"ROLE OF VISUAL INSPECTION WITH ACETIC ACID AND HPV DNA TESTING IN DETECTION OF CERVICAL INTRAEPITHELIAL NEOPLASIA – A PROSPECTIVE STUDY"

By

Dr. SIMARAN JEET
(REG.NO. BJ0110006)

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

Under the Guidance of

Dr. (Mrs.) ANITA DALAL MD
Professor

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"ROLE OF VISUAL INSPECTION WITH ACETIC ACID AND HPV DNA TESTING IN DETECTION OF CERVICAL INTRAEPITHELIAL NEOPLASIA – A PROSPECTIVE STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. (Mrs.) ANITA DALAL** **MD** Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum – 590010.

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LIST OF ABBREVIATIONS USED

‘p’ value	- Probability value
AAR	- Age Adjusted Incidence Rate
ACCP	- Alliance for Cervical Cancer Prevention
AIIMS	- All India Institute of Medical Sciences
ASCUS	- Atypical Squamous Cells of Undetermined Significance
CI	- Confidence interval
CIN	- Cervical Intraepithelial Neoplasia
DA	- Diagnostic accuracy
DALY	- Disability adjusted life years
DVI	- Direct Visual Inspection
ELISA	- Enzyme linked immuno sorbent assay
HBCR	- Hospital Based Cancer Registries
HIV	- Human Immunodeficiency Virus
HPV	- Human Papilloma Virus
HPV-DNA	- Human Papilloma Virus- Deoxyribonucleic acid
HR	- High risk
HSIL	- High grade Squamous Intra epithelial Lesion
IARC	- International Agency for Research on Cancer
K	- Kappa
LSIL	- Low grade Squamous Intra epithelial Lesion
n	- Total Number
NCRP	- National Cancer Registry Programme
NPV	- Negative Predictive Value
PAP	- Papanicolaou
PBCR	- Population Based Cancer Registries

PPV	- Positive Predictive Value
RCI	- Reid Colposcopic Index
RNA	- Ribonucleic acid
SCC	- Squamous cell carcinoma
SD	- Standard deviation
SIL	- Squamous Intra epithelial Lesion
US	- United States
VIA	- Visual Inspection with Acetic acid
VIAM	- Visual Inspection with Magnification
VILI	- Visual Inspection with Lugol's Iodine
WHO	- World Health Organization

ABSTRACT

Background and objective

Cervical cancer is an important public health problem that deserves urgent attention. In the developing countries control of cervical cancer is viable through screening modalities such as visual screening methods like visual inspection with acetic acid/visual inspection with Lugol's iodine (VIA/VILI) and recently Human Papilloma virus deoxyribose nucleic acid (HPV-DNA). This study was aimed to assess test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and to assess the performance when HPV DNA testing and VIA are combined.

Methodology

This one year cross-sectional screening interventional study was conducted on a total of 204 women referred to Colposcopy Clinic, at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Test results of VIA, colposcopy, HPV DNA and biopsy were obtained.

Results

Most of the women (50%) had age between 30 to 34 years with the mean age of 36.75 ± 35.50 years. Most of the women (54.90%) had studied upto college. 46.57% complained vaginal discharge and 33.82% backache. VIA, and HPV DNA test was positive results in 33.33% and 21.57%. The colposcopic findings among 16 women (7.84%) showed positive test results which included 11 (5.39%) cases of CIN 2, four cases (1.96%) of CIN 3 and one case of SCC

(0.49%). Of the 204 women, 73 (35.78%) underwent biopsy. Among them, four women (5.48%) revealed CIN 3 and one case (1.37%) of SCC.

Conclusion

Overall, VIA and HPV positive tests showed diagnostic accuracy of 93.63% with positive likelihood ratio of 13.26 and negative likelihood ratio of 0.21 whereas VIA or HPV positive 55.39% diagnostic accuracy with positive likelihood ratio of 2.18 (CI 95%).

Keywords:

Cervical cancer; Colposcopy; Cervical biopsy; Human papilloma virus Deribonucleic acid test; Cervical cancer screening; Visual inspection with acetic acid.

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Chapter 1

Introduction

INTRODUCTION

Cervical cancer is the second most common malignancy in women worldwide, and it remains a leading cause of cancer-related death for women in developing countries. Cervical cancer is an important public health problem that deserves urgent attention. The burden of cervical cancer in India is enormous accounting for about 20% of all cancer related deaths in women and is the number one cause of death due to cancer in middle aged Indian women.[1]

The lifetime risk of being diagnosed with cervical cancer is 0.78% and the lifetime risk of dying from cervical cancer is 0.26%.[2] A World Bank report estimated that women with cervical cancer die about 18 years earlier than they would have otherwise.[3]

In India an estimated 1.5 lakh women develop cervical cancer annually. This is about one fourth of global burden of cervical cancer.[4]

The incidence of cervical cancer is declining slowly necessitating concerted and organized control measures. Control through primary prevention has become a distinct reality though a prophylactic vaccine, which may take quite some time for its widespread use. Thus control of cervical cancer through secondary preventive measures is the only viable solution now.

Screening modalities such as visual screening methods like visual inspection with acetic acid / visual inspection with Lugol's iodine (VIA/VILI) and recently Human Papilloma virus deoxyribose nucleic acid (HPV-DNA) can be explored.

VIA has arisen as a promising alternative for developing countries because it is inexpensive and fast and requires a low level of training and no special equipment. It is based on acetowhitening, with the CIN turning white when exposed to 5% acetic acid (vinegar). These characteristics make VIA a realistic alternative for low-resource settings. Some previous reports have observed that VIA can reach similar or better results than the Pap smear in the detection of CIN. Further, it is important to mention that there had been no prior experience with using VIA in a high-resource setting in a developing country. In general, VIA has demonstrated high sensitivity for detecting CIN and cervical cancer, but it is limited by low specificity.[5-7]

VILI involves examination of the cervix with the naked eye to identify mustard-yellow areas on the cervix after application of Lugol's iodine.

A multi-centre study in India and Africa involving around 49,000 women concurrently evaluated VIA and VILI by independent providers, using a common protocol.[8]

The pooled sensitivity and specificity to detect high-grade CIN were 92 and 85%, respectively, as opposed to 77 and 86% for VIA, thus indicating a higher sensitivity than VIA in this study but similar specificity was observed. In a Latin American study involving about 3000 women, VILI had a significantly lower sensitivity of 53% and a specificity of 78% to detect high-grade CIN.[9]

HPV DNA testing has shown very high sensitivity and is being recommended in high-resource countries.[10,11]

However, its current price and technology requirements make this option unrealistic for poor areas[12] until a low-cost, same-day HPV test and realistic strategies are developed.[13]

Although data from population-based cancer registries indicate a slow but steady decline in cervical cancer incidence rates over the last two decades, the risk of disease is still high, particularly in rural areas. Despite the high burden of disease and the increasing absolute number of cases due to population growth, there are no organised screening programmes for cervical cancer prevention anywhere in India.[14]

Hence there is a clear need for a viable, accurate and effective screening method for control of cervical cancer.

In view of the above the present study was planned to assess the test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and also to assess the performance when HPV DNA testing and VIA are combined to find out the probable best screening option.

Chapter 2

Objectives

OBJECTIVES

Objectives of the present study were;

1. To assess the test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions

2. To assess the performance when HPV DNA testing and VIA are combined to find out the probable best screening option.

Chapter 3

Review of Literature

REVIEW OF LITERATURE

Cervical cancer is the second most common malignancy in women worldwide, and it remains a leading cause of cancer-related death for women in developing countries.[1] In the United States, cervical cancer is relatively uncommon.[15]

The incidence of invasive cervical cancer has declined steadily in the United States over the past few decades; however, it continues to rise in many developing countries. The change in the epidemiological trend in the United States has been attributed to mass screening with Papanicolaou tests. Furthermore, cervical cancer is a preventable disease, primarily with newly approved human papillomavirus (HPV) vaccines and secondarily through treatment of preinvasive disease.[15]

Papanicolaou test screening is recommended in women who meet screening criteria, regardless of symptoms. However, symptoms, abnormal Papanicolaou test results, or women with a gross lesion of the cervix are best evaluated with colposcopy and biopsy.[15]

The treatment of cervical cancer varies with the stage of the disease. For early invasive cancer, surgery is the treatment of choice. In more advanced cases, radiation combined with chemotherapy is the current standard of care. In patients with disseminated disease, chemotherapy or radiation provides symptom palliation.[15]

HISTORICAL ASPECTS

In a now famous paper an Italian physician, Rigoni-Stern (1842), analyzed death certificates of women in Verona during the period 1760–1839 and noted a high frequency of cervical cancer in married women, widows and prostitutes, but their rare occurrence in virgins and nuns. He concluded that the development of this type of cancer should be related to sexual contacts. The rapid development of bacteriology in the second part of the 19th century resulted in early attempts to link cervical cancer to sexually transmitted infectious events, without reproducible data until the end of the 1960s. At this time first reports appeared incriminating a virus infection, Herpes simplex type 2, as candidate for cervical cancer etiology. Although initially a number of confirmatory data have been published, a large scale prospective study performed in former Czechoslovakia failed to confirm these results.[16]

In the early 1970s studies on the possible role of human papillomaviruses (HPV) in cancers were initiated. Skin and genital warts were well known among ancient Greek and Romans. In the 1970s the plurality of human papillomavirus types became apparent. An early suggestion for antigenic differences between cutaneous and genital wart papillomavirus particles originated from electron microscopic analysis of particle agglutination studies. Antisera to skin wart virus reacted with both, skin and genital wart viruses, whereas antisera to genital wart virus reacted only with the genital wart virus particles. This study has not been reproduced; the basis for this observation is still not understood.[16]

Experiments trying to establish a relationship between papillomavirus infections and cervical cancer were initiated in 1972. They were based on anecdotal reports in the medical literature of rare malignant conversion of genital warts (condylomata acuminata) into squamous cell carcinomas, resulting in the hypothesis that cervical cancer may arise from infections with the virus found in condylomata acuminata.[16]

The speculation appeared to be boosted by negative attempts to demonstrate herpes simplex type 2 DNA in cervical cancer biopsies. The isolation of novel HPV types from genital warts, HPV 6, and laryngeal papillomas , HPV 11, permitted direct approaches to answer this question.[16]

In 1976 and 1977 Meisels and Fortin postulated that koilocytotic cells found in cervical smears of patients with flat dysplastic lesions represent the cytopathogenic change of a papillomavirus infection. Initially these authors hypothesized that the discovery of such koilocytotic cells permitted a differentiation between the koilocyte-positive “benign” proliferations from koilocyte-negative lesions, assumed to represent “truly premalignant” cells. The demonstration of typical papillomavirus particles within koilocytotic cells by and by confirmed the HPV-mediated cytopathic effect as proposed by Meisels and Fortin.[16]

Southern blot hybridizations with HPV 11 DNA permitted the detection of this DNA in one out of 24 cervical carcinoma biopsies. By using HPV 11 as probe, it was possible to isolate a novel HPV DNA directly from cervical cancer biopsies, subsequently labelled as HPV 16. Shortly thereafter, the same group

isolated and partially characterized HPV 18 DNA from cervical cancer biopsies as well as from several cervical cancer derived cell lines (among them HeLa cells). Within the same year it was possible to demonstrate HPV 16 DNA in typical precursor lesions of ano -genital cancers, Bowenoid papulosis and 1 year later in cervical intraepithelial neoplasias. Without reviewing here the subsequent burst of molecular and epidemiological data within the following years, among others a few major steps deserve mentioning.[16]

Early in 1985 the selective transcription of E6 and E7 genes in cervical cancer and specific deletions occurring in the course of integration of viral DNA into host cell DNA were established. Within the same year this was confirmed by another group. The interaction of E6 protein with p53, resulting in degradation of this protein, and of E7 with pRb, blocking the function of the latter, were important for the initiation and understanding of intracellular events resulting in immortalization and eventually in a transformed phenotype of the viral genome harbouring cells. Cell transformation by these viral oncogenes was initially shown for rodent cells and shortly thereafter also for human keratinocytes. In addition, induction of tumors in transgenic animals clearly demonstrated the oncogenic potential of these genes. Global epidemiological studies identified HPV 16, 18 and a few others as major risk factors for cervical cancer. The interruption of intra- and extracellularly triggered pathways as a precondition for malignant conversion, as well as the essential role of viral oncoprotein expression for the maintenance of the malignant phenotype, the serology of HPV infections, and the recent development of HPV vaccines have been covered in several reviews.[16]

Today it is very well established that infection with specific types of HPV can cause cervical cancer. The intervention with vaccines permits today the statement that essential precursor lesions of this cancer are efficiently prevented. Although more than 95% of cervical cancer biopsies contain high risk HPV genomes, this figure does not necessarily imply that all of these tumors are caused by these infections. Long-term follow-up studies of vaccinated women, particularly after achieving a broad protection against the majority of high risk HPV types, will provide a better basis for more accurate estimates. Cervical cancer, on the global scale, represents the second most frequent cancer in women. Thus, specific HPV types emerge as one of the most important infectious carcinogens in humans.[16]

EPIDEMIOLOGY

Distribution, prevalence and incidence of Cervical Cancer

Global scenario

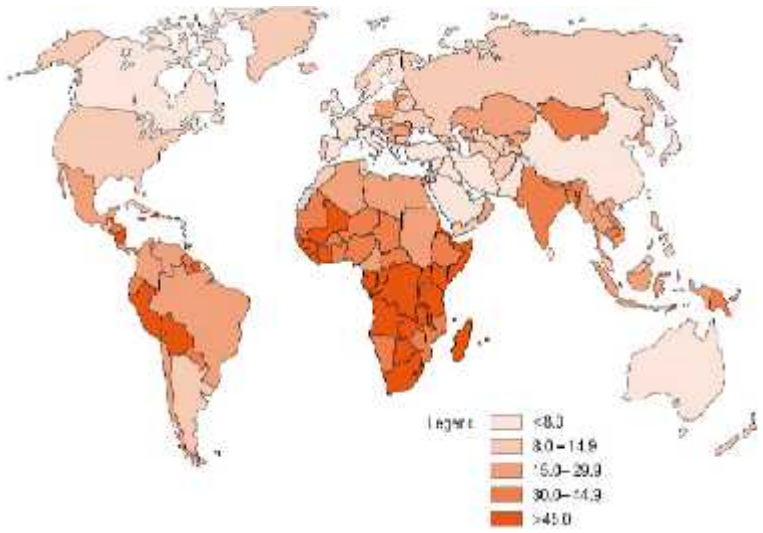


Figure 1. Global burden of cervical cancer: Age standardized incidence rates (Per 100,000 women)[17]

The American Cancer Society estimated that in the United States in 2010, 12,200 new cases of cervical cancer would be diagnosed.[18] In addition, more than 50,000 cases of carcinoma in situ are diagnosed each year. Internationally, 500,000 new cases are diagnosed each year. Unlike the United States, where the annual incidence is 6.8 cases or less per 100,000 women, rates in parts of South America and Africa range as high as 52.8 cases per 100,000 women.[19]

Global Cervical Cancer Burden[20]

In 2004, cervical cancer was the fifth most common cause of cancer related death among women in the world, and had:

- 489,000 new cases.
- An age-standardized incidence rate (global) of 16 per 100,000 women in 2002.
- One year prevalence of 381,033, and 5-year prevalence of 1.41 million in 2002.
- 268,000 deaths (3.6% out of 7.4 million cancer deaths).
- Nine age-standardized deaths per 100,000 in 2002.
- 3,719,000 DALYs (disability adjusted life-years).

Indian Scenario[20]

In 2004, cervical cancer was the third largest cause of cancer related mortality in India, and had:

- An age-standardized incidence rate of 30.7 per 100,000 women in 2002.

- One year prevalence of 101,583 and five year prevalence of 370,243 in 2002.
- 72,600 deaths (nearly 10% out of 729,600 cancer deaths).
- 6.5 deaths per 100,000.
- 9.5 age-standardized deaths per 100,000

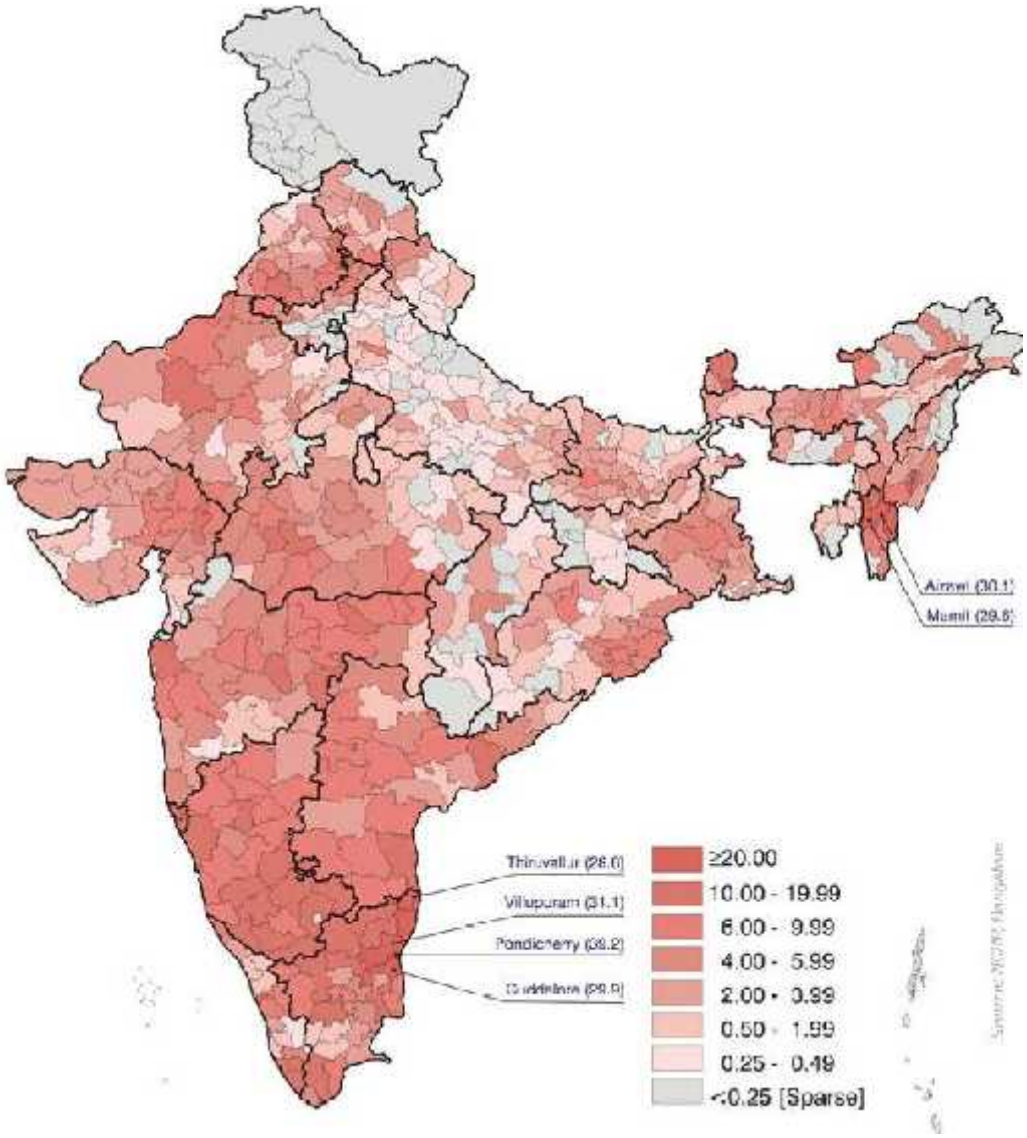


Figure 2. District wise comparison of age adjusted incidence of cervical cancer (per 100,000 population)[20]

As of 2002, the one year prevalence of cervical cancer in India was 1.01,583, and the 5 year prevalence was 3,70,243, accounting for approximately

26% of global prevalence, and 83% of total prevalence in South Central Asia. In India, the age-adjusted incidence of cervical cancer (30.7 per 1,00,000 women, 1,32,082 incident cases) is the highest relative to that of all other types of cancer, and is higher than the average for the South Central Asia region. By 2025, the number of new cervical cancer cases in India is projected to increase to 2,26,084. Cervical cancer is the leading cancer among women in terms of incidence rates in two out of the 12 Population Based Cancer Registries (PBCRs) in India, and has the second highest incidence rate after breast cancer in the rest of the PBCRs. The age-adjusted incidence is highest in Chennai and lowest in Thiruvanathapuram, the capital of Kerela.[20]

India has a disproportionately high burden of cervical cancer. Although its age standardised death rate of 9.5 deaths per 100,000 population is representative of global rates, it accounts for nearly one-third of global cervical cancer deaths. Cervical cancer is the third largest cause of cancer mortality in India after cancers of the mouth and oropharynx, and oesophagus, accounting for nearly 10% of all cancer related deaths in the country. Among women, it is the leading cause of cancer mortality, accounting for 26% of all cancer deaths. According to IARC estimates, mortality from cervical cancer is expected to witness an increase from 74,118 deaths in 2002 to 132,745 deaths by 2025.[20]

Crude and age adjusted incidence rates per 100,000 population of cervical cancer in 12 Indian population based cancer registries (PBRCs) in India[20]

PBRC	Crude incidence rate	Age-adjusted incidence rate
Bangalore	18.8	21.7
Barshi	42.7	22.4
Bhopal	22.2	24.5
Chennai	24.4	30.6
Delhi	16.3	22.7
Mumbai	14.6	18.0
Ahmedabad	16.2	13.4
Karunagappally	19.2	15.0
Kolkata	17.5	19.9
Nagpur	19.1	23.2
Pune	20.5	22.5
Thiruvanathapuram	13.1	10.9

Another measure of disease burden is Disability Adjusted Life Years (DALYs). At a rate of 113 age-adjusted DALYs per 100,000 population, cervical cancer accounts for 26.5% of global cervical cancer DALYs, and 11.6% of total cancer DALYs in India.[20]

Race- and age-related demographics

In the United States, cervical cancer is more common in Hispanic, African American, and Native American women than in white women. The Center for Disease Control and Prevention's Surveillance of Screening-Detected Cancers (Colon and Rectum, Breast, and Cervix) United States, 2004–2006 reported that incidence rates of late-stage cervical cancer were highest among women aged 50-79 years and Hispanics.[21] However, cervical cancer may be diagnosed in any woman of reproductive age.

Etiology

Early epidemiological data demonstrated a clear association between cervical cancer and sexual activity. Major risk factors observed were sex at a young age, multiple sexual partners, promiscuous male partners, and history of sexually transmitted diseases. However, the search for a potential sexually transmitted carcinogen was unsuccessful until breakthroughs in molecular biology enabled scientists to detect viral genome in cervical cells.

Strong evidence now implicates human papillomaviruses (HPVs) as prime suspects.[22-24] HPV viral DNA has been detected in more than 90% of squamous intraepithelial lesions (SILs) and invasive cervical cancers compared with a consistently lower percentage in controls. Both animal data and molecular biologic evidence confirm the malignant transformation potential of papilloma virus–induced lesions. Squamous intraepithelial lesions (SILs) are found predominantly in younger women, while invasive cancers are detected more often in women 10-15 years older, suggesting slow progression of cancer.

HPV infection occurs in a high percentage of sexually active women. Most of these infections clear spontaneously within months to a few years, and only a small proportion progress to cancer. This means that other crucial factors must be involved in the process of carcinogenesis.

Three main factors have been postulated to influence the progression of low-grade SILs to high-grade SILs. These include the type and duration of viral infection, with high-risk HPV type and persistent infection predicting a higher risk for progression; host conditions that compromise immunity, such as multiparity or poor nutritional status; and environmental factors such as smoking, oral contraceptive use, or vitamin deficiencies.

In addition, various gynaecologic factors significantly increase the risk for cervical cancer. These include early age of first intercourse and higher number of sexual partners.

Human papillomavirus

Human papilloma virus is a sexually transmitted infection. Transmission occurs through infected genital skin, mucus membranes, or bodily fluids from a partner with overt or subclinical infection. The predominant HPV risk factor is the number of sexual partners in ones lifetime. There is no doubt that this infection and cervical cancer are sexually transmitted by infected partners. There are more than 100 HPV types (DNA viruses), 40 of which have been found in the cervico-vaginal area. There are high risk types (Oncogenic HPV 16 and HPV 18) and low risk, non cancer causing types, including those responsible for common genital warts (HPV 6 and HPV 11).[2]

Human papilloma virus infection of the genital tract might be clinical (Condyloma accuminatum, or genital warts) but most are subclinical and can be diagnosed cytologically (Papanicolaou test) Visual tests (VIA,VILI), Virological test (DNA detection).[25]

Most HPV infections are transient (3/4th of low risk HPV types resolve between an initial and a subsequent assessment). The median HPV DNA duration is 8 months. The lifetime risk of being diagnosed with cervical cancer is 0.78% and the lifetime risk of dying from cervical cancer is 0.26%.[2]

Beral postulated that exposure to sexually transmitted infection is an important determinant of cervical cancer.[26] Zur Hausen suggested that, HPV infection and HPV viral gene expression have emerged as necessary, but not sufficient factors for cancer induction.[27]

Reviewing the epidemiological evidence linking HPV to cervical cancer, Bosch et al concluded that over 90% of cervical cancers could be attributed to certain HPV types. The central role of HPV in cervical carcinogenesis has far-reaching implications in the prevention of this cancer. Molecular Virology of HPV is a small, double-stranded DNA virus that is a member of the papovavirus group. The subtypes of HPV are not serotype viruses but are genotypes in which the typing scheme is based on the similarity of one HPV type to the other known HPV types at the DNA level. The central HPV-DNA repository is in Heidelberg and this facility assigns a new type of HPV after adequate studies.[28]

The viral genome of HPV consists of approximately 7900 nucleotides, and all viral gene transcription occurs off one strand. The HPV genome may be

divided into three parts based on the function of the encoded genes: the early (E) region E6, E7, E1, E2, E4 and E5 and the late (L) region L1, L2 and L3 and a non coding region which harbours the origin of replication and transcription control signals essential for the regulatory functions of the genome. Stringent measures have to be adopted to avoid contamination of the specimen for PCR diagnosis. PCR has been shown to be more sensitive than Filter in situ Hybridisation and Southern Blot analysis in the detection of HPV in cervical scrapes.[29]

HPV is a heterogeneous group of viruses that contain closed circular double-stranded DNA. The viral genome encodes 6 early open reading frame proteins (E1, E2, E3, E4, E6, E7), which function as regulatory proteins, and 2 late open reading frame proteins (L1, L2), which make up the viral capsid.[15]

Till date, 77 different genotypes of HPV have been identified and cloned, among which types 6, 11, 16, 18, 26, 31, 33, 35, 39, 42, 43, 44, 45, 51, 52, 53, 54, 55, 56, 58, 59, 66, and 68 have the propensity to infect ano-genital tissues.[15]

The HPVs that infect the human cervix fall into 2 broad risk categories. The high-risk types, mostly HPV 16 and 18, are found in 50-80% of SILs and in up to 90% of invasive cancers. Although less common, types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 should also be considered carcinogenic.[30]

The major difference between the 2 types is that after infection, the low-risk HPVs are maintained as extra chromosomal DNA episomes, while the high-risk HPV genome is found integrated into the host cellular DNA. The recombination event often leaves E6 and E7 directly coupled to the viral

promoter and enhancer sequences, allowing their continued expression after integration.[15]

Because E7 binds and inactivates the Rb protein while E6 binds p53 and directs its degradation, the functional loss of both *TP53* and the *RB* genes leads to resistance to apoptosis, causing uncensored cell growth after DNA damage. This ultimately results in progression to malignancy.[15]

Human immunodeficiency virus

The role of human immunodeficiency virus (HIV) infection in the pathogenesis of cervical cancer is not fully understood. Studies have shown a higher prevalence of HPV infection in HIV-seropositive women than in seronegative women, and the HPV prevalence was directly proportional to the severity of immunosuppression as measured by CD4 counts.[30]

Impaired lymphocyte function has been postulated to enhance latent or subclinical HPV activity, resulting in a higher rate of persistent infection. Whether HIV has a synergistic effect on HPV infection, either by direct molecular interaction or through an indirect immunologic effect, remains unclear.[30]

SCREENING FOR CERVICAL CANCER

Screening is considered optimal when the smallest amount of resources is used to achieve the greatest benefit. It should be simple, minimally invasive, easy to perform, cost-effective and highly sensitive to the largest number of people.[32] The main barriers to screening include a lack of accessibility, a lack of comfort

and privacy in health centers, high cost of services, anxiety related to waiting for test results and an overall fear of cancer.[33]

Cervical cancer accounts for 7% of all female malignancies in developed countries in contrast to 24% in developing countries. This difference is mainly due to the inaccessibility of a feasible screening technique in developing countries.[33]

Cervical cancer screening began in 1943 with the introduction of Pap smear by Papnicolaou and Traut. Now the Pap test is probably the most used cervical cancer- screening test. However the various disadvantages of Pap Smear has lead to the development of various low cost screening methods. In 1980's WHO started advocating visual inspection methods for the screening of cervical cancer.

The various cervical cancer screening methods are:

- Pap Smear
- Visual Inspection with acetic acid (VIA)
- Visual inspection with Lugol's iodine (VILI)
- HPV-DNA testing
- Liquid based cytology
- Speculoscopy
- Cervicography

1. Pap Smear

Pap smear is the most effective cervical cancer screening test at present. It is responsible for the drastic reduction in the morbidity and mortality of cervical cancer. In most developed countries, women are advised to have their first Pap smear soon after becoming sexually active and to repeat the test every one to three years. But in developing countries, most women never have a Pap smear in their lifetime.[34]

Conventional Pap smears is collected by taking sample from the ectocervix and the endocervix using the Ayre spatula and endocervical brush, fixed in 95% ethanol and stained by the modified Papanicolaou method. Final cytological diagnoses are classified as:

Comparison of different classification

Pap Smear	WHO Classification	SIL Bethesda
I	Normal	Normal
II	Inflammatory	Inflammatory-HPV,ASCUS
III	CIN I	LSIL
IV	CIN II, CIN III, CIS	HSIL
V	Squamous Cell Carcinoma	Squamous Cell Carcinoma

Advantages[33]

- High specificity (90-95%)[34-36]

Disadvantages[33]

- Low sensitivity (20-35%)[34-36]
- Difficult to locate the lesion
- Need for laboratory with high human expertise
- Follow up visit required for report
- High cost

The minimum requirements for establishing an effective Pap smear screening effort include:[34]

- Well-trained providers, including nurses, midwives, and physicians' assistants.
- Examination rooms and laboratories stocked with the necessary supplies and equipment.
- Linkages, including transportation, to reliable laboratories with appropriately trained technicians.
- Strategies for ensuring the quality of Pap smear samples and the accuracy of interpreting them.
- Proven systems for timely communication of Pap smear results to screened women.
- Effective referral and follow-up systems for diagnosis and treatment of abnormalities.
- In low-resource settings often there is a lack of these requirements, thus making Pap smear programs ineffective.

Owing to these problems ACCP has studied alternative approaches to screening and treatment of precancerous disease aiming to reach women and provide them with a screening test at least once in their lifetime.[34]

2. Liquid-based cytology

Involves the collection of cell samples from the cervix and the sampling device is vigorously stirred in a vial of preservative, producing a suspension of cells which is transferred to a slide as a thin layer. In the laboratory, the cells are collected either by extraction across a special filter (Thin Prep) or by layering onto a density reagent.

Advantages

- Allows removal of blood and other extraneous material providing better visualization of the cells.
- Increased sensitivity but lower specificity compared to conventional Pap smear.[33]
- Residual specimens are available for additional testing such as 'reflex' HPV testing in cases of equivocal ASCUS cytology results.

3. Visual Inspection with acetic acid (VIA)

Screening for cervical cancer by VIA was advocated by WHO for screening of cervical cancer in low resource settings where cytology was not available.[34]

Visual screening relies only on the naked eye of a trained clinician and some basic clinic supplies. Visual inspection with acetic acid involves swabbing the cervix with 4% acetic acid (vinegar) solution and visual examination by a trained health provider. Visual inspection with acetic acid has demonstrated high sensitivity for detecting CIN and cervical cancer, but it is limited by low specificity.[34]

Visual inspection with acetic acid is based on acetowhitening, with the CIN turning white when exposed to 4% acetic acid (vinegar). Application of 4% acetic acid causes a reversible coagulation, or precipitation of the cellular proteins. It also causes swelling of the epithelial tissue, columnar and any abnormal squamous epithelial areas in particular, dehydration of the cells, and it helps in coagulating and clearing the mucous secretions on the cervix. The normal squamous epithelium appears pink and the columnar epithelium red, due to the reflection of light from the underlying stroma, which is rich in blood vessels. Thus, the effect of acetic acid depends upon the amount of cellular proteins present in the epithelium. Areas of increased nuclear activity and DNA content exhibit the most dramatic white colour change.[37]

Advantages[34,37]

- Requires only low-technology equipment.
- The result is available within one minute.
- Simple test.
- Inexpensive.
- Easy to carry out in large population.

- Does not require any laboratory.
- Can be performed by trained paramedical workers and medical workers.
- These characteristics make VIA a realistic alternative for low-resource settings.

Disadvantages[34,37]

- There is difficulty in standardizing quality control.
- Competent trained personnels are required
- Presence of inflammation, infection, and metaplasia affect the results
- High rate of false positive results
- Wide inter-observer variation.

4. Visual inspection with Lugol's iodine (VILI)

In an effort to increase the accuracy of visual screening, some centers have used an iodine solution to stain abnormal cells. Visual inspection with Lugol's iodine is also known as Schiller's test because it is similar to the Schiller's iodine test that was widely used in the 1930s before the development of Pap smears. Recent data show that visual screening with Lugol's iodine may have higher accuracy than screening with acetic acid.[34]

Lugol's iodine stains glycogen-rich vaginal epithelium cells. Proliferative lesions, like CIN or cancer, are composed of cells that contain less glycogen than the surrounding epithelium. These lesions appear as non-staining areas when Lugol is applied to the cervix. Visual inspection with Lugol's iodine was always

performed after VIA, because Lugol's iodine usually stains the cervix for 30 to 60 min, sometimes for many hours.[34,37]

As with VIA, the main purpose of VILI is not to ascertain the diagnosis, but to distinguish between a normal and an abnormal cervix.

- Negative – homogeneous staining of the cervix is obtained after application of Lugol's iodine.
- Positive – a well-delimited non-staining area is present.

5. HPV DNA testing

Within the past five years, guidelines recognizing the value of HPV testing in both primary cervical screening and in the management of abnormal cervical cytology have been established in the US and are being considered in Europe. This trend has occurred because of the definitive association of high risk (HR) HPV with cervical cancer and the overwhelming evidence that the sensitivity of HR HPV testing for lesions with a diagnosis of cervical intraepithelial neoplasia grade 2 or more severe (CIN 2+) is substantially higher than that of cytology. This higher sensitivity offers a number of advantages, including, most importantly, the potential of reducing cervical cancer rates while reducing the number of screens in a lifetime necessary to achieve this goal.[38]

In comparison with cytology, HPV testing is highly reproducible, is more easily monitored, provides an objective test outcome and can easily be automated. The lower specificity of HPV testing in younger women is due to a higher prevalence of transient infections. Cytology has a higher PPV than HPV

testing, which reduces the costs associated with referral for colposcopy. However, in well-screened populations,[39,40] some interval cancers still occur that could potentially be avoided using a more sensitive screening method such as HPV testing.

The higher sensitivity of HPV testing also leads to a higher negative predictive value, suggesting that the screening interval can be safely lengthened if HPV testing is used.[38] The International Agency for Research on Cancer (IARC) concluded that there is sufficient evidence that HPV testing can reduce the incidence and mortality from cervical cancer and that it is likely to be at least as effective as cytology (IARC 2005).[41]

Basic principles suggest that the most appropriate use of two tests is to perform the most sensitive test first and follow this with the more specific test for those who test positive initially. Tests employing HPV E6/E7 mRNA, p16 or other biomarkers may help distinguish transient from persistent HPV infections, but these still require clinical validation. Recent data support type-specific testing for HPV 16 and 18 as a highly specific marker for risk for CIN 2+.[38]

In recent decades other alternatives have been explored, such as human papillomavirus (HPV) DNA testing.[42] HPV DNA testing has shown very high sensitivity (85-95%)[37] and is being recommended in high-resource countries.[42-44] However, its current price and technology requirements make this option unrealistic for poor areas[32] until a low-cost, same-day HPV test and realistic strategies are developed.[42]

HPV DNA tests can use cervical or vaginal samples, often obtained with a endocervical cytobrush. The samples are collected either by trained personnel or, in the case of vaginal sampling, by the woman herself. Once collected, the sample is stored in a preservative solution until testing.[33]

The test utilizes non radioactive Ribo Nuceic Acid (RNA) probes in a modified Enzyme Linked Immuno Sorbent Assay (ELISA) procedure to report the presence or absence of 13 strains of high risk HPV- DNA.

These tests are most effective among women at the highest risk for precancerous lesions (women aged 30 or older) because of the greater likelihood that a positive result at that age signals a persistent HPV infection that could progress to cancer. But this diagnostic step may be difficult to implement in low-resource settings where appropriately trained specialists or necessary equipment is lacking.

Commercially available HPV DNA tests are relatively expensive and involve sophisticated processing in a laboratory. Moreover, results are not immediately available. These factors combined with difficulty in collecting specimens limit the applicability of this test. Until it is possible to produce the test in a simpler way to use and less expensive, HPV DNA testing is unlikely to reach its full potential in reducing cervical cancer. A new and rapid HPV DNA test is being developed for the market in low and middle income countries. It will have a lower cost per test and will be simpler to perform. Moreover, it will be portable and will allow for field tests and results will be available faster.

However, it will take several more years for its complete development, commercialization and recommendation.

For women who have had sexual intercourse, there is a good chance for HPV infection. While the cumulative lifetime incidence of HPV infection is 70% to 80% in many countries, the vast majority of women with HPV infection will not develop cancer. This group of women should have a HPV DNA testing before getting HPV vaccines.

Colposcopy

Colposcopy is a diagnostic procedure, most commonly used in the diagnosis of cervical intraepithelial neoplasia and lower genital tract carcinoma. Colposcopy was first described by Hans Hinselman of Germany in 1925. He believed that the earliest signs of cancer occur as minute ulcers or tumors which could be recognized by means of suitable magnification and illumination.[36]

Colposcopy is a technique meant primarily to assist the physician in the examination of the visible portion of the female genital tract. It provides the clinician with additional dimensions in the evaluation of the physiology and pathology of the uterine cervix. In addition to evaluating the epithelial pattern, colposcopy also evaluates changes in the terminal vascular network of the cervix which reflects the biochemical and metabolic changes in the cervical tissue. Colposcopy goes a long way towards obviating the difficulty of diagnosing a lesion without physically removing it.[36]

Many women during the reproductive period have some cervical changes which is difficult to differentiate by unaided eye whether they are ectopy, metaplasia, inflammation or neoplasia. Colposcopy makes it possible to localize the lesion, to evaluate its extent and to obtain a directed biopsy when required. Colposcopy is very accurate in differentiating invasive and non-invasive lesions and also in differentiating inflammatory atypias from neoplasia. In a patient with fully visible squamo-columnar junction, the false negative rate of colposcopy is very low.[36]

Unless cervical cancer is suspected, the routine use of an intermediate diagnostic step (such as colposcopy) between screening and treatment is generally not efficient and may result in reduced programmatic success and increased cost.

Colposcopy guided biopsy

It is the gold standard and the definitive diagnostic test. Colposcopy allows for the identification and histological sampling of the most clinically significant areas of an identified lesion by allowing directed rather than random biopsy, thus increasing the chance for accurate diagnosis.

A prospective study of 1,921 asymptomatic women living in Lima, Peru, was conducted to assess visual inspection with acetic acid (VIA) as a screening tool for use in a well-equipped health center in Peru, carried out in 1999 and 2000. The women underwent a complete clinical evaluation, including a Pap smear and VIA. Participants with any positive test were referred for colposcopy and biopsy. More women were tested positive by VIA than on the Pap smear

(6.9% vs. 4.2%; p=0.0001). There were 35 women with histologic cervical intraepithelial neoplasia grade 1 (CIN1); of these, 15 were detected by Pap smear and 20 by VIA (p=0.4). A diagnosis of CIN 2 or 3 (CIN 2–3) was confirmed in a total of 13 cases; Pap smear detected 5 of the cases and VIA 11 of the cases (p=0.06). The positive predictive value for detection of CIN 2+ was 8.3% for VIA and 6.3% for Pap Smear.[42]

In a study to assess the performance indicators of visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) in four Latin American centres, overall test positivity was 11.6% for VIA, 23% for VILI. VIA was positive in 61.8% of the women with CIN 1, 57.0% of those with CIN 2, 35.0% of women with CIN 3 and in 21 of 28 (75%) of women with cancer. Approximately 10% of women with no detectable disease had an abnormal VIA. Regarding VILI, 83.3% of women diagnosed with CIN 1 and 62.5% of those with CIN 3 had an abnormal test. VILI failed to detect one of three cases of cancer. Both the sensitivity, specificity and positive predictive value of VIA and VILI in detecting CIN 2 or CIN 3 could be significantly improved depending on the combination with Pap smear.[36]

Large community based cross- sectional study was conducted in the suburbs of Africa to evaluate the feasibility and performance of VIA and VILI for cervical cancer screening in a primary health care setting using biopsy as the reference. Test was done by nurse and physician and the sensitivity, specificity and negative predictive value for VIA- nurse/physician are 55.5% / 71.1%, 64.6% / 71.3%, 96.8%/98.6%. The corresponding values for VILI- nurse/ physician were 44.0%/68.3%, 74.6%/76.2% and 96.7%/97.2%.[45]

Another cross- sectional study with 4,444 women aged 25-65 years were examined. It was conducted in Kerala, India to evaluate the test characteristics of VIA and VILI. It showed the sensitivities of low-threshold VIA, high-threshold VIA, VILI and cytology to detect CIN 2 or worse disease were 88.6%, 82.6%, 87.2%, 81.9% respectively and the corresponding specificities were 78.0%, 86.5%, 84.7% and 87.8%.[46]

Eleven cross sectional studies involving 56,939 women aged 25 to 65 years were screened with 4%acetic acid (VIA) and with Lugol's Iodine (VILI) by health workers. All women were investigated with colposcopy and biopsied when necessary. Of the screened women 16.1% and 16.4% were positive on examination using VIA and VILI respectively; 1,063 were diagnosed with HSIL. The sensitivity, specificity, positive and negative predictive values for VIA was 76.8%, 85.5%, 9.4% and 99.9% respectively. The values for VILI were 91.7%, 85.4%, 10.9% and 99.8% respectively. VILI appeared to be more accurate visual test for use in screening and treatment program because of higher sensitivity and could be used in low resource settings.[47]

In a study where 300 women between the age group of 25 to 65 years were examined. VIA and VILI was performed and Pap smear was also taken in all the patients. Cervical biopsy was taken for cytology, VIA or VILI positive patients. Sensitivity for Pap, VIA and VILI are 52.6%, 80% and 78.9% respectively and the specificity was 84.8%, 74.4% and 74.4% respectively. Positive predictive values are 45.5%, 72.2% and 57.7% respectively and the Negative predictive value were 77.5%, 80% and 88.9%.[48]

Recently a study conducted on VILI in India concluded that the sensitivity and specificity of VILI could be increased by combining another method like VIA.[49]

Inference from the reviewed literature is that the conventional Pap test plays an important role in the screening of cervical cancer and in the drastic reduction of cervical cancer in the developed countries. VIA, VILI are simple, inexpensive methods which can be equally useful in the screening of cancer cervix in the low resource settings. The studies where VIA and VILI were compared, sensitivity and specificity of VILI was found to be better than VIA.

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 during the period of January 2011 to March 2011.

Study design

This was a one year cross-sectional screening interventional study.

Study period

This study was conducted during the period January 2011 to December 2011.

Source of data

All women referred to Colposcopy Clinic, Department of Obstetrics and Gynaecology at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum

Sample size

A total of 204 women were included in the study.

Sampling technique

The sample size was calculated based on the formula.

$$n = \frac{4\ Z\alpha^2\ p\ q}{d^2}$$

Where, $Z\alpha$ = Constant

d = Error

p = Prevalence

q = (100 - p)

n = Sample size

The eligible pool will be 288 women, 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 hence enabling us to meet our sample size of 204.

Selection criteria

Inclusion criteria

- Persistent vaginal discharge.
- Post coital bleeding.
- Unhealthy cervix on examination.
- Inter menstrual bleeding.
- Screen positive status.

Exclusion criteria

- Less than 30 years of age.
- Unmarried women.
- Prior total hysterectomy done.

- Obvious growth on cervix.
- Pregnancy.

Ethical clearance

Prior to the commencement, the study was approved by the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

All the participants fulfilling selection criteria were explained about the purpose of the study and the need for cervical cancer screening. A written informed consent was obtained from all the participants before enrollment (Annexure I).

Method of collection of data

After the enrollment, demographic data such as age, education, marital status, obstetric history, complaints, was recorded on a predesigned and pretested proforma (Annexure II).

Procedure

Further participants were subjected to speculum examination starting with a direct visual evaluation of the cervix to identify squamo- columnar junction, abnormal vaginal discharge, cervical polyp, Nabothian follicle or cysts, leukoplakia, condyloma, growth, ectropion and erosion.

Sample collection for HPV testing

Brush was inserted 1 to 1.5 cm into the cervical os until the largest outer bristle of the brush touched the ectocervix and rotated three times clockwise and anti clockwise without inserting. The brush was then removed from the canal carefully, avoiding touching the bristles to the outside of the tube or any other object. Brush was inserted to the bottom of the transport tube and shaft snapped off at score line and capped securely.

Interpretation of results

- Cut-off ratio of 0 to 0.90 was considered as normal.
- Ratio of more than 0.91 was considered as positive for high risk HPV infection.

VIA

VIA involved gentle application of 5% acetic acid using a small piece of cotton to avoid bleeding. After one minute a naked-eye evaluation was performed under 100 watt illumination.

Colposcopy

Colposcopy was performed in all participants by a gynecologist trained in colposcopy. A cervical biopsy was obtained in cases where colposcopy revealed a precancerous lesion using cervical punch biopsy forceps by the study gynecologist.

Blinding

The gynaecologist performing colposcopy was blinded to the results of VIA.

Statistical analysis

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data was expressed as rates, ratios and proportions and continuous data was expressed as mean ± standard deviation (SD). Concordance of tests was determined by kappa statistics.

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

Following this test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and when HPV DNA testing and VIA are combined to find out the probable best screening option was determined by the sensitivity, specificity, positive and negative predictive value and diagnostic accuracy was calculated.

Chapter 5

Results

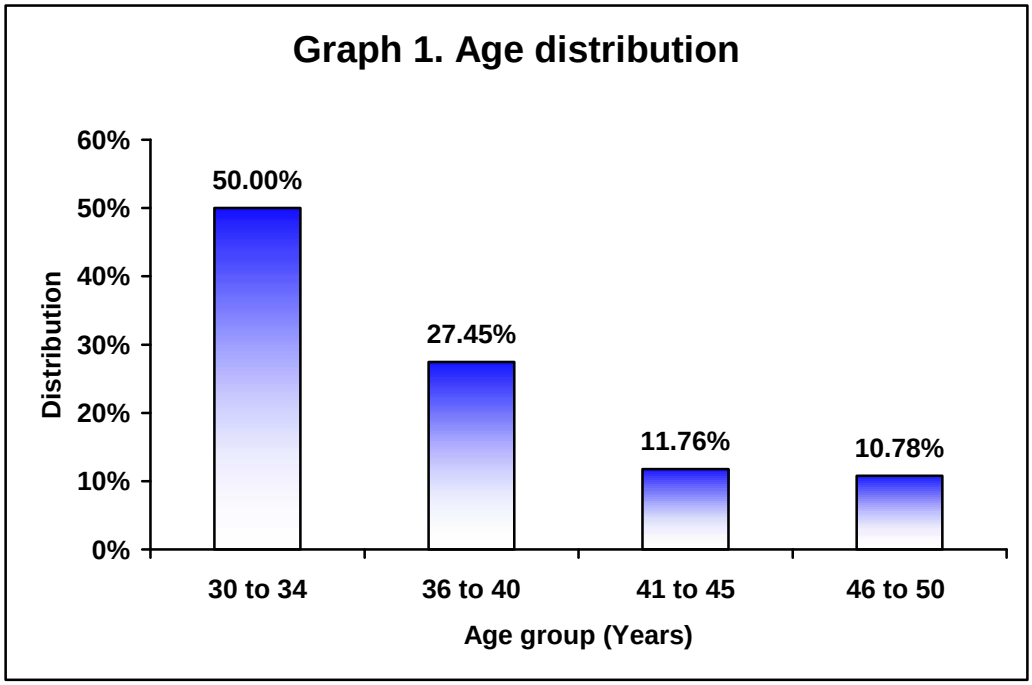
RESULTS

The present one year cross-sectional screening interventional study was conducted on a total of 204 women referred to Colposcopy Clinic, Department of Obstetrics and Gynaecology at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum.

Test results of VIA, colposcopy, HPV DNA and biopsy were carried out. The gynaecologist performing colposcopy was blinded to the results of VIA. The data obtained was coded and entered into Microsoft excel spread sheet and analysed. The results obtained were tabulated and presented as below.

Table 1. Age distribution

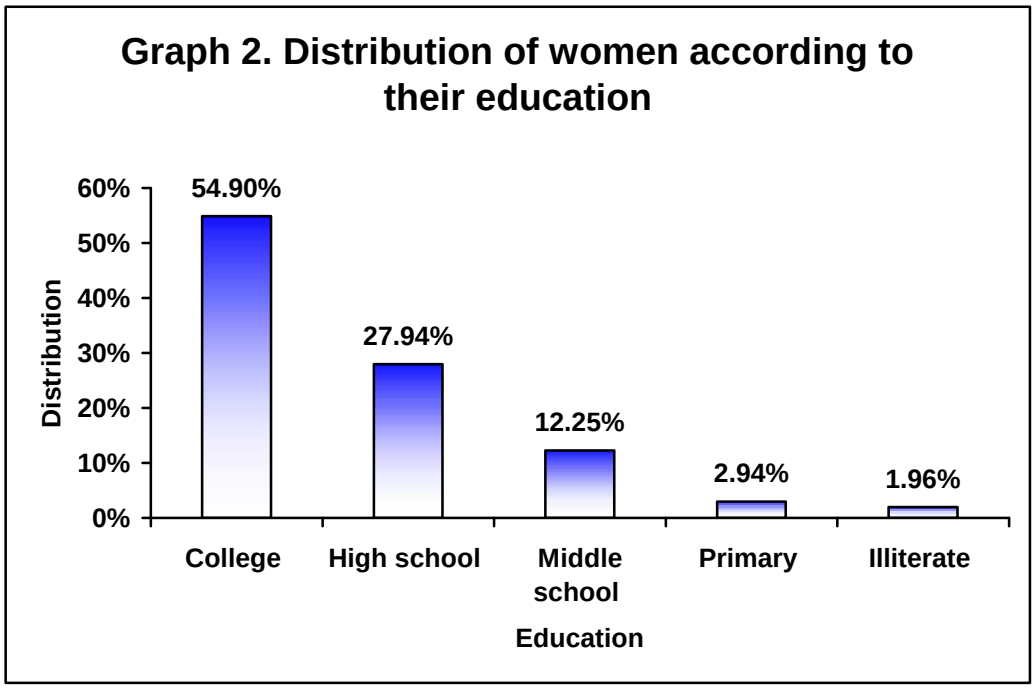
Age group (Years)	Distribution (n=204)	
	Number	**Percent**
30 to 35	102	50.00
36 to 40	56	27.45
41 to 45	24	11.76
46 to 50	22	10.78
Total	**204**	**100.00**



In this study of the 204 women, most of the women (50%) were between 30 to 34 years followed by 27.45% between 36 to 40 years, 11.76% between 41 to 45 years and 10.78% between 46 to 50 years. Overall, the mean age was 36.75 ± 35.50 years and the median age was 35.5 years with range being 24 as minimum to 52 as maximum.

Table 2. Distribution of women according to their education

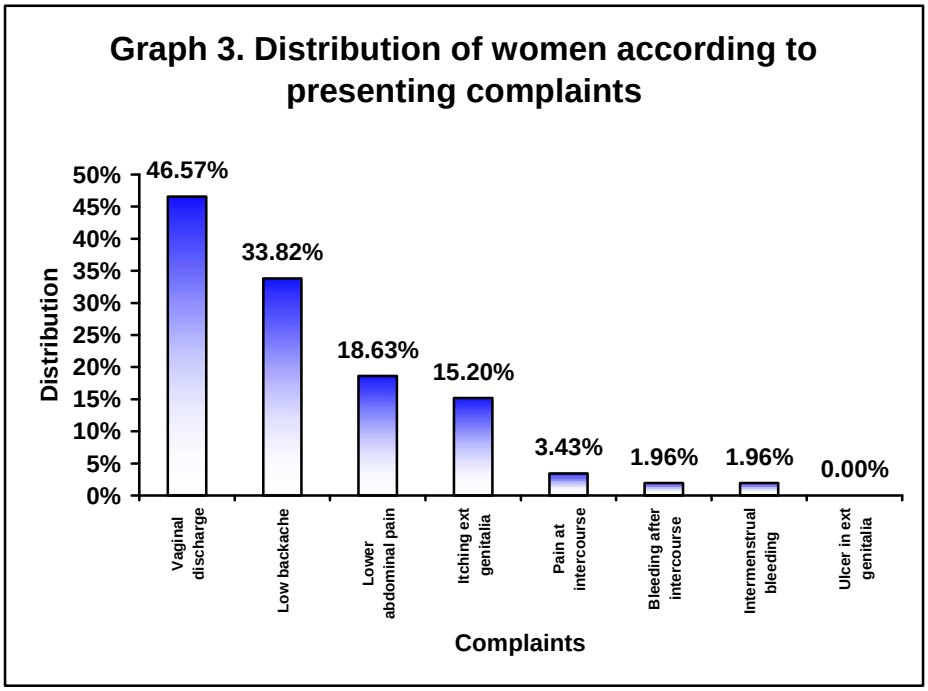
Education	Distribution (n=204)	
	Number	**Percent**
College	112	54.90
High school	57	27.94
Middle school	25	12.25
Primary	6	2.94
Illiterate	4	1.96
Total	**204**	**100.00**



In this study of the 204 women, most of the women (54.90%) had studied upto college and 27.94% had high school education.

Table 3. Distribution of women according to presenting complaints

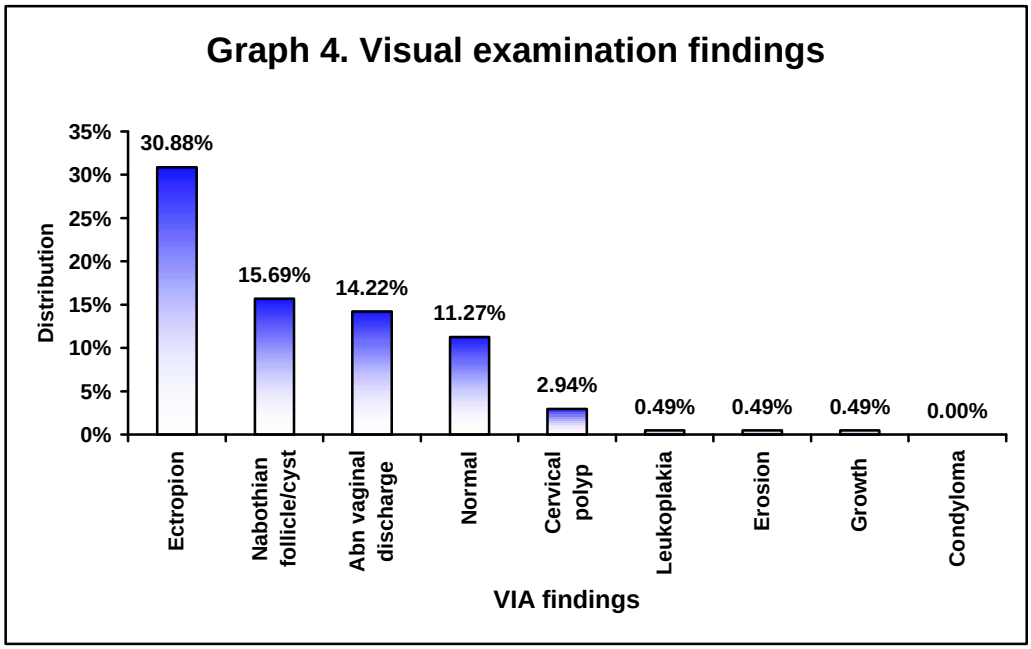
Complaints	Distribution (n=204)	
	Number	Percent
Vaginal discharge	95	46.57
Low backache	69	33.82
Lower abdominal pain	38	18.63
Itching in external genitalia	31	15.20
Pain at intercourse	7	3.43
Bleeding after intercourse	4	1.96
Intermenstrual bleeding	4	1.96
Ulcer in external genitalia	0	0.00



In this study 46.57% of the women reported vaginal discharge and 33.82% reported backache.

Table 4. Visual examination findings

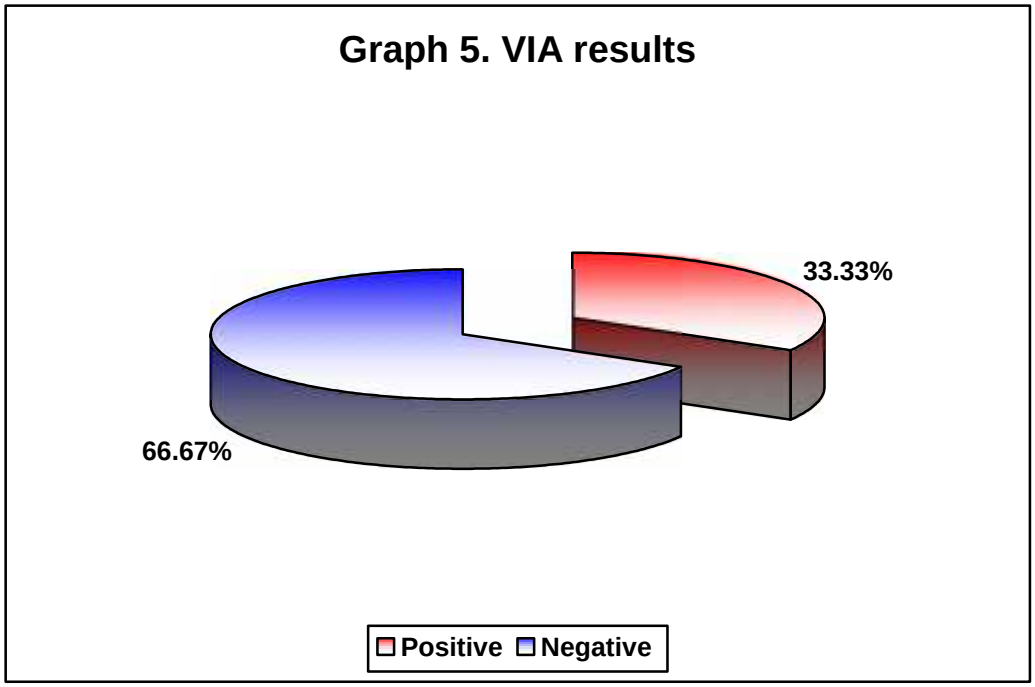
Findings	Distribution (n=204)	
	Number	Percent
Ectropion	63	30.88
Nabothian follicle/cyst	32	15.69
Abnormal vaginal discharge	29	14.22
Normal	23	11.27
Cervical polyp	6	2.94
Leukoplakia	1	0.49
Growth	1	0.49
Erosion	1	0.49
Condyloma	0	0.00



The visual examination revealed most cases with ectropion (30.88%) women.

Table 5. VIA results

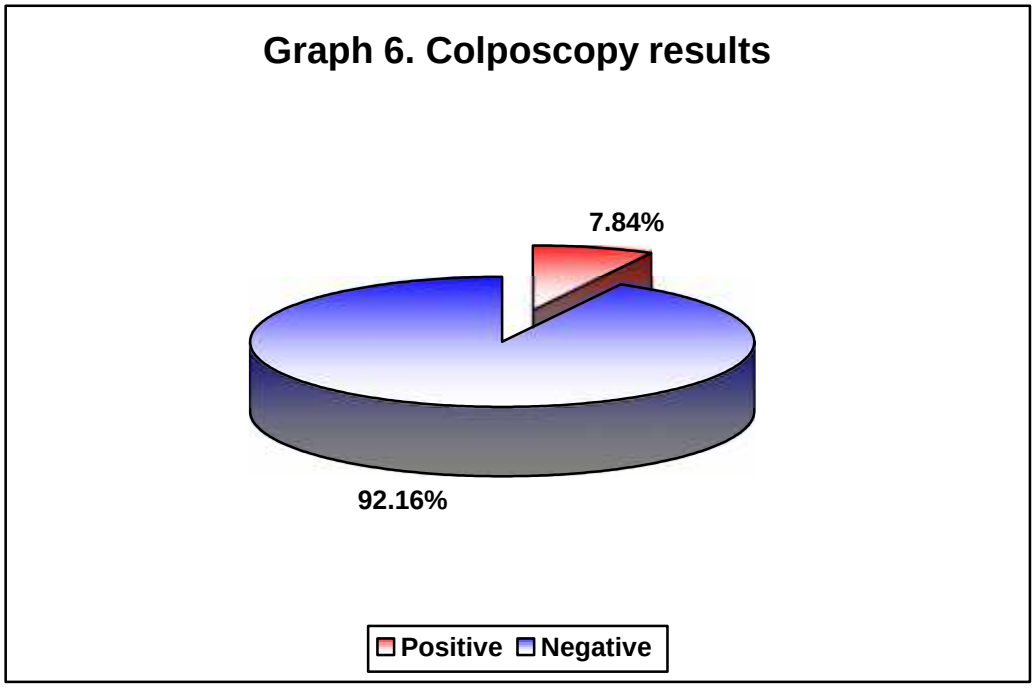
Results	Distribution (n=204)	
	Number	**Percent**
Positive	68	33.33
Negative	136	66.67
Total	**204**	**100.00**



In the present study of the 204 women, VIA was positive in 68 cases (33.33%).

Table 6. Colposcopy results

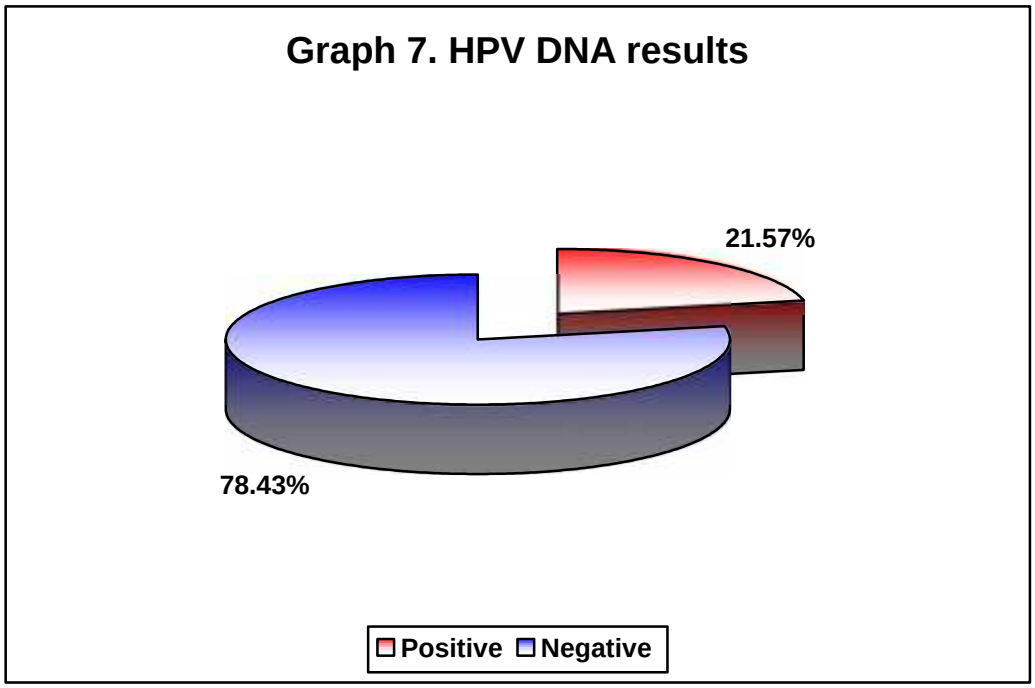
Test results	Findings	Distribution (n=204)	
		Number	**Percent**
Negative	Benign	141	69.12
	CIN 1	47	23.04
	Total	*188*	*92.16*
Positive	CIN 2	11	5.39
	CIN 3	4	1.96
	SCC	1	0.49
	Total	*16*	*7.84*
Total	**Total**	**204**	69.12



The colposcopic findings among 16 women (7.84%) showed positive test results.

Table 7. HPV DNA results

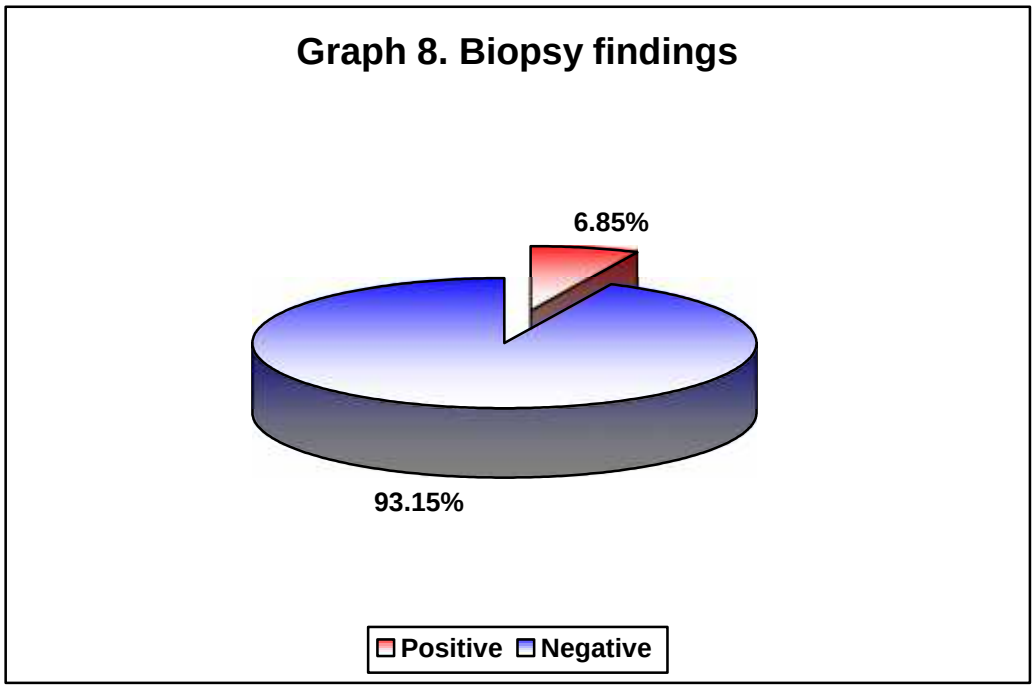
Results	Distribution (n=204)	
	Number	**Percent**
Positive	44	21.57
Negative	160	78.43



The HPV DNA test was positive among 44 (21.57%) women.

Table 8. Biopsy results

Test results	Findings	Distribution (n=73)	
		Number	**Percent**
Negative	Benign	62	84.93
	CIN 1	6	8.22
	Total	*68*	93.15
Positive	CIN 2	0	0.00
	CIN 3	4	5.48
	SCC	1	1.37
	Total	*5*	6.85
Total	**Total**	**73**	**100.00**



Out of 204, 73 (35.78%) underwent biopsy. The biopsy findings in four women (5.48%) revealed CIN 3 and one case (1.37%) of SCC.

Table 9. Correlation of VIA with final disease status as established by reference standard

VIA test results	Final diagnosis					Total
	Negative		Positive			
	Benign	CIN 1	CIN 2	CIN 3	SCC	
Positive	58	6	0	3	1	68
Negative	135	0	0	1	0	136
Total	193	6	0	4	1	204

Table 10. Diagnostic efficacy of VIA with CIN 2 as disease threshold

VIA	Final diagnosis		Total
	Positive	Negative	
Positive	4	64	**68**
Negative	1	135	**136**
Total	**5**	**199**	**204**
k=0.067;			**p=0.025**

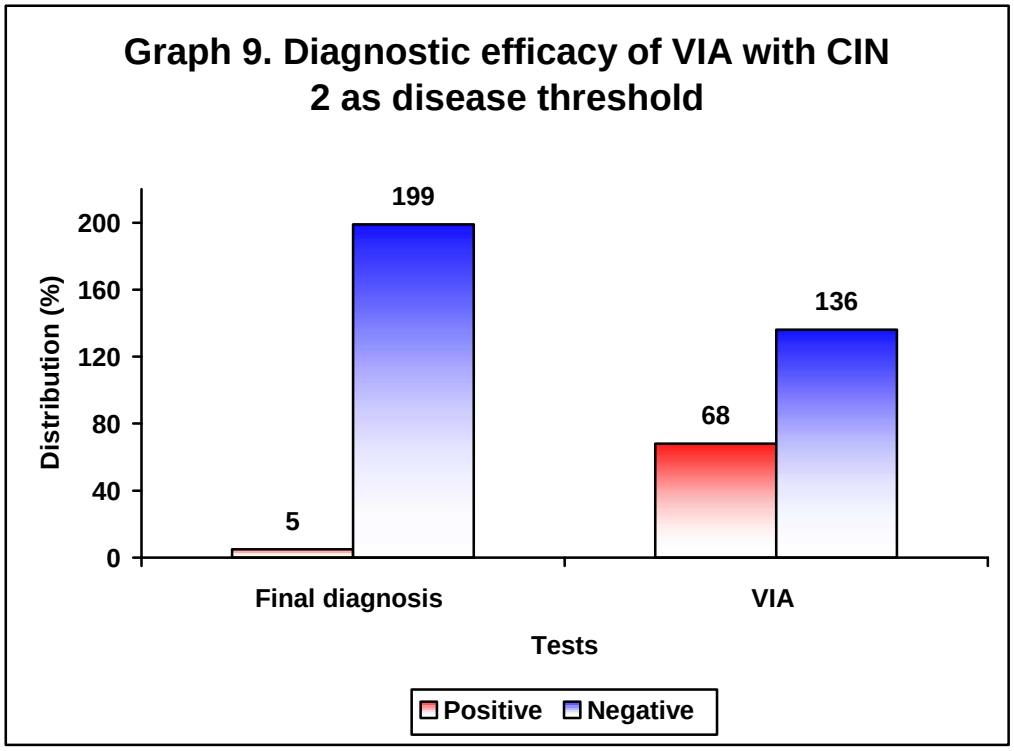
Sensitivity=80% (CI=95% [0.37-0.96]);

Specificity=67.84%; (CI=95% [0.61-0.73]);

PPV=5.88%;

NPV=99.26;

DA=68.14%



In the present study VIA test findings revealed 68 positive and 136 negative cases. Of the 68 positive cases the final diagnosis was positive among 4 cases which showed three cases of CIN 3 and one case of SCC. Out of 136 VIA negative cases, one case was diagnosed as CIN 3. Based on these findings the sensitivity of VIA compared to final diagnosis was 80% with specificity of 67.84%, PPV of 5.88% and NPV of 99.26% showing the diagnostic accuracy of 68.14%. The kappa statistics for agreement between VIA and biopsy was 0.067, which is statistically significant ($p<0.025$)

Table 11. Correlation of HPV DNA test with final disease status as established by reference standard

HPV DNA test	Final diagnosis					Total
	Negative		Positive			
	Benign	CIN 1	CIN 2	CIN 3	SCC	
Positive	38	1	0	4	1	44
Negative	155	5	0	0	0	160
Total	193	6	0	4	1	204

Table 12. Diagnostic efficacy of HPV DNA test with CIN 2 as disease threshold

HPV DNA test	Final diagnosis		Total
	Positive	Negative	
Positive	5	39	**44**
Negative	0	160	**160**
Total	**5**	**199**	**204**

k=0.167; **p<0.001**

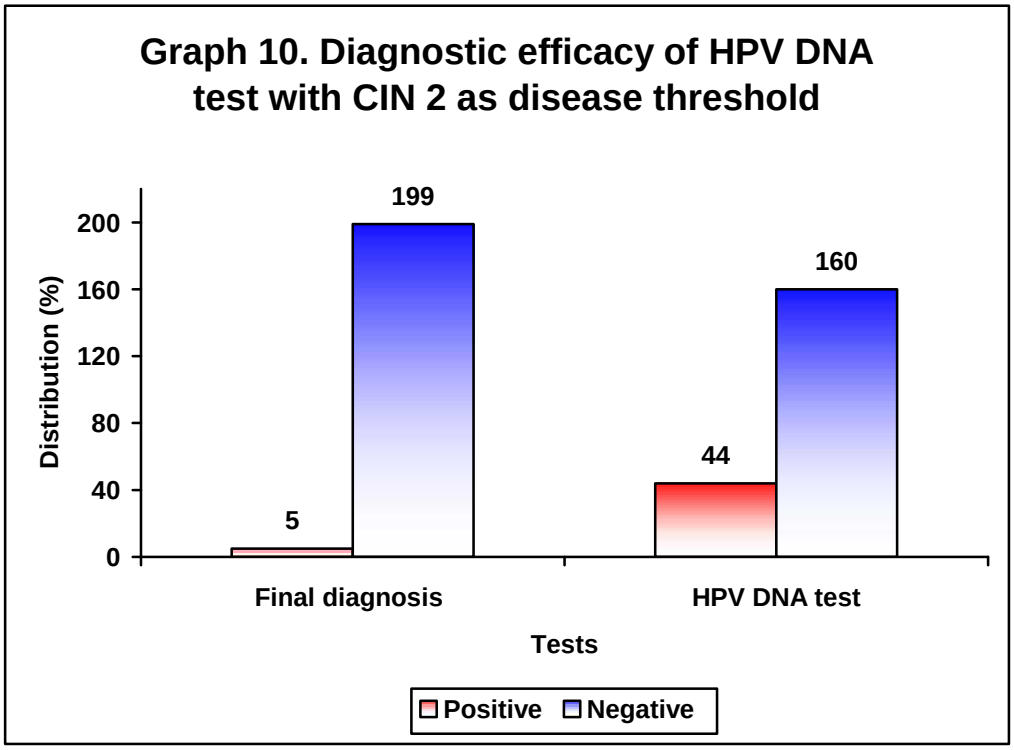
Sensitivity=100% (CI=95% [0.56-1.00])

Specificity=80.40% (CI=95% [0.74-0.85])

PPV=11.36%

NPV=100%

DA=80.88%



In the present study HPV DNA test findings revealed 44 positive and 160 negative cases. Of the 44 positive cases the final diagnosis was positive among five cases which showed four cases of CIN 3 and one case of SCC. Of the 160 HPV DNA test negative cases none of case had positive final diagnosis. Based on these findings the sensitivity of HPV DNA test compared to final diagnosis was 100% with specificity of 80.40%, PPV of 11.36% and NPV of 100% showing the diagnostic accuracy of 80.88%. The kappa statistics for agreement between HPV-DNA test and biopsy was 0.167, which is statistically significant ($p<0.001$)

Table 13. Correlation of VIA positive and HPV DNA test positive with final disease status as established by reference standard

VIA and HPV DNA test	Final diagnosis					Total
	Negative		Positive			
	Benign	CIN 1	CIN 2	CIN 3	SCC	
Both test Positive	11	1	0	3	1	16
Either test Negative	182	5	0	1	0	188
Total	193	6	0	4	1	204

Table 14. Diagnostic efficacy of VIA positive and HPV DNA positive with CIN 2 as disease threshold

VIA and HPV DNA test	Final diagnosis		Total
	Positive	Negative	
Positive	4	12	**16**
Negative	1	187	**188**
Total	**5**	**199**	**204**
k=0.357;			**p<0.001**

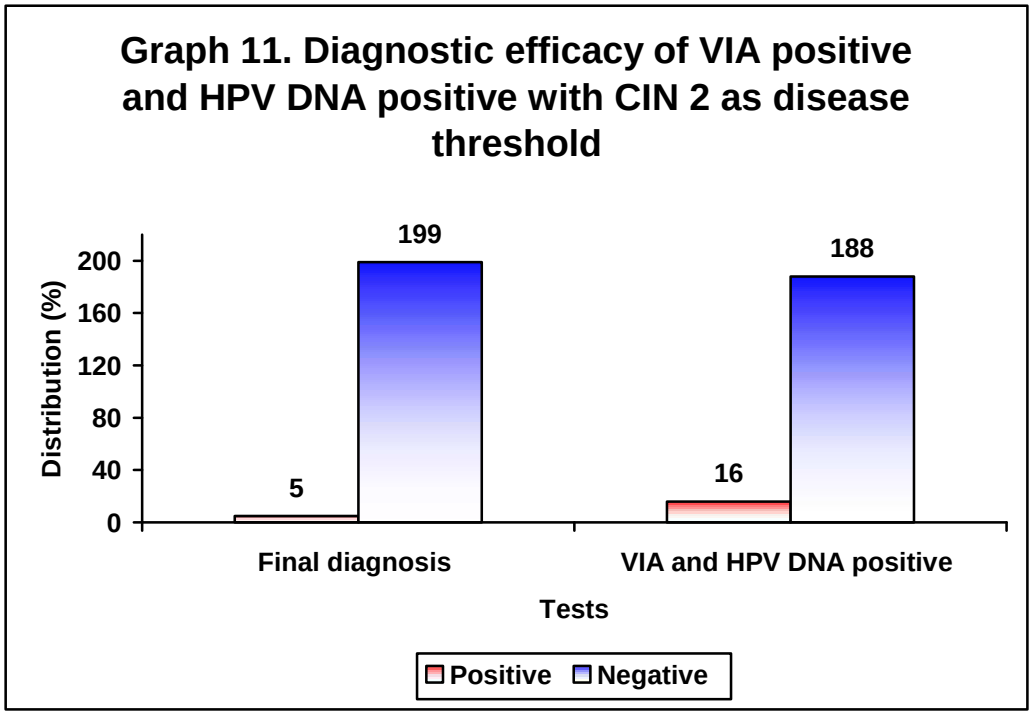
Sensitivity=80% (CI=95% [0.37-0.96])

Specificity=93.96% (CI=95% [0.89-0.96])

PPV=25%

NPV=99.46%

DA=93.63%



In the present study 16 cases had VIA and HPV DNA test positive. Among them the final diagnosis was positive in four cases which showed three cases of CIN 3 and one case of SCC. In 188 cases with either test negative one case had final diagnosis of CIN 3. Based on these findings, the sensitivity of both HPV DNA and VIA compared to final diagnosis of CIN 2 as disease threshold showed 80% sensitivity with specificity of 93.96%, PPV of 25% and NPV of 99.46% showing diagnostic accuracy of 93.63%. The kappa statistics for agreement between VIA positive and HPV-DNA test positive and final diagnosis was 0.357, which was statistically significant ($p<0.001$).

Table 15. Correlation of VIA positive or HPV DNA positive with final disease status as established by reference standard

VIA or HPV DNA test	Final diagnosis					Total
	Negative		Positive			
	Benign	CIN 1	CIN 2	CIN 3	SCC	
Either test positive	85	6	0	4	1	96
Both test Negative	108	0	0	0	0	108
Total	193	6	0	4	1	204

Table 16. Diagnostic efficacy of VIA positive or HPV DNA positive with CIN 2 as disease threshold

VIA or HPV DNA test	Final diagnosis		Total
	Positive	Negative	
Either test positive	5	91	**96**
Both test Negative	0	108	**108**
Total	**5**	**199**	**204**

k=0.040; **p=0.016**

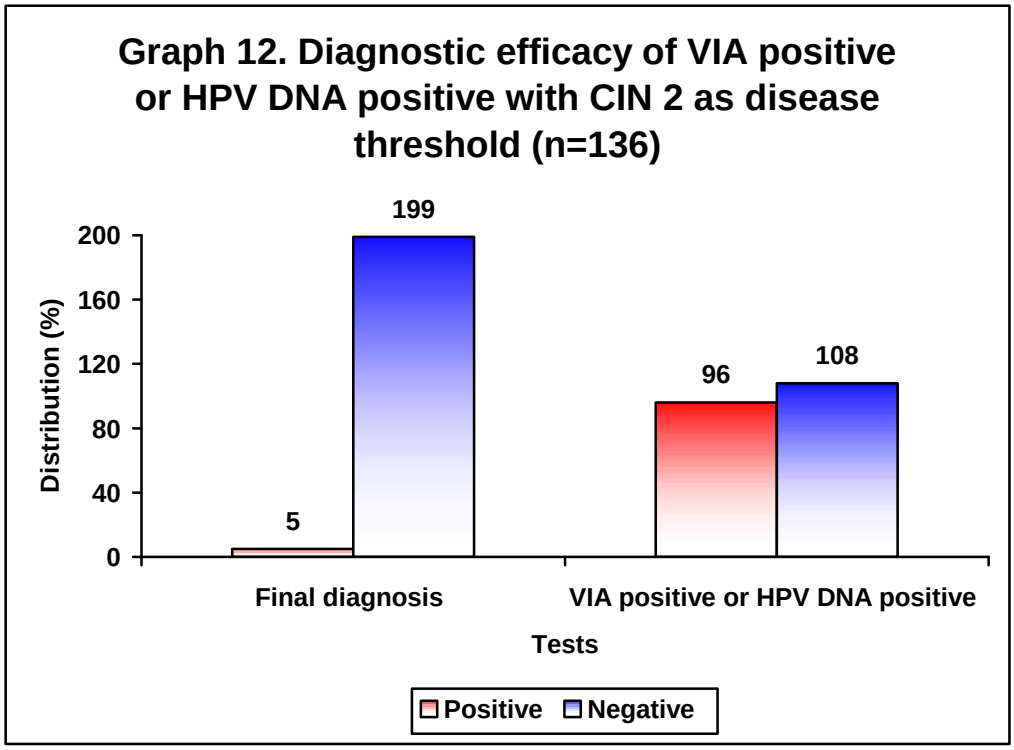
Sensitivity= 100% (CI=95% [0.56-1.00])

Specificity=54.27% (CI=95% [0.47-0.61])

PPV=5.21%

NPV=100%

DA=55.39%



In this study VIA or HPV DNA test was positive in 96 cases. Among them the final diagnosis was positive in five cases which showed four cases of CIN 3 and one case of SCC. Of the 108 cases with VIA and HPV DNA negative, the final diagnosis showed benign lesions in all the cases. Based on these findings the sensitivity of VIA positive or HPV DNA positive compared to final diagnosis was 100% with specificity of 54.27%, PPV of 5.21% and NPV of 100% showing diagnostic accuracy of 55.39%. The kappa statistics for agreement between VIA positive or HPV-DNA positive and final diagnosis was 0.055, which was statistically significant (p=0.016).

Table 17. Comparison of the diagnostic efficacy of VIA, HPV DNA, VIA and HPV DNA positive and VIA or HPV DNA positive with CIN 2 as disease threshold

Diagnostic efficacy	VIA (CI=95%)	HPV (CI=95%)	VIA and HPV positive (CI=95%)	VIA or HPV positive (CI=95%)
Sensitivity (%)	80.00%	100%	80.00%	100%
Specificity (%)	67.84%	80.40%	93.96%	54.27%
PPV (%)	5.88%	11.36%	25.00%	5.21%
NPV (%)	99.26%	100%	99.46%	100%
DA (%)	68.14%	80.88%	93.63%	55.39%

Table 20. Likelihood ratio of screening test

Screening tests	Likelihood ratio	
	Positive	Negative
VIA	2.48 [0.61-0.73]	0.29 [0.05-1.70]
HPV DNA	5.10 [3.85-6.76]	-
VIA and HPV positive	13.26 [6.57-26.77]	0.21 [0.03-1.22]
VIA or HPV positive	2.18 [1.88-2.54]	-

The above table shows comparison of sensitivity, specificity, PPV, NPV and diagnostic accuracy. It was observed that, VIA and HPV positive tests showed diagnostic accuracy of 93.63% with positive likelihood ratio of 13.26 and negative likelihood ratio of 0.21 whereas VIA or HPV positive 55.39% diagnostic accuracy with positive likelihood ratio of 2.18 (CI 95%).

Chapter 6

Discussion

DISCUSSION

Invasive cervical cancer is preceded by a long premalignant phase known as cervical intraepithelial neoplasia. The goal of cervical cancer screening is the detection and treatment of precancer before cancer develops.[36]

To detect cervical intraepithelial neoplasia grades 2 or 3, which are considered to be true precancerous lesions, we need a well implemented secondary prevention system that provides screening for all women as well as treatment of detected abnormalities according to local policy. The Papanicolaou (Pap) smear has been shown to be highly effective in developed countries that have widespread screening programs.[36]

In developing countries, because of the lack of trained cytotechnologists and cytology laboratories, there is often a long interval (1–3 months) between the Pap screening and when the test result is available. Additionally, only a small percentage of women with positive Pap smears have diagnostic evaluation and treatment, because of the lack of health centers that are able to treat preinvasive lesions. These problems with Pap smears have stimulated research on alternative tests, including visual inspection with acetic acid (VIA). VIA has demonstrated high sensitivity for detecting CIN and cervical cancer, but it is limited by low specificity. VIA is based on aceto whitening, with cervix turning white when exposed to 5% acetic acid (vinegar). VIA has the advantage of requiring only low-technology equipment, and the result is available within a couple of minutes. These characteristics make VIA a realistic alternative for low-resource settings.[36]

Within the past five years, guidelines recognizing the value of HPV testing in both primary cervical screening and in the management of abnormal cervical cytology have been established in the US and are being considered in Europe. This trend has occurred because of the definitive association of high risk HPV with cervical cancer and the overwhelming evidence that the sensitivity of high risk HPV testing for lesions with a diagnosis of cervical intraepithelial neoplasia grade 2 or more severe (CIN 2+) is substantially higher than that of cytology.[38]

Hence, the present study was planned to assess the test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and also to assess the performance when HPV DNA testing and VIA are combined to find out the probable best screening option.

This one year cross-sectional screening interventional study was conducted on a total of 204 women referred to Colposcopy Clinic, at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Test results of VIA, colposcopy, HPV DNA and biopsy were obtained. The gynaecologist performing colposcopy was blinded to the results of VIA.

In this study most of the women (50%) were aged between 30 to 34 years followed by 27.45% between 36 to 40 years. Overall, the mean age was 36.75 ± 35.50 years and the median age was 35.5 years with range being 24 as minimum to 52 as maximum. These findings were comparable with a study[50] done in our institution to assess the interobserver variability of VIA between nurse and physician wherein, maximum number of women (42.6%) were in the age group

of 30 to 39 years with mean age of 35 years. Similarly another study[49] from Andhra Pradesh reported most of the participants (48%) in the age groups of 25 to 34 years whereas a study[44] from Mumbai reported 84% women between 30 to 49 years. A study[9] from Brazil reported mean age of 37.9 years, with 90% central range of 26–56 years.

In this study of the 204 women, most of the women (54.90%) had studied upto college and 27.94% had high school education. A study[49] from Andhra Pradesh reported 69.4% women with no formal education whereas a study[44] from Mumbai reported 78% literate women. The educational status of the women enrolled in this study was better when compared to the other studies that is, only 1.96% women were illiterate in this study.

In the present study most of the women complained of vaginal discharge (46.57%) and backache (33.82%). Unhealthy cervix was seen on speculum examination in 38 women. The visual examination revealed ectropion in 30.88% women. A study[51] from AIIMS, New Delhi reported vaginal discharge in 80 women, irregular vaginal bleeding in 13 women and post coital bleeding in one woman. In another study[50] from our institution persistent white discharge per vaginum was the commonest complaint (64.2%) followed by suspicious looking cervix in 21.4%, post menopausal bleeding in 6.6% and postcoital bleeding in 5.6%.

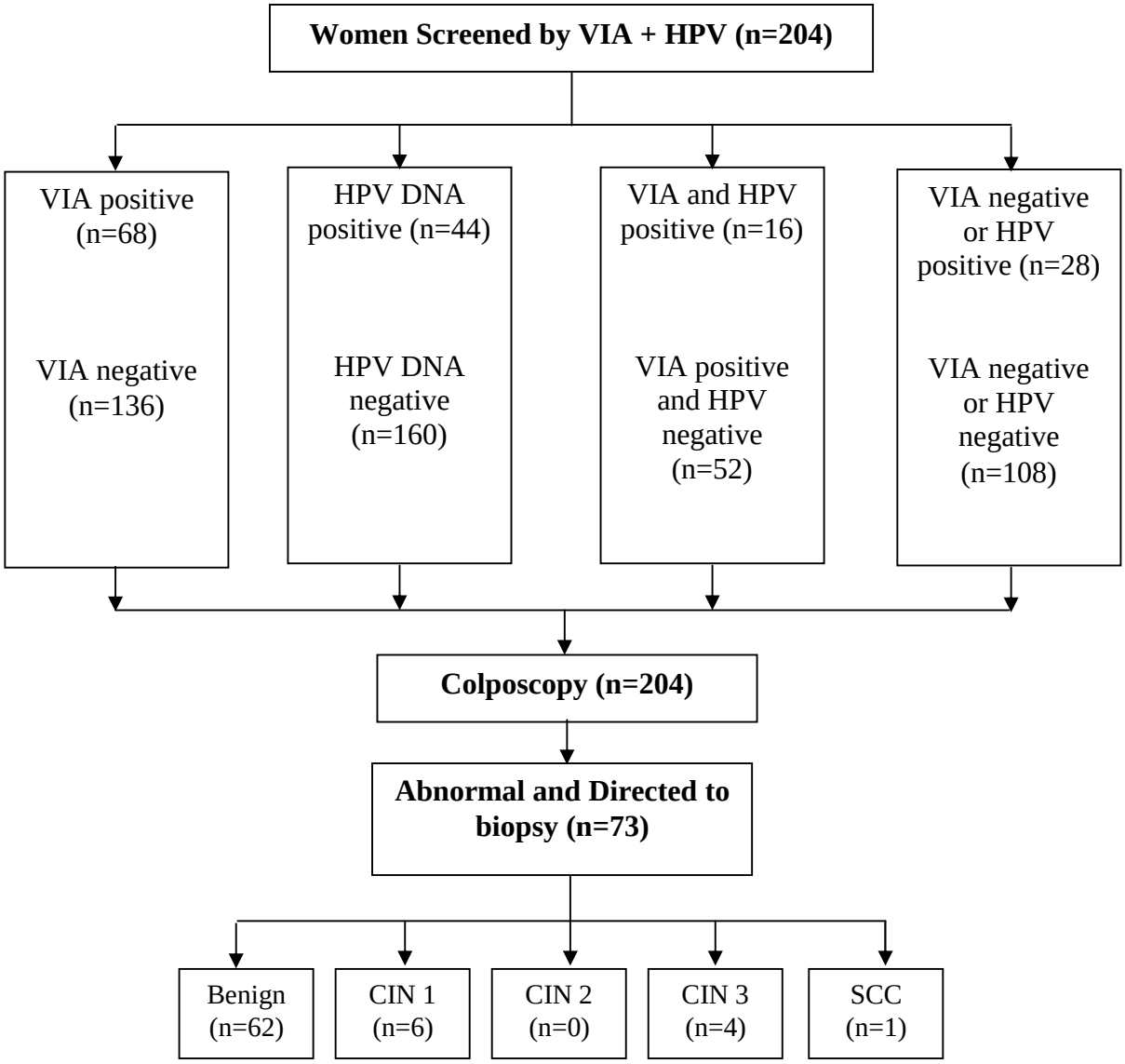


Figure 3. Flow chart of women screened

In the present study of the 204 women VIA and HPV DNA test was positive in 33.33% and 21.57% women respectively. The colposcopic findings among 16 women (7.84%) showed positive test results of which CIN 2 was observed in 5.39%, CIN 3 in 1.96% and SCC in 0.49% women. Out of 204, 73 (35.78%) underwent biopsy and HSIL findings were recorded in five women

(6.85%) which revealed CIN 3 in four women (5.48%) and one case (1.37%) of SCC.

In a study[51] from AIIMS, New Delhi results of VIA, Pap smear, colposcopy and biopsy, if indicated, were available for 100 cases. HPV results were available for 94 patients. Biopsy was taken in 60 patients. There were two cases of CIN 1, three cases of CIN 2, three cases of CIN 3 and two cases of invasive squamous cell carcinoma.

Another study[9] from Brazil reported overall test positivity of 11.6% for VIA, 23.0% for VILI, 2.2% for Pap smear (LSIL threshold), 1.1% for Pap smear (HSIL threshold) and 17.1% for hybrid capture II.

In a study[44] from Mumbai positive results for VIA, VIAM and VILI tests were 12.7%, 14.8% and 17% respectively and 2.7% cytology results were positive and 7.6% of HPV test results were positive.

A similar study[50] from our institute to assess the interobserver variability of VIA between nurse and physician reported VIA as positive in 149 cases (36.7%) by physician and in 199 cases (49.01%) by nurse. Of the study population 110 cases (27%) were VIA positive and 168 cases (41.37%) were VIA negative by both physician and nurse resulting in a moderate agreement between the two (k=0.366). Of the 69 biopsy confirmed CIN 1 lesions 52 were reported VIA positive by physician 48 by nurse. Of the 31 high grade lesions (CIN 2 and CIN 3) 5 cases were missed by the physician and 9 cases by the nurse. All cases of early invasive carcinoma were picked by both the physician and nurse.

Close to 80% of invasive cancer cases occur in developing countries, where either there are no screening programs or the programs are poorly developed and inefficient. Most of these programs are based on Pap smears and try to mimic the good results obtained in developed countries. Unfortunately, their results have been suboptimal due to lower coverage of women at risk, no standardized quality control systems, and a lack of follow-up and treatment of positive cases. For these reasons, in recent decades other alternatives have been explored, such as human papillomavirus (HPV) DNA testing and VIA.[42]

HPV DNA testing has shown very high sensitivity and is being recommended in high-resource countries. However, its current price and technology requirements make this option unrealistic for poor areas until a low-cost, same-day HPV test and realistic strategies are developed. VIA has arisen as a promising alternative for developing countries because it is inexpensive and fast and requires a low level of training and no special equipment. Some previous reports have observed that VIA can reach similar or better results than the Pap smear in the detection of CIN. Further, it is important to mention that there had been no prior experience with using VIA in a high-resource setting in a developing country. In general, the sensitivity of VIA has been shown to be equal to or better than the Pap smear's, while its specificity has been lower.[45]

Visual inspection based methods have many advantages: they are less expensive than cytology based screening, easy to administer and train appropriate health care workers, and provide real-time results. They may be a viable screening option in low-resource settings such as India;[52] however, their long-term effectiveness in reducing cervical cancer incidence and mortality has not yet

been established. Preliminary data from an Indian cluster randomised control trial based in Tamil Nadu suggests that screening using the VIA method substantially reduces incidence of, and mortality from, cervical cancer [incidence hazard ratio of 0.75 (0.55–0.95) and mortality hazard ratio of 0.65 (0.47–0.89)].[53]

In the present study VIA test findings revealed 68 positive and 136 negative cases. Of the 68 positive cases the final diagnosis was positive among 4 cases which showed three cases of CIN 3 and one case of SCC. Out of 136 VIA negative cases, one case was diagnosed as CIN 3. Based on these findings the sensitivity of VIA compared to final diagnosis was 80% with specificity of 67.84%, PPV of 5.88% and NPV of 99.26% showing the diagnostic accuracy of 68.14%. The kappa statistics for agreement between VIA and biopsy was 0.067, which is statistically significant ($p<0.025$) VIA meets most generally agreed criteria of a good screening test. In a workshop Proceedings on alternatives for Cervical Cancer Screening and Treatment in Low-Resource Settings, delegates reviewed studies and reported sensitivity for VIA was consistently 60 to 70% and the specificity was approximately 70%.[54] A study[55] from Iran reported sensitivity and specificity of VIA as 74.3% and 94%, respectively, that were very similar to cytology values for detecting CIN I or other preinvasive lesions. Another study[6,56] reported better results with visual inspection. They detected 90.1% of true positive cases, with a qualified specificity (limited biopsies) of 92.2%. In a study[9] from Brazil using the CIN 2 cut-off point, VIA and VILI as stand-alone tests performed very similarly in terms of sensitivity, detecting roughly 50% of the lesions. However, VIA was more specific (89%) than VILI (77%). Importantly, both tests showed very low PPV: 6.6% for VIA and, even more

impressive, close to 3% for VILI. The NPV of VIA (99.2 %) matched that of VILI (99.3%). In a cohort of 4444 women examined with Pap smear, VIA and VILI in Kerala, India, recently achieved more than 80% sensitivity and specificity with VIA, associated with 17.5% PPV.[57] VIA was far less sensitive, but showed comparable specificity and lower PPV. The results were equal with VILI, which reached 87.2% sensitivity, 84.7% specificity and 16.6% PPV.[6] The sensitivity and specificity of the VIA test in the present study was comparable with these studies.

In the present study HPV DNA test findings revealed 44 positive and 160 negative cases. Of the 44 positive cases the final diagnosis was positive among five cases which showed four cases of CIN 3 and one case of SCC. Of the 160 HPV DNA test negative cases none of case had positive final diagnosis. Based on these findings the sensitivity of HPV DNA test compared to final diagnosis was 100% with specificity of 80.40%, PPV of 11.36% and NPV of 100% showing the diagnostic accuracy of 80.88%. The kappa statistics for agreement between HPV-DNA test and biopsy was 0.167, which is statistically significant ($p<0.001$). HPV testing is highly reproducible, is more easily monitored, provides an objective test outcome and can easily be automated. In a review of 14 studies,[58] the average sensitivity and specificity of HPV DNA testing were 85% and 84%. On average, the sensitivity of HPV DNA testing was 27% higher than that of cytology in absolute terms, and its specificity is 8.4% lower. The performance of HPV DNA testing in women older than 30 years, however, was significantly better, with the average sensitivity and specificity increasing to 89% and 90%. In addition, testing for high-risk types of HPV DNA has a very high NPV, that is, the

likelihood of having no disease if the HPV DNA test is negative. In a number of cross-sectional studies in different populations and age groups, the NPV of HPV DNA testing was consistently greater than 97% using either the Hybrid Capture assay hc2 or PCR-based assays, with most studies reporting values greater than 99% and some reporting 100%.[59]

In a study[9] from Brazil, HPV tests were positive in 15.5% of women with no detectable disease, but was positive in 52.3% of women with CIN 1, reaching 100.0% (three of three cases) in women diagnosed with cancer. Interestingly, 96.6% of women with CIN 3 had a positive hybrid capture II, whereas only 67.7% of those with CIN 2, also considered high-grade disease, had a positive HPV test. A study[49] from Andhra Pradesh reported sensitivity and specificity of 61.2% and 91.9% respectively.

A study[44] from Mumbai reported sensitivity, specificity, and predictive values of the positive and negative tests for detecting HSIL. HPV testing had a higher specificity than the visual tests, but a lower specificity than cytology. The positive predictive values (PPV) of the visual tests ranged from 6.5 to 7.0%, while the PPV of HPV testing was 12.1%, and the highest PPV was calculated for cytology (37.8%). The negative predictive values of all tests exceeded 99.3%. The sequential test combinations resulted in a significant increase in specificity (greater than 99.0% for combinations of visual and laboratory-based tests) compared with that for the single tests, but a substantial reduction in sensitivity Combining a visual test with cytology or HPV testing in parallel resulted in a substantial increase in sensitivity and a moderate decrease in specificity

compared with those of single tests. Although the combination of VILI and HPV testing in parallel gave the highest sensitivity (92.0%), the specificity was 79.9%.

In study[49] from Andhra Pradesh HPV DNA testing had the best sensitivity and specificity when defining cases as CIN2+ or CIN3+ (84.2% and 81.3% for CIN2+; 100% and 80.72% for CIN3+). Accordingly, the HPV DNA test showed both high positive predictive value (11.5%) and negative predictive value (99.4%) for CIN2+.

In the present study 16 cases had VIA and HPV DNA test positive. Among them the final diagnosis was positive in four cases which showed three cases of CIN 3 and one case of SCC. In 188 cases with either test negative one case had final diagnosis of CIN 3. Based on these findings, the sensitivity of both HPV DNA and VIA compared to final diagnosis of CIN 2 as disease threshold showed 80% sensitivity with specificity of 93.96%, PPV of 25% and NPV of 99.46% showing diagnostic accuracy of 93.63%. The kappa statistics for agreement between VIA positive and HPV-DNA test positive and final diagnosis was 0.357, which was statistically significant ($p<0.001$). Similarly, VIA or HPV DNA test was positive in 96 cases. Among them the final diagnosis was positive in five cases which showed four cases of CIN 3 and one case of SCC. Of the 108 cases with VIA and HPV DNA negative, the final diagnosis showed benign lesions in all the cases. Based on these findings the sensitivity of VIA positive or HPV DNA positive compared to final diagnosis was 100% with specificity of 54.27%, PPV of 5.21% and NPV of 100% showing diagnostic accuracy of 55.39%. The kappa statistics for agreement between VIA positive or HPV-DNA

positive and final diagnosis was 0.055, which was statistically significant (p=0.016).

A study[51] from AIIMS, New Delhi reported that, the nature of sequential testing, the hypothetical net specificity in all schemes involving VIA was higher than the value observed for VIA as a stand-alone test. The simulated test combination involving VIA and HPV demonstrated the best balance of sensitivity and specificity (87.7% and 95.4%). The simulated parallel combination that resulted in the highest net sensitivity was that of VIA/HPV and VIA/Pap (both 100%). However, the net specificity was only 45.9% and 52.2% respectively. HPV and Pap demonstrated the best balance of sensitivity and specificity (87.5% and 89.1%).

In a study[49] from Andhra Pradesh among women screened, substantial differences in test performance for Pap smear, VIA, and HPV DNA tests were observed. As expected, adjustment for verification bias decreased sensitivity and increased specificity for all tests.

Combining VIA and VILI with Pap smear and HPV testing markedly improved their performance as screening tools. Many ongoing studies are paving the way for new screening strategies for cervical cancer.[57,60,61,62] These reports are almost universally consonant in that the combination of screening techniques may improve the overall sensitivity and, in some instances, specificity and predictive values. However, strategies to deal with the increasing costs and the larger number of women to be referred for colposcopy need to be developed further.

Chapter 7

Conclusion

CONCLUSION

In the present study of the 204 women VIA, and HPV DNA test was positive results in 33.33% and 21.57%. The colposcopic findings among 16 women (7.84%) showed positive test results which included 11 (5.39%) cases of CIN 2, four cases (1.96%) of CIN 3 and one case of SCC (0.49%). Of the 204 women, 73 (35.78%) underwent biopsy. Among them, four women (5.48%) revealed CIN 3 and one case (1.37%) of SCC.

The sensitivity of VIA compared to final diagnosis was 80% with specificity of 67.84%, PPV of 5.88% and NPV of 99.26% showing the diagnostic accuracy of 68.14%.

The sensitivity of HPV DNA test compared to final diagnosis was 100% with specificity of 80.40%, PPV of 11.36% and NPV of 100% showing the diagnostic accuracy of 80.88%.

The sensitivity of both HPV DNA and VIA compared to final diagnosis of CIN 2 as disease threshold showed 80% sensitivity with specificity of 93.96%, PPV of 25% and NPV of 99.46% showing diagnostic accuracy of 93.63%. The sensitivity of VIA positive or HPV DNA positive compared to final diagnosis was 100% with specificity of 54.27%, PPV of 5.21% and NPV of 100% showing diagnostic accuracy of 55.39%.

Overall VIA and HPV positive tests showed diagnostic accuracy of 93.63% with positive likelihood ratio of 13.26 and negative likelihood ratio of

0.21 whereas VIA or HPV positive 55.39% diagnostic accuracy with positive likelihood ratio of 2.18 (CI 95%).

Cervical cancer accounts for the highest number of deaths due to cancer among women in India. The role of pap smear for cervical cancer screening has long been established in the West but it is not a very feasible test for a resource limited setting. Alternative methods such as VIA may be very useful in a resource limited setting but VIA and VILI may not perform well as stand alone tests, so adjunctive tests is one way of improving specificity of the test, in this study the joint test qualities of VIA and HPV were compared and from our results we could conclude VIA followed by HPV test would be an effective efficacy approval to identify women who need further treatment.

Chapter 8

Summary

SUMMARY

Cervical cancer is an important public health problem that deserves urgent attention. The burden of cervical cancer in India is enormous and is the number one cause of death due to cancer in middle aged Indian women. In the developing countries control of cervical cancer is viable through screening modalities such as visual screening methods like visual inspection with acetic acid/visual inspection with Lugol's iodine (VIA/VILI) and recently Human Papilloma virus deoxyribose nucleic acid (HPV-DNA). The present study was planned to assess the test performance of HPV DNA testing and VIA for detection of high grade cervical intraepithelial lesions and also to assess the performance when HPV DNA testing and VIA are combined to find out the probable best screening option.

This one year cross-sectional screening interventional study was conducted on a total of 204 women referred to Colposcopy Clinic, at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. Test results of VIA, colposcopy, HPV DNA and biopsy were conducted. The gynaecologist performing colposcopy was blinded to the results of VIA.

Most of the women (50%) had age between 30 to 34 years with the mean age of 36.75 ± 35.50 years. 46.57% of the women complained vaginal discharge and 33.82% backache. In the present study of the 204 women VIA, and HPV DNA test was positive results in 33.33% and 21.57%. The colposcopic findings among 16 women (7.84%) showed positive test results which included 11 (5.39%) cases of CIN 2, four cases (1.96%) of CIN 3 and one case of SCC

(0.49%). Of the 204 women, 73 (35.78%) underwent biopsy. Among them, four women (5.48%) revealed CIN 3 and one case (1.37%) of SCC.

Overall VIA and HPV positive tests showed diagnostic accuracy of 93.63% with positive likelihood ratio of 13.26 and negative likelihood ratio of 0.21 whereas VIA or HPV positive 55.39% diagnostic accuracy with positive likelihood ratio of 2.18 (CI 95%).

Chapter 9

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Annexures

Annexure I

ANNEXURE I – CONSENT FORM

"CONCURRENT EVALUATION OF VISUAL INSPECTION WITH ACETIC ACID AND HPV DNA TESTING IN DETECTION OF CERVICAL CANCER – A PROSPECTIVE STUDY"

Principal Investigator: Dr. Simaran Jeet Postgraduate Student

Guide **:** Dr. Bhavana Sherigar Associate Professor

We request you to be a participant in above said research to be conducted at KLE'S Hospital from Sep 2010 to Sep 2011 conducted by DR SIMARAN JEET, Postgraduate student in the Dept. of Obstetrics and Gynecology at J.N. Medical College, Belgaum. Ph No 9986468972

Your participation in this study is your voluntary decision whether or not to participate will not affect your current or future relationship with the KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre.

Procedure Involved

The doctor /health care worker explained to me in detail about how the sample would be taken and send for HPV DNA testing by Hybrid capture2 assay. This procedure will be followed by application of 5 % acetic acid to my cervix with a cotton swab .If the tests come as positive I would be subjected to further treatment with colposcopy or colposcopy guided biopsy as ill be at the risk of developing cervical cancer.

Risk and benefits

There are no risks involved in this procedure. If any complications arise during the procedure then the patients will be treated with best of our knowledge. There will be no compensation or payment for such medical treatment.

If you attain any complication during the procedure you may contact Dr. Bhavana Assosiate professor and Dr. Simaran postgraduate in the dept of obstetrics and gynecology.

During the course of study you will be informed of any significant new findings such as changes in risks and benefits resulting from participation in the research.

Privacy and Confidentiality

The only people who will know that you are a research participant are members of the research team. No information about you or provided by you, during the research will be disclosed to others without your written consent. When the results of the research are published or discussed the conferences, no information will be disclosed that would reveal your identity. Any information obtained in connections with this study and that can be identified with you remain confidential and will be disclosed only with your permission.

Voluntary participation

Your participation in this study will help us identify a superiority of Hybrid capture 2 assay over other tests in early detection and early treatment of

cervical cancer in patients. You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research.

If you have any questions about your rights or research as research participant you may contact Dr. V.D. Patil, Principal JNMC, Belgaum. Ph No 08312473777. You will be given a copy of this form for your information and to keep for your records.

Statement of Consent

To voluntarily agree to take part in this study I must sign on the line below: If you chose to take part in this study I may withdraw at any time I am not giving up any of my legal rights, by signing this form. My signature below indicates that I have read or have read to me this entire consent form including the risks and benefits and had all questions answered, I will be given a copy of this consent form.

Signature of the Subject:

Name: Date:

Signature of the authorized representative:

Name: Date:

Relation to the Subject:

Signature of the witness:

Name: Date:

Signature of the investigator:

Name: Date:

Annexures

Annexure II

ANNEXURE II – PROFORMA

1.Serial No._____

2.Date of testing [ ] [ ] [ ] [ ]

3.Name_____

4.Address;_____

_____

5.Age (in years) [ ] [ ]

6.Education: [ ]

1.Nil

2Primary

3.Middle

4.High school

5.College

6.Not Known

7. Marital Status: [ ]

1.Married

2.Widow

3.Seperated

8.When did you have your last menstruation? [ ] [ ]

9.Age at marriage or first sexual intercourse? [ ] [ ]

10.Total no.pf pregnancy/miscarriages [ ] [ ]

11.Do you suffer from the following

[ ] Excessive vaginal discharge

[ ] Itching in the external genitalia

[ ] Ulcer in the external genitalia

[ ] Lower abdominal pain

[ ] Pain during sexual intercourse

[ ] Bleeding after intercourse

[ ] Intermenstrual bleding

[ ] Low backache

12.Visual Exmination findings

[ ] Squamocolumnar junction fully seen

[ ] Normal

[ ] Abnormal vaginal discharge

[ ] Cervical Polyp

[ ] Nabothian follicle/cysts

[ ] Leukoplakia

[ ] Condyloma

[ ] Growth

[ ] Ectropion

[ ] Erosion

13Finding one minute after application of 5% acetic acid [ ]

1 Negative

2 Positive

3 positive for invasive cancer

14 If VIA positive, does the acetowhite lesion extend into the endocervical canal?

1 Yes

2 No

15 If VIA positive, How many quadrants are involved in acetowhite lesion? [ ]

0 None

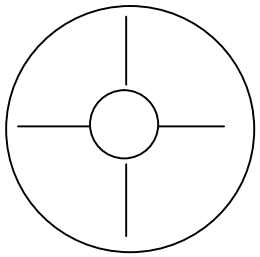
1 One

2 Two

3 Three

4 Four

16.Schematic representation of VIA lesions of SCJ



17. Colposcopy impression based on RCI

18.Biopsy taken [ ]

1 yes

2 No

19.HPR DNA by Hybrid Capture 2 Assay [ ]

Report._____

_____

_____

_____

_____

20. Histopathological report

_____

_____

_____

21.Action taken [ ]

1.Antibiotics given

2.Follow up after 9-12months

3.Advised Cryotherapy

4.Advised LEEP

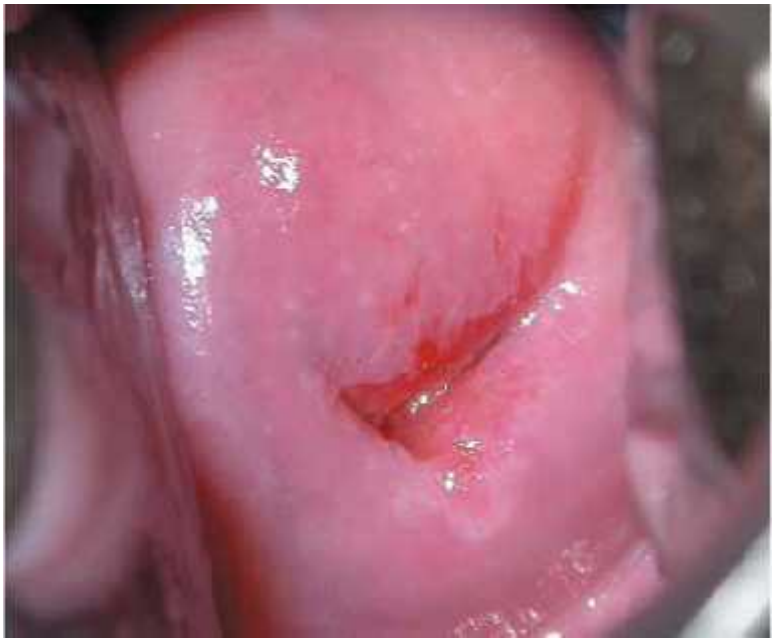
5.Advised Hysterectomy

6.Advised Radiotherapy

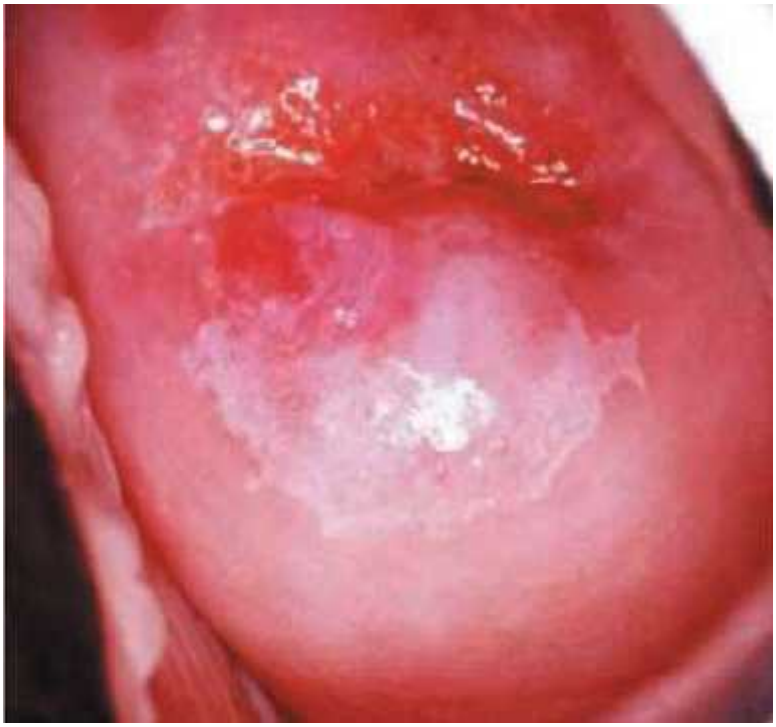
Annexures

Annexure III

ANNEXURE III – PHOTOGRAPHS

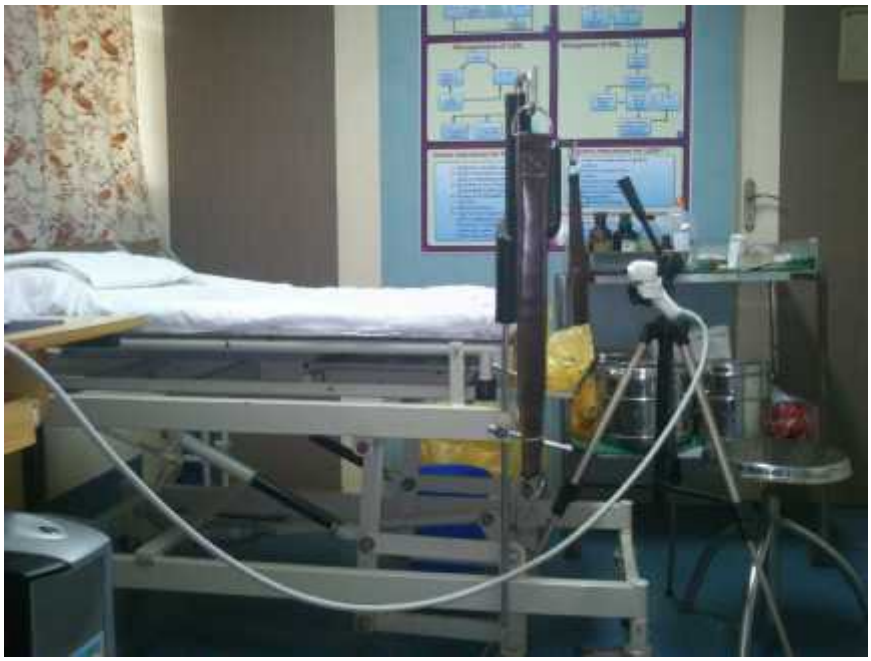


Photograph 1. VIA findings - Negative



Photograph 2. VIA findings – Positive

Photograph 3. HPV DNA testing unit



Photograph 4. Colposcopy clinic

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																							
															Visual examination with acetic acid											Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
1	EN01	30	5	1	26	2	+	+	-	-	+	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	Normal	BN	20.98	+	Y	Normal	BN
2	EN02	32	5	1	22	2	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 2/3, RCI 7	C3	0.34	-	Y	CIN 1	C1
3	EN03	32	4	1	21	2	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	Cervical ectopy	BN	0.53	-	N	-	-
4	EN04	31	4	1	20	1	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.21	-	Y	ECC	BN
5	EN05	34	5	1	22	2	-	-	-	+	-	-	-	+	+	-	-	-	+	-	-	-	-	+	-	1	CIN 1	C1	40.99	+	Y	CIN 1	C1
6	EN06	34	5	1	22	2	+	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	Cervical ectopy, inflammation	BN	0.60	-	Y	Endocervical polyp	BN
7	EN07	32	5	1	24	1	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	+	-	1	CIN 1, RCI 2, Ectopy	C1	0.45	-	Y	Cervicitis	BN
8	EN08	32	1	3	24	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-	1	Cervical ectopy	BN	0.40	-	N	-	-
9	EN09	32	5	1	26	3	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	+	-	+	-	1	CIN 1, RCI 1	C1	0.68	-	Y	Cervicitis	BN
10	EN10	34	4	1	24	4	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.41	-	N	-	-
11	EN11	34	4	1	23	1	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.44	-	N	-	-
12	EN12	34	4	1	30	1	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+	-	1	Cervical ectopy, ISM, Polyp	BN	1.07	-	Y	Endocervical polyp	BN
13	EN13	40	5	1	24	2	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.99	-	Y	Normal	BN
14	EN14	34	4	1	16	3	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.43	-	N	-	-
15	EN15	44	3	1	26	2	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Unsatisfactory with senile changes	BN	0.35	-	N	-	-
16	EN16	32	5	1	28	1	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.29	-	N	-	-
17	EN17	34	5	1	24	3	-	-	-	-	-	-	-	+	+	-	-	-	+	-	-	-	-	-	-	-	CIN 1, Acute chronic cervicitis	C1	537.37	+	N	-	-
18	EN18	42	5	1	20	3	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	+	1	CIN 1	C1	0.17	-	Y	ECC	BN
19	EN19	31	5	1	20	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.70	-	N	-	-
20	EN20	49	5	1	20	2	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Ectopy	BN	0.37	-	N	-	-
21	EN21	33	5	1	22	4	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	+	-	+	1	Ectropion, ISM	BN	0.41	-	N	-	-
22	EN22	30	5	1	20	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	+	2	CIN 1, RCI 2, HPV	C1	0.51	-	Y	ECC	BN
23	EN23	34	5	1	12	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	CIN 1, RCI 1	C1	0.67	-	Y	ECC	BN
24	EN24	36	4	1	12	2	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Ectropion	BN	37.75	+	N	-	-
25	EN25	34	5	1	22	2	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.99	-	Y	Mild reactive atypia	BN
26	EN26	31	5	1	22	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	+	2	Invasive Cervical Cancer	HG	0.62	-	Y	Cervivitis	BN
27	EN27	34	5	1	16	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	1	CIN 1, Chronic cervicitis	C1	0.50	-	Y	Cervivitis	BN
28	EN28	38	5	1	24	2	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	+	2	Normal	BN	0.71	-	Y	ECC	BN
29	EN29	34	5	1	24	1	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.33	-	N	-	-

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																				
															Visual examination with acetic acid											Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
30	EN30	48	5	1	24	2	+	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	Endocervical polyp	BN	0.69	-	N	-	-
31	EN31	44	5	1	24	3	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+	-	2	CIN 1, RCI 2	C1	0.42	-	N	-	-
32	EN32	34	5	1	22	3	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.72	-	Y	ECC	BN
33	EN33	34	5	1	24	2	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.53	-	N	-	-
34	EN34	38	5	2	24	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.99	-	N	-	-
35	EN35	40	4	1	22	2	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	+	-	3	CIN 1	C1	1.06	+	Y	Cervicitis	BN
36	EN36	36	5	1	28	2	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.39	-	N	-	-
37	EN37	38	4	1	24	2	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	1	Normal	BN	0.37	-	Y	Sq metaplastic, mod dysplasia	BN
38	EN38	34	4	1	22	3	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.78	-	N	-	-
39	EN39	36	5	1	20	3	-	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.18	-	Y	Cervicitis	BN
40	EN40	32	3	2	21	4	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	Ectopy, Trichomonias	BN	144.40	+	N	-	-
41	EN41	36	1	3	22	3	+	-	-	-	-	-	-	-	+	+	-	-	+	-	-	-	-	-	+	+	2	CIN 1, RCI 1	C1	232.50	+	Y	Cervicitis	BN
42	EN42	34	4	1	24	3	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Cervical ectropian	BN	0.42	-	N	-	-
43	EN43	37	4	1	24	2	-	-	-	+	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	CIN 1	C1	0.13	-	N	-	-
44	EN44	48	2	3	28	3	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	+	-	+	-	1	CIN 1	C1	0.15	-	Y	ECC	BN
45	EN45	35	4	1	24	2	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	Cervical ectropian	BN	0.17	-	N	-	-
46	EN46	38	5	1	24	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.12	-	N	-	-
47	EN47	38	5	1	30	2	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.12	-	Y	Cervicitis	BN
48	EN48	33	2	1	24	3	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	1	CIN 2, MRCI 2	C2	0.13	-	Y	CIN 1	C1
49	EN49	36	5	1	32	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	+	-	2	CIN 2, MRCI 2	C2	0.03	-	Y	CIN 1	C1
50	EN50	42	3	1	25	3	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	Ectopy, ISM	BN	0.33	-	N	-	-
51	EN51	44	5	1	22	4	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	+	-	+	-	1	ISM, RCI	BN	537.37	+	Y	ECC	BN
52	EN52	38	5	1	17	4	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	ISM	BN	3.04	+	N	-	-
53	EN53	32	5	1	22	1	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	ISM	BN	0.12	-	N	-	-
54	EN54	47	3	1	22	3	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	ISM	BN	1.19	+	N	-	-
55	EN55	47	1	1	45	6,2	+	-	-	-	-	-	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	Unsatisfactory (Frichomonasis)	BN	1.08	+	N	-	-
56	EN56	37	5	1	18	2	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	8.04	+	N	-	-
57	EN57	32	5	1	20	2	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1, RCI 1	C1	3.49	+	Y	ECC	BN
58	EN58	30	5	1	17	2	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	HPV Infection	BN	38.11	+	N	-	-

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																			
															Visual examination with acetic acid												Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
59	EN59	37	5	1	17	2	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	Ectopy	BN	2.00	+	N	-	-
60	EN60	43	5	1	23	3	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.61	+	N	-	-
61	EN61	30	4	1	25	2	+	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	+	-	+	-	1	Ectopy, ISM, HPV Infection	BN	0.12	-	N	-	-
62	EN62	40	1	1	15	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	3	CIN 1, RCI 1	C1	1.20	+	Y	ECC	BN
63	EN63	32	3	1	21	3	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	Ectopy, ISM	BN	1107.46	+	Y	ECC	BN
64	EN64	32	5	1	24	3,2	+	+	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	2.20	+	N	-	-
65	EN65	32	5	1	22	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	Ectopy	BN	0.80	-	N	-	-
66	EN66	45	4	1	16	4	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	1	Chronic ECC	BN	0.60	-	Y	ECC	BN
67	EN67	47	5	1	21	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	+	-	1	Satellite lesion	BN	0.46	-	N	-	-
68	EN68	46	4	1	24	2	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.20	-	N	-	-
69	EN69	32	4	1	20	1	-	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.35	-	N	-	-
70	EN70	48	4	1	24	3	-	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.39	-	N	-	-
71	EN71	32	3	1	21	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	+	1	CIN 2, RCI 3	C2	0.26	-	Y	Chronic cervicitis	BN
72	EN72	49	3	1	22	4	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion, ISM	BN	0.22	-	N	-	-
73	EN73	32	4	1	22	2	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion, ISM	BN	0.30	-	N	-	-
74	EN74	32	3	1	25	1	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	1	HPV Infection	BN	0.63	-	N	-	-
75	EN75	43	5	1	22	3	+	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	+	-	+	+	2	CIN 1	C1	1.26	+	Y	Cervicitis	BN
76	EN76	34	4	1	20	2	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Cervical ectropy	BN	0.57	-	N	-	-
77	EN77	39	4	1	28	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	2	CIN 1, Ectropian	C1	0.64	-	Y	Cervicitis	BN
78	EN78	42	5	1	24	2	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	1	Cervical ectopy	BN	0.38	-	N	-	-
79	EN79	40	4	1	16	2	+	+	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	CIN 2/3, MRCI 5	C3	57.83	+	Y	CIN 3	C3
80	EN80	41	4	1	22	4	+	-	-	-	-	-	-	+	+	-	-	-	+	-	-	-	-	-	-	-	-	CIN 1, MRCI 1	C1	0.10	-	Y	Normal	BN
81	EN81	31	4	1	21	4	-	-	-	-	-	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	ISM	BN	0.12	-	N	-	-
82	EN82	34	5	1	18	1	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	2	CIN 2, MRCI 2	C2	0.12	-	Y	Cervicitis	BN
83	EN83	39	2	1	22	4	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	Cervical ectropian, ISM	BN	0.13	-	N	-	-
84	EN84	30	3	1	24	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	1	Cervical ectropian	BN	0.15	-	N	-	-
85	EN85	34	4	1	28	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion, ISM	BN	0.14	-	N	-	-
86	EN86	50	5	1	28	2	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.12	-	Y	Normal	BN
87	EN87	39	3	1	32	5	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	4	CIN 1/2, MRCI 3	C1	0.09	-	Y	ECC	BN

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																				
															Visual examination with acetic acid												Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
88	EN88	48	2	1	22	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	2	Ectropion	BN	0.13	-	N	-	-
89	EN89	30	2	1	22	2	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	+	-	4	Ectropion, HPV Infection	BN	0.06	-	N	-	-
90	EN90	31	4	1	22	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	CIN 1, ISM	C1	0.19	-	Y	Cervicitis	BN
91	EN91	40	4	1	30	3	-	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	0.17	-	Y	Cervicitis	BN
92	EN92	50	4	1	24	3	-	-	-	+	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.27	-	N	-	-
93	EN93	32	5	1	22	2	+	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	CIN-2	C2	0.25	-	Y	ECC	BN
94	EN94	46	4	1	21	2	-	+	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.19	-	N	-	-
95	EN95	32	5	3	21	2	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Ectopy, ISM	BN	0.38	-	N	-	-
96	EN96	32	5	1	24	2	+	+	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	Satellite lesion	BN	0.16	-	N	-	-
97	EN97	32	5	3	22	1	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Ectopy, ISM	BN	0.30	-	N	-	-
98	EN98	32	5	1	24	1	-	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	+	-	+	+	2	CIN 2	C2	0.38	-	Y	Cervicitis	BN
99	EN99	34	5	1	30	1	+	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	3.70	+	N	-	-
100	EN100	32	5	1	24	1	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.35	-	N	-	-
101	EN101	36	5	1	22	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	CIN 2, MRCI 2	C2	0.17	-	Y	Cervicitis	BN
102	EN102	36	5	1	24	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.76	-	N	-	-
103	EN103	38	5	1	22	3	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.12	-	N	-	-
104	EN104	40	5	1	24	1	-	+	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	+	-	1	CIN 1, MRCI 2	C1	0.11	-	Y	Cervicitis	BN
105	EN105	32	3	1	15	3	+	-	-	+	+	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	Normal	BN	0.51	-	N	-	-
106	EN106	32	5	1	24	2	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	Normal	BN	0.32	-	N	-	-
107	EN107	31	5	1	21	2	+	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	+	-	-	Satellite lesion	BN	0.24	-	N	-	-
108	EN108	35	5	1	20	1	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.54	+	N	-	-
109	EN109	32	4	1	24	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	+	-	-	-	-	Ectopy, ISM	BN	0.30	-	N	-	-
110	EN110	34	3	1	22	2	+	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	1	CIN 1, RCI 0	C1	1.13	+	Y	Cervicitis	BN
111	EN111	34	5	1	25	1	+	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	+	-	+	-	1	CIN 1, MRCI 0	C1	1.27	+	Y	Cervicitis	BN
112	EN112	34	5	1	27	2	+	+	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1, RCI 2	C1	2.06	+	Y	Cervicitis	BN
113	EN113	38	4	1	21	2	+	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	+	-	1	CIN 1, RCI 0	C1	0.84	-	Y	Cervicitis	BN
114	EN114	34	5	1	26	1	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.09	-	N	-	-
115	EN115	38	3	1	28	1	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	+	2	CIN 1	C1	29.29	+	Y	CIN 3	C3
116	EN116	33	4	1	28	1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Cervical ectopy, ISM	BN	0.84	-	N	-	-

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																			
															Visual examination with acetic acid											Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
117	EN117	34	3	1	26	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	Ectopy	BN	0.67	-	N	-	-
118	EN118	36	5	1	30	2	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	+	-	1	CIN 1	C1	0.45	-	Y	Cervicitis	BN
119	EN119	38	5	1	24	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Ectopy	BN	0.30	-	N	-	-
120	EN120	33	5	1	22	1	-	+	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+	-	1	CIN 2	C2	296.56	+	Y	Chronic cervicitis	BN
121	EN121	38	5	1	20	2	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	CIN 1	C1	0.72	-	N	-	-
122	EN122	40	5	1	24	3	+	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.45	+	Y	Cervicitis	BN
123	EN123	36	4	1	21	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.01	+	N	-	-
124	EN124	36	4	1	22	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	42.35	+	N	-	-
125	EN125	42	2	1	24	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	2.17	+	Y	CIN 3	C3
126	EN126	36	3	3	24	1	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Chronic trichomoniases	BN	1.30	+	N	-	-
127	EN127	34	4	1	22	3	+	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	0.90	-	N	-	-
128	EN128	36	5	1	25	1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	2	CIN 1, Ectopy	C1	0.20	-	Y	Normal	BN
129	EN129	37	3	1	19	1	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.60	-	N	-	-
130	EN130	40	5	1	22	1	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	0.33	-	Y	CIN 1	C1
131	EN131	41	4	1	22	1	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Ectopy, ISM	BN	0.66	-	N	-	-
132	EN132	31	5	1	22	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectopy	BN	0.79	-	N	-	-
133	EN133	47	5	1	21	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	Ectopy, ISM	BN	0.81	-	N	-	-
134	EN134	44	5	1	22	4	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Chronic TV, Senile changes	BN	0.24	-	N	-	-
135	EN135	40	5	1	20	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	2	CIN 2	C2	79.49	+	Y	Infiltrating SCC	SCC
136	EN136	40	4	1	20	1	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	1.04	+	Y	Cervicitis	BN
137	EN137	42	5	1	22	1	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.01	+	N	-	-
138	EN138	33	4	1	21	2	+	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	Ectropion, Senile polyp	BN	0.12	-	N	-	-
139	EN139	30	4	1	21	2	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	+	-	1	CIN 1, RCI 1	C1	0.24	-	Y	Cervicitis, squamous metaplasia	BN
140	EN140	34	5	1	24	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.26	-	N	-	-
141	EN141	34	5	1	20	2	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.11	-	N	-	-
142	EN142	35	5	1	24	2	+	-	-	-	-	-	-	-	+	-	+	+	-	-	-	-	-	-	+	-	1	CIN 1, RCI 2	C1	0.15	-	Y	Cervicitis	BN
143	EN143	34	5	1	22	2	+	-	-	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	+	-	1	CIN 1, RCI 1	C1	0.26	-	Y	Normal	BN
144	EN144	34	5	1	21	1	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	5.49	+	N	-	-
145	EN145	31	5	1	20	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.59	-	N	-	-

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																									
															Visual examination with acetic acid											Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
146	EN146	31	5	1	22	1	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	Ectopy, ISM	BN	0.31	-	N	-	-
147	EN147	30	5	1	23	3	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	Ectopy, ISM	BN	0.62	-	N	-	-
148	EN148	32	5	1	18	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.42	-	N	-	-
149	EN149	49	4	1	20	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.57	-	N	-	-
150	EN150	42	4	1	23	3	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-	1	Ectropion	BN	0.42	-	N	-	-
151	EN151	33	5	1	21	1	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	Trichomoniasis	BN	0.44	-	N	-	-
152	EN152	40	4	1	22	1	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	Candidiasis	BN	0.70	-	N	-	-
153	EN153	35	5	1	20	1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	Ectropion, Candidiasis	BN	0.59	-	N	-	-
154	EN154	40	5	1	23	1	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.86	-	N	-	-
155	EN155	36	4	1	20	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	+	-	2	Normal	BN	0.48	-	N	-	-
156	EN156	40	5	1	21	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.62	-	N	-	-
157	EN157	33	4	1	23	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.61	-	N	-	-
158	EN158	49	5	1	20	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.48	-	N	-	-
159	EN159	40	5	1	24	2	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	+	2	Candidiasis	BN	0.70	-	N	-	-
160	EN160	36	5	1	22	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.27	-	N	-	-
161	EN161	34	5	1	20	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	Candidiasis	BN	0.54	-	N	-	-
162	EN162	33	3	1	23	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.95	-	N	-	-
163	EN163	30	4	1	21	1	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	+	-	1	Normal	BN	0.93	-	N	-	-
164	EN164	32	3	3	22	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.49	+	N	-	-
165	EN165	38	5	1	24	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	1.03	+	N	-	-
166	EN166	30	3	1	21	2	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	CIN 1	C1	0.42	-	Y	Cervicitis	BN
167	EN167	47	3	3	24	2	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	Normal	BN	0.23	-	N	-	-
168	EN168	44	5	1	21	1	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	+	-	+	-	2	CIN 1, Cervical ectopy	C1	0.28	-	Y	ECC	BN
169	EN169	32	4	1	20	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	1	Normal	BN	0.21	-	Y	Cervicitis	BN
170	EN170	38	4	1	22	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Senile changes on colposcopy	BN	0.26	-	N	-	-
171	EN171	38	4	1	24	2	-	-	-	+	-	-	-	+	-	-	-	+	+	-	-	-	-	-	-	-	CIN 1	C1	0.32	-	Y	ECC	BN
172	EN172	41	4	1	20	1	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	0.21	-	Y	Cervicitis	BN
173	EN173	41	4	1	23	2	-	-	-	+	-	-	-	+	-	-	-	-	+	-	-	-	-	-	+	-	1	CIN 1	C1	0.27	-	Y	CIN 1	C1
174	EN174	40	5	1	21	1	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	CIN 1	C1	0.26	-	N	-	-

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																										
															Visual examination with acetic acid											Colposcopy		HPV DNA Test		Biopsy findings											
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis								
175	EN175	48	5	1	19	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.28	-	N	-	-							
176	EN176	48	4	1	23	2	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.26	-	N	-	-							
177	EN177	38	3	3	20	2	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.21	-	N	-	-							
178	EN178	31	5	1	22	1	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.23	-	N	-	-							
179	EN179	44	4	1	24	3	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	+	-	1	CIN 1	C1	0.31	-	Y	Cervicitis	BN							
180	EN180	34	4	1	19	1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.26	-	N	-	-							
181	EN181	41	5	1	18	3	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.50	-	N	-	-							
182	EN182	44	5	1	22	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Ectropion	BN	0.42	-	N	-	-							
183	EN183	42	5	1	22	2	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	CIN 2/3, RCI 3	C3	0.30	-	Y	Mild dysplasia	BN							
184	EN184	34	3	1	25	1	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	+	-	-	-	-	CIN 2/3, RCI 6	C3	0.35	-	Y	Cervicitis	BN							
185	EN185	44	3	1	26	3	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	CIN 1	C1	0.21	-	N	-	-							
186	EN186	40	3	1	21	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	CIN 1	C1	0.27	-	N	-	-							
187	EN187	32	5	1	26	2	+	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	Cervical ectopy	BN	0.58	-	N	-	-							
188	EN188	30	5	1	20	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	1	CIN 1, Ectropian	C1	0.11	-	Y	Cervicitis	BN							
189	EN189	38	5	1	21	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.91	-	N	-	-							
190	EN190	35	5	1	24	2	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	Cervical ectopy, ISM	BN	0.23	-	N	-	-							
191	EN191	49	5	1	24	2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.17	-	N	-	-							
192	EN192	32	5	1	23	1	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	Normal	BN	1.06	+	N	-	-							
193	EN193	32	5	1	19	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.91	-	N	-	-							
194	EN194	31	4	1	19	1	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.95	-	N	-	-							
195	EN195	34	5	1	20	1	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	167.50	+	N	-	-							
196	EN196	42	3	1	23	3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	167.50	+	Y	Cervicitis	BN							
197	EN197	37	5	1	24	1	+	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	+	-	+	-	1	CIN 2	C2	411.89	+	Y	CIN 3	C3							
198	EN198	44	5	1	20	2	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	Normal	BN	0.02	-	N	-	-							
199	EN199	36	4	1	21	2	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	Normal	BN	0.16	-	N	-	-							
200	EN200	47	5	1	22	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	20.98	+	Y	Normal	BN							
201	EN201	38	4	1	23	3	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.58	-	N	-	-							
202	EN202	34	5	1	24	1	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	Normal	BN	0.33	-	N	-	-							
203	EN203	31	5	1	20	2	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	Normal	BN	0.70	-	N	-	-							

MASTER CHART

Serial number	Identification Number	Demography			Obst history		Complaints								Screening																			
															Visual examination with acetic acid													Colposcopy		HPV DNA Test		Biopsy findings		
		Age (Years)	Education	Marital status	Age at marriage (Years)	Pregnancies / Miscarriages	Vaginal discharge	Itching in ext genitalia	Ulcer in ext genitalia	Lower abdominal pain	Pain at intercourse	Bleeding after intercourse	Intermenstrual bleeding	Low backache	SCM junction	Normal	Abn vaginal discharge	Cervical polyp	Nabothian follicle/cyst	Leukoplakia	Condyloma	Growth	Ectropian	Erosion	VIA findings	Endocervical canal	Quadrants involved	Findings	Diagnosis	Report	Diagnosis	Biopsy	Findings	Final diagnosis
204	EN204	36	4	1	20	2	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	+	-	2	Normal	BN	0.48	-	N	-	-

MASTER CHART

Serial number	Identification Number	Treatment
1	EN01	5
2	EN02	4
3	EN03	1
4	EN04	1
5	EN05	5
6	EN06	2
7	EN07	2
8	EN08	1
9	EN09	2
10	EN10	2
11	EN11	2
12	EN12	3
13	EN13	2
14	EN14	2
15	EN15	1
16	EN16	1
17	EN17	4
18	EN18	2
19	EN19	1
20	EN20	2
21	EN21	2
22	EN22	1
23	EN23	2
24	EN24	2
25	EN25	2
26	EN26	5
27	EN27	1
28	EN28	2
29	EN29	1

MASTER CHART

Serial number	Identification Number	Treatment
30	EN30	2
31	EN31	1
32	EN32	1
33	EN33	1
34	EN34	1
35	EN35	4
36	EN36	1
37	EN37	2
38	EN38	2
39	EN39	2
40	EN40	1
41	EN41	3
42	EN42	1
43	EN43	1
44	EN44	2
45	EN45	2
46	EN46	1
47	EN47	1
48	EN48	2
49	EN49	3
50	EN50	1
51	EN51	1
52	EN52	2
53	EN53	1,2
54	EN54	1,2
55	EN55	1
56	EN56	2
57	EN57	2
58	EN58	1

MASTER CHART

Serial number	Identification Number	Treatment
59	EN59	1,2
60	EN60	1
61	EN61	2
62	EN62	2
63	EN63	1,2
64	EN64	1,2
65	EN65	1
66	EN66	1,2
67	EN67	2
68	EN68	1
69	EN69	1
70	EN70	1
71	EN71	1
72	EN72	1
73	EN73	1
74	EN74	1
75	EN75	2
76	EN76	1
77	EN77	1
78	EN78	1
79	EN79	4
80	EN80	2
81	EN81	1,2
82	EN82	2
83	EN83	1
84	EN84	2
85	EN85	1
86	EN86	2
87	EN87	1

MASTER CHART

Serial number	Identification Number	Treatment
88	EN88	1
89	EN89	2
90	EN90	1
91	EN91	1
92	EN92	2
93	EN93	1
94	EN94	2
95	EN95	1
96	EN96	1
97	EN97	2
98	EN98	1
99	EN99	5
100	EN100	2
101	EN101	1
102	EN102	1
103	EN103	2
104	EN104	2
105	EN105	2
106	EN106	2
107	EN107	2
108	EN108	1,2
109	EN109	2
110	EN110	3
111	EN111	1,2
112	EN112	3
113	EN113	2
114	EN114	2
115	EN115	1,2
116	EN116	2

MASTER CHART

Serial number	Identification Number	Treatment
117	EN117	2
118	EN118	1
119	EN119	1
120	EN120	3
121	EN121	2
122	EN122	1
123	EN123	3
124	EN124	3
125	EN125	3
126	EN126	2
127	EN127	2
128	EN128	2
129	EN129	2
130	EN130	2
131	EN131	2
132	EN132	2
133	EN133	2
134	EN134	1
135	EN135	3
136	EN136	3
137	EN137	3
138	EN138	2,3
139	EN139	1,2
140	EN140	2
141	EN141	2
142	EN142	1
143	EN143	1
144	EN144	2
145	EN145	2

MASTER CHART

Serial number	Identification Number	Treatment
146	EN146	2
147	EN147	2
148	EN148	2
149	EN149	2
150	EN150	2
151	EN151	2
152	EN152	2
153	EN153	2
154	EN154	2
155	EN155	2
156	EN156	2
157	EN157	2
158	EN158	2
159	EN159	2
160	EN160	2
161	EN161	2
162	EN162	2
163	EN163	2
164	EN164	2
165	EN165	2
166	EN166	1
167	EN167	2
168	EN168	2
169	EN169	1
170	EN170	2
171	EN171	2
172	EN172	2
173	EN173	1,2
174	EN174	1

MASTER CHART

Serial number	Identification Number	Treatment
175	EN175	2
176	EN176	2
177	EN177	2
178	EN178	2
179	EN179	1,2
180	EN180	2
181	EN181	2
182	EN182	2
183	EN183	2
184	EN184	2
185	EN185	2
186	EN186	2
187	EN187	1
188	EN188	1
189	EN189	2
190	EN190	1
191	EN191	1
192	EN192	2
193	EN193	2
194	EN194	2
195	EN195	2
196	EN196	2
197	EN197	3
198	EN198	1
199	EN199	2
200	EN200	2
201	EN201	2
202	EN202	1
203	EN203	1

MASTER CHART

Serial number	Identification Number	Treatment
204	EN204	2

Annexures

Annexure IV

ANNEXURE IV – MASTER CHART

-	-	Negative
+	-	Positive
1	-	Antibiotics given
2	-	Follow up after 9 to 12 months
3	-	Advised Cryotherapy
4	-	Advised LEEP
5	-	Advised Hysterectomy
6	-	Advised Radiotherapy
BN	-	Benign
C1	-	Cervical intraepithelial neoplasia 1
C2	-	Cervical intraepithelial neoplasia 2
C3	-	Cervical intraepithelial neoplasia 3
CIN	-	Cervical intraepithelial neoplasia
DNA	-	Deribonucleic acid
ECC	-	Endocervical cervicitis
EN	-	Enrolment
HG	-	High grade
HPV	-	Human papilloma virus
ISM	-	Immature squamous metaplasia
MRCI	-	Modified Reid’s Colposcolic Index
Obst history	-	Obstetric history
RCI	-	Reid’s colposcopy index
SCC	-	Squamous cell carcinoma
SCM	-	Sqamo columnar junction
TV	-	Trichomonas vaginalis
VIA	-	Visual inspection with acetic acid