study done in India in 2003.[53] VIA was positive in 116 cases (46.4%) by physician and in 117 cases (46.8%) by nurse (Table 1). VILI positive cases by physician were 108 (43.2%) and by nurse were 110 (44%). Of the study population, 106 cases (42%) were VIA positive and 123 cases (49.2%) were VIA negative by both physician and nurse resulting in an almost perfect agreement between the two (k=0.831). Bhatla et al study had moderate agreement (k=0.57) between VIA findings between the doctor and nurse. VILI was positive in 101 cases (40.4%) and negative in 133 cases (53.2%) by both physician and nurse, with almost perfect agreement between the two (k=0.87), which was comparable to a study done at New Delhi, India (k=.89). In a study done for inter rater variability for VIA on static images between experts, moderate to substantial agreement was observed.[62]

Contrary to the study[53] done in New Delhi, India, our study showed higher sensitivity by physician (100%) as compared to nurse (88.23%) but specificity by both physician and nurse were almost comparable (57.5% and 56.2%). VILI results by physician also had superior sensitivity to that of nurse (82.3% versus 76.47%) and specificity of 59.65% and 58.36% by physician and nurse respectively. Two CIN 2 lesions were missed by nurse on VIA examination as the acetowhite areas were less dense although physician labelled them as positive. If Denny's criteria had been followed in the present study and all white lesions considered positive, the sensitivity would have increased further but with reduction in the positive predictive value of the test. This is an important programmatic consideration as this would lead to an unacceptably high burden of referrals for further disease characterization.

Because of the subjective nature of the VIA test, it has high false positive rate. Even in this study both physician and nurse had false positive rate of 42.2% and 43.7% respectively. Both physician and nurse were aware that colposcopy would be done on the same day so cases were over diagnosed in order to ensure that no case was missed.

As observed in this study, the physician with a better clinical skill level who was familiar with gynaecological examination and various pathological conditions of cervix comprehended the proceedings of the training session better than the nurse. This was reflected as better test performance by the physician. This study emphasizes the fact that VIA is provider dependent. As standardization of the test is difficult we feel that intensive training with periodic

reinforcement is essential for providers who have limited knowledge regarding cervical pathology.

Chapter 7

Conclusion

CONCLUSION

Based on the results of the present study it may be concluded that, visual inspection can be performed reliably by trained nurses and doctors and is an effective screening option in low resource settings. However, intensive training and periodic reinforcement sessions are needed so as to reduce the false positive results.

Chapter 8

Summary

SUMMARY

Cervical cancer is an important public health problem that deserves urgent attention. It is an important area of action for any cancer control programme because of the burden of disease, and the potential for effective prevention via screening. The present study was aimed to evaluate and compare predictive value of visual inspection methods and assess the concordance of results between physician and nurse for cervical cancer screening as compared to colposcopy and histopathology.

The present cross-sectional study was conducted at Colposcopy Clinic, Outpatient department, Obstetrics and Gynaecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from December 2010 to July 2012. A total of 250 women were studied. All sexually active women from age 20 to 50 years attending Colposcopy Clinic with complaints of persistent vaginal discharge, inter menstrual bleeding, post coital bleeding, suspicious looking cervix and positive screen test were included in the study. VIA and VILI by both physician and nurse and the findings were interpreted independently. This was followed by colposcopy done by a gynaecologist blinded to the results of VIA and VILI and directed biopsy was taken if indicated. Negative colposcopy and histopathology were considered as the reference standard. Test positivity was defined by histopathology report of cervical intraepithelial neoplasia 2 (CIN 2) and above.

VIA by doctor had a higher sensitivity (100% versus 88.23%) and higher specificity (57.5% versus 56.2%) when compared with the nurse. There was

almost perfect agreement between their VIA findings (kappa=0.83). VILI findings of doctor had a sensitivity and specificity of 82.3% and 59.65% respectively, while nurse had a sensitivity of 76.47% and specificity of 58.36%. There was almost perfect agreement (kappa=0.87) between VILI by the doctor and nurse.

Visual inspection can be performed reliably by trained nurses and doctors and is an effective screening option in low resource settings.

Chapter 9

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Annexures

Annexure I

ANNEXURE I

PARTICIPANT'S INFORMATION AND CONSENT FORM

Sr. No: _____

Patient's Name (Mrs.): _____

I hereby request you to participate in the study **"INTEROBSERVER VARIABILITY OF VISUAL INSPECTION METHODS BETWEEN PHYSICIAN AND NURSE FOR CERVICAL CANCER SCREENING: A CROSS SECTIONAL STUDY"** conducted by Dr. **** *****, Post Graduate in M.S Obstetrics and Gynaecology under the guidance of Dr. **** *****, Associate Professor, Department of Obstetrics and Gynaecology, J. N. Medical College, Belgaum under KLE University, Belgaum.

I request you to enroll yourself to participate in this study as you are eligible for participating. Cancer cervix is the commonest genital malignancy and leading cause of death among women in India. It can be easily prevented by screening and treating at an earlier stage known as the pre-cancerous stage. Screening for precancerous lesions can be done by visual inspection methods. The objective of this study is to evaluate and compare test performance of visual inspection with acetic acid (VIA) and Visual inspection with Lugol's iodine (VILI) by physician and nurse for cervical cancer screening and to know the feasibility and effectiveness of training the nurses so that we can achieve a better coverage and quality results. Your participation may benefit you and others undergoing same procedure. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of

your knowledge. All information collected about you during the course of this study will be kept confidential.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with KLES PRABHAKAR KORE HOSPITAL. If you decide to participate, you are free to withdraw at any time according to the existing protocol.

There are no financial incentives promised to you for being a part of this study. You will not be charged any extra cost.

PROCEDURE

If you agree to enroll in my study the following steps are followed:

a) As you are eligible for this study, dilute vinegar (5% acetic acid) will be applied to the mouth of the womb (cervix) and visually inspected after 1 min under 100 watt bulb both by physician and nurse followed by application of Lugol's iodine.

b) Following visual inspection methods, magnified inspection of the cervix with an instrument called colposcope will be done. If colposcopy reveals any abnormality examination of a sample of tissue (biopsy) of the cervix will be recommended before the treatment is provided.

BENEFITS

Early detection of precancerous lesions at a treatable stage before they progress to invasive cancer.

RISKS INVOLVED

Mild irritation after the application of acetic acid. If biopsy is taken then minimal bleeding from the biopsy site which will subside without any treatment.

ALTERNATIVE

Even if you decline to participate in this study, you will get the routine line of management**.**

PRIVACY AND CONFIDENTIALITY

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission except:

1) In emergency to protect your rights and welfare.
2) If required by law.

AUTHORIZATION TO PUBLISH RESULTS

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

COMPENSATION

In event of injury related to the study, treatment will be made available through KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr. ***** ******, Post Graduate Student, J. N. Medical College, Belgaum. Phone no. ***** *****.

QUERIES

If you have any question about the study you may please contact the Chief investigator Dr. **** ******, Professor of department of Obstetrics and

Gynaecology, J.N.M.C. Belgaum, Ph. No. ***** *****, Dr. **** ******, Post Graduate Student, Department of Obstetrics and Gynaecology, J. N. M. C. Belgaum. Ph. No. ***** ******.

If you have any questions regarding rights of participants you may please contact Chairman of ethical committee, JNMC, Belgaum. Ph. No. ***** *****.

Consent for participation in research trial:

Participant's Name: _____

Signature or left thumb print: _____

Address: _____

_____

Telephone No: _____

Witness name: _____

Signature: _____

Investigator's Name: _____

Signature: _____

Date: _____

Annexures

Annexure II

ANNEXURE II – PROFORMA

"INTEROBSERVER VARIABILITY OF VISUAL INSPECTION METHODS BETWEEN PHYSICIAN AND NURSE FOR CERVICAL CANCER SCREENING: A CROSS SECTIONAL STUDY"

Serial. No. : _____ **OP No: _____**

Date: [ ][ ]-[ ] [ ]-[ ] [ ]

1. Patient Name: _____
2. Age : [ ] [ ]
3. Husband's Name: _____
4. Socio economic status:_____
5. Residential Address: _____

   _____
6. Residence Phone No.:_____
7. Mobile No.:_____
8. Education: [ ]

   1. Nil
   2. Primary
   3. Middle
   4. High school
   5. College

9. Marital status: [ ]

   1= Married, 2= Widow, 3= Separated

10. History

Chief Complaints: (use: 0=No, 1=Yes)

Intermenstrual bleeding [ ]

Post coital bleeding [ ]

Post menopausal bleeding [ ]

Recurrent episodes of white discharge per vagina [ ]

Menstrual History:

Age of Menarche: [ ]

Past Menstrual Cycle: _____

Present Menstrual Cycle: _____

LMP: [ ][ ]-[ ] [ ]-[ ] [ ]

Obstetric History:

ML _____

Para _____ Living_____ Abortion _____

Contraception: Use of OC pills Yes / No

Sterilization: _____

Past History: [ ] DM, [ ] HTN, [ ] TB, [ ] Previous surgeries, [ ] STDs

Family History: [ ] DM, [ ] HTN, [ ] TB in the family

Personal History: (use: 0=No, 1=Yes)

Age of 1st intercourse [ ] [ ]

Multiple sexual partner [ ]

Tobacco: Smoking/ Chewing [ ]

HIV [ ]

11. General Physical Examination:

    Pallor [ ]

    Pedal edema [ ]

    BP:

    PR:

12. Systemic Examination:

    CVS: _____

    RS: _____

    P/S: _____

    SCJ Visualized (use: 0=No, 1=Yes) [ ]

    P/V:

    A. Uterine size (0=Normal, 1=Enlarged) [ ]

    B. Cervical motion tenderness (0=No, 1=Yes) [ ]

    C. Adnexal tenderness (0=No, 1=Yes) [ ]

    D. Adnexal Mass (0=No, 1=Yes) [ ]

PROFORMA FOR VIA AND VILI BY PHYSICIAN

13. Findings 1 min after application of 5% Acetic acid. [ ]

    1. Negative

    2. Positive

    3. Positive (Invasive cancer)

14. If VIA is positive, does the aceto white lesion extend into the endocervical canal? [ ]

    1. Yes

    2. No

15. If VIA positive, how many quadrants are involved with aceto white lesions? [ ]

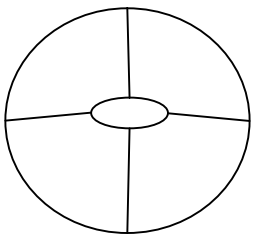
    1. One

    2. Two

    3. Three

    4. Four

16. Diagram of VIA positive lesions and SCJ.



17. Findings of VILI. [ ]

    1. Negative

    2. Positive

    3. Positive (Invasive carcinoma)

18. If VILI positive, how many quadrants do not take up iodine staining? [ ]

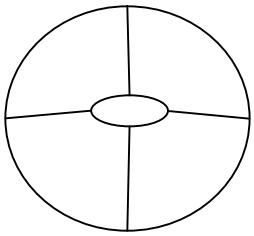
    1. One

    2. Two

    3. Three

    4. Four

19. Diagram of VILI positive areas.



PROFORMA FOR VIA AND VILI BY NURSE

13. Findings 1 min after application of 5% Acetic acid. [ ]

    1. Negative

    2. Positive

    3. Positive (Invasive cancer)

14. If VIA is positive, does the aceto white lesion extend into the endocervical canal? [ ]

    3. Yes

    4. No

15. If VIA positive, how many quadrants are involved with aceto white lesions? [ ]

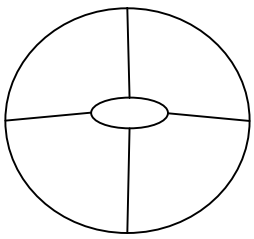
    1. One

    2. Two

    3. Three

    4. Four

16. Diagram of VIA positive lesions and SCJ.



17. Findings of VILI. [ ]

    1. Negative

    2. Positive

    3. Positive (Invasive carcinoma)

18. If VILI positive, how many quadrants do not take up iodine staining? [ ]

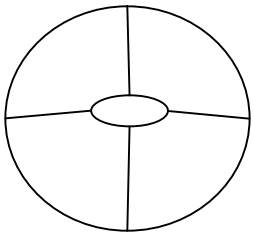
    1. One

    2. Two

    3. Three

    4. Four

19. Diagram of VILI positive areas.

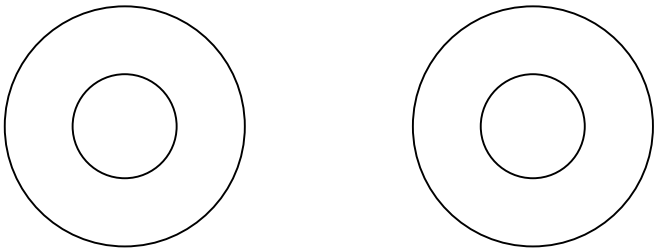


20. Patient will be subjected to colposcopy Date: **[ ] [ ]- [ ] [ ]- [ ] [ ]**

1. Squamocolumnar junction [ ]

(0=Not seen, 1= Partially seen, 2=Fully seen, 9= Not able to comment)

2. Diagram of Colposcopic findings (mark with colour) (also mark site of biopsies taken with respective numbers)



3. If lesion(s) present, how many quadrants are involved? [ ]

(0=none, 1=One, 2=Two, 3=Three, 4=Four, 9=Not able to comment)

4. Mucosal bleeding easily induced [ ]

(0=No, 1= Yes, 9=Not done/not able to comment

Colposcopic Diagnosis: (use:0 =No, 1=Yes)

a. Unsatisfactory [ ]

b. WNL [ ]

c. Ectopy [ ]

d. Inflammation/ Infection [ ]

e. Nabothian Follicle [ ]

f. Condyloma [ ]

g. Squamous Metaplasia – Mature [ ]

h. Squamous Metaplasia- Immature [ ]

i. Atrophic [ ]

j. HPV infection [ ]

k. CIN 1 [ ]

l. CIN 1 / 2 [ ]

m. CIN 2 / 3 [ ]

n. Invasive Cancer [ ]

o. Healing / Post traumatic [ ]

p. Chronic cervicitis [ ]

21. Modified Reid Colposcopy Index:_____

22. If the colposcopic diagnosis is HPV infection / CIN 1-3, is the entire lesion visualized on the ectocervix? (1=Yes, 2=No) [ ]

Additional remarks: _____

23. Biopsy taken? (1=Yes, 2=No)

24. Biopsy report [ ]

Number of biopsy:

Site of Biopsy:

Microscopy:

Impression:

25. ECC taken? (1=Yes, 2=No) [ ]

26. ECC report (if taken): _____

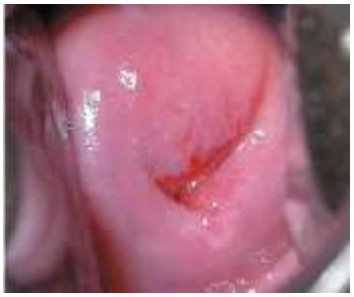
27. Treatment advised [ ]

1. Antibiotics given
2. Follow up after 9-12 months
3. Cryotherapy
4. LEEP
5. Hysterectomy
6. Radiotherapy

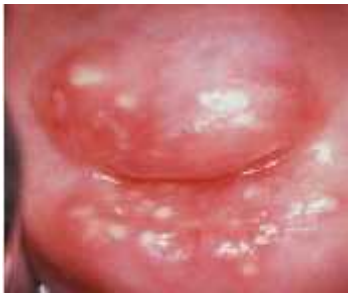
Annexures

Annexure III

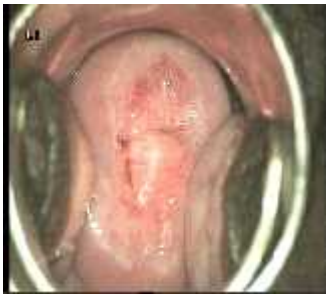
ANNEXURE III – PHOTOGRAPHS



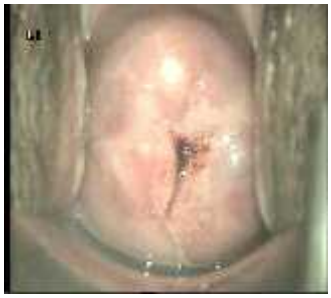
Photograph 3. VIA negative



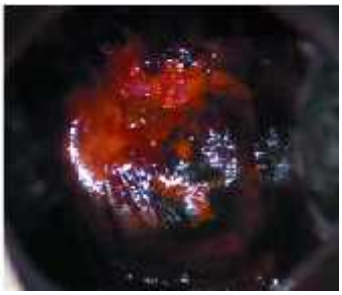
Photograph 4. VIA negative



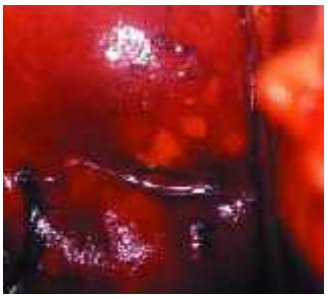
Photograph 5. VIA positive



Photograph 6. VIA positive



Photograph 7. VILI negative



Photograph 8. VILI negative

Photograph 9. VILI positive

Photograph 10. VILI positive

Annexures

Annexure IV

ANNEXURE IV – KEY TO MASTER CHART

ECC	-	Endocervical curettage
HIV	-	Human immunodeficiency virus
MRCI	-	Modified Reid Colposcopic Index
OCP	-	Oral contraceptive pills
P/S	-	Per Speculum
VIA	-	Visual Inspection by Acetic acid
VILI	-	Visual Inspection by Lugol's Iodine

Age :

1	20-30 years
2	31-40 years
3	41-50 years

Education:

1	Illiterate
2	Primary
3	Middle
4	High school
5	College

Inclusion criteria:

1	WDPV
2	Intermenstrual bleeding
3	Post coital bleeding
4	Post menopausal bleeding
5	Screen positive
6	Suspicious cervix

Age of menarche:

1	11 years
2	12 years
3	13 years and above

Married life (ML):

1	1-10 years
2	11-20 years
3	21-30 years
4	31-40 years

Parity:

1	Nulliparous
2	Para 1
3	Para 2
4	Para 3
5	Para 4 & above

Oral contraceptive pill use/ HIV infection:

1	No
2	Yes

Sterilization:

1	No
2	Yes

Age of Coitus:

1	15-18 years
2	19-22 years
3	23-26 years
4	27-30 years
5	31-34 years

Per speculum :

0	Cervix & vagina healthy
1	WDPV
2	Erosion
3	Unhealthy
4	Others

VIA & VILI examination by Physician and Nurse:

1	Positive
2	Negative

Colposcopy:

1	Benign
2	CIN 1
3	CIN ½
4	CIN 2/3
5	Invasive carcinoma

Biopsy report:

0	Not taken
1	Benign
2	CIN 1
3	CIN 2
4	CIN 3
5	Invasive carcinoma

ECC report:

0	Not taken
1	Normal
2	Chronic endocervicitis

Treatment advised:

1	Antibiotics
2	Follow up after 9-12 months
3	Cryotherapy
4	Leep
5	Hysterectomy

Final diagnosis:

1	Benign & CIN 1
2	CIN 2, CIN 3 & Invasive carcinoma

MASTER CHART

Serial number	Age (Years)	Education	Marital status	Inclusion criteria	Age of menarche	Married life	Parity	OCP use	Sterilization	Age of coitus	Multiple sex partners	Tobacco	HIV	Per speculum	VIA by Physician	VILI by physician	VIA by nurse	VILI by nurse	Colposcopy	MRCI	Biopsy taken	Number of Biopsy	Biopsy Site	Biopsy Impression	ECC	Treatment advice	Final diagnosis
1	1	2	1	1	2	1	3	0	0	2	0	0	0	3	1	1	1	1	2	0	1	1	1 o'clock	2	0	2	1
2	2	3	1	3	2	2	2	0	0	3	0	0	0	1	1	1	1	1	2	0	1	1	10 o'clock	2	0	2	1
3	1	1	1	1	4	1	2	0	0	2	0	0	0	4	1	2	2	2	1	-	0	-	-	0	0	2	1
4	2	1	1	1	2	2	3	0	1	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
5	1	4	1	1	2	2	4	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
6	2	1	1	1	2	1	3	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
7	2	5	1	1	4	1	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
8	2	4	1	1	2	2	5	0	1	1	0	0	0	4	1	2	1	2	1	-	0	-	-	0	0	1	1
9	3	5	1	1	5	1	2	0	0	5	1	0	0	1	1	1	1	1	2	2	1	1	2 o'clock	1	0	2	1
10	1	5	1	5	4	1	3	0	0	3	0	0	0	1	1	1	2	1	2	0	1	1	12 o'clock	1	0	2	1
11	3	5	1	1	4	3	4	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
12	2	5	1	1	4	2	3	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
13	2	5	1	1	4	2	3	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
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15	2	1	1	5	4	2	3	0	1	3	0	0	0	2	1	1	1	1	2	0	1	1	4 o'clock	1	2	1	1
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17	3	3	1	1	4	3	4	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
18	2	3	1	1	4	3	4	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
19	1	5	1	1	2	1	2	0	0	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
20	2	5	1	1	4	2	2	0	0	3	1	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
21	2	2	1	1	4	3	4	0	1	1	0	0	0	2	1	1	1	1	2	1	1	1	2&11 o'clock	1	0	3	1
22	1	4	1	1	2	1	3	0	1	3	1	1	1	2	1	2	1	2	1	-	0	-	-	0	0	2	1
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24	2	5	1	1	4	1	3	1	0	2	1	0	0	4	2	2	2	2	1	-	0	-	-	0	0	2	1
25	2	4	10	1	4	2	3	0	1	2	0	0	0	2	1	1	1	1	1	1	1	3	2,6&10 o'clock	1	0	2	1
26	1	3	1	2	2	1	2	0	0	2	0	0	0	2	1	1	1	1	2	1	1	1	12 o'clock	2	0	2	1
27	2	3	1	1	2	2	4	0	0	1	0	0	0	1	1	1	1	1	2	1	1	1	5 o'clock	1	0	3	1
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36	1	5	1	1	4	1	3	0	0	3	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	3	1
37	3	4	1	1	5	3	3	1	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
38	1	4	1	1	3	1	3	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
39	3	5	1	2	2	3	3	0	1	2	0	0	0	3	1	1	1	1	3	3	1	2	3 & 7 o'clock	2	0	5	1
40	2	1	1	6	4	2	4	0	1	1	0	0	0	4	2	2	2	2	1	-	0	-	-	0	0	2	1
41	3	4	1	1	1	3	4	0	1	3	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	2	1
42	3	4	1	6	3	3	3	0	1	2	0	0	0	3	1	1	1	1	2	0	1	1	11 o'clock	3	0	4	2
43	2	4	1	3	3	2	4	0	0	2	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	2	1
44	2	5	1	1	4	2	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
45	2	3	1	5	3	2	3	0	0	2	1	0	0	3	1	1	2	2	2	2	1	2	6&12 o'clock	3	0	3	2
46	1	2	1	1	2	1	3	0	0	2	0	0	0	1	2	2	1	1	1	-	0	-	-	0	0	2	1
47	1	3	1	1	3	1	2	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
48	2	4	1	1	2	2	4	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
49	1	5	1	1	3	1	3	0	0	2	0	0	0	3	2	2	1	1	1	-	0	-	-	0	0	2	1
50	2	3	1	1	3	3	4	0	0	1	0	0	0	3	1	1	1	1	4	6	1	2	6 & 12 o'clock	5	0	5	2
51	2	1	1	1	4	2	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
52	2	5	1	1	2	1	2	0	0	2	0	0	0	3	1	1	1	1	3	3	1	1	2 o'clock	1	0	3	1
53	3	5	1	1	2	3	3	0	0	2	0	0	0	3	2	2	1	1	2	1	1	1	4 o'clock	2	0	3	1
54	2	1	1	1	2	2	3	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
55	2	4	1	3	3	2	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	2	2	1
56	3	1	1	1	2	3	4	0	0	2	0	0	0	3	1	1	1	1	2	0	1	3	12,2&6 o'clock	2	1	3	1
57	3	5	1	1	1	3	3	0	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
58	1	4	1	3	2	1	3	1	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
59	2	5	1	2	3	1	3	0	1	3	0	0	0	2	1	1	1	1	2	1	1	2	12 & 6 o'clock	2	0	3	1
60	3	5	1	1	3	2	3	0	1	3	0	0	0	1	1	1	2	2	1	-	0	-	-	0	0	2	1
61	3	4	1	1	2	3	4	0	1	3	0	0	0	4	1	1	2	2	1	-	0	-	-	0	1	2	1
62	1	1	1	1	2	3	3	0	0	1	0	0	0	4	1	1	1	1	1	1	1	1	2 o'clock	1	0	2	1
63	3	3	1	1	4	4	3	0	0	4	0	0	0	1	2	2	2	2	1	-	0	-	-	0	1	2	1
64	2	1	1	1	3	2	3	0	0	1	0	0	0	0	1	1	1	1	2	0	1	1	1 o'clock	1	0	2	1
65	1	4	1	1	2	1	3	0	0	2	0	0	0	4	2	2	2	2	1	-	0	-	-	0	0	3	1

MASTER CHART

Serial number	Age (Years)	Education	Marital status	Inclusion criteria	Age of menarche	Married life	Parity	OCP use	Sterilization	Age of coitus	Multiple sex partners	Tobacco	HIV	Per speculum	VIA by Physician	VILI by physician	VIA by nurse	VILI by nurse	Colposcopy	MRCI	Biopsy taken	Number of Biopsy	Biopsy Site	Biopsy Impression	ECC	Treatment advice	Final diagnosis
66	2	4	1	1	3	2	3	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
67	3	1	1	4	3	3	4	0	0	2	0	0	0	2	1	1	1	1	2	1	1	1	6 o'clock	1	0	3	1
68	1	5	1	1	3	1	3	1	0	3	0	0	0	1	1	1	1	1	2	0	1	1	6 o'clock	1	0	3	1
69	2	4	1	1	3	1	3	0	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
70	1	5	1	1	4	1	2	0	0	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
71	2	4	1	1	2	2	3	0	1	2	0	0	0	4	1	1	1	1	2	1	1	1	6 o'clock	4	0	4	2
72	3	5	1	3	2	2	3	1	0	2	0	0	0	1	1	1	1	1	2	2	1	2	3 & 6 o'clock	2	0	4	1
73	1	5	1	1	2	1	3	0	0	2	0	0	0	4	2	2	2	2	1	-	0	-	-	0	0	2	1
74	1	5	1	1	2	1	2	0	0	3	0	0	0	1	1	2	1	2	2	2	1	1	12 o'clock	3	0	4	2
75	2	5	1	2	2	2	3	0	0	1	0	0	0	1	2	2	2	2	1	-	1	1	polypectomy	1	0	2	1
76	1	5	1	1	4	1	3	0	1	2	0	0	0	2	1	2	2	2	1	-	1	1	11 o'clock	1	0	2	1
77	2	5	1	1	4	2	3	0	0	3	0	0	0	1	1	2	1	2	3	2	1	1	12 o'clock	2	0	4	1
78	1	3	1	1	3	1	2	0	0	1	0	0	0	0	1	1	1	1	2	2	1	2	11 & 5 o'clock	1	0	3	1
79	3	3	1	1	2	3	4	0	1	2	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	2	1
80	2	3	1	1	4	1	3	0	1	3	0	0	0	2	1	1	1	1	2	-	1	1	10 o'clock	1	0	2	1
81	3	4	1	1	5	4	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	2	2	1
82	2	2	1	2	4	1	4	0	1	2	0	0	0	3	1	1	1	1	1	-	1	2	11 o'clock	1	0	2	1
83	3	1	2	5	4	3	3	0	1	2	0	0	0	3	1	1	1	1	2	2	1	1	11 o'clock	1	0	2	1
84	3	1	1	4	1	4	5	0	0	2	0	0	0	3	1	1	1	1	5	-	1	3	12,4&6 o'clock	5	0	5	2
85	3	5	1	2	4	4	3	0	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
86	3	2	1	2	3	3	3	0	1	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
87	3	5	2	1	4	3	3	0	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
88	1	5	1	1	4	1	2	1	0	2	0	0	0	3	1	1	1	1	2	1	1	1	11 o'clock	1	0	3	1
89	2	5	1	1	2	2	3	0	1	3	1	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
90	2	1	1	1	1	2	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
91	1	5	1	1	2	1	3	1	0	2	0	0	0	2	1	1	1	1	1	-	0	-	-	0	0	2	1
92	2	2	1	1	3	1	3	0	0	2	0	0	0	1	1	1	1	1	1	-	0	-	-	0	0	1	1
93	1	1	1	5	2	1	3	0	0	2	0	0	0	1	1	1	1	1	3	3	1	2	11 & 4 o'clock	2	0	3	1
94	1	2	1	1	1	1	2	0	0	2	0	0	0	1	1	2	2	2	1	-	0	-	-	0	0	3	1
95	2	1	1	1	2	2	4	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
96	2	3	1	1	1	1	2	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
97	1	2	1	1	2	1	2	0	0	2	0	0	0	1	1	1	1	1	2	1	1	1	4 o'clock	1	0	3	1
98	2	3	1	1	3	1	3	1	0	3	0	0	0	0	1	1	1	1	2	2	1	1	1 o'clock	1	0	3	1
99	3	5	1	1	2	3	3	0	1	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	2	5	1
100	1	4	1	1	2	1	2	0	0	3	0	0	0	1	1	1	1	1	2	2	1	2	12,2&5 o'clock	1	0	3	1
101	2	5	1	2	2	1	2	0	0	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
102	1	4	1	1	3	1	3	0	1	1	0	0	0	2	2	2	1	2	1	-	0	-	-	0	0	2	1
103	3	3	1	1	2	2	3	0	0	2	0	0	1	2	1	1	1	1	3	3	1	2	4 & 6 o'clock	1	0	3	1
104	1	3	1	1	2	1	2	0	0	3	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
105	2	2	1	6	2	3	4	0	0	2	0	0	0	3	1	1	1	1	1	-	0	-	-	0	0	2	1
106	2	4	1	3	4	2	4	0	1	2	0	0	0	2	1	1	1	1	1	-	0	-	-	0	0	3	1
107	1	4	1	1	2	1	3	0	0	2	0	0	0	3	1	1	1	1	2	3	1	1	11 o'clock	1	0	2	1
108	1	4	1	3	1	1	2	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
109	1	3	1	1	2	1	3	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
110	2	4	1	1	3	2	3	0	1	1	0	0	0	0	2	2	1	2	1	-	0	-	-	0	0	2	1
111	2	5	1	1	4	2	2	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
112	1	4	1	1	2	2	3	0	0	1	0	0	0	1	2	2	1	1	1	-	0	-	-	0	0	1	1
113	1	4	1	1	3	2	4	0	0	1	0	0	0	3	1	1	1	1	3	4	1	3	2,4&5 o'clock	1	0	3	1
114	1	3	1	1	2	2	4	0	1	1	0	0	0	2	1	1	1	1	1	-	1	1	12 o'clock	1	0	2	1
115	2	3	1	1	2	1	3	0	0	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
116	2	3	1	1	2	2	2	0	0	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
117	3	2	1	3	3	3	4	0	1	1	0	0	0	3	1	1	1	2	5	-	1	2	10 & 4 o'clock	5	0	5	2
118	1	2	1	1	2	1	2	0	0	1	0	0	0	0	1	1	1	1	1	-	0	-	-	0	0	1	1
119	2	2	2	1	4	2	2	0	0	1	0	0	1	0	2	2	2	2	1	-	0	-	-	0	0	2	1
120	1	3	1	1	3	1	2	0	0	1	0	0	0	1	1	1	1	1	1	-	1	1	6 o'clock	1	0	3	1
121	2	5	1	3	3	1	3	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
122	1	4	1	1	2	1	2	0	0	1	0	0	0	1	1	1	1	1	2	2	1	1	12 o'clock	1	0	5	1
123	2	5	1	2	2	2	3	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
124	1	5	1	1	2	1	3	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
125	2	3	1	1	2	1	3	0	1	2	0	0	0	1	1	2	1	2	1	-	0	-	-	0	0	1	1
126	2	4	1	1	4	1	2	0	0	4	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	3	1
127	2	2	1	1	2	1	3	0	0	4	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
128	2	4	1	1	1	2	3	0	0	2	0	0	0	1	1	1	1	1	4	5	1	2	12 & 6 0'clock	1	0	5	1
129	1	4	1	1	2	1	2	0	0	3	0	0	0	1	2	2	1	1	1	-	0	-	-	0	0	1	1
130	2	3	1	1	1	2	3	0	0	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1

MASTER CHART

Serial number	Age (Years)	Education	Marital status	Inclusion criteria	Age of menarche	Married life	Parity	OCP use	Sterilization	Age of coitus	Multiple sex partners	Tobacco	HIV	Per speculum	VIA by Physician	VILI by physician	VIA by nurse	VILI by nurse	Colposcopy	MRCI	Biopsy taken	Number of Biopsy	Biopsy Site	Biopsy Impression	ECC	Treatment advice	Final diagnosis
131	1	3	1	1	2	1	4	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
132	2	1	1	1	2	2	5	0	1	2	0	0	0	1	1	1	1	1	2	1	1	1	12 & 5 o'clock	1	0	1	1
133	1	2	1	1	3	1	2	1	0	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
134	2	4	1	2	2	3	5	0	1	1	0	0	0	2	2	2	2	2	2	1	1	1	12 & 6 0'clock	0	0	1	1
135	1	5	1	1	2	1	2	0	0	2	0	0	0	1	1	1	1	1	2	1	1	1	10 & 6 o'clock	2	0	2	1
136	2	1	1	1	2	2	3	0	1	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
137	2	1	1	1	3	2	4	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
138	3	1	1	1	2	2	4	0	1	1	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	2	1
139	2	4	1	1	2	2	4	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
140	3	3	1	2	2	2	4	0	1	2	0	0	0	3	1	2	1	2	1	-	1	2	polypectomy	1	0	2	1
141	2	2	1	3	2	2	4	0	1	1	0	0	0	3	1	1	1	1	1	-	0	-	-	0	0	2	1
142	1	3	1	2	3	2	5	0	1	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
143	1	4	1	1	2	1	4	0	1	1	0	0	0	3	1	1	1	1	2	2	1	2	2 & 11 o'clock	2	0	3	1
144	3	3	1	1	3	3	4	0	0	2	0	0	0	3	1	1	1	1	1	-	0	-	-	0	0	2	1
145	2	1	1	1	2	2	4	0	1	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	1	1
146	2	1	1	1	2	3	4	0	1	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
147	2	2	1	1	2	2	3	0	1	2	0	0	0	4	1	1	1	1	2	1	1	3	11,12&4 o'clock	1	0	3	1
148	3	1	1	4	2	3	4	0	1	1	0	0	0	3	1	1	2	2	2	1	1	2	6 o'clock,polyp	1	2	3	1
149	2	1	1	1	2	2	3	0	1	2	0	0	0	2	1	1	1	1	2	2	1	2	11 &5 o'clock	1	0	3	1
150	3	3	1	1	2	3	4	0	0	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
151	2	3	1	1	2	2	1	0	0	1	0	0	0	1	1	1	1	1	4	3	1	3	6,1& 11 o'clock	3	0	4	2
152	1	2	1	6	2	2	3	0	1	4	0	0	0	3	1	1	1	1	2	1	1	3	11,5&7 o'clock	1	0	3	1
153	1	4	1	1	2	1	3	0	0	2	0	0	0	3	2	1	1	1	2	1	1	1	1 o'clock	1	0	3	1
154	1	3	1	1	2	2	2	1	0	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
155	1	2	1	1	4	1	3	0	0	1	0	0	0	2	1	1	1	1	1	-	1	1	1 o'clock	2	0	3	1
156	2	4	1	2	3	2	3	0	0	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
157	2	1	1	1	1	2	4	0	0	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
158	3	1	1	6	1	2	5	0	0	5	0	0	0	3	1	1	1	1	5	-	1	4	4 quadrant	5	0	5	2
159	3	1	1	1	2	3	4	0	0	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
160	2	4	1	1	2	3	5	0	1	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
161	3	1	1	1	2	4	4	0	0	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
162	1	5	1	1	3	1	2	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
163	2	1	1	1	2	2	3	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
164	1	3	1	1	2	1	2	0	0	1	0	0	0	1	2	2	2	2	2	2	1	2	11 & 12 o'clock	1	0	3	1
165	3	4	1	1	4	2	3	0	1	4	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
166	3	1	1	4	2	4	5	0	0	1	0	0	0	3	1	1	1	1	5	-	1	4	4 quadrant	5	0	5	2
167	3	2	1	3	2	4	3	0	1	2	0	0	0	3	1	1	1	1	5	-	1	1	4 o'clock	5	0	5	2
168	3	4	1	2	2	3	3	0	1	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
169	2	4	1	1	4	2	4	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
170	3	5	1	1	3	3	3	0	0	3	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
171	3	5	1	2	2	3	4	0	1	2	0	0	0	1	1	1	1	1	2	0	1	1	6 o'clock	1	0	3	1
172	2	2	1	1	3	3	3	0	1	2	0	0	0	1	2	1	1	1	1	-	1	1	6 o'clock	1	0	3	1
173	3	1	1	1	1	4	4	0	0	2	0	0	0	3	1	1	1	1	5	-	1	4	4 quadrant	5	0	5	2
174	3	4	1	1	3	3	4	0	1	1	0	0	0	1	1	1	1	1	1	-	0	-	-	0	0	2	1
175	2	4	1	5	2	2	3	0	1	2	0	0	0	1	1	2	1	2	4	6	1	2	4 & 8 o'clock	4	0	4	2
176	3	4	1	1	2	3	3	0	1	4	0	0	0	1	2	1	2	1	1	-	0	-	-	0	0	2	1
177	2	1	1	2	2	1	1	0	0	2	0	0	0	2	1	2	1	2	2	1	1	2	12 & 3 o'clock	2	0	3	1
178	1	3	1	1	2	2	3	0	0	2	0	0	0	1	1	1	1	1	1	-	1	1	12 o'clock	1	0	2	1
179	2	1	1	4	2	2	3	0	1	3	0	0	0	3	1	1	1	1	2	3	1	2	4 & 7 0'clock	1	0	3	1
180	2	4	1	1	3	2	4	0	1	2	0	0	0	1	1	1	1	1	1	-	1	2	3 & 7 o'clock	1	0	2	1
181	3	4	1	2	2	3	3	0	1	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
182	2	5	1	1	3	1	2	0	0	4	0	0	0	0	1	2	1	1	2	2	1	1	12 o'clock	1	0	3	1
183	3	3	1	1	2	2	4	0	1	3	0	0	0	1	1	1	1	1	2	2	1	1	12 o'clock	1	0	3	1
184	3	2	1	3	1	3	3	0	0	3	0	0	0	2	2	2	2	2	2	2	1	1	3 o'clock	1	0	3	1
185	2	4	1	1	2	2	3	0	1	2	0	0	0	2	1	1	1	1	3	3	1	2	3 & 9 o'clock	1	0	3	1
186	2	5	1	1	2	2	3	0	1	2	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
187	1	5	1	1	2	2	3	0	1	2	0	0	0	2	2	1	2	1	1	-	1	1	4 o'clock	1	0	2	1
188	2	4	1	1	4	2	3	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
189	1	1	1	3	2	1	2	0	0	1	0	0	0	3	1	1	1	1	2	1	1	1	12 o'clock	1	0	3	1
190	1	3	1	1	3	1	3	0	1	2	0	0	0	2	1	2	1	2	1	-	0	-	-	0	0	2	1
191	2	5	1	1	4	2	4	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
192	2	4	1	1	2	2	3	0	1	4	0	0	0	2	1	1	1	1	2	1	1	1	12 o'clock	1	0	3	1
193	2	3	1	1	3	1	5	0	0	2	0	0	0	1	1	1	1	1	1	1	1	1	12 o'clock	1	0	3	1
194	3	5	1	1	1	3	3	0	1	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
195	3	4	1	2	2	4	5	0	0	1	0	0	0	3	1	1	1	1	3	3	1	2	1 & 7 o'clock	3	0	5	2

MASTER CHART

Serial number	Age (Years)	Education	Marital status	Inclusion criteria	Age of menarche	Married life	Parity	OCP use	Sterilization	Age of coitus	Multiple sex partners	Tobacco	HIV	Per speculum	VIA by Physician	VILI by physician	VIA by nurse	VILI by nurse	Colposcopy	MRCI	Biopsy taken	Number of Biopsy	Biopsy Site	Biopsy Impression	ECC	Treatment advice	Final diagnosis
196	2	1	1	1	2	3	4	0	1	2	0	0	0	3	1	1	1	1	4	3	1	3	5,12&1'o clock	1	0	5	1
197	1	3	1	1	2	1	4	0	1	1	0	0	0	1	1	1	1	1	1	-	1	2	1 & 4 o' clock	1	0	2	1
198	1	4	1	1	2	1	2	0	0	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
199	2	5	1	1	4	2	2	0	0	2	0	0	0	2	1	1	1	1	1	-	0	-	-	0	0	2	1
200	1	1	1	3	2	2	4	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	3	1
201	2	2	1	1	2	1	2	0	0	5	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	1	1
202	2	3	1	1	2	2	3	0	1	2	0	0	0	2	1	1	1	1	2	1	1	1	12 o'clock	1	0	2	1
203	3	1	1	1	2	3	5	0	0	1	0	0	0	3	1	1	1	1	2	1	1	4	4 quadrant	1	0	2	1
204	2	2	1	1	4	3	4	0	1	1	0	0	0	1	1	1	1	1	2	0	1	1	4 o'clock	1	0	2	1
205	2	5	1	1	2	1	3	0	1	4	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
206	1	3	1	2	2	1	3	0	0	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
207	2	4	1	1	2	1	3	0	1	2	0	0	0	2	2	1	2	1	2	-	1	1	12 o'clock	1	0	2	1
208	2	4	1	2	2	3	5	0	0	1	0	0	0	2	1	1	1	1	2	1	1	1	2 o'clock	1	0	3	1
209	2	5	1	1	2	2	4	0	0	3	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
210	3	2	1	1	1	3	3	0	1	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
211	3	5	1	6	2	3	4	0	1	3	0	0	0	3	1	1	1	1	2	2	1	2	12 & 6 o'clock	2	0	2	1
212	2	4	1	1	2	2	3	0	0	3	0	0	0	3	1	1	1	1	2	2	1	2	10 & 6 o'clock	2	0	3	1
213	1	4	1	1	2	1	3	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
214	3	5	1	1	3	3	3	0	0	4	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
215	2	3	1	1	2	2	3	0	1	2	0	0	0	2	1	1	1	1	2	2	1	1	12 o'clock	2	0	2	1
216	2	3	1	1	2	2	3	0	1	2	0	0	0	3	1	1	1	1	2	1	1	1	2 o'clock	1	0	3	1
217	2	5	1	1	2	2	3	0	1	2	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
218	1	4	1	1	3	1	2	0	0	2	0	0	0	1	1	1	1	1	2	2	1	1	12 o'clock	2	0	2	1
219	1	1	1	1	2	1	2	0	0	2	0	0	0	1	1	1	1	1	2	2	1	2	11 & 1 o'clock	2	0	3	1
220	2	5	1	1	2	2	3	0	1	3	0	0	0	1	1	1	1	1	3	3	1	2	12 & 8 o'clock	1	0	3	1
221	2	3	1	1	4	2	3	0	1	3	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
222	1	3	1	1	2	2	3	0	0	1	0	0	0	1	1	1	1	2	2	2	1	1	2 o'clock	2	0	2	1
223	2	2	1	1	3	2	3	0	0	2	0	0	0	2	1	1	1	1	2	3	1	2	10 & 6 o'clock	2	0	3	1
224	1	4	1	1	2	1	3	0	0	2	0	0	0	2	1	1	2	1	2	2	1	1	5 o'clock	2	0	3	1
225	2	5	1	1	5	2	3	0	1	3	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
226	2	3	1	1	2	2	4	0	1	1	0	0	0	0	2	2	2	2	1	-	0	-	-	0	0	2	1
227	1	4	1	1	2	2	3	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
228	2	1	1	1	3	2	3	0	1	2	0	0	0	1	1	1	1	1	2	1	1	1	10 o'clock	2	0	3	1
229	2	4	1	1	4	3	4	0	1	1	0	0	0	3	2	2	2	2	1	-	1	1	2 o'clock	1	0	2	1
230	2	1	1	1	2	3	4	0	1	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	1	1
231	1	4	1	1	2	1	3	0	1	2	0	0	0	0	1	1	1	1	3	3	1	1	2 o'clock	2	0	3	1
232	1	1	1	1	3	1	3	1	0	1	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
233	1	1	1	1	1	2	3	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
234	1	4	1	2	2	1	3	0	0	1	0	0	0	2	1	1	1	1	2	1	1	1	3 o'clock	2	0	2	1
235	2	5	1	2	3	2	4	0	1	2	0	0	0	3	1	1	1	1	5	1	1	4	4 quadrant	3	0	5	2
236	2	3	1	1	2	3	3	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
237	2	4	1	2	2	2	5	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	2	1
238	3	1	1	1	2	2	3	0	1	2	0	0	0	1	1	1	1	1	2	1	1	1	12 o'clock	2	0	2	1
239	3	4	1	1	3	3	3	0	1	3	0	0	0	1	1	1	1	1	2	1	1	1	2 o'clock	2	0	2	1
240	2	2	1	1	3	2	3	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
241	2	5	1	1	2	2	3	0	1	1	0	0	0	1	1	2	2	1	2	0	1	1	12 o'clock	3	0	5	2
242	3	4	1	1	3	3	4	0	1	2	0	0	0	0	2	2	2	2	2	0	1	1	8 o'clock	1	0	2	1
243	3	2	1	6	2	3	3	0	0	2	0	0	1	3	1	1	1	1	5	-	1	4	4 quadrant	5	0	5	2
244	1	5	1	1	2	1	2	0	0	2	0	0	0	2	2	1	2	2	2	0	1	1	4 o'clock	1	0	1	1
245	2	3	1	1	2	2	3	0	1	1	0	0	0	2	2	2	2	2	1	-	0	-	-	0	0	1	1
246	1	5	1	1	2	1	3	0	1	2	0	0	0	1	2	2	2	2	1	-	0	-	-	0	0	2	1
247	2	1	1	1	1	3	3	0	0	1	0	0	0	1	1	1	1	1	2	1	1	1	6 o'clock	1	0	2	1
248	3	4	1	1	2	3	3	0	1	2	0	0	0	1	1	1	1	1	3	3	1	2	2 & 7 o'clock	1	0	2	1
249	3	5	1	1	2	3	4	0	1	2	0	0	0	3	1	1	1	1	2	1	1	1	10 o'clock	1	0	2	1
250	1	5	1	1	3	1	3	0	1	2	0	0	0	3	2	2	2	2	1	-	0	-	-	0	0	2	1