"COMPARISON OF VISUAL INSPECTION WITH ACETIC ACID AND PAP SMEAR IN DETECTING PREMALIGNANT LESIONS OF CERVIX"

BY

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Under the guidance of

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ABBREVIATIONS

ASCUS - Atypical Squamous cells of undetermined significance

AWA-Acetowhite area

CIN - Cervical intraepithelial lesion

CIS - Carcinoma in situ

DAWA (dense)- Dense acetowhite area

HAWA(HAZY)- Hazy acetowhite area

HIV- Human Immunodeficiency Virus

HPV - Human papilloma virus

HSIL - High grade squamous intraepithelial lesion

IMB- Inter menstrual bleeding

INF- Inflammation

LBC - Liquid based cytology

LSIL - Low grade squamous intraepithelial lesion

NVP- Negative predictive value

PCB- Post-coital Bleeding

PMB- Post menopausal bleeding

PMOL- pre malignant oral lesions

PPV- Positive Predictive Value

RCI - Reid colposcopy index

SCC- Squamous Cell Carcinoma

SCJ-squamocolumnar junction

SES- Socio-economic Status

VIA - Visual inspection with acetic acid

VILI - Visual inspection with Lugol's iodine

TZ- Transformation Zone

WDPV- White discharge per vagina

SE- socioeconomic status

ABSTRACT

Background -

Worldwide cervical cancer comprises approximately 12% of all cancers in women with 1,22,844 new cases reported annually in India. Cervical cancer progress slowly for a decade as it is preceded by intraepithelial histological changes, VIA, Pap smear and colposcopy can be utilized as a tool for cytological analysis of cervix, early identification of risk factors and preinvasive lesions of cervix and hence early diagnosis and treatment of cervical cancer even in rural areas.

Objectives-

1. To compare VIA with PAP smear in detecting premalignant lesions of cervix.
2. To correlate VIA and pap smear findings with colposcopic findings.
3. To localize the lesion by colposcopy and obtain biopsy wherever necessary.

Methods-

Prospective study of 200 women attending gynecology OPD at BLDE (DEEMED TO BE UNIVERSITY)'s Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura between *OCTOBER 2016 – AUGUST 2018* were included in the study.

Results-

The incidence of premalignant and malignant lesions of the cervix was 7%. Cervical cytology was normal in16%, inflammatory in 77.5%, ASCUS in 4%, LSIL in 1.5%, HSIL in 0.5% and squamous cell carcinoma in 0.5%.

Maximum number of patients with ASCUS and LSIL were in the age group of 35-39 years and 40-44years and HSIL and Squamous cell carcinoma occurred in the age group of 25-29 years and 30-34years respectively.

ASCUS, LSIL and HSIL were seen in parity 3-5 and Malignancy in parity >3 observed mostly in low socioeconomic status.

All abnormal Pap smears mainly presented with white discharge PV, pain abdomen and with irregular PV bleeding as the second most common and erosion and cervicitis as the most common clinical picture. Cervical biopsy confirmed HSIL and Invasive carcinoma cytology.

Conclusion-

In India, cytology, a low cost and easily accessible test, is the most logical screening modality although it has a very low sensitivity but detection rates could be further improved using liquid based cytology and the use of endocervical cytobrush.

Key words –Cervix; VIA; Pap smear; Colposcopy; Biopsy Screening

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INTRODUCTION

INTRODUCTION

Worldwide cervical cancer comprises approximately 12% of all cancers in women with an incidence of five lakh new cases reported each year of which almost one fourth of it occurs in India [1]. About 1,22,844 new cervical cancer cases are diagnosed annually in India and 67,477 cervical cancer deaths have been reported annually in India [2]. It is the second most common cancer in women worldwide but the most common in developing countries like INDIA. It accounts for 80% of cervical cancer deaths in developing countries like India [3].

Cervical cancer being a public health problem is a priority concern for the WHO programmers on cancer control. Cervical screening is currently acknowledged as the most effective approach for cervical cancer control. The dramatic reduction in the incidence of cervical cancer in developed countries is because of widespread use of an effective cytological screening test i.e. Papanicolaou Smear, which can identify the premalignant and malignant lesions of the uterine cervix, which cannot be detected or even suspected by history and clinical examination [4]. The various degrees of cervical intraepithelial lesions precede invasive cancer. Once these precursor states have been identified by cytology, further progress of the disease can be prevented by simple therapeutic maneuvers and continued follow up.

Cervical cancer is regarded as the most preventable and treatable cancer in women through early diagnosis and appropriate treatment of pre-invasive and early invasive diseases. Early detection of cervical abnormality at appropriate time is the early need for the gynecologist, so as to prevent its progression from cervical intraepithelial neoplasia to invasive cancer thereafter.

The factors like easy accessibility of cervix, propensity of cervical epithelial cells to exfoliate, rapid turnover of epithelial cells, evidence of wide spectrum of

histological changes ranging from mild atypia to frank malignancy and apparently prolonged natural history of disease help for early detection. Thus, they provide the best potential for control of progression of the epithelial abnormality to frank carcinoma by selective screening of population.

Epidemiological data indicates that incidence of cervical cancer has continued to be high due to poor hygiene, early marriage, multiparty, lack of screening facility. Cytological services in India are available since last 20 years, but it still remains the luxury available only for a few urban females. To control the disease, cytological screening should be undertaken routinely and intensively [5].

Various screening methods are available like cytology by Pap smear, visual inspection of cervix with acetic acid and/or Lugol's iodine, HPV- DNA Test, Liquid based cytology etc.

Pap smear is an effective method of cervical cancer screening. It is the laboratory method to examine the exfoliated or scraped cells to detect dysplasia. It is a simple routine outpatient procedure which is less expensive, with minimal or no side-effects, easy to do with higher specificity, done without anesthesia. It also detects various infection and inflammation with characteristic cytological appearances.

In a country like India, intention of screening women for cervical cancer is to utilize limited and available resources for a targeted population, for the early detection of cervical changes. However in many developing countries like INDIA, the existing programs are failing to achieve a major impact.

Screening women for cervical cancer can save lives. However among young women, cervical cancer is relatively rare and too frequent screening can lead to high costs and adverse effects associated with over treatment. Before 2012 cervical cancer screening guidelines of the American College Of Obstetricians and Gynecologists

(ACOG), American Cancer Society (ACS) and U.S Preventive Services Task Force (USPSTF) differed on age to start and how often to get screened for cervical cancers.

In 2012, all the three-organization recommended that, [6]

1. Screening by Papanicolaou test (Pap) should not be used for women aged less than 21 years, regardless of initiation of sexual activity.
2. A screening interval of three years should be maintained by Pap smear for women aged 21-30 years. HPV test is not recommended.
3. Women aged 30-65years should have a Pap test and a HPV test (co-testing) every 5 years or is even acceptable to have a Pap test alone every 3 years.

NEED FOR THE STUDY

The most common among Indian women is cervical cancer. In developing countries, including India, it is not possible to launch nationwide cytology screening programs for cervical cancers because of population explosion and lack of skills. As a result of these severe limitations, World Health Organization, suggested to use alternative strategies, like visual inspection of cervix for the control of cervical cancer[1].

Initially only visual inspection study was done without using acetic acid. In that study, certain high-risk clinical signs were identified. These high-risk signs were identified in about 60% of cervical cancer patients in early clinical stages. This was in sharp contrast to the detection of cervical cancer in the "Cancer Clinic" where less than 5% women reported at an early stage. This technique, however, picked up about 12% false positive results. Thus, there was a distinct need to improve the sensitivity and specificity of visual inspection and hence application of acetic acid was found to be useful. [1]

Cervical cancer is the leading cause of death among women in developing countries. Cervical cancer can be prevented as the premalignant lesions can be detected early. This prevention can be achieved by using relatively inexpensive technologies like PAP smear and visual inspection with acetic acid to detect abnormal cervical tissue before it progresses to invasive cervical cancer [2].

Screening for cervical lesions has proven successful in the industrialized world, with the reduction in incidences of cervical cancer by 80% in countries with organized screening programs [3].

Visual inspection with acetic acid was used as primary screening tool to detect premalignant lesions of cervix [4].

A review study observed cervical cancer to be relatively neglected disease in terms of advocacy and indicated cytology, Human Papilloma Virus (HPV) testing. Visual inspection of cervix using acetic acid (VIA) is known to be accurate and effective method to detect cervical intraepithelial neoplasia (CIN) or cervical cancer and could contribute to the reduction of disease in low resource setting [5].

Cervical cancer develops from well-defined precursor lesion over a varied period of time. The key to reduce morbidity and mortality from cervical cancer is by detection of those early pre-cancerous lesion known as Cervical Intraepithelial Neoplasia (CIN) which results from persisted infection with Human Papilloma Virus (HPV) [6].

Early detection of premalignant lesions can help to prevent cervical cancer. Hence there is need to identify an easily applicable, low cost and sensitive, cervical cancer screening test which will be helpful in low resource set up. The present study is visual inspection with acetic acid and PAP smear will be done to detect the premalignant lesions of cervix.

OBJECTIVE OF THE STUDY

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PRIMARY OBJECTIVES-

1. To compare VIA with PAP smear in detecting premalignant lesions of cervix.
2. To correlate VIA and pap smear findings with colposcopic findings.
3. To localize the lesion by colposcopy and obtain biopsy wherever necessary.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE

After the introduction of cellular pathology by Dr. Virchow in the middle of the 19th century, the development of staining methods for dry preparations by P. Ehrlich made it possible to carry out exact study of cells. At the turn of the century, Widal extended this method, applying it to the cytological examination of exudates and transudates [7].

The study of exfoliated cells dates back to the middle of the 19th century. As early as in 1843, Walshe took notice of small tissue fragments exfoliated from malignant growth of the respiratory tract [8]. In studying the characteristics of malignancy, friability of growth is because of high cellularity and lack of stromal support. This makes it possible for malignant cells to get exfoliated [9]. One of the earliest references of studies of desquamated cells for the purpose of diagnosing cancer is that of Beale, 1860, who reported the finding of malignant cells in the sputum of a case of cancer of the pharynx. Malignant cells in smear of fresh sputum from cases of carcinoma of the lungs were reported by Hampelu in 1876 and 1887, Menetriu in 1886, Betschardt in 1895 and others.

Diagnostic cytology as a method of investigation depends on the fact that cells exfoliated/collected from surface reflect many features of underlying tissue. Cytological smears of other body fluids were also utilized, at a very early date, for the diagnosis of malignancy. Thus, Sandess in 1864 reported finding fragments of malignant cells in the urine of a patient with cancer of the bladder. Further observation on cells of the urine was made by Dickinson et al in 1869. As early as in 1892, Ferguson et al recommended microscopic examination of the urine sediments as the best way, exclusive of cystoscopy, for diagnosing tumors of the bladder.

Though the study of exfoliated cells dates back to the middle of nineteenth century, the main progress in the field of cytology was achieved within last four decades.

In 1847 Pouchet published his Pouchet's monogram on Ovulation, which deals with normal cytological changes in human vaginal smear. **It** is also the first publication in the field of Gynecological cytological changes [10].

Lucke & Klebs in 1867, found malignant cells in smears of ascitic fluid, in cases of malignant tumors of ovary. Later in 1875 Quinke used this principle in the examination of transudates and exudates. In this application, however, the use of smear was soon suspended by the sectioning of sedimented cells as described by Bakrendberg in 1895[11]. Ramirez in 1928, in Mexico, gave the first precise description of the vaginal cycle based on cytological smears. During the years 1925 to 1942, a large number of basic and detailed studies of physiological cytology were published, mostly by Papanicolaou's team [12].

Originally, the vaginal smear technique was employed by Stockard and Papanicolaou in 1917 to analyze sex cycle in guinea pig [13]. Its value as a method, for determining the morphologic and functional states of the female reproductive organs resulted in its general adaptation as a standard method for the study of the sex cycles of the female mammals and study of problems related to sex physiology and endocrinology. This initiated an area of unprecedented activity which led to significant advances in these fields. Much of the progress which has been made toward an understanding of the mammalian sex hormones can thus be accredited to exfoliative cytology.

The scope and significance of the vaginal smear was widened considerably by its application to the humans. The study of normal cellular forms, characteristic of the various phases of the sex cycle was subsequently expanded to include the many

aberrant types found in pathologic conditions and more particularly in cancer. The cytological characteristics of cancer cells are often striking, capturing one's attention immediately by the contrast to those of the non-malignant forms. This fact, coupled with the interest which has always been connected with studies related to cancer, has caused reawakening to the possibilities of using the cytological method in the diagnosis of malignant lesions.

In 1927 Dierks, on the basis of study of 30 women was the first to show cyclical changes in the vaginal epithelium and in the same year Pacconi published similar findings.

In 1933 Papanicolaou published detailed description of his fundamental observations on the epithelial changes in vagina during the menstrual cycle of women [13]. Murray 1938, De Allende and Orias 1947, Litchwitz and Fitussi 1947, Fundel 1950 and others confirmed his observations.

In India, Kishore and Agarwal in 1936, were the earliest workers to study cytohormonal changes in vagina.

The introduction of different staining technique by Shorr (1941) and Papanicolaou (1942) marked a considerable step forward in the development of gynecologic cytology [14].

Papanicolaou and Traut presented their famous monogram "Diagnosis of uterine cancer by vaginal smear" in 1943[13]. They examined smears from 3014 women at the Cornell University Hospital for women and arrived at correct diagnosis in 98.4% of Cervical carcinoma and 90.7% cases of Corpus carcinoma. They detected 179 carcinomas (127 cervix and 52 corpus) which were confirmed histologically.

A most helpful step forward was taken when Ayre introduced his spatula in 1947[15].

In 1948, American Cancer Society recognized the importance for early detection of Genital malignancy and recommended that further cytological laboratories should be set up in order to promote early diagnosis.

Achenbach R.R. et al (1951) studied the validity of cervical smear in the diagnosis of carcinoma of cervix. During a period of 3 years, 11, 871 cervical smears from 9,748 patients were examined and a total of 398 cases of malignancy were found [16].

Wied G.L.et al (1962) studied the cytology of 300 cytologically diagnosed dysplasia cases, histological confirmation was present in 279 cases [17].

Original PAP fixative was a modification of Carnoy's fluid (equal parts of alcohol, acetic acid and chloroform) and fixed the smears within one minute. It was too rapid and over fixation was easy. Way in 1963, used equal parts of ethyl alcohol and ether as fixative, successfully, which continues till date [14].

In 1967, Richart proposed the term cervical intraepithelial neoplasia [18]. This has been convincingly established through the work on cytogenetics (Kirkland et al, 1967), micro spectrophotometry (Wilbanks et al, 1967) and culture & auto radio Graphy (Richart, 1973).

Around 1960, the study of cytology attained a good momentum in India. In 1960 – 1963, Wahi, Luthra and Mali at S.N.Medical college, Agra, in a mass screening project, studied 4,919 smears from 39,587 women attending Gynecology OPD; out of these 1.7% showed carcinoma of cervix and 20% showed dysplastic changes. In 1969 they studied Cervical dysplasia and its significance [19].

Padma Rao studied 3,582 cases over 10 years from 1961 to 1972 and detected 56 positive cases i.e. 1.5%.

The 'Indian Academy of Cytologists' was established on 5th November 1969, with main objective to encourage various activities in clinical cytology and to standardize terminology.

TweeddaleD.N.et al (1972) studied 12 cases of micro invasive squamous cell cancer of cervix. They reported that the cytological smears of micro invasive lesions contained greater percentages of non-keratinizing and keratinizing cancer cells and fewer parabasal like cells. The histologic pattern of the micro invasive lesion parallels its cytological counterpart [20].

Tovell H.M.M. et al (1976) examined Pap smears from 254 patients, which showed cervical intraepithelial neoplasia or early invasive carcinoma. The accuracy of cytology in predicting the degree of CIN and early invasive carcinoma was 84.5% [21].

S. Panda and Mahapatra studied cervical cytology in unhealthy cervices of 510 cases with dysplasia in 9.5% and in situ lesions in 1.57% in 1977.

Usha Saraiyya and Mohini Garud screened 7,988 cases in 1981. The incidence of dysplasia was 3.2% and most of cases were of cervical erosion.

In 1986 M.S.Nanavati and Darshan Mehta studied 3,613 cases with 2.8% abnormal smears. The dysplasia was 1.6% and carcinoma of cervix 1.2%.

Lozowski M.S. et al (1982) studied 170 cases with abnormal cervical smears out of which histological correlation was available in 157 cases, accuracy of cytologic reporting was 41 % in mild to moderate dysplasia, 29% in severe dysplasia [22].

LullaM.and Saraiya U.B.49 (1983) studied 90 cases of cervical intraepithelial neoplasia. Cytohistological correlation was seen in 74% cases [23].

Carmichael J.A. et al (1984) reviewed 299 cervical Papanicolaou smears and obtained agreement within 1 degree of deviation from original diagnosis in 237 smears (79.3%) [24].

Parker A and Ueki M. (1986) compared preoperative cervical cytology with subsequent histology in 441 cases. The surgical specimens included total hysterectomies, cone biopsies and colposcopically directed punch biopsies. There was a precise correlation in 66% cases. The false negative rate was 11.5% and false positive rate 11.2% [25].

Sugimori L. et al (1987) examined the cytology of micro invasive squamous cell carcinoma in 53 cases. They reported that the cellular features are characterized by the presence of tumor cells in sheets, highly increased course nuclear chromatin, pleomorphic cancer cells and presence of nucleoli. Cytohistological correlation was present in 42% cases [26].

Soost H.J. et al (1991) studied 748, 871 cytological smears from 277, 842 women over a ten-year period. Positive cytological diagnoses were validated by a subsequent histological examination within 1year. Predictive value of a negative cytological examination was 99.8%. Predictive value of a positive cytological examination was 73.4% for mild to moderate dysplasia, 90.6% for severe dysplasia / Ca in situ, 94.5% for diagnosis of micro invasive carcinoma and 95.5% for diagnosis of invasive carcinoma. The cytological screening had sensitivity of 80% and specificity of 99.4% [27].

Dibonito L. et a1(1993) investigated 1000 women who had cervical smears and tissue sampling obtained during the same colposcopic evaluation. Cytological diagnosis of CIN I were 96, CIN II were 44, CIN III including carcinoma in situ were 39, invasive carcinoma were 2, atypical cases were 56. Sensitivity was 76.3%, with sensitivity increasing with CIN grade. Specificity was 93%. Positive predictive value was 80.2% and Negative predictive value was 91.3%. False negatives were 8.7% due to sampling errors [28].

Kashyap V et a1 (1995) screened, 1,1741 cervical smears over a period of 10 years and confirmed diagnosis with biopsy. A total of 1910 cases with dysplasia and 213 cases with malignancy were detected. The exact agreement in diagnosis between cytology and histology of dysplasia cases was found to be 61.9% and in malignancy 90.1% [29].

Murthy N.S. and Mathew A. (1999) studied cytological smears of 1,17,471 women, out of which 213 had malignant lesions. Malignancy was confirmed histologically in 192 (91 %) women of 213 cytologically diagnosed malignant cases [30].

Kim Y. et al (2002) studied cervical cytology smears from 18 cases of small cell carcinoma of cervix diagnosed between 1986 and 2001. Most cases showed minimal cytoplasm, finely stippled chromatin, prominent nuclear molding and smearing effect. Cytological smears diagnosed or suggested 79% of squamous cell carcinoma cervix before histologic confirmation. The tumor cells were arranged mostly in clusters of varying sizes with no typical architectural pattern. The tumors had very pleomorphic cells and recognizable nucleoli [31].

Khodakarami & Nahid [32], in 2010 studied, to compare the sensitivity, specificity, positive and negative predictive values (PPV and NPV), and accuracy of Pap smear, visual inspection with acetic acid (VIA). Their study indicated that screening with VIA allows detecting the presence of cervical neoplasia with an accuracy as good as or even better than the Pap test [32].

Albert SO et al [33], in 2012, studied the comparison of sensitivity, specificity, PPV, NPV and accuracy of visual inspection using acetic acid (VIA) with that of the Pap smear. In this study, VIA was noted to have the same sensitivity (60%) and negative predictive value (99.4%) as Pap smear. It has slightly lower specificity

(94.4%) and diagnostic accuracy (98.6%) than Pap smear, while its positive predictive value is about half (50%) of that of Pap smear. Over all, VIA seemed to be comparable to Pap smear for screening of pre-invasive lesion of the cervix [33].

Khan M et al[34],in 2012, studied the diagnostic accuracy of visual inspection of cervix using 3% acetic acid as a screening test for early detection of cervical cancer taking histopathology as the gold standard. There were 500 subjects, who underwent visual inspection of cervix with acetic acid.

Karimi-Zarchi M et al [35], in 2013, studied a comparison of 3 ways of conventional PAP smear, liquid based cytology and colposcopy versus cervical biopsy for early diagnosis of premalignant lesions. This study demonstrated that, general colposcopy method has a higher sensitivity in diagnosis of any cervical lesions compared to conventional PAP smear and liquid-based PAP smear and also statistically significant relationship was found between them. However, in the comparison of the conventional PAP smear and liquid-based PAP smear, no significant relation was observed [35].

Satyanarayana L et al [36], in 2014, did a comparative study of cervical cancer screening methods in a rural community setting of North India. The aim of their study was to demonstrate the performance of aided visual cervical screening tests as against conventional Pap smear testing in a rural community. A total of 65.6% (4988/7604) eligible women of 30-59 years age group were screened. Screen positivity rates by Pap (ASCUS and above) and VIA were 2.6% and 9.7% respectively. Sensitivity and specificity of detecting the CIN III lesions were 87.5 and 98.8% for Pap, 50.0% and 96.7% for VIA respectively. VIA screening demonstrated as a feasible primary screening test for detecting high grade CIN and as to perform better when the Pap test is not feasible [36].

ZF Jesmin et al [37], in 2015, studied, clinical effectiveness of visual inspection with acetic acid and colposcopy-based management of cervical intraepithelial neoplasia. Primary objective of their study was to update clinical efficacy of colposcopy-based diagnosis. WHO health bulletin in 2001 suggested that VIA may be considered as a suitable early detection test of cervical cancer in the context of early clinical diagnosis in low-income countries. Colposcopy is the gold standard for diagnosis of CIN and colposcopy based management eradicate CIN in 75% of cases[37].

The foremost field of application of cytology is vaginal cytology. It has been used:

1. To detect physiological changes in vagina. It means to note the cells in the vagina at birth, at menarche, in reproductive age during pregnancy, during puerperium and after menopause.
2. To detect ovulation. As a part of infertility work up, to detect the day of ovulation.
3. To know the hormonal status of female. In this case smear is taken from middle one third lateral vaginal walls.
4. As adjunct in diagnosing hormone secreting ovarian tumour.
5. To diagnose genital pathology of vagina, cervix, uterus, tubes and ovaries.
6. To diagnose the type of infection.
7. To detect genital cancer.

Today the foremost field of application of vaginal cytology is in the screening for cancer, since it is the site of the origin of the most common malignant diseases in the female is cervical carcinoma [38]. Cervical smear is very much advantageous since:

1. Carcinoma cervix is a prolonged pathological process. It takes years to develop into invasive carcinoma. Almost 10-15 years gap exist between CIN

to invasive carcinoma [39]. Thus, due to its natural course, it offers sufficient time for its detection at the earliest stage and thus chance of a complete cure.

2. Also, it is multifocal in origin. Since smear includes larger area of cervix than biopsy, it increases the chance of detection of cervical malignancy.

It has been recognized that one of the salient features of the cytological approach is the possibility, which it offers for recognition of cancer cells at earlier stage. This has been demonstrated by the large number of pre-invasive carcinomas of cervix detected in recent years by the use of smear method in different laboratories. The new interest has been created in the study of cytological and histological changes in early carcinogenesis.

The recently acquired evidence of the distinctive cytological patterns in the early developmental stages of cervical carcinoma, in contrast to that of the more advanced stages have provided more sensitive criteria for the diagnosis of early cancer, and possibly a means of prognosis based on the prevailing cytological pattern.

Knowledge of the cytology of early cancer is still fragmentary. The only organ in which actual progress has been achieved is the cervix, largely because of its accessibility to biopsy for the confirmation of positive smear findings. The correlation between the cytological and histologic picture in the early stages of malignancy is much more difficult in other less accessible organs.

A negative histological result should never be accepted as a proof especially with positive clinical findings. One should advice repeat smear. This can be due to tendency of carcinoma to necrose at the surface. The swab may very easily pick up necrotic tissue and no diagnostic cells. Thus superficial necrosis in advanced cases may lead to negative incorrect diagnosis. So clinical suspicion must never be discarded on hand of a negative cytology.

HISTOLOGY OF CERVIX

Epithelial Lining of The Cervix

Uterine cervix consists of ectocervix and endocervix.

Ectocervix: It is the vaginal portion of the cervix, which extends downwards from the external os to the reflection of the cervical epithelium on to the vaginal fornix. It is lined by non-keratinizing stratified squamous epithelium, continuous with that of the vagina.

The non-keratinizing squamous epithelium of ectocervix is composed of four layers:

1. Basal Layer 2. Parabasal layer 3. Intermediate Layer 4. Superficial Layer

1. **Basal Layer:** It is a single row of immature cells with large nuclei and small amount of cytoplasm. It is the source of epithelial cell regeneration.
2. **Para basal Layer:** It consists of 2-4 rows of immature cells that have normal mitotic Figures and provide the replacement cells for the overlying epithelium.
3. **Intermediate Layer:** It contributes to the majority of epithelial thickness. It includes 4-6 rows of cells with large amount of cytoplasm in a polyhedral shape, separated by an intercellular space. Intercellular bridges where differentiation of glycogen production occurs can be identified with light microscopy.
4. **Superficial Layer:** It has squamous cells, non-keratinized type. It includes 5-8 rows of flattened cells with small uniform nuclei and a cytoplasm filled with glycogen. The nucleus becomes pyknotic and the cells detach from the surface (exfoliation). These cells form the basis for Papanicolaou (Pap) testing.

Endocervix: It is the portion of the cervix from external os to internal os. The mucous membrane lining the endocervical canal is thrown into folds, which consists of anterior and posterior columns from which, radiate circumferential folds to give the appearance of tree trunk and branches, hence the name 'arborvitae'. Histologically the endocervix differs considerably from the endometrium. It is covered by a single layer of tall columnar epithelium with mucus at the top and basal nuclei which, on the top of the folds but not in the crypts and glands, are ciliated.

In cervical smears, endocervical cells appear as cells arranged in "Picket fence"; parallel rows of cells or "Honey Comb" pattern; the nuclei are basal with glandular chromatin, cytoplasm is finely vacuolated and faintly basophilic. Beneath this, there are patches of cubical 'basal or reserve' cells from which new surface cells are believed to develop and which can undergo squamous metaplasia.

Endocervical glands are simple, tubular & branching glands. The glands which dip into the stroma are of complex racemose type and are lined by secretory columnar epithelium. There is no stroma unlike the corpus and the lining epithelium rests on a thin basement membrane.

SQUAMOCOLUMNAR JUNCTION (SCJ)

It is the meeting point of columnar epithelium that lines the endocervical canal with squamous epithelium that lines the ectocervix. It is a dynamic point. It varies in relation to hormonal level of estrogen and hence in different phases of life. e.g. puberty, pregnancy and menopause.

In the presence of estrogen, the vaginal epithelium accumulates glycogen. The Lactobacilli act on glycogen to produce the acidic pH (lactic acid) of vagina. This moves the squamocolumnar junction downwards.

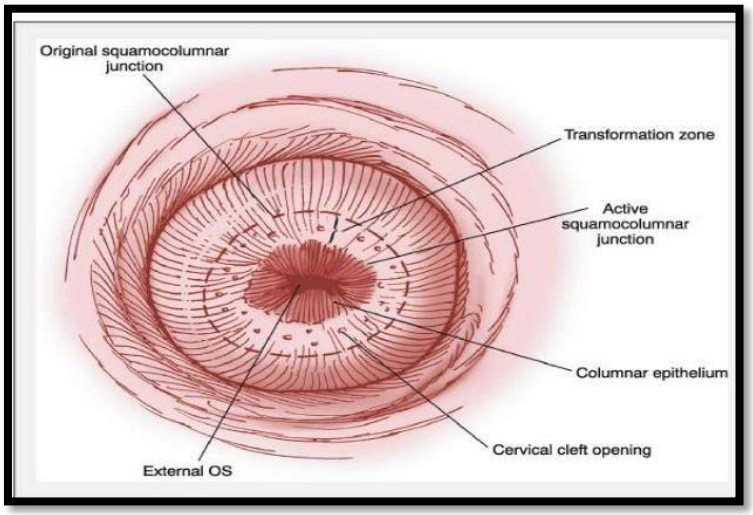
The metaplasia extends from the original SCJ outside to the newly developed (physiologically active) SCJ inside. This area is called as TRANSFORMATION ZONE (TZ) or Transitional Zone. It may be 1 - 10 mm width with variable histological features. It consists of endocervical stroma and glands covered by squamous epithelium.

The zone is not static but is in dynamic state. Two mechanisms are involved in the process of replacement of endocervical columnar epithelium by squamous epithelium.

a. By squamous metaplasia of the sub columnar reserve cells
b. Squamous epidermalization by ingrowth of the squamous epithelium of the ectocervix under the columnar epithelium. Initially squamous cells are immature but ultimately become mature and indistinguishable from the adjacent squamous epithelium.

The metaplastic process is very active at the time of menarche and during and after first pregnancy. These metaplastic cells have got the potentiality to undergo atypical transformation by trauma or infection [40].

Figure 1- Transformation zone



NATURAL HISTORY OF NEOPLASIA OF CERVIX

Cervical cancer doesn't develop suddenly from normal tissues but is preceded by intraepithelial histopathological changes.

Ever since the 1st population studies conducted in the 1950s in the United States, certain facts about pre-cancerous lesions of the uterine cervix became apparent. They are:

- Pre-cancerous lesions of cervix occurred generally several years earlier than those with invasive carcinoma.
- Pre-cancerous lesions did not necessarily progress to invasive cancer in a period of month or year.
- Some of the pre-cancerous lesions regressed spontaneously.
- There were marked cytological and histological differences amongst the various pre-cancerous lesions with regard to the degree of abnormality and cellular configuration.
- Incidence of invasive carcinoma in the population was much less considering the rate of discovery of the pre-cancerous lesions, indicating that not all of the pre-cancerous lesions progressed into invasive carcinomas within the lifetime of the patient.
- CIN-l may progress to invasive cancer without going through the stages of CIN II and III. This is called "Jumping" of the lesion. This is extremely uncommon.

All dysplastic lesions are not potentially malignant. Majority of mild and moderate lesions revert to normal and majority of severe lesions progress to malignancy but a few lesions remain unchanged also. The risk of manifestation of malignancy is reported to be as follows:

- Mild dysplasia to malignancy -3.42%
- Moderate dysplasia to malignancy -20.9%
- Severe dysplasia to malignancy -71.5%

Mild dysplasia takes 5 years to change to CIS, whereas moderate dysplasia to CIS takes 3 years, and severe dysplasia progresses very fast i.e. within a year time to CIS. These observations led to a number of attempts to investigate the frequency with which the CIN progress to invasive cancer.

Oster 1993 reviewed the literature and has summarized regression, persistence and progression rates [41].

TABLE 1: Life cycle of unstable cervical epithelium

	Progression	Persistence	Progression to CIS	Progression to Invasion
CIN I	57%	32%	11%	1%
CIN II	43%	35%	22%	5%
CIN III	32%	<56%	0	>12%

	Normal	CIN I, II	CIN III/CISS	Invasion
Duration of disease progression (years)	0	5	10	20
Age of Patient (Years)	-	25-30	30-35	40-45

At present we cannot identify which individuals with CIN have the potential for malignant progression. A blanket approach to treatment is therefore necessary. Current opinion largely favors the treatment of patients with CIN II or III lesions,

although conservative management may be justified for CIN I, (Robertson J.R. et al., 1988.)

TERMINOLOGY AND NOMENCLATURE

In spite of the fact that the significance of the cytological screening and the intraepithelial lesions has been recognized since the beginning of 20th century, general acceptance of uniform terminologies for such lesions was not determined which led to instances in which the results were of overwhelmingly positive character, leaving no doubt as to their final interpretation and on the other hand, there were cases in which there is strong but not fully convincing evidence of malignancy [42].

These considerations led **Papanicolaou and Traut** in 1941 to classify cytological smears [8]. They divided the smear in to 5 groups.

Group I - Absence of atypical or abnormal cells

Group II - Atypical cytology but no evidence of malignancy

Group III - Cytology suggestive of but not conclusive of malignancy

Group IV - Cytology strongly suggestive of malignancy

Group V - Cytology conclusive for malignancy

This classification received a lot of criticism, mainly because of lack of diagnostic precision in group III and uniformity in the number of grades used and absence of clinicopathological expression. The international Academy of Cytology has therefore prohibited its use in official publication and recommends the use of nomenclature with an inherent histopathological prognosis.

This was modified and **WHO** recommended (1952-1973) that cytology smears should be classified as:

Group I - Normal

Group II - Inflammatory

Group III - Dysplasia

Mild dysplasia

Moderate dysplasia

Severe dysplasia

Group IV - Carcinoma in situ

Group V - Invasive carcinoma/ squamous cell carcinoma

In 1967, Ralph M. Richart introduced the term cervical intraepithelial neoplasia (CIN) [43]. It is a single descriptive term which would embrace all grades of dysplasia as well as carcinoma in situ under single heading &graded as I - IV. Later on, he used only 3 grades of CIN from I - III because of excellent evidence that there was no significant or meaningful difference between CIN grade III (severe dysplasia) and CIN grade IV (carcinoma in situ).

Richart's Classification

CIN - Mild dysplasia

CIN II - Moderate dysplasia

CIN III - Severe dysplasia and Carcinoma in situ

In 1975, WHO correlated **CIN** with various grades of dysplasia and CIS When 1/3rd or less of the distance from basement membrane to the surface is involved, the lesion is called CIN-l, when more than 1/3rd but less than 2/3rdis involved it is CIN-II, when more than 2/3rd involved, it is CIN III, full thickness involvement was called CIS and is now included in CIN III.

In an attempt to establish consensus in cervical cytological terminology, in 1988, the National Cancer Institute held a workshop, which met in Bethesda, Maryland and proposed a new system for reporting cervical cytology. This is referred to as "The Bethesda System" which was revised in 2001[44].

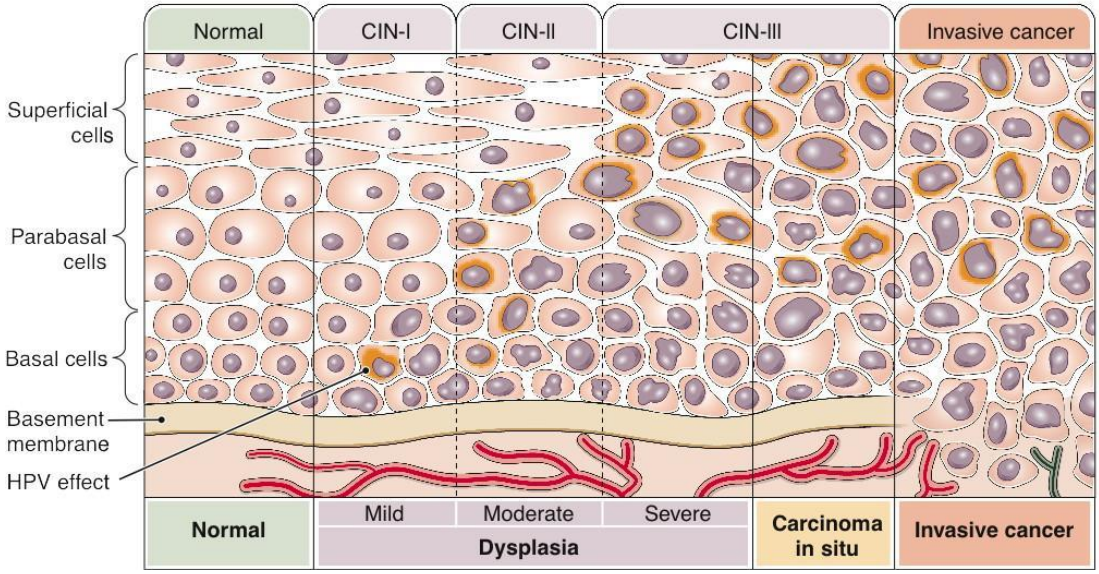


Figure 2- CLASSIFICATION OF DYSPLASIA

CRITERIA FOR SPECIMEN ADEQUACY AS PER BETHESDA SYSTEM

Following criteria for satisfactory specimen

1. Appropriate labeling and identifying inflammation.
2. Relevant clinical information.
3. Adequate number of well preserved and well visualized squamous epithelial cells.
4. An adequate endocervical transformation zone component.

Well preserved and visualized squamous epithelial cells should be spread on more than 10% of the slide surface. An adequate endocervical, transformation zone component should consist, and a minimum of 2 clusters of well-preserved endocervical or squamous metaplastic cells with each cluster composed of a minimum of at least five appropriate cells.

A Specimen is "Satisfactory for evaluation but limited by" if any of the following apply

1. Lack of pertinent clinical patient information.
2. Partially observing blood, inflammation, thick areas, poor fixation air drying artifact, contaminant etc., which preclude interpretation of approximately 50-75% of epithelial cells.
3. Lack of endocervical transformation zone component as defined above.

A Specimen is "Unsatisfactory for evaluation" if any of the following apply

1. Lack of patient identification on the specimen and! or requisition form.
2. A technically unacceptable slide is defined as one that is broken and cannot be repaired or as having cellular material that is inadequately preserved.
3. Scanty squamous epithelial components.
4. Observing blood, inflammation, thick areas, poor fixation, air-drying artifact, contaminant etc., which preclude interpretation of approximately 75% or more of the epithelial cells.

BETHESDA SYSTEM FOR REPORTING CERVICAL / VAGINAL CYTOLOGY (2001) [14] [45]

Specimen type

Indicate conventional smear (Pap smear) vs. liquid-based.

Specimen adequacy

- Satisfactory for evaluation (Describe presence or absence of endocervical/ transformation zone component and any other quality indicators, e.g. partially obscuring blood, inflammation, etc.)
- Unsatisfactory for evaluation (specify reason)
- Specimen rejected/not processed (specify reason)
- Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

General categorization (optional)

- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality: See "Interpretation/result"

  (Specify 'squamous' or 'glandular' as appropriate.)
- Other: See "Interpretation/result"

(e.g. endometrial cells in a woman> 40 years of age)

Automated review

If case examined by automated device, specify device and result.

Ancillary testing

Provide a brief description of the test methods and report the result so that it is easily understood by the clinician.

Interpretation/result

Negative for intra epithelial lesion or malignancy

(When there is no cellular evidence of neoplasia, state this in the "General categorization" above and/or in the "Interpretation/result" section of the report, whether or not there are organisms or other nonneoplastic findings.)

Organisms

- Trichomonas vaginalis.
- Fungal organisms morphologically consistent with Candida spp.
- Shift in flora suggestive of bacterial vaginosis.
- Bacteria morphologically consistent with Actinomyces spp.
- Cellular changes consistent with Herpes simplex virus like ground glass nuclei (margination of nuclei), molding and multinucleation.

Other nonneoplastic findings

(Optional to report; list not inclusive):

- Reactive cellular changes associated with inflammation (includes typical repair) radiation, intrauterine contraceptive device (IUD)
- Glandular cells in post hysterectomy status
- Atrophy

Other

- Endometrial cells (in a woman> 40 years of age) (Specify if negative for squamous intraepithelial lesion')

Epithelial cell abnormalities

Squamous cell

- Atypical squamous cells of undetermined significance (ASC-US) cannot exclude HSIL(ASe-H)

- Low-grade squamous intraepithelial lesion (LSIL) encompassing: HPV/mild dysplasia/CIN 1
- High-grade squamous intraepithelial lesion (HSIL)encompassing: moderate and severe dysplasia, CIS/CIN 2 and CIN 3; with features suspicious for invasion (if invasion is suspected).
- Squamous cell carcinoma.

Glandular cell

- Atypical

  Endocervical cells

  Endometrial cells

  Glandular cells

  Atypical

  Endocervical cells, favor neoplastic

  Glandular cells, favor neoplastic
- Endocervical adenocarcinoma in situ
- Adenocarcinoma

  Endocervical

  Endometrial

  Extrauterine

  Not otherwise specified (NOS)

TABLE 2: Comparison of Different Classification Systems [46]

Bethesda System	**Dysplasia/CIN**	**Papanicolaou System (Class)**
Within normal limits	Normal	I
Infection (organism should be specified)	Inflammatory atypia (organism)	II
Reactive and reparative changes		
Squamous cell abnormalities Atypical squamous cells 1.Of undetermined significance 2.Exclude high grade lesions	Squamous atypia, HPV atypia, exclude LSIL, Exclude HSIL, HPV atypia	II
Low grade squamous intraepithelial lesion (LSIL)	Mild dysplasia CIN I	
High grade squamous intraepithelial lesion (HSIL)	Moderate dysplasia CIN II Severe Dysplasia CIN III Carcinoma in situ	III IV
Squamous cell carcinoma	Squamous cell carcinoma	V

The Cancer prevention and control division of National Cancer Institute Participants, unanimously approved the following recommendation.

A. The cytopathology report is a medical consultation

1. The cytopathology has the ultimate responsibility for the diagnostic evaluation and reporting.
2. The referring physician bus an obligation to include all the patient clinical information in the request for cytological evaluation, so that the cytopathologist can consult effectively.

3. The cytopathologist should determine whether the specimen is adequate for diagnostic evaluation, if it is unsatisfactory or less than optimal this should be noted in the report.

B. The Papanicolaou classification of reporting is not acceptable in modern practice of diagnostic cytology

1. Pap classification does not reflect current understanding of cervical/vaginal neoplasia.
2. The Pap classification has no equivalent m diagnostic histopathological terminology.
3. The Pap classification does not provide diagnosis for non-cancer entities.
4. As a result of numerous provided idiosyncratic modifications, the specific Papanicolaou classification no longer reflects diagnostic interpretations uniformly.

C. The Bethesda system should serve as a guideline for cytopathology reports of cervical/vaginal specimens

1. Provide for effective communication among cytopathologist and referring physicians.
2. Facilitate cytological and histological correlation.
3. Facilitate research into the epidemiology, biology and pathology of cervical lesions.
4. Provide reliable data for National and International Statistical Analysis and comparisons.

CYTOLOGICAL SCREENING FOR CERVICAL CANCER

Advantages of diagnostic cytology:

1. It is outpatient basis procedure.

2. Pap smears do not diagnose cancer, but they detect 95% of cervical cancers at a stage when they cannot be seen with the naked eye.
3. Suitable specimen can be collected with minimal discomfort to the woman.
4. Collection techniques are simple and inexpensive.
5. Making repeated or serial investigations feasible.
6. Use of cytology may make biopsy unnecessary. It covers wide areas as compared to biopsy so considering multifocal origin of cancer cervix cytology offers better chance to catch the disease.
7. In cancer diagnosis, cytology may diagnose it before it is clinically evident.
8. Asymptomatic infections can be diagnosed.
9. Scrap cytology provides cells from whole of the portio vaginalis of the cervix including endocervical canal whereas cervical biopsies provide biopsy specific reports and may miss other parts of the cervix.

Limitations/Disadvantages of Cytology:

1. Provision of adequate clinical history, age, sex, relevant family history, H/O surgery/hormonal therapy, hygiene and addiction.
2. Collection of specimens –it will be impossible to collect the specimen. Specific site and method of collection should be mentioned, since different sites and methods have different normal ranges.
3. Collection of suitable specimens should be with as little contamination as possible. Also, it should be affected by immediate fixation and accurate identification.
4. Avoid laboratory hazards of poor selection of material, delay in processing, drying distortion inadequate fixation, poor staining and contamination.

5. Sound knowledge of cellular structure and staining is essential. Also, one should know normal physiological changes.
6. Complete examination of specimen to come to the conclusion. It is the time consuming and frequently monotonous.
7. Also, it is inconclusive about the invasion of tumour.
8. It has to be used with other diagnostic tools like colposcopy, cervical biopsy[47][48]

Thus, it is clear that it is equally important to get the good smear as well as to stain the smear properly. Papanicolaou's stain is the stain universally accepted. The comparative study of Papanicolaou stain and acridine fluorescent staining was done in 1979, which showed Pap staining to be better diagnostic aid though it is time consuming and requires expert personal to comment.

Merits of Papanicolaou Staining:

1. Staining Material is easily available.
2. Stained slides can be stored for years.
3. Cyto-morphological features are easily recognized.

Demerits:

1. It takes more than one hour.
2. Nuclei are not distinguishable from pseudo nucleoli [49].

Sensitivity and specificity of Pap smear in recent reviews of cervical cytology assessment, the sensitivity of the Pap test in detecting CIN 2-3 ranged from 47% to 62% and specificity ranged from 60% to 95% [50] [51]

The technique to be used for cervical cancer screening involves taking samples from the ectocervical and endocervical canal. The vaginal pool samples should be abandoned because it adds little to the diagnostic accuracy of the technique.

The cervix should be exposed and any mucous discharge should be gently wiped away. ‘A small cytobrush or saline-moistened, cotton tipped application should be inserted into the endocervical canal and twisted to collect a sample from the endocervix. Then, the broad end of Ayres spatula should be used to scrape the cervix in a 360^{o} fashion. Alternatively, a glass or plastic pipette with a large rubber suction bulb may be used to aspirate a sample of secretion from the endocervical canal [52].

By whatever technique, the endocervical specimen is an important part of the screening test [53] [54]. When all the samples have been collected, they are spread as rapidly as possible on a glass microscope slide and fixed immediately in 95% ethyl alcohol. When a cervical dysplasia or other abnormality is known to exist, it may be helpful to use two slides and send the endocervical and ectocervical samples on separate slides in order to provide a large cell spread for diagnostic interpretation. Commercial spray or dropper fixatives are quite satisfactory. Once fixed, the slide can be dried for shipment to the laboratory.

Newer techniques of cervical cytology:

It is obvious that improvement in the conventional Pap test technique is necessary. False-negative errors occur in sampling, preparation, and interpretation. Sampling errors occur because a lesion is too small to exfoliate cells or the device used did not pick up the cells and transfer them to the glass slide. Preparation errors may occur because of poor fixation on the glass slide, leading to air-drying and an inability to interpret the results. The slide may also be too thick and obscured by vaginal discharge, blood, or mucus. The thick slide also leads to poor fixation because the fixative does not penetrate the cell sample. Interpretive errors occur when the slide contains diagnostic cells that the screening technician did not identify.

Using a liquid-based medium to collect the cytological sampling and preserve the collected cervical cells can alleviate sampling and preparation errors [55]. The sample is then processed to provide a uniform, thin layer of cervical cell without debris on a glass slide. The AHRQ (agency for health care research and quality) reported that liquid-based cytology assessment improved the sensitivity of the Pap test to a stated goal of 80%. The cell sample is collected with endocervical brush used in combination with a plastic spatula or with a plastic brush [56] [57]. The sample is then rinsed in a vial containing liquid preservative. With this technique, 80%-90% of the cells are transferred to the liquid media, as compared with the only 10% - 20% transferred to the glass slide with conventional cytological testing. In addition, using liquid-based media eliminates air drying [58]. The cells are retrieved from the vial by passing the liquid through the filter, which traps the larger epithelial cells, separating them from the small blood and inflammatory cells. This process leads to a thin layer of diagnostic cells properly preserved and more easily interpreted by the cytologist [59] [60]. This technique reduces by 70% - 90%, the rate of unsatisfactory samples encountered with conventional cytological testing [61]. Liquid-based cytology is now commonly performed by most of the laboratories in United States.

A second new technology for assessment of cervical cytology is the Auto Pap Screening System, which has been approved by the U.S. Food and Drug Administration for primary screening and rescreening of samples initially interpreted as normal. This technique uses an automated microscope coupled to a special digital camera. The system scans the slide and uses computer imaging technique to analyze each field of view on the slide. Computer algorithms are then used to rank each slide on the basis of the probability that the sample may contain abnormality. The selected slides are then reviewed by a cytopathologist. This technique has reduced the false-

negative rate by 32% [62]. The Auto Pap Screening System currently is not in wide spread use.

Since the discovery of cyto-diagnosis of cancer cervix by Papanicolaou smear, this method is been widely used by many, like Graham and Mein (1949),Wahi and Mali Jain (1950), Ayre (1957), Zinson (1957), Phuja (1963), Mali and Wahi (1966), Samuel (1967), Rao Purandare (1973).

Over the years, the procedure of Papanicolaou smear has undergone considerable modifications as per the requirements and changing aims [63]. For remote centers, fast fixation Kits for 'posting' are designed. Rapid staining techniques 'Shorrs technique' is adopted by some as an alternative.

During the past decade much progress has been made in the adaptation of the cytological method for diagnosis of cancer. Achievement of proper diagnostic technique should go hand in hand with correct application of it in right place i.e. the technique should be utilized to divert the attention of medical practitioners to this point.

It is the poor, non-metropolitan woman mostly in middle income countries which is at high risk of developing malignancy and she is the one which is less likely to get screened [64] [65]. Also increasing efforts are being made to divert the flow of resources towards the high-risk population. Firstly, detailed study of epidemiology of cancer cervix was made and high-risk factors were found out [66]. Attention is diverted to them either by reaching out to them by ambulatory medical squad or by making them come up to medical help by health awareness through community health education. This screening of reproductive age group will help us reducing the burden and make carcinoma preventable by early detection.

Despite this noteworthy progress, we are still far from our ultimate goal, the attainment of which will depend on the gradual accumulation of observations in the field of applied cytology but to a greater extent of future advances in our fundamental concepts of the morphological and physiological properties of the cells and its application. There is no satisfactory formula available that provides an accurate cost benefit analysis of this screening technique. It is only possible to appraise the value of cytology in terms of improvement in the morbidity of cervical cancer.

Programmes with shorter intervals are much likely to detect the lesions early and to eradicate them preventing the development of invasive cancer, although at a higher cost.

The similarity between family planning programmes and cervical neoplasia detection programmes is that their population of interest is almost identical, namely women in the reproductive age group who are sexually active. When both programmes are combined significant accomplishment is possible at low cost.

Figure 3- Pap smear showing normal cytology

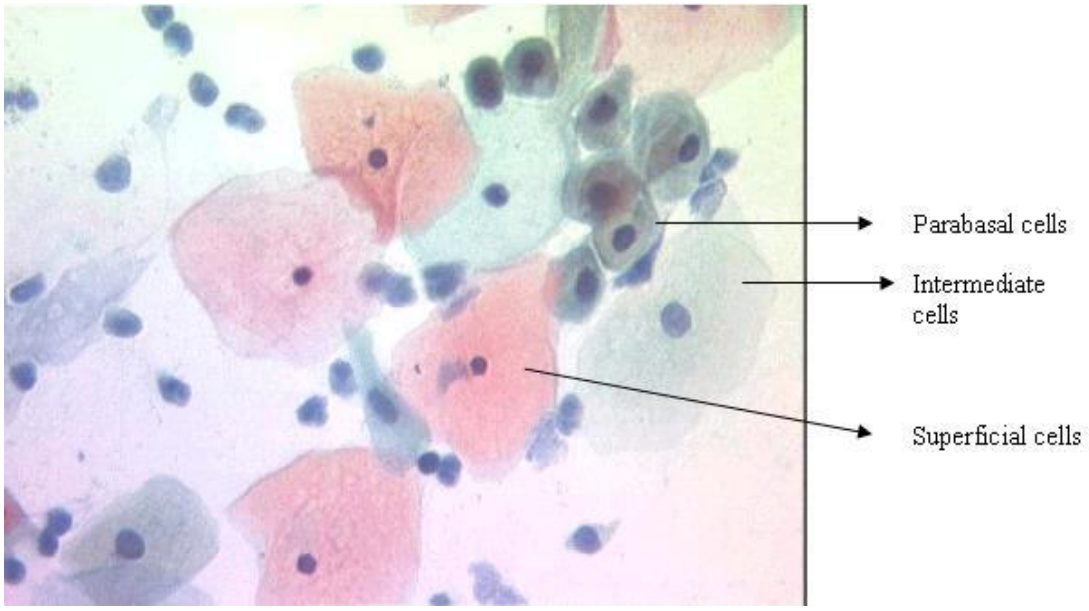


Figure 4- Pap smear showing inflammatory changes

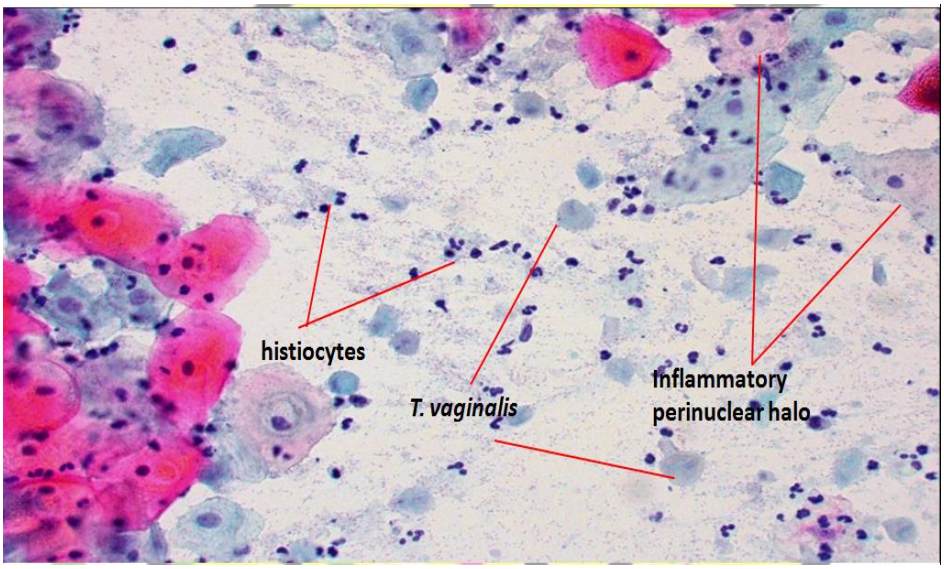


Figure 5- Pap smear showing ASCUS changes

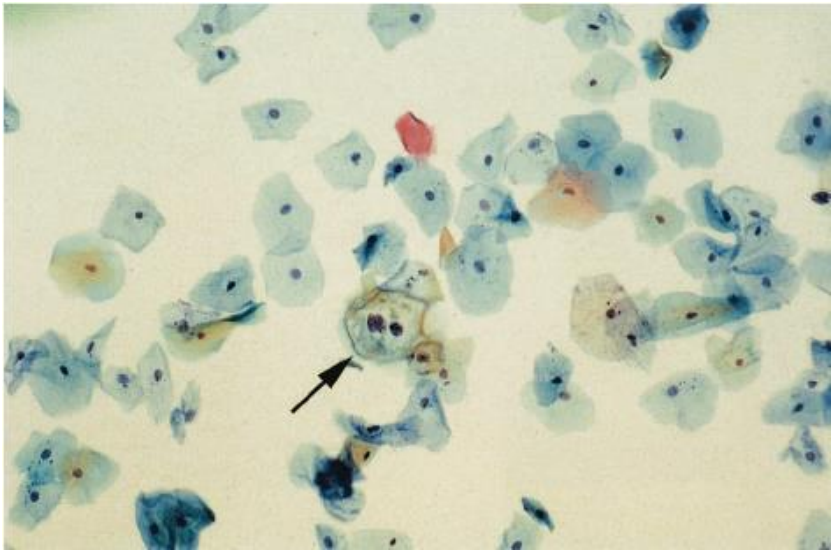


Figure 6- Pap smear showing LSIL

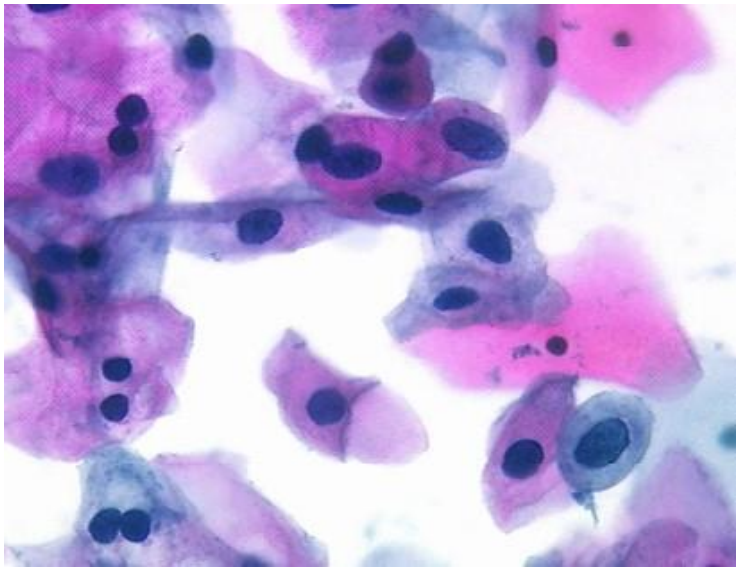


Figure 7- Pap smear showing HSIL

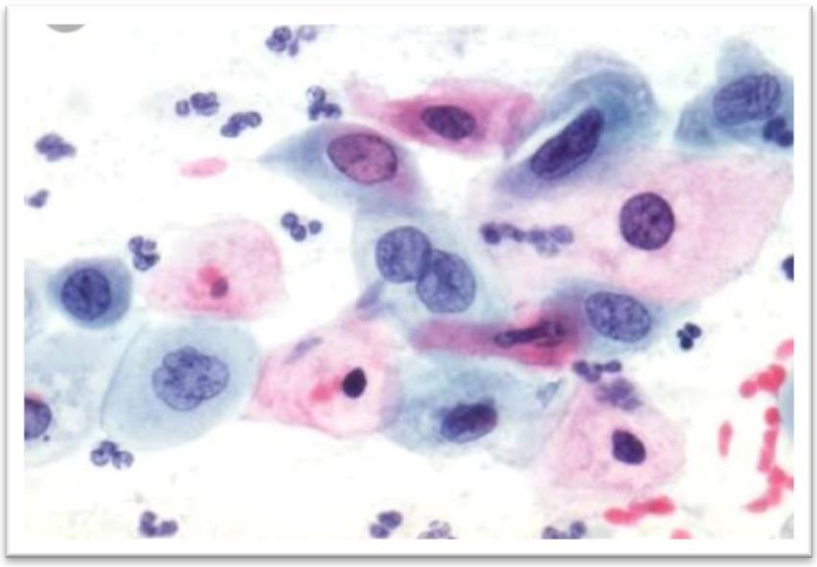
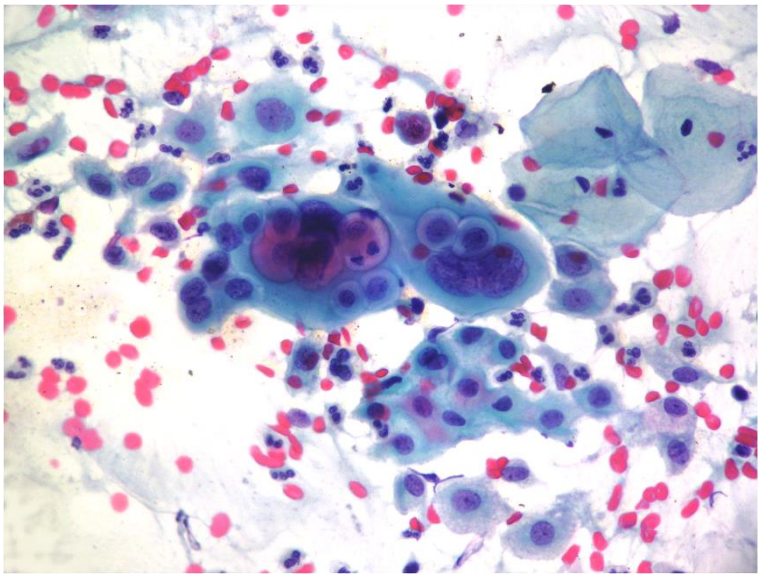


Figure 8- Pap smear showing Squamous cell carcinoma



AETIOPATHOGENESIS OF CERVICAL CANCER:

1) **Age -** It occurs at about 2 peaks of age, at 30-35 years and 50-55 years of age. Pre-invasive lesions occur 10years before.
2) **Sexual activity, marriage and childbearing** –Sexually active woman is **two** to **four** times more likely to develop cancer than in sexually inactive woman. Young ageat first intercourse, multiple sexual partners and high parity have been implicated as the risk factors for CIN and cervical cancer.
3) **Race –** The women of certain races, notably orthodox Jews are almost immune to cervical cancer. Carcinoma cervix is unusually common in Africans.
4) **Social and economic factors –** The disease is more prevalent among women belonging to low socioeconomic status.
5) **Coitus –** The practice of coitus is now established as being a prime cause of cervical malignant disease. It is almost unknown in groups of nuns and virgins. Early age of 1st intercourse and multiple partners are associated with higher risk of developing cervical cancer.
6) **Infection with HPV (Human Papilloma Virus)–** HPV infection has been detected in up to 99% of women with squamous cervical carcinoma. Specific HPV types are associated with cervical cancer. Low risk includes types 6,11,42,44 and high-risk types include 16,18,31,33,35,39,45,51,52,56,58. HPV subtypes 16 and 18 are found in 62% of cervical carcinomas. The mechanism by which HPV affects cellular growth and differentiation is through the epitheliotropic infection→oncogenic HPV DNA integrates with human genome→upregulation of viral oncogenes→expression of E6 and E7 oncoproteins→interference of tumor suppression genes→host cell immortalization and HPV induced neoplastic transformation[39].

7) **Risk associated with smoking**- It seems consistent that the risk of cervical cancer is invariably associated with human papillomavirus (HPV) infection partly via sexual transmission. Active smoking may also be related to cervical cancer because tobacco smoke constituents/metabolites or mutagens/carcinogens will be conveyed to the cervical mucus and act as independent initiators/promoters in the carcinogenesis or interact with the oncogenes of HPV.

8) **HIV and cervical neoplasia**- strong association between HIV and HPV infections and evidence of more rapid progression of HPV infections to cervical neoplasia in HIV infected women.

9) **Use of OC Pills**- OC Pills predispose to cervical neoplasia hence women on OC pills are advised for yearly pap smear for monitoring of changes in cervical epithelium. **Colposcopy**[70]-Colposcopy means to look at the vagina (i.e. colpo means vagina, scope means to look). It was first described by Hans Hinselman of Germany in 1925. It is performed using a colposcope, an optical instrument that supplies magnification (typically 5 - 25x) and often records photo Figures. Magnification provided by colposcope is 6-40 times. Blue/ green filter is used for visualization of vascular pattern, as they appear dark and visibly contrasted against the surrounding epithelium. It allows accurate delineation of suspicious areas for tissue biopsy. Colposcopy is required in abnormal Pap smear cytology, to locate abnormal areas, to obtain directed biopsy, for conservative therapy under colposcopic guidance and for follow up of cases treated conservatively.

Indications for colposcopy include-

1. Pap smear consistent with HPV infection, dysplasia, or cancer (LSIL or HSIL)
2. Pap smear with ASCUS favor dysplasia or repeated ASCUS
3. Pap smear with repeated unexplained inflammation

4. Abnormal appearing cervix

5. Infection with oncogenic HPV

6. Aceto-positivity in visual inspection with acetic acid (VIA) and visual inspection with acetic under magnification (VIAM)

8. Leukoplakia of cervix

Lesions that are more likely to be missed or under-read by colposcopic examination include endocervical lesions and necrotic lesions.

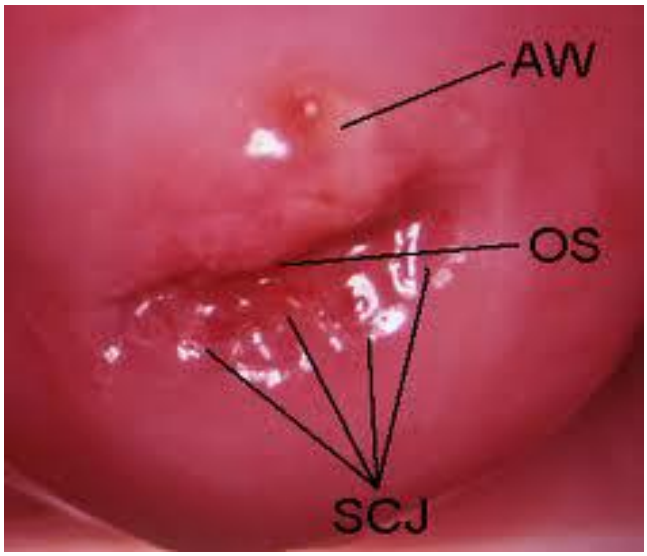


Figure 9- Normal Colposcopic Image

AW-acetowhite area

SCJ-squamocolumnar junction

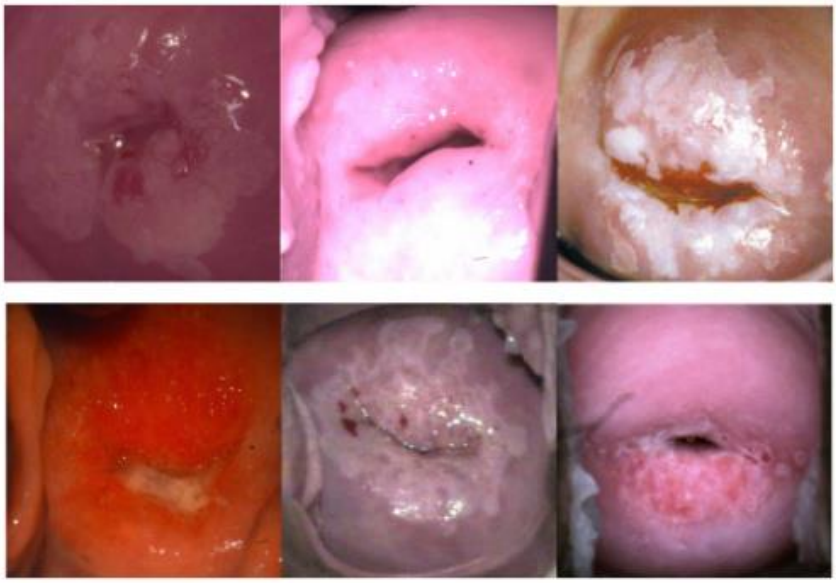


Figure 10- Abnormal Colposcopic Images

Contraindications*:1)* No absolute contraindications exist.

2) The patient's inability to tolerate a standard speculum examination.

Active cervicitis and vulvovaginitis should be treated before undergoing the examination because inflamed tissues can alter the ability to obtain an accurate assessment.

Coppleson's Grading System

Grade I (Insignificant)- Shiny or semitransparent acetowhite epithelium. Borders are not sharp. No punctuations or mosaic. Short inter-capillary distance. Absent atypical vessels.

Grade II (Significant)- Dense aceto-white epithelium or grey opaque epithelium, borders are sharp. Vessels are dilated and irregular and coiled. Coarse punctuations, mosaic, atypical vessels and irregular surface.

Role of Colposcopy in screening

Colposcopy greatly enhances diagnostic accuracy. When used complimentary to cytology, sensitivity of colposcopy is between 87-99%. But its specificity is lower and varies between 23-87%.

Problems encountered in colposcopy may arise due to: -

1. **Inadequate expertise**: An inexperienced colposcopist may find difficulty in assessment of various lesions. Recognition of squamo-columnar junction is crucial to identify the upper limit of the lesion. A less experienced colposcopist may give more importance to minor grades of mosaic or punctations than major grades of acetowhite epithelium leading to biopsy from a wrong area.
2. **Interpretive problems and limitations**: There are various conditions which create confusion in colposcopic differentiation. Immature or active metaplastic epithelium may be difficult to differentiate from early grades of CIN. Vascular pattern may lead to confusing picture. Colposcopy maybe unsatisfactory at times.
3. **Failure to follow standard diagnostic protocol**: Deviation from an established protocol increases the probability of inaccurate diagnosis resulting in inappropriate treatment which may prove disastrous [71].
4. In post-menopausal women due to atrophic changes, the squamo columnar junction gets flushed in to the vagina which makes it difficult for visualization and examination to report the findings.

Colposcopic Directed Biopsy:

Biopsy should be taken under colposcopic guidance from a point within the most abnormal area. Histopathology provides the final confirmation of diagnosis in most situations, even though certain conditions cannot be pinpointed such as inflammatory conditions. It is of paramount importance in deciding the modality of

treatment and type of surgery. Thus, it is imperative to have active interaction between the colposcopist, cytologist and histopathologist to correlate their findings for achieving optimum results in the management of female lower genital tract lesions[72].

Cervicography[67]**-**

This method was first described by Adolf Stafl in 1981. A photo Figure of the cervix is taken after the application of 3-5% solution of acetic acid. Cerviscope is a special camera equipped with an extension tube and ring flash. After development, the film is projected on 2 x 2 m screen and a colposcopy expert reads the picture from a distance of 150 cm. The Cervigram is interpreted as negative, atypical or positive. The Cervigrams are treated as

1. Negative
2. Atypical – recommending repeat cervigram and Pap test in 6 to 12 weeks
3. Positive – with colposcopy recommended.

In summary, Cervicography alone has an inferior sensitivity compared to cytology, and therefore is not recommended in settings where adequate cytology services are available. As an adjunct to Pap smear screening, Cervicography may increase the sensitivity for detecting cervical abnormalities but will decrease the specificity, potentially resulting in increased referrals for colposcopy. It is useful when a colposcopist is not available for spot evaluation.

Down staging screening of cancer cervix-

According to WHO it is defined as the detection of disease in an earlier stage (when still curable) by nurses and other paramedical workers by using a simple speculum for visual inspection of the cervix. It is an experimental approach suggested by WHO as alternative to regular cytological screening.

In the developing countries, where effective mass screening cannot be extended and the majority of cases of carcinoma cervix are diagnosed at an advanced stage, down staging screening offers at least an early detection of disease. The strategy is however, not expected to lower the incidence of cancer cervix but it can certainly minimize the cancer death through early detection.

Objective of the visual examination is solely, to be able to recognize clinically normal from abnormal cervix and refer abnormal looking cases for further evaluation and diagnosis. All findings should be carefully recorded in the provided printed forms. The gross appearance of the cervix is classified into Normal, Abnormal or Suspicious of Malignancy.

Normal Cervix- A normal cervix appears smooth, round, pink lubricated with clear mucoid secretion and has a central hole the "external os". The shape of the external os varies with parity, being round in a nulliparous woman and slit like or cruciate in a multipara. Cervix in postmenopausal women appears atrophic.

Abnormal Cervix- This category will include all benign looking lesions, like

1. Hypertrophy
2. Redness or Congestion
3. Irregular surface/ Distortion
4. Simple erosions (that do not bleed on touch)
5. Cervical polyps (with smooth surface)
6. Abnormal discharge (foul smelling, dirty/ greenish, white/ cheesy, bloodstained)
7. Nabothian follicles
8. Ectropion

Suspicious of Malignancy- Malignancy should be suspected when there is erosion that bleeds on touch or a growth with an irregular surface. Both of these lesions may be friable and bleed on touch or may be accompanied with an offensive discharge.

Second generation category-

Polar Probe- Real time electronic device is used for detection of cervical neoplasia. It detects the existence of cervical cancer and pre-cancer by measuring two sets of physical parameters, voltage decay and scattering of various wavelengths of light by different tissues. When applied directly to cervix the device instantly recognizes six types of tissues from normal to abnormal tissue. It may be used in primary screening or as an adjunct to cytology. Excellent discrimination of polar probe at high-grade end of spectrum and its ability to give instantaneous results makes it appear as high risk, poorly compliant population in rural areas and in developing countries where return visit colposcopy is especially difficult. The sensitivity is similar to that of cytology and specificity better than cytology in some settings.

NEW SCREENING TECHNOLOGIES UNDER INVESTIGATION

AIMED AT IMPROVING PAP TEST ACCURACY

New technologies for cytology screening are intended to reduce the false negative rate, improve sensitivity and specificity of screening, improve the adequacy of the pap smear and potentially improve laboratory productivity.

Liquid- Based Cytology

a) Thin Layer preparation/ Thin Prep FDA approved-

Interpretation of Pap smear slides maybe hindered by poor sampling, uneven cell distribution or improper fixation of the slide. Important findings may be obscured by uneven sample distribution, cellular clumping and debris.The Liquid based/ thin layer preparation system is designed to correct this problem. It improves the sensitivity of the Pap test to the stated goal of 80%. The cell sample is obtained with a cytobrush, and Ayre spatula or a cervical broom device. The sample is not smeared directly on a glass slide. Instead the sample is rinsed in a vial containing liquid preservative. This technique transfers 80 – 90% of the cells to the liquid media, as compared with only 10 – 20% transferred to the glass slide with conventional cytology testing. The technique removes most mucus protein and fresh red blood cells from preparation, distributes the cells uniformly, improves fixation and the preservation of the cellular architecture, maintains diagnostic clusters and ensures uniform sampling of the material removed from the cervix. It eliminates air dying.

Furthermore, this method provides representative residual material in collection media that can be used for additional / adjunctive testing (ex-HPV testing). The cells are retrieved from the vial by passing the liquid through a filter, which traps the larger epithelial cells, separating them from the small blood and inflammatory cells. A predetermined number of cells are drawn onto a filter membrane, which is then applied to a glass slide in a monolayer. This leads to a thin layer of diagnostic cells properly preserved and more easily interpreted by cytologist. This technique reduces the rate of unsatisfactory smears encountered with conventional cytological testing by 70 to 90 %.

There are some disadvantages with this technique. Interpretation of monolayers is different from conventional studies, requiring retraining of cytotechnologists and cytopathologists. Cells may be overlooked because they may resemble benign metaplastic cells. Also, glandular abnormalities are more difficult to assess.

b) Cytorich/ Surepath – Awaiting FDA approval

It uses collection technique similar to that employed by Thin Prep. Unlike thin prep, however, Cytorich is approved for use only with broom like device. Mixing the solution separates the clumps of cells. Centrifuging against a density gradient separates debris and inflammatory cells. Cells are suspended and allowed to settle onto a slide by gravity. The slide is then stained and evaluated by a cytopathologist. This process reduces the number of unsatisfactory slides and results in increased sensitivity.

Automated cytological screening-Interpretation of cervical cytology is considered to be very difficult (Richart,1995). The training programs for cytotechnologists are long, require an educated student and require a high degree of discipline and pattern recognition skills. Even after completing an adequate training program, cytotechnologists require several years of practical experience before they can make consistent diagnosis on the normality of the smears. Hence it is not surprising that false negative rates are high. Manual re-screening is possible to reduce this rate, but this comes at the expense of increased false positives, longer screening time and diminished productivity. Methods of computer assisted screening currently available -

Auto Pap screening system- has been approved by the U.S F.D. A for primary screening and rescreening of samples initially read as normal. This technique uses an automated microscope coupled to a special digital camera. The system scans

the slides and uses computer imaging techniques to analyze each field of view on the slide. Computer algorithms are then used to rank each slide on the basis of the probability that the sample may contain abnormality. It selects 10-20% of slides labeled as normal following routine screening by cytotechnologist with the highest probability of having abnormal cells. The algorithm includes a variety of visual characteristics, such as shape and optical density of the cells. The selected slides are then reviewed by a cytotechnologist or cytopathologist, for which of the cells are likely to be abnormal. This technique reduces false negative rate by 32%. It is not in widespread use. It has been shown to be superior to conventional pap test screening in identifying ASCUS, LSIL and HSIL

Pap Net- uses neural network computing technology to improve accuracy in Pap smear screening. It uses the computer to spot suspicious patterns not obvious to the naked eye and displays the abnormal cells on a high-resolution color video screen for interpretation and diagnosis by a skilled laboratory technician. Received FDA approval for the automated rescreening of Pap smears that have been read as normal.

Auto Cyte - Uses slides that are prepared by the thin layer cytology systems (Cyto Rich Method) and can screen up to 300 slides within 24 hours. For each abnormal slide, the most significant abnormal cellular features and the interpretation of each are captured, stored and processed by a series of algorithms. These images are presented to a human reviewer who then determines whether manual review is required. After the human reviewer has entered an opinion, the device reveals its determination based on a ranking as to whether manual review is warranted. When human reviewer and computer agree that no review is needed, a diagnosis of 'within normal limits' is given.

Manual review is required for any case if designated by either the cytologist or the computer ranking.

HPV DNA detection and typing

Cervical cancer and its precursor are principally, of not exclusively, by HPV infection (Schiffman 1993). The prevalence of HPV varies dramatically, depending on the age group and techniques used to detect the virus. It is much more common in the younger patients than the older. There is also recent evidence that, in many women HPV infection is transient and is cleared within the first 12 – 24 months. Therefore, in younger women, HPV infection is more a marker of sexual activity than of cervical cancer risk, whereas the persistence of HPV in older (less sexually active) is an indication of increased cervical cancer risk. Primary screening for HPV DNA in younger women may probably detect many women with cervical HPV, few of whom have significant disease. This will lead to many unnecessary colposcopic evaluations. However, in older women, in whom the prevalence of disease is lower and its significance is greater, HPV testing may offer a sensitive and specific way of detecting women at risk of developing squamous intraepithelial lesion.

Table 3:The tests for HPV

1.	PCR
2.	Hybrid capture tube test
3.	Hybrid capture II test
4.	HPV test(called the DNA with PAP)
5.	Pretest-HPV-proofer

HPV detection by PCR- PCR and southern blotting are highly sensitive and highly specific tests, can detect even a single molecule of HPV DNA. During the past 10 years, PCR has been the "gold standard" technique in HPV diagnosis. DNA is extracted by the high-salt

method. HPV DNA is detected by PCR with primer GP05+ and GP06+. Confirmation of the specificities of the PCR products is done by hybridization with digoxigenin-labeled oligonucleotide probes specific for HR HPV types. After hybridization, the positive spots on the film are graded according to the signal intensities as weak, moderate or strong. Approximately 20 copies of HPV, i.e., 20 SiHa cells mixed with 200 ng of human fibroblast DNA, give a weakly positive signal. The recognized disadvantages of PCR are its extremely high analytical sensitivity and potential for contamination, leading to false-positive results.

HPV detection by DNA test- The hybrid capture technique is based on the formation of RNA-DNA hybrids between HPV DNA that may be present in clinical specimens and complementary unlabeled HPV RNA probes. The RNA-DNA hybrids are captured and immobilized by anti-hybrid antibodies. Immobilized hybrids are reacted with a monoclonal antibody reagent that is conjugated to alkaline phosphatase, and the complexes are detected via a chemiluminescent substrate reaction. In HCT, a tube luminometer is employed, whereas in HC II, a microplate luminometer reads the light output and displays the assay results as relative light units (RLU). HPV positivity or negativity is based on comparison to a standard positive reference (RLU of a clinical specimen divided by the mean RLU of three positive calibrator references).

The HCT Probe B cocktail detects a limited number of high-risk HPV types, including HPVs 16, 18, 31, 33, 35, 45, 51, 52, and 56 and has been reported to have a diagnostic sensitivity similar to that of the Pap smear. HC II detects HPV types at an increased sensitivity compared to that of HCT. The advantage of this test is that it may provide a semi quantitative measure of viral load. It has been suggested that viral load may lend prognostic and diagnostic value

HPV detection by mRNA test- Persistent expression of E6/ E7 oncogenes could serve as an indicator of progression to cervical intraepithelial neoplasia and invasive cancer. E6/ E7 mRNA transcripts are detected by mRNA based molecular techniques and may therefore be of higher prognostic value and improve the specificity and PPV compared to HPV DNA testing in screening. Generally malignant transformation of the cervical cells is

indicated by expression of 2 to 1000 copies of HPV E6, E7 mRNA per cell. Total mRNA is extracted using the RNeasy Mini protocol. Individual identification of E6/ E7 mRNA full-length transcripts from HPV 16, 18, 31, 33 and 45 is performed with the PreTect HPV Proofer assay. Several investigators have found that among older women, the combination of a Pap smear and HPV DNA screening detects more than 95% of patients with high grade lesions, 100% with invasive cancers and 70% with low grade lesions.

One of the most promising roles of HPV testing is to determine which women with single smear showing ASCUS require colposcopic evaluation.

Advantages

• High positive predictive value (PPV)

• The ease with which the specimens can be collected even by unsophisticated medical personnel

• Does not require the extensive training that conventional cytological screening personnel must undergo

• More sensitive than unaided visual inspection of cervix

• Potential for applying it to large populations at low cost.

The use of HPV DNA testing in addition to cytology improves the sensitivity compared to HPV testing alone. According to the recommendations, HPV DNA testing can be added to cytology for screening of women over age 30 years. If results are negative for both HPV DNA and cytology, there is no need to screen again for 3 years. If the cytology is negative but the DNA test is positive, repeat screening with both cytology and HPV DNA testing is indicated in 6 – 12 months. If repeated results are positive for either cytology or HPV DNA, the clinician should proceed to colposcopy.

Pap smear

It is an in-office, non-invasive method for performing direct visual screening of examination of cervix. It has been approved by the FDA for use in all women undergoing Pap smears.

TREATMENT-

The treatment of cervical cancer depends upon the age of the patient, desirability of the woman to retain her reproductive function, the type of lesion present and the stage of the disease.

Below Table 4 gives a brief and concise overlook on the options available for treatment of cervical cancer.

Table 4: Standard Treatment Options for Cervical Cancer[73]

In situ carcinoma of the cervix (this stage is not recognized by FIGO)	Conization
	Hysterectomy for post reproductive patients
	Internal radiation therapy for medically inoperable patients
Stage IA cervical cancer	Conization
	Total hysterectomy
	Modified radical hysterectomy with lymphadenectomy
	Radical trachelectomy
	Intracavitary radiation therapy
Stages IB, IIA cervical cancer	Radiation therapy with concomitant chemotherapy
	Radical hysterectomy and bilateral pelvic lymphadenectomy with or without total pelvic radiation therapy plus chemotherapy
	Radical trachelectomy is used in stage I cervical cancer to maintain fertility
	Neoadjuvant chemotherapy is used in young women with bulky stage IB-IIB disease desiring for fertility sparing surgery
	Radiation therapy alone
	Intensity Modulated Radiation Therapy (IMRT) is used for recurrent carcinomas which spares the normal tissues
Stages IIB, III, and IVA cervical cancer	Radiation therapy with concomitant chemotherapy 1. Early stage IA2, IB, IIA after radical hysterectomy 2. As primary treatment for stage IB,

	IIA. 3. Locally advanced like stage IIB-IVA as primary therapy
	Interstitial brachytherapy A-stage IB,IIB and above if a)distorted anatomy b)narrow vagina and obliterated fornices c)loss of endocervical canal B-bulky primary disease C-bulky parametrial disease D-extensive para vaginal or distal vaginal involvement E-persistent or recurrent carcinoma cervix post EBRT and post brachytherapy F-carcinoma of cervical stump G-prior supra cervical hysterectomy H-presence of fistula and/or adjacent organ invasion
	Neoadjuvant chemotherapy A-in young women with bulky stage IB-IIB disease desiring for fertility sparing surgery B-locally advanced cervical carcinoma
Stage IVB cervical cancer	Palliative radiation therapy
	Palliative chemotherapy
Recurrent cervical cancer	Radiation therapy and chemotherapy
	Palliative chemotherapy
	Pelvic exenteration

MATERIAL AND METHODS

MATERIAL AND METHODS

METHODS OF COLLECTION OF DATA:

SOURCE OF DATA:

Prospective study of 200 women attending gynecology OPD at BLDE (DEEMED TO BE UNIVERSITY)'S, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura.

PERIOD OF STUDY: OCTOBER 2016 – AUGUST 2018

Sample size calculation

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

Where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate

A sample size of 185 (~200) were allowed for the comparison of visual inspection with acetic acid and pap smear as screening methods for premalignant lesions of cervix with 95% confidence level and margin of error of ±7% with finite population correction.

Statistical analysis

Data were represented using Mean ±SD, and analyzed by Chi square test for association, comparison of means using t test, ANOVA for comparison, sensitivity, specificity, positive predictive value and negative predictive values.

METHODS OF COLLECTION OF DATA:

Informed consent was taken from each woman. Relevant obstetrics and gynecology history was taken and recorded.

INCLUSION CRITERIA:

1. Age between 25-65 years
2. Chronic cervicitis
3. Symptoms like vaginal discharge, post coital bleeding, postmenopausal bleeding, intermenstrual bleeding and persistent leucorrhoea not responding to antibiotics.
4. Normal looking cervix but symptomatic.

EXCLUSION CRITERIA:

1. Menstrual bleeding at the time of examination
2. Cancer cervix
3. Clinical evidence of acute pelvic infection
4. Pregnancy

METHODOLOGY IN BRIEF:

METHOD-

200 patients as per the inclusion and exclusion criteria attending gynecology OPD, BLDE (Deemed To Be University)'s Shri.B.M.Patil medical college and hospital were considered for the study and patients were subjected to VIA and PAP smear and colposcopy and colposcopy assisted biopsy if necessary after taking informed consent.

Materials required-

a) Pair of sterile gloves

b) Cusco's speculum

c) Ayre's spatula

d) Clean glass slides

e) Fixative solution

Status of the hygiene of women was classified into three grades-Good, Average and Poor. This was judged by asking following questions.

Que. 1) Whether she uses sanitary pads or not?

Que. 2) Whether she takes bath daily or not?

Que. 3) Whether she uses soap during bath or not?

Que. 4) Whether she washes genitalia after urination or not?

Scoring of Status of Hygiene:

Question No.	**Yes (Score=0)**	**No (Score=1)**
Que. 1	0	1
Que. 2	0	1
Que. 3	0	1
Que. 4	0	1

Score 0 = good hygiene

Score 1-3 = average hygiene

Score 4 = poor hygiene

Method

1. Naked eye examination of the cervix done after introducing Cusco's speculum.
2. Cytologic specimen collection by using Ayre's spatula.

Procedure

When a patient who fulfilled the criteria of the study, came to the Gynaecology OPD, the procedure was explained to the patient in detail, clinical details were noted and entered into the proforma and written consent was taken.

The patient was put in dorsal position after emptying the bladder. Per speculum examination was done without using lubricants. Naked eye examination of the cervix was done to evaluate its color, shape, size, presence of any lesions, discharge. The cervical smear was then taken by means of the scrape technique using the Ayre's spatula.

The longer end of the spatula was inserted into the external os and rotated through 360° maintaining firm pressure so as to scrape the squamo-columnar epithelial junction throughout its circumference [74]. Care was taken to include all abnormal looking areas. The spatula was then withdrawn without touching the vaginal walls to avoid contamination with cells from the lower genital tract.

The smear was made by spreading the scraped material evenly, with a circular motion on a glass slide having the patient's identity labeled. It was then fixed in fixative solution, which contains 95% alcohol and ether for 15-30 minutes and then sent to the cytopathology laboratory.

The smears were stained according to modification of Papanicolaou (1942)

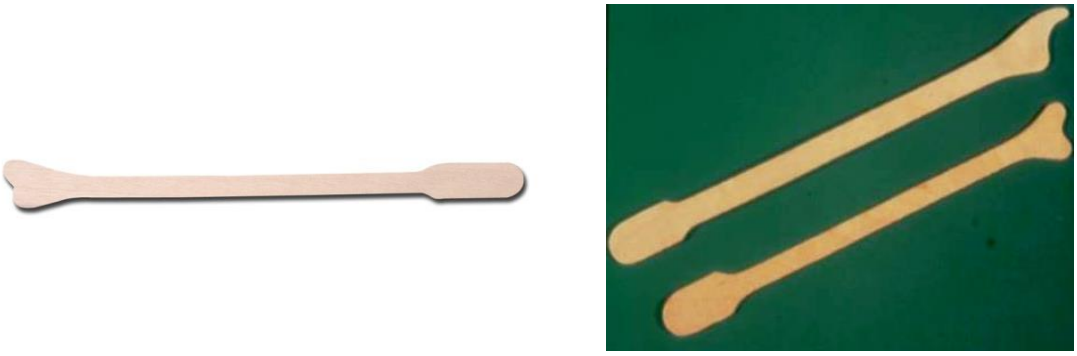


Figure 11- Ayre's Spatula

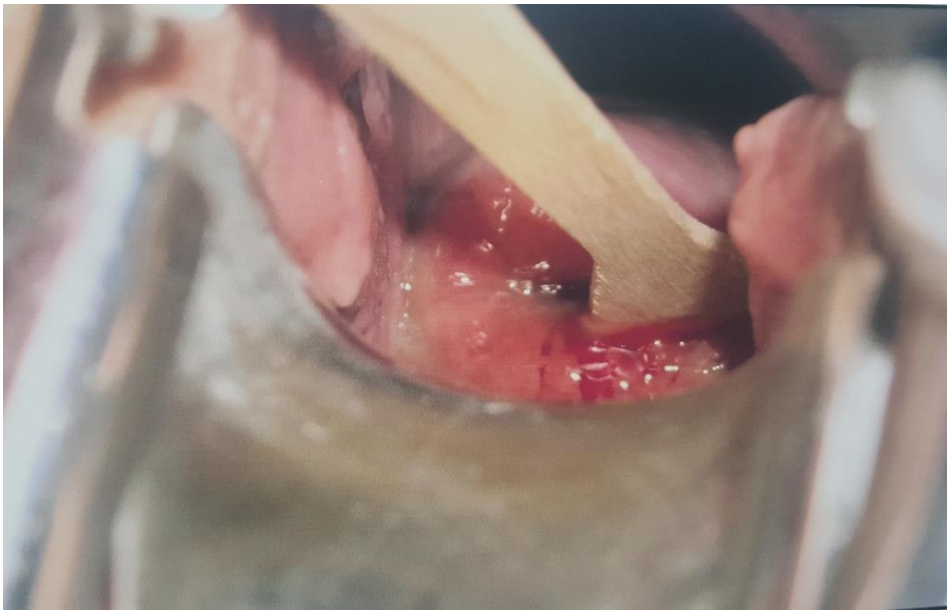


Figure 12 - Scraping technique by Ayre's spatula

Figure 13- Slide preparation of Pap smear

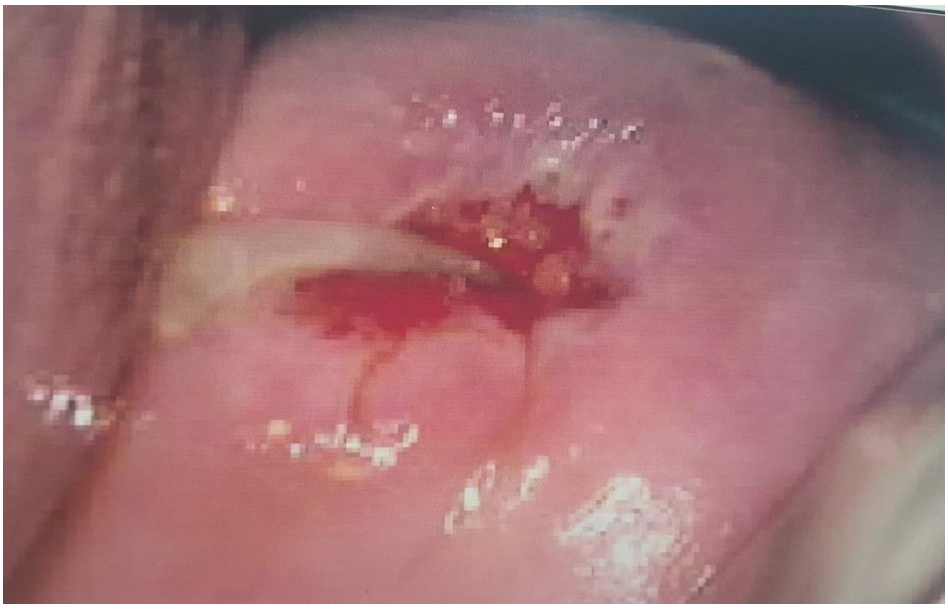


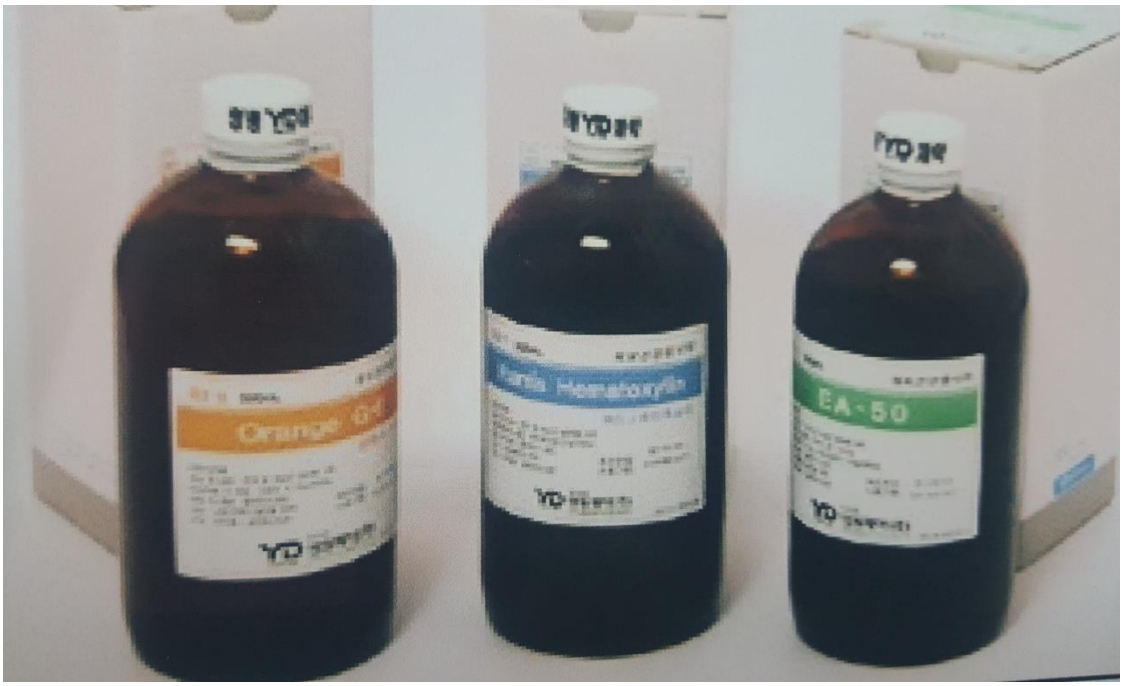
Figure 14 – cervical erosion

Procedure

1. Transfer the slides directly into the fixative without delay after taking smear to 90%, 70%, 50% alcohol – 2 min, each.
2. Rinse in water – 1 min.
3. Stain with Harris Hematoxylin – 5 min.
4. Rinse in water – 2 min
5. Differentiate in 0.5% aqueous HCL – 10 sec approximately
6. Rinse in water – 2 min
7. 'Blue' in Scott's tap water substitute – 2 min
8. Rinse in water – 2 min
9. Dehydrate in 50%, 70%, 80% alcohol – 2 min each
10. Stain in Orange G6 – 2 min
11. Rinse in 95% alcohol – 2 min
12. Stain in EA 50 – 3 min
13. Rinse in 95% alcohol – 1 min
14. Clean in Xylol, 3 changes – 10 dips
15. Mount in Distrene 80 Dibutyl Phosphate Xylene (DPX)

The smears were classified as per Bethesda System (2001) [75][76]

Figure 15 - Pap stains used



Pap smear results were considered as positive (abnormal) when they are ASCUS and more (LSIL, HSIL, Invasive lesion). The plan was to evaluate these women further by cervical punch biopsy where a portion of cervix was taken and the tissue was then processed and viewed under microscope.

All patients with inflammatory smear and unhealthy cervix were treated with a course of oral antibiotics (Doxycycline 100mg BD, Metronidazole 400mg BD) for a period of 2 weeks. On persistence of unhealthy cervix and inflammatory smear on Pap smear- direct cervical punch biopsy was taken.

PAP SMEAR:

METHOD -

Patient was put in dorsal position. Labia parted and the Cusco's self-retaining speculum will be introduced without the use of lubricant or jellies. Cervix was exposed. The squamo-columnar junction was scraped with Ayer's spatula by rotating the spatula all around The scrapings are evenly spread onto glass slide, and immediately fixed by dipping the slide in the jar containing equal parts 95% ethanol.

BETHESDA SYSTEM OF CYTOLOGY REPORTING-

1. Squamous cell abnormalities

a. Atypical squamous cells(ASC)

- Ascus – atypical cells of undetermined significance
- ASC- H – cannot rule out high- grade lesion

b. Low – grade squamous intra epithelial lesion (LSIL)- includes CIN 1

c. HIGH –grade squamous intraepithelial lesion (HSIL) includes CIN 2, 3

d. Squamous cell carcinoma

2. Glandular abnormalities

a. Atypical glandular cells

b. Adenocarcinoma in situ

c. Adenocarcinoma

3. Other malignant neoplasms.

VISUAL INSPECTION WITH ACETIC ACID AND COLPOSCOPY-

After taking the cytology specimen, the cervix was painted with a cotton wool soaked in 5% acetic acid, wait for two minutes. The cervix was examined after 2 minutes for acetowhite reaction. Suspicious or visible lesions were noted and subjected for colposcopy and colposcopy guided biopsy. **Information Agency for Research on Cancer (IARC) guidelines for reporting VIA test results**[76].

Positive VIA test:

a. Sharp, distinct, well defined, dense acetowhite areas with or without raised margins, abutting the squamo-columnar junction

b. Strikingly dense acetowhite areas in the columnar epithelium

c. Condyloma and leukoplakia occurring closer to the squamo-columnar junction turning intensely white after application of acetic acid

Negative VIA test:

a. No acetowhite lesion observed on the cervix

b. Polyps protruding from the cervix with bluish-white areas

c. Nabothian cysts appearing as button like areas or as whitish acne or pimples

d. Faint line-like or ill-defined aceto-whitening at the squamo-columnar junction

e. Dotted areas in the endocervix

f. Shiny, pinkish, cloudy, bluish-white lesions, faint patchy lesions or doubtful lesions with ill-defined, indefinite margins blending with the rest of the cervix.

g. Angular, irregular, digitalizing acetowhite lesions resembling geographical regions far away from the transformation zone (satellite lesions)

h. Streak-like aceto-whitening in the columnar epithelium

i. When red spots are observed in the cervix against a pinkish-white hue

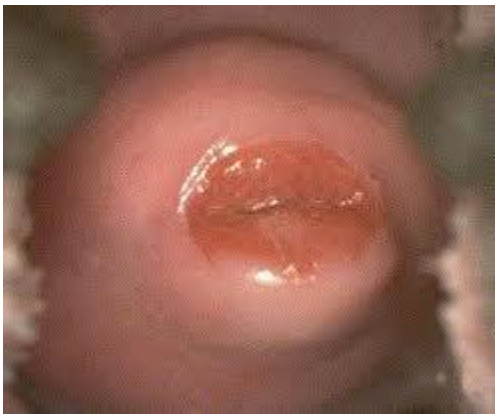


Figure 16- Normal- Negative VIA

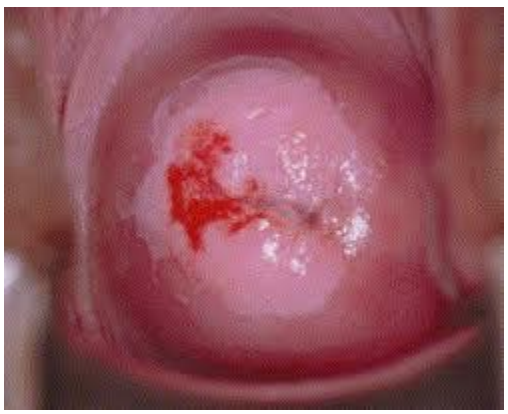
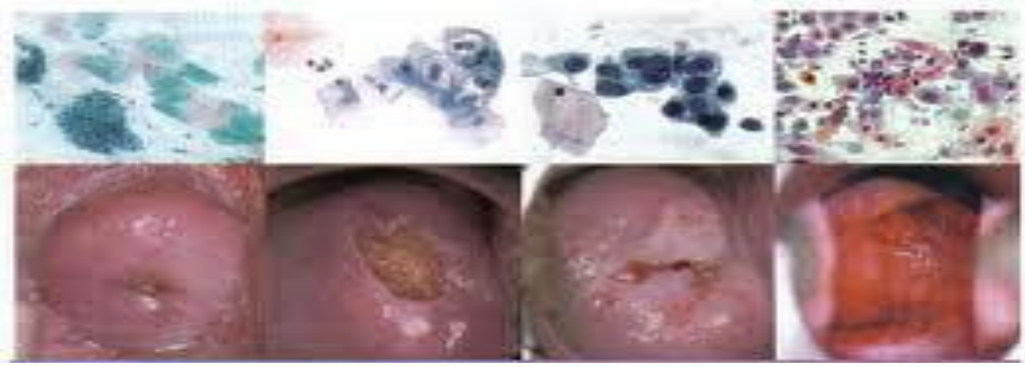


Figure 17- Positive VIA



Transient infection Persistent HPV

Figure 18-HPV

COLPOSCOPY FINDINGS

- The findings include major and minor details of lesion, transformation zone and squamo-columnar junction demarcation, biopsy sight, and imprints of vascular pattern after application of acetic acid.
- Biopsy details.

At colposcopy the 200 cases were categorized into 5 groups [97]

- Normal (N)
- Unsatisfactory
- CIN-I, II, III
- Invasive cancer
- Others (inflammation, ulcer etc.)

After histological examination they were finally grouped into: [98]

- Normal (N)
- Changes consistent with repairs
- CIN-I, II, III
- Micro invasive cancer
- Invasive cancer.

Colposcopy:

In all women colposcopy was done. Colposcopy was performed using normal saline, green filter and acetic acid. Findings were recorded and colposcopy diagnosis was made based on Modified Reid Colposcopic Index (RCI) [69]. Ried et al (1983) defined three objective categories based on colposcopic index using four colposcopic signs i.e. colour, margin (including surface contour) and vascular pattern Each category is offered scores of 0 to 2.

Summation of scores is done.

Scores of 0-2: Predictive of minor lesion (CIN1 or HPV)

3-5: Middle grade lesion (CIN1 – II)

6-8: Significant lesion (CIN II – III)

Table 5: Combined colposcopic index [70]

Colposcopic sign	0(zero)	1(one)	2(two)
Margin	Condylomatous or micropapillary contour, indistinct aceto-whitening, flocculated or feathered margins. Angular jagged lesions. Satellite lesions and aceto-whitening beyond the transformation zone.	Regular lesions with straight outlines	Rolled peeling edges. Internal demarcation between areas of differing appearance
Colour	Shiny, snow-white color, indistinct aceto-whitening	Intermediate shade (shiny gray)	Dull oyster white
Vessels	Fine- caliber vessels, poorly formed patterns	No abnormal vessel	Definite punctations and mosaicism
Iodine	Positive iodine uptake	Partial iodine	Negative staining of significant lesion

Figure 19: Colposcope

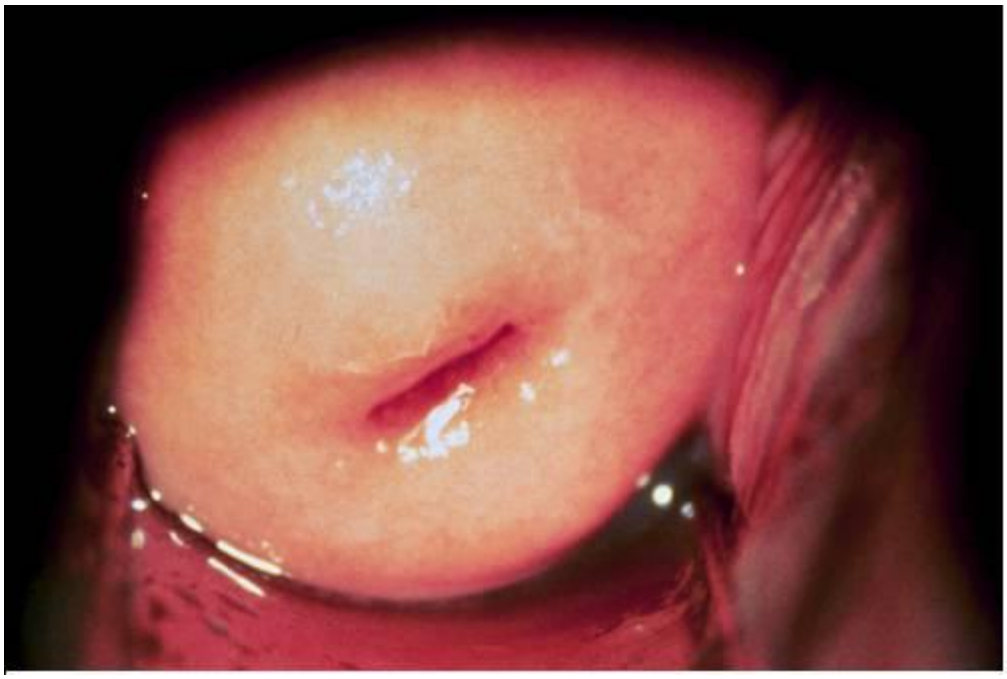


Figure 20: Normal cervix

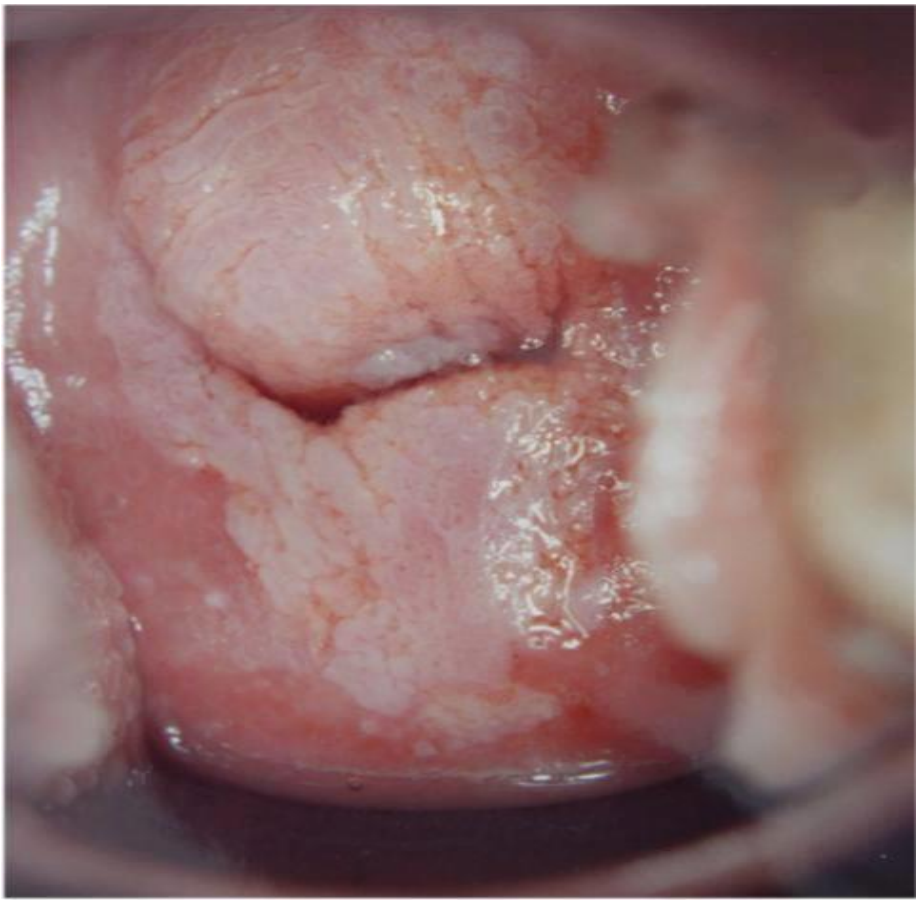


Figure 21: Sharp, distinct, well-defined, dense acetowhite areas with or without raised margins abutting the squamocolumnar junction (HSIL)

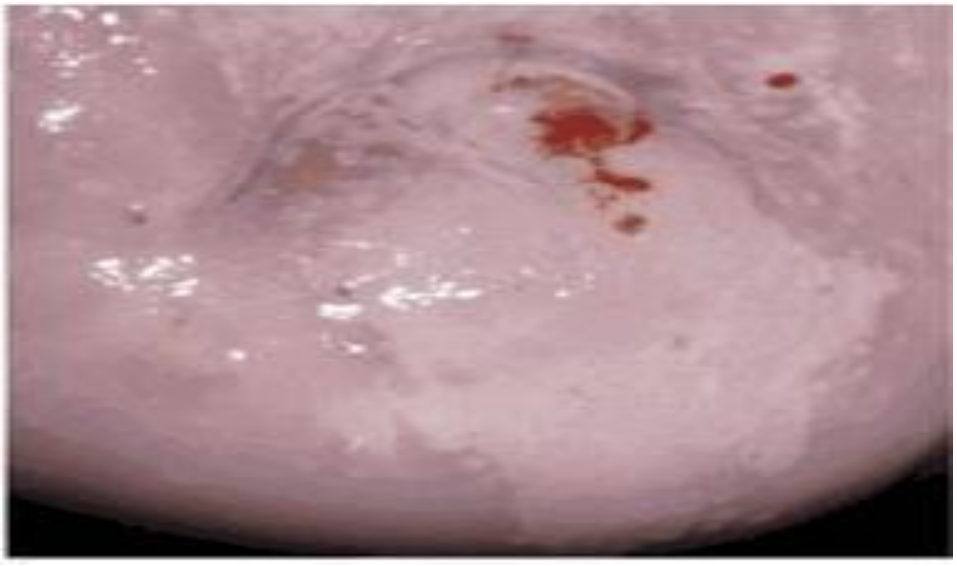


Figure 22: Strikingly dense acetowhite areas (LSIL)

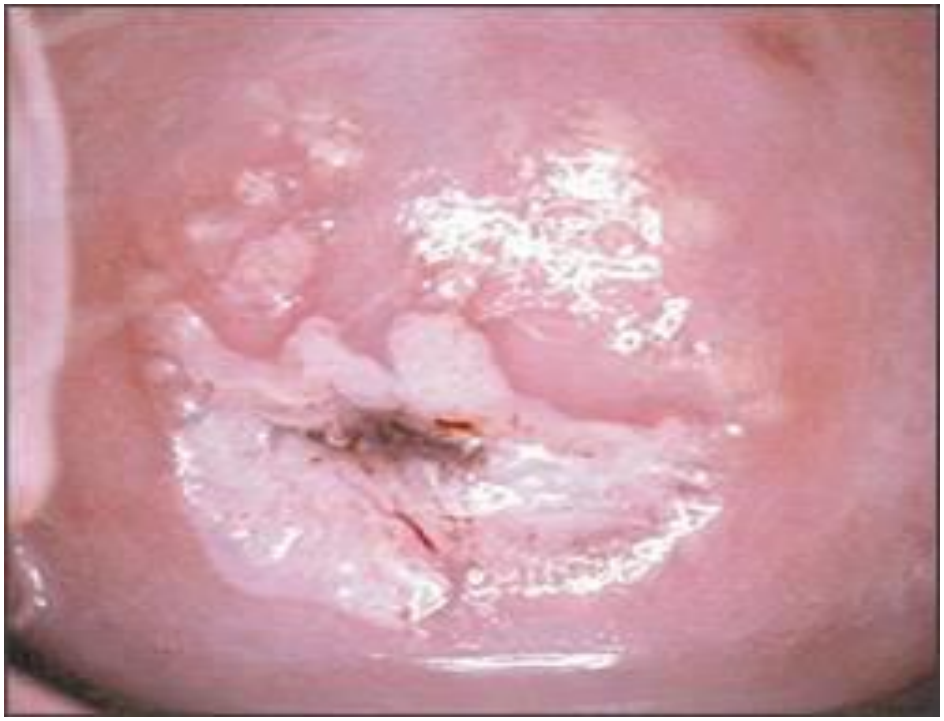


Figure 23: Strikingly dense acetowhite areas in the columnar epithelium

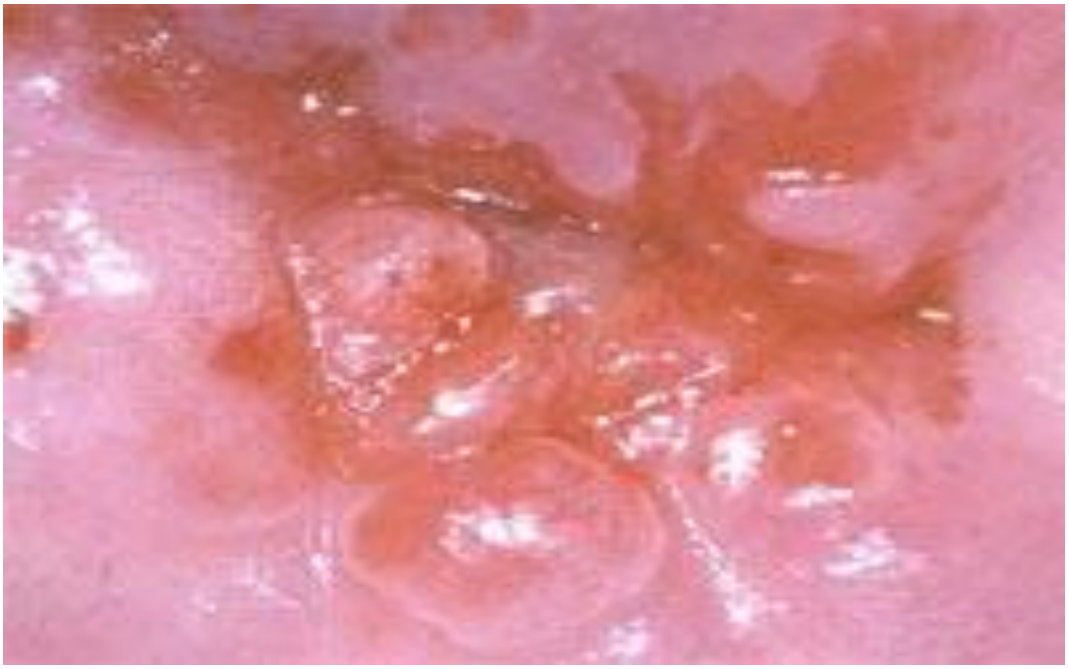


Figure 24: Strikingly dense acetowhite areas with atypical vascular pattern (HSIL)

Colposcopic guided biopsy:

Biopsy was taken from abnormal area under colposcopy guidance using cervical punch biopsy forceps. Four quadrant biopsies were taken from ectocervix at the squamocolumnar junction, if no abnormality was detected on colposcopy. The specimen was sent for histopathological examination in formalin solution. Slides were analyzed by senior consultant pathologist. Biopsy results were categorized as

1. Cervicitis/ metaplasia
2. CIN-1 (mild dysplasia/ correlating with LSIL)
3. CIN-2/3 (moderate to severe dysplasia/ correlating with HSIL)
4. Squamous cell carcinoma

OBSERVATIONS

AND

RESULTS

RESULTS

The study was performed on 200 women who attended the Department of Obstetrics and Gynaecology at Shri B.M.Patil Medical College & Research Hospital, Vijayapura. The objectives of the study were to correlate the findings in women using, PAP smear, visual inspection aided by acetic acid test (VIA), colposcopy and colposcopic directed biopsies wherever necessary, in detecting the premalignant lesions of the cervix and to find the efficacy of individual tests. The detailed analysis of the study conducted and the results are computed together after all the tests were employed to arrive at a conclusion.

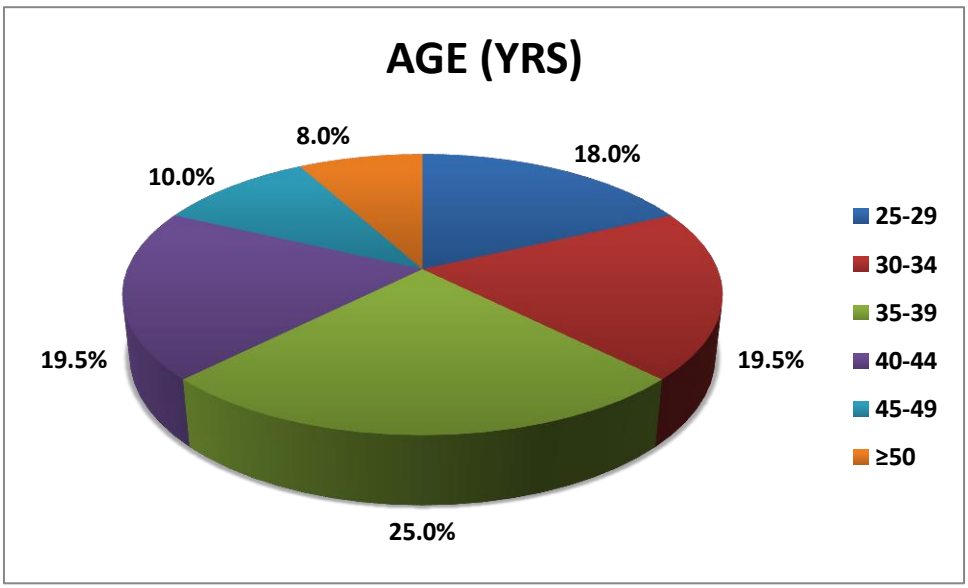
1. Age distribution

The 200 women who were in the study group belonged to the age group of 25-65 years. The Table 1 and the Graph 1 shows age wise distribution of cases. Maximum number of cases were in the age group of 35-39 years i.e.50 cases (25%). The mean age was 36.73 years.

TABLE: 6 DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (YRS)	N	%
25-29	36	18
30-34	39	19.5
35-39	50	25
40-44	39	19.5
45-49	20	10
≥50	16	8
Total	200	100

GRAPH 1: DISTRIBUTION OF CASES ACCORDING TO AGE



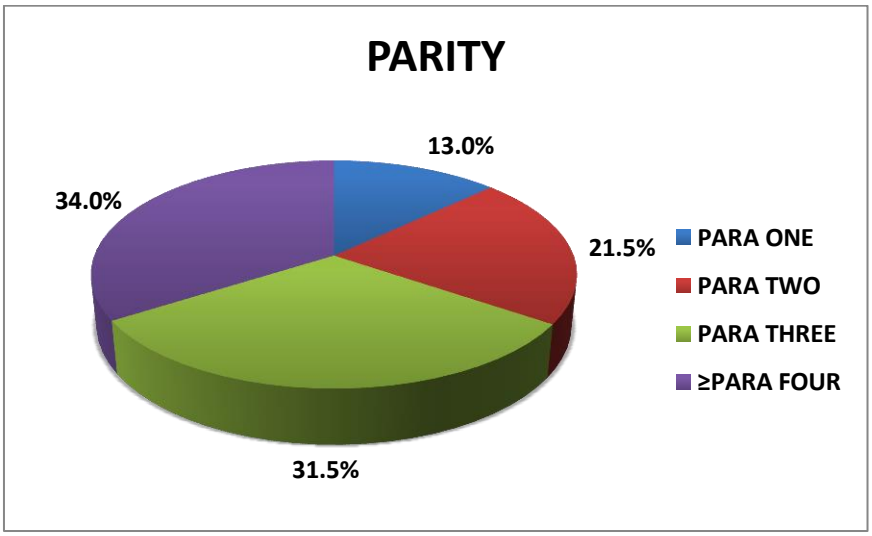
2. According to parity

The women in the study group were para one to grand multipara. Majority of study group were in para 3 (31.5%) and ≥ para 4 (34%) group.

TABLE: 7 DISTRIBUTION OF CASES ACCORDING TO PARITY

PARITY	N	%
PARA ONE	26	13
PARA TWO	43	21.5
PARA THREE	63	31.5
≥PARA FOUR	68	34
Total	200	100

GRAPH 2: DISTRIBUTION OF CASES ACCORDING TO PARITY



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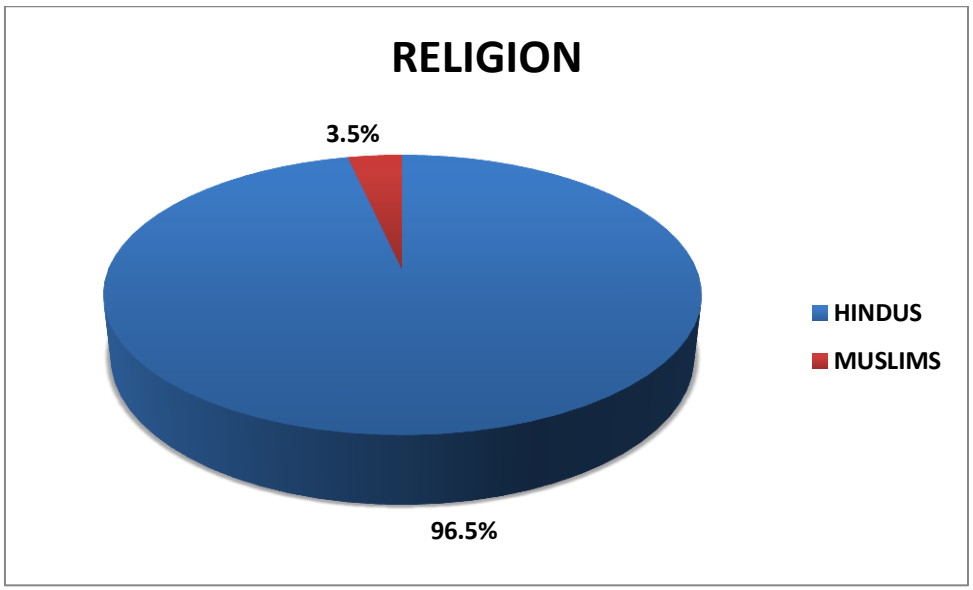
3. According to religion

Hindus were 96.5%while 3.5 % of patients were Muslims

TABLE: 8 DISTRIBUTION OF CASES ACCORDING TO RELIGION

RELIGION	N	%
HINDUS	193	96.5
MUSLIMS	7	3.5
Total	200	100

GRAPH: 3 DISTRIBUTION OF CASES ACCORDING TO RELIGION



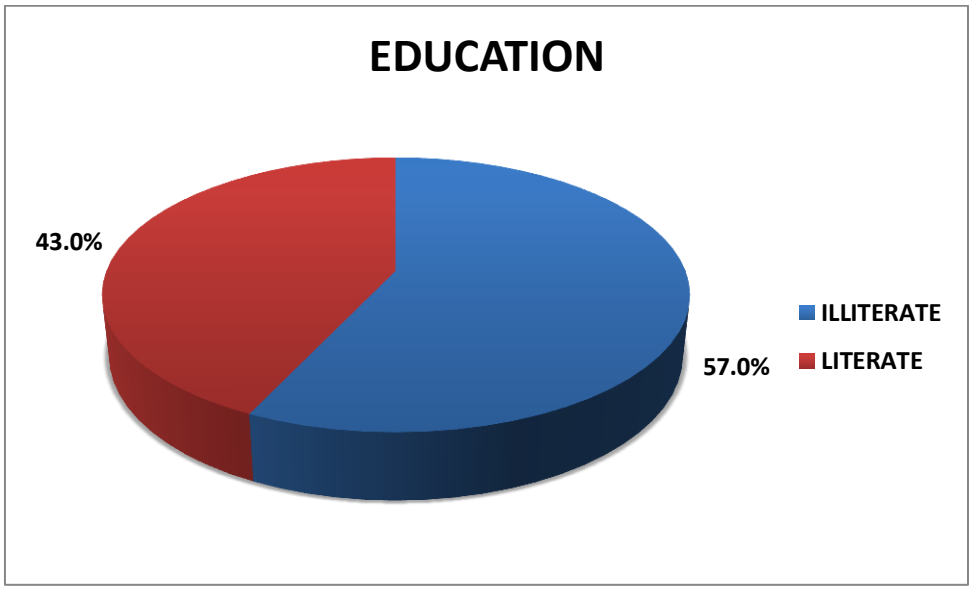
4. According to education

Out of 200 cases, 86 were literate and 114 cases were illiterate.

TABLE: 9 DISTRIBUTION OF CASES ACCORDING TO EDUCATION

EDUCATION	N	%
ILLITERATE	114	57
LITERATE	86	43
Total	200	100

GRAPH: 4 DISTRIBUTION OF CASES ACCORDING TO EDUCATION



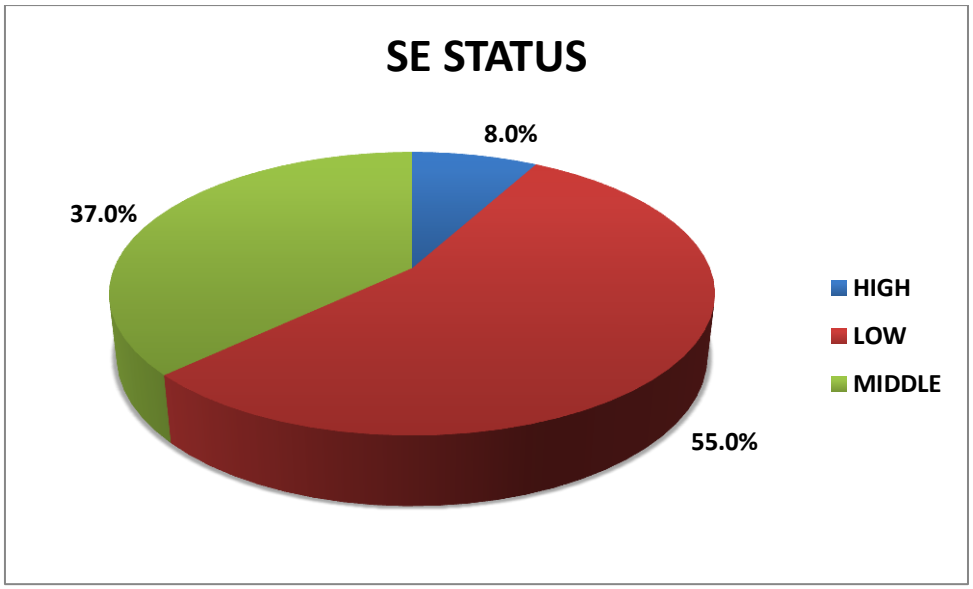
5. According to Socioeconomic status

Out of 200 cases, 110 cases were from low SE status.

TABLE: 10 DISTRIBUTION OF CASES ACCORDING TO SE STATUS

SE STATUS	N	%
HIGH	16	8
LOW	110	55
MIDDLE	74	37
Total	200	100

GRAPH: 5 DISTRIBUTION OF CASES ACCORDING TO SE STATUS

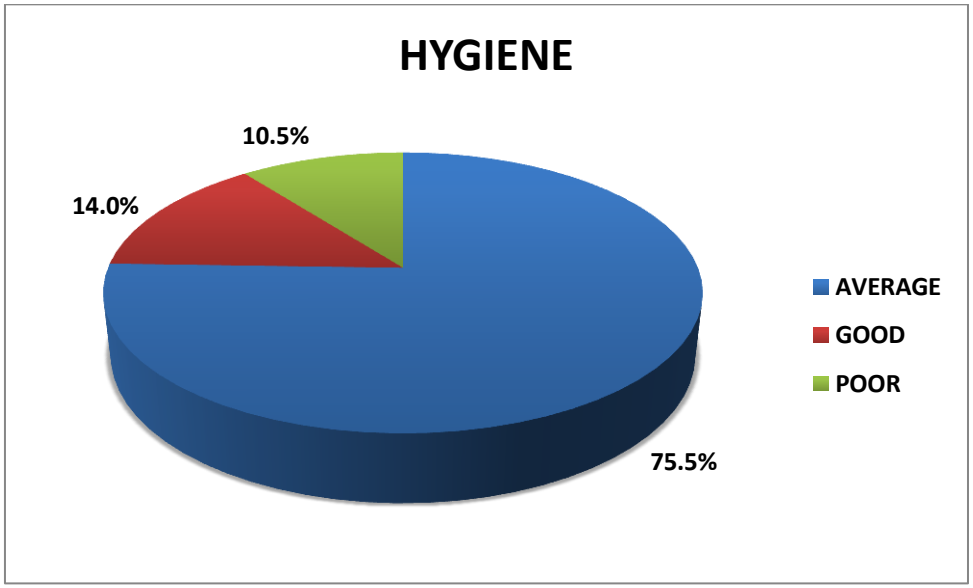


6. According To Hygiene

TABLE: 11 DISTRIBUTION OF CASES ACCORDING TO HYGIENE

HYGIENE	N	%
AVERAGE	151	75.5
GOOD	28	14
POOR	21	10.5
Total	200	100

GRAPH: 6 DISTRIBUTION OF CASES ACCORDING TO HYGIENE

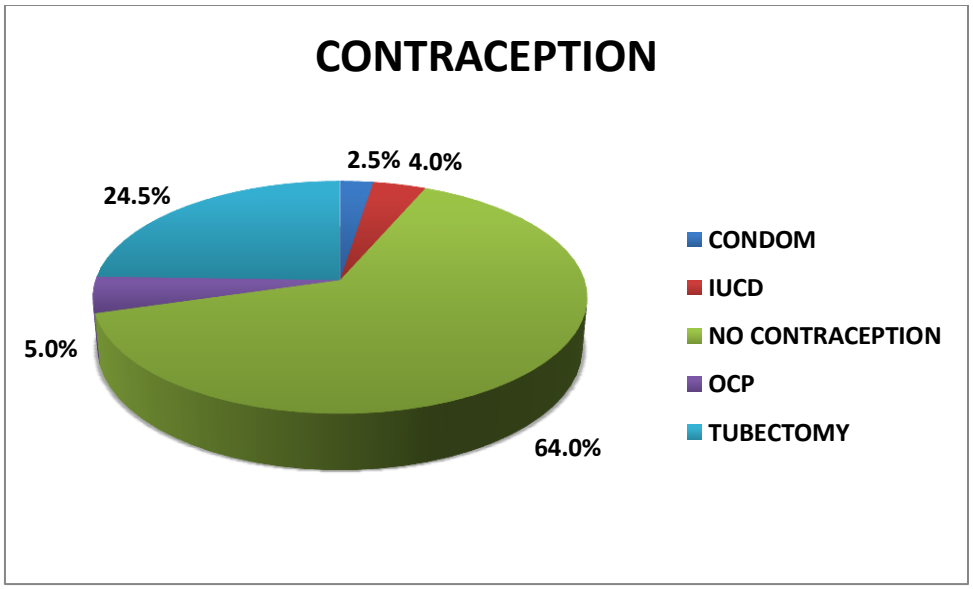


7. According to contraception

TABLE: 12 DISTRIBUTION OF CASES ACCORDING TO CONTRACEPTION

CONTRACEPTION	N	%
CONDOM	5	2.5
IUCD	8	4
NO CONTRACEPTION	128	64
OCP	10	5
TUBECTOMY	49	24.5
Total	200	100

GRAPH : 7 DISTRIBUTION OF CASES ACCORDING TO CONTRACEPTION



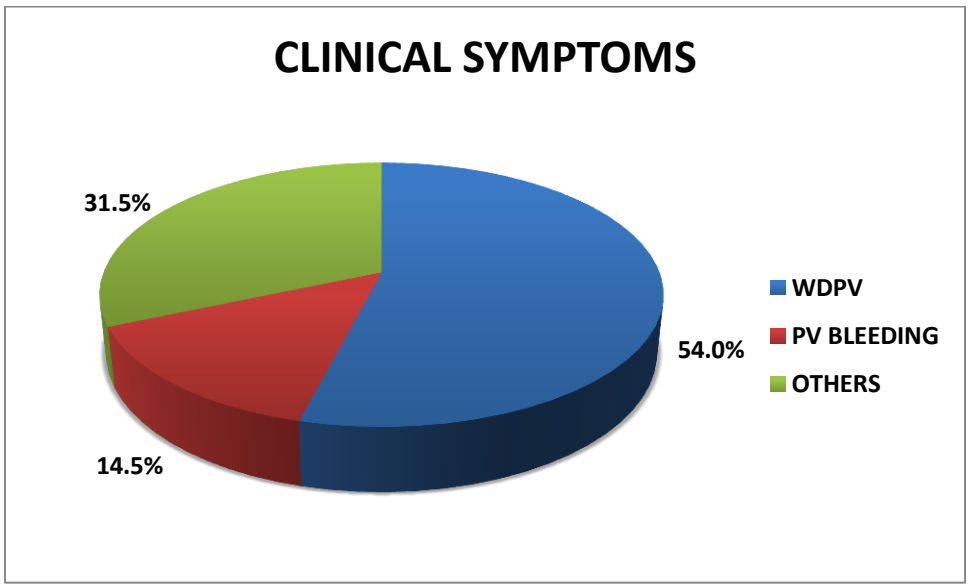
8. According to clinical symptoms

The women in the study group presented with symptoms of white discharge per vagina, per vaginal bleeding (post coital bleeding, inter menstrual bleeding, post-menopausal bleeding), pain abdomen and backache. The Table 8 and Graph 8 shows the various symptoms with which the patients presented and the distribution of cases with each of the symptoms. The commonest symptom was white discharge per vagina

TABLE: 13 DISTRIBUTION OF CASES ACCORDING TO CLINICAL SYMPTOMS

CLINICAL SYMPTOMS	N	%
WDPV	108	54
PV BLEEDING	29	14.5
OTHERS	63	31.5
Total	200	100

GRAPH 8: DISTRIBUTION OF CASES ACCORDING TO CLINICAL SYMPTOMS



WDPV- White discharge per vagina

Per Vaginal bleed

Others (pain abdomen, backache)

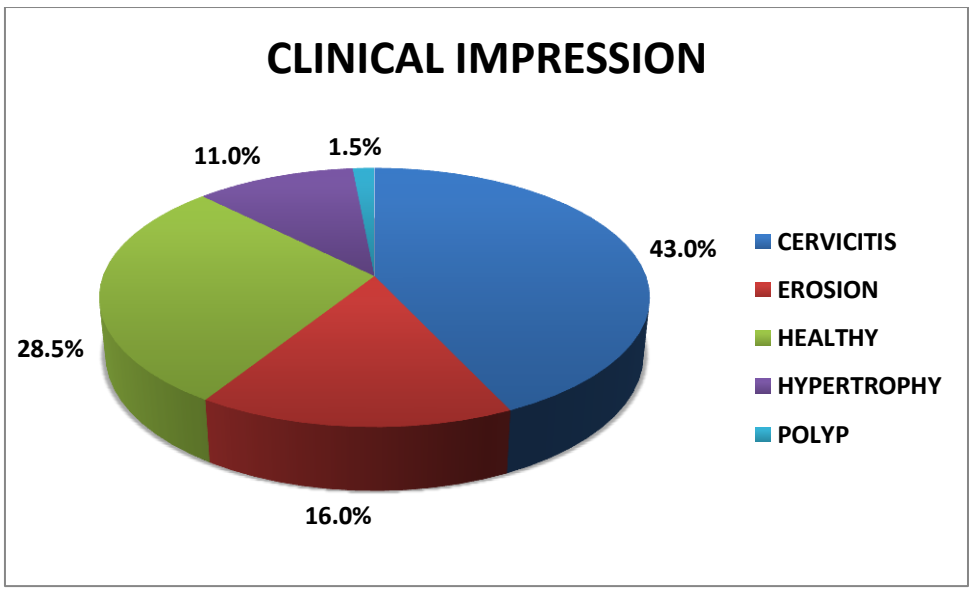
9. According to clinical impression

The maximum number of cases had cervical erosion (43%) followed by healthy cervix (28.5%).The women recruited for the study were subjected to visual inspection aided by acetic acid (VIA), where in 3-5% of dilute acetic acid was applied to the cervix and observed by naked eyes. Test was considered positive result by the presence of acetowhite area and the others negative. The Table 4 and Graph 4 show the number of positive and negative cases on VIA..

TABLE 14: DISTRIBUTION OF CASES ACCORDING TO CLINICAL IMPRESSION

CLINICAL IMPRESSION	N	%
CERVICITIS	86	43
EROSION	32	16
HEALTHY	57	28.5
HYPERTROPHY	22	11
POLYP	3	1.5
Total	200	100

GRAPH:9 DISTRIBUTION OF CASES ACCORDING TO CLINICAL IMPRESSION



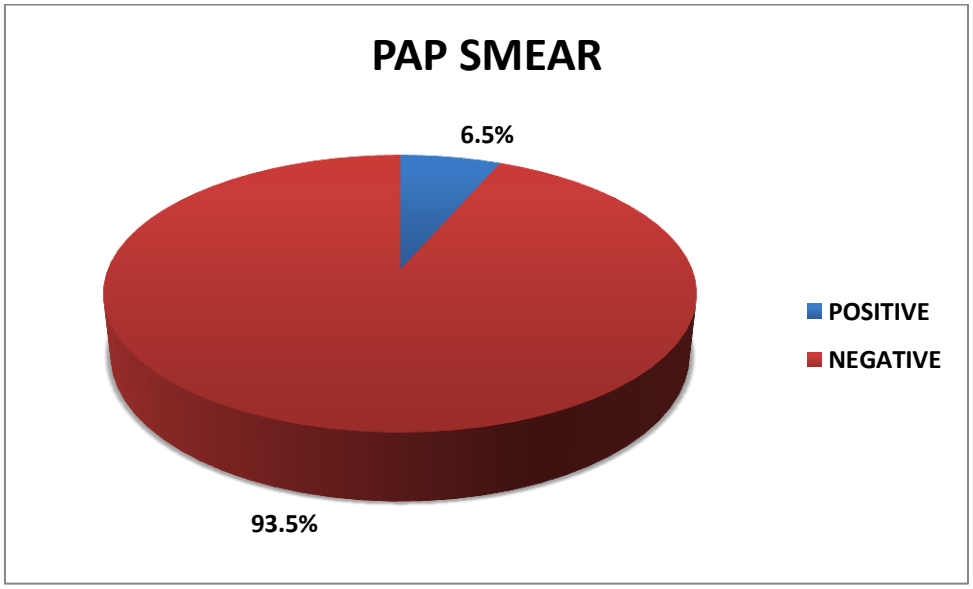
10. According to PAP smear

Out of 200 cases, 13 had positive PAP smear findings

TABLE: 15 DISTRIBUTION OF CASES ACCORDING TO PAP SMEAR

PAP SMEAR	N	%
POSITIVE	13	6.5
NEGATIVE	187	93.5
Total	200	100

GRAPH: 9 DISTRIBUTION OF CASES ACCORDING TO PAP SMEAR



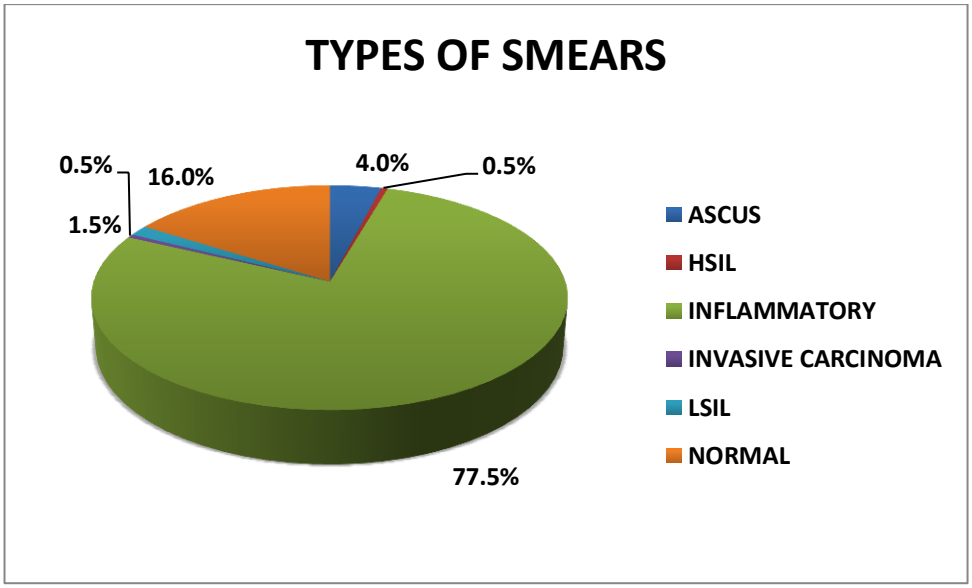
11. According to type of smear

Normal smears in 16.0% patients, Inflammatory smears in 77.50%, ASCUS in 4%, LSIL in 1.5%, HSIL in 0.5% and Invasive Carcinoma in 0.5% patients.

TABLE: 16 DISTRIBUTION OF CASES ACCORDING TO TYPES OF SMEARS

TYPES OF SMEARS	N	%
ASCUS	8	4
HSIL	1	0.5
INFLAMMATORY	155	77.5
INVASIVE CARCINOMA	1	0.5
LSIL	3	1.5
NORMAL	32	16
Total	200	100

GRAPH: 11 DISTRIBUTION OF CASES ACCORDING TO TYPES OF SMEARS



12. According to VIA

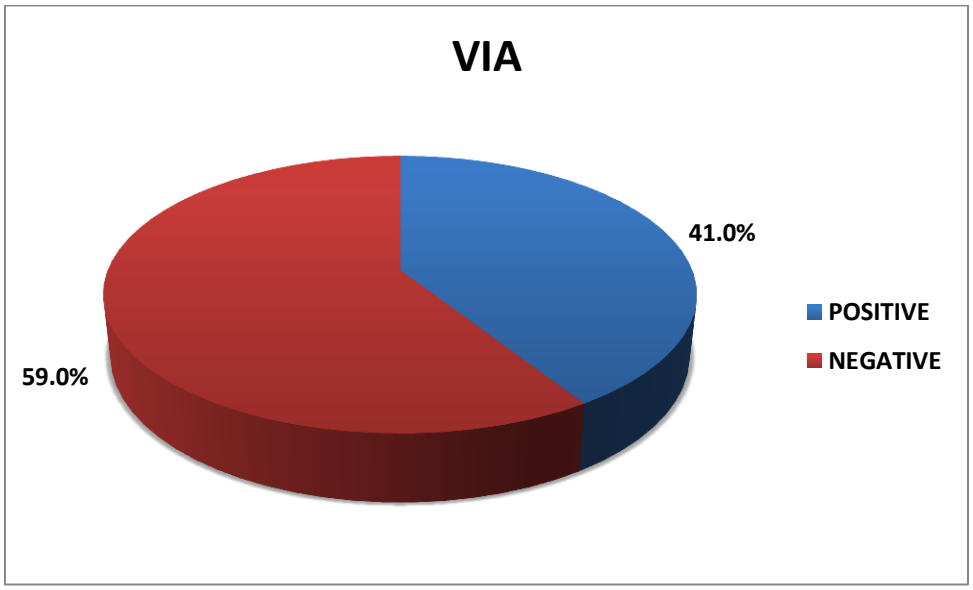
82 women out of 200 had a positive result and 118 out of 200 had a negative result on VIA.

Examination of cervix by Colposcopy is the gold standard screening method used in the study. All the cases were subjected to colposcopy examination.

TABLE: 17 DISTRIBUTION OF CASES ACCORDING TO VIA

VIA	N	%
POSITIVE	82	41
NEGATIVE	118	59
Total	200	100

GRAPH: 12 DISTRIBUTION OF CASES ACCORDING TO VIA



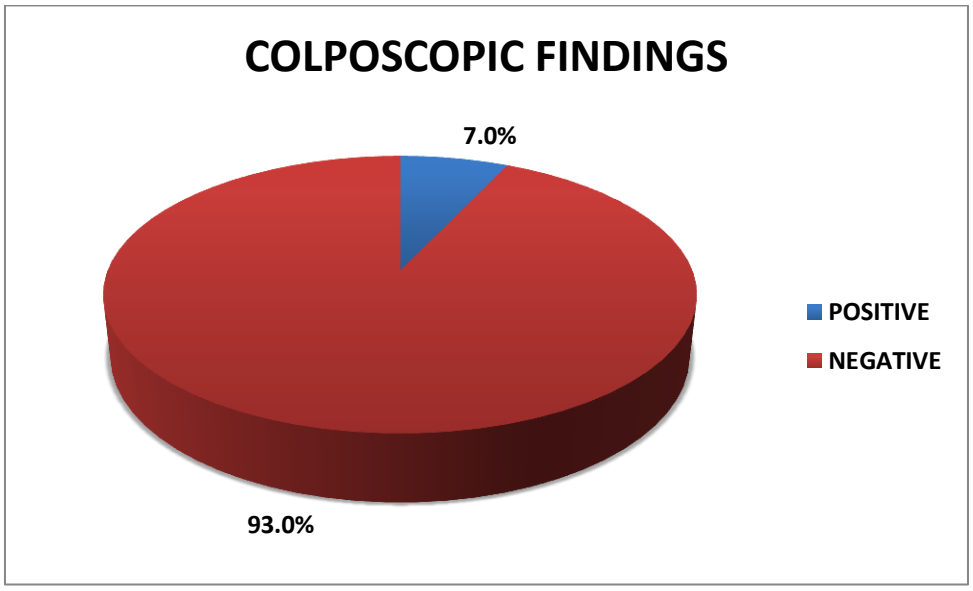
13. According to colposcopic findings

On Colposcopy 14 women were found to have a positive result (7%) and the remaining were normal. Colposcopy was considered positive if it revealed lesions of hazy acetowhite and dense acetowhite areas. Among the 14 women with abnormal colposcopies there were 8 cases of hazy acetowhite areas, 6 cases of dense acetowhite areas.

TABLE: 18 DISTRIBUTION OF CASES ACCORDING TO COLPOSCOPIC FINDINGS

COLPOSCOPIC FINDINGS	N	%
POSITIVE	14	7
NEGATIVE	186	93
Total	200	100

GRAPH: 13 DISTRIBUTION OF CASES ACCORDING TO COLPOSCOPIC FINDINGS



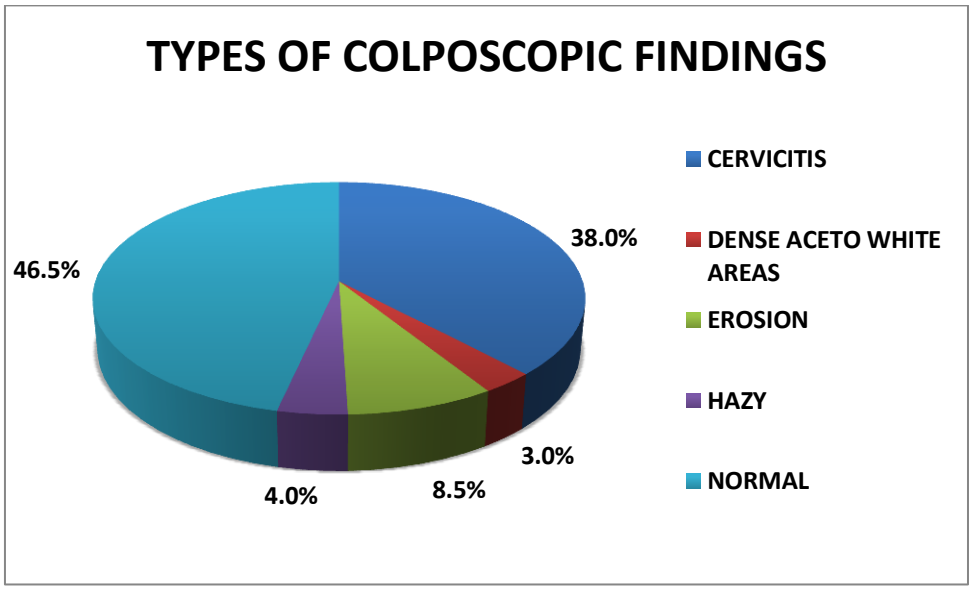
14. According to types of colposcopic findings

Out of 200 cases 46.5% were normal, 38% had cervicitis, 8.5 % had erosion, 4 % had hazy aceto white areas and 3% dense aceto white areas.

TABLE: 19 DISTRIBUTION OF CASES ACCORDING TO TYPES OF COLPOSCOPIC FINDINGS

TYPES OF COLPOSCOPIC FINDINGS	N	%
CERVICITIS	76	38
DENSE ACETO WHITE AREAS	6	3
EROSION	17	8.5
HAZY	8	4
NORMAL	93	46.5
Total	200	100

GRAPH: 14 DISTRIBUTION OF CASES ACCORDING TO TYPES OF COLPOSCOPIC FINDINGS



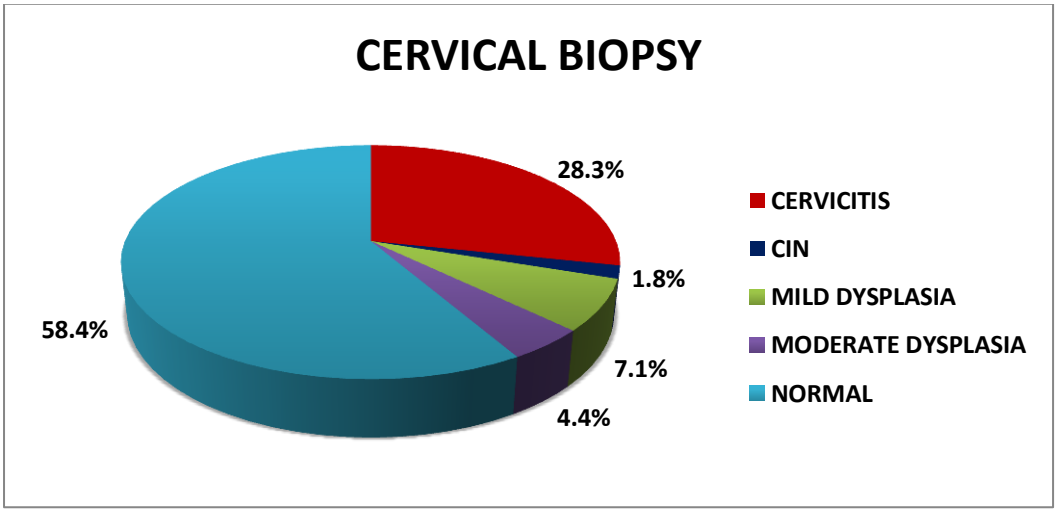
15. According to cervical biopsy

In our study, out of 200 cases, 113 had abnormal cervical findings, and were subjected to punch biopsy. 58.4% were normal,28.3% had cervicitis,7.1 % had mild dysplasia,4.4 % had moderate dysplasia and 1.8 % were CIN.

TABLE:20 DISTRIBUTION OF CASES ACCORDING TO CERVICAL BIOPSY

CERVICAL BIOPSY	N	%
CERVICITIS	32	28.3
CIN	2	1.8
MILD DYSPLASIA	8	7.1
MODERATE DYSPLASIA	5	4.4
NORMAL	66	58.4
Total	113	100.0

GRAPH: 15 DISTRIBUTION OF CASES ACCORDING TO CERVICAL BIOPSY



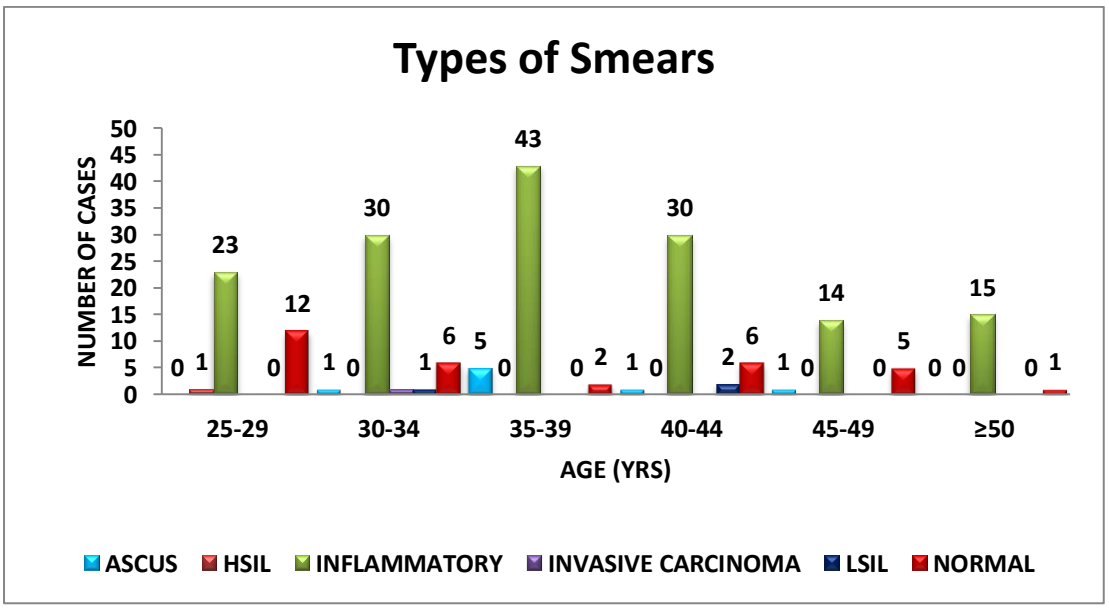
16. Association of type of smears and age

Majority of normal smears were seen in 25-29 years (37.5%), 35-39 years predominantly had inflammatory smears (27.7%). ASCUS 35-39 years with 62.5 % whereas HSIL and Malignancy was found in 25-29 and 30-34 respectively (No statistical significance was noted in association of age group with cytology report)

TABLE: 21 ASSOCIATION OF TYPE OF SMEARS AND AGE

AGE (YRS)999	Types of Smears												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
25-29	0	0	1	100.0	23	14.8	0	0.0	0	0.0	12	37.5	0.064
30-34	1	12.5	0	0.0	30	19.4	1	100.0	1	33.3	6	18.8	
35-39	5	62.5	0	0.0	43	27.7	0	0.0	0	0.0	2	6.3	
40-44	1	12.5	0	0.0	30	19.4	0	0.0	2	66.7	6	18.8	
45-49	1	12.5	0	0.0	14	9.0	0	0.0	0	0.0	5	15.6	
≥50	0	0	0	0.0	15	9.7	0	0.0	0	0.0	1	3.1	
Total	8	100	1	100.0	155	100.0	1	100.0	3	100.0	32	100.0	

GRAPH:16 ASSOCIATION OF TYPE OF SMEARS AND AGE



17. Association of type of smears and parity

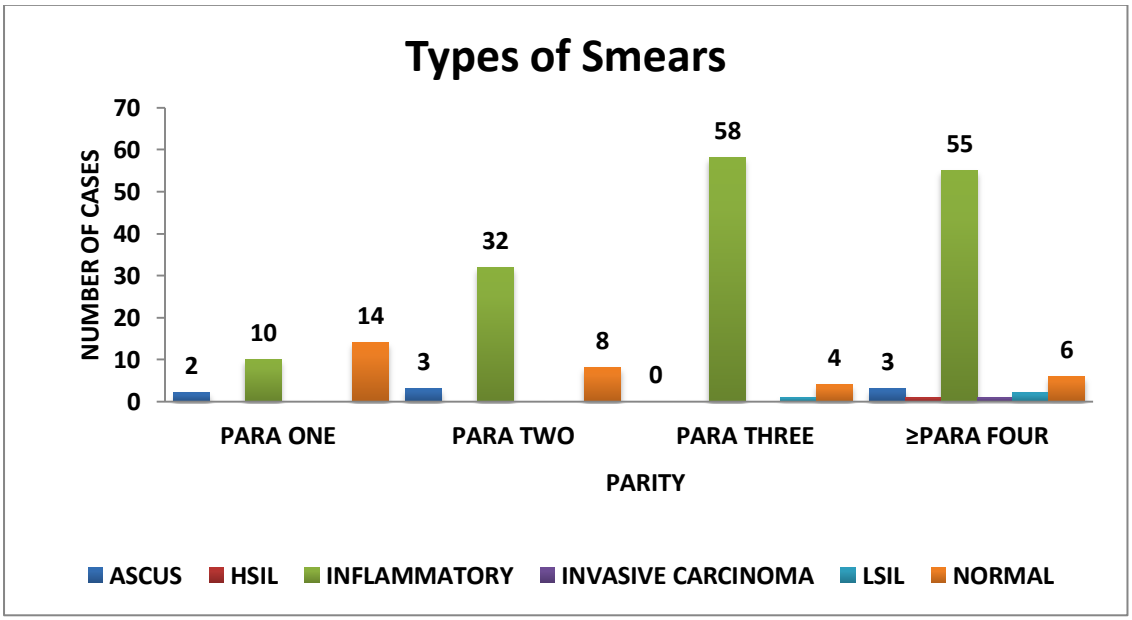
There is a significant association with parity and type of smear. The above table shows majority of para one women having normal smear (43.8%), patients with parity three showing inflammatory smears (37.4%), ASCUS in parity two and ≥4 (37.5% respectively), LSIL and HSIL in parity ≥4 (66.7%and 100% respectively) and Malignancy in parity ≥4(100%).

TABLE: 22 ASSOCIATION OF TYPE OF SMEARS AND PARITY

PARITY	Types of Smears												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
PARA ONE	2	25.0	0	0.0	10	6.5	0	0.0	0	0.0	14	43.8	
PARA TWO	3	37.5	0	0.0	32	20.6	0	0.0	0	0.0	8	25.0	
PARA THREE	0	0.0	0	0.0	58	37.4	0	0.0	1	33.3	4	12.5	<0.001*
≥PARA FOUR	3	37.5	1	100.0	55	35.5	1	100.0	2	66.7	6	18.8	
Total	8	100.0	1	100.0	155	100.0	1	100.0	3	100.0	32	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 17 ASSOCIATION OF TYPE OF SMEARS AND PARITY



18.Association of type of smears and clinical symptoms

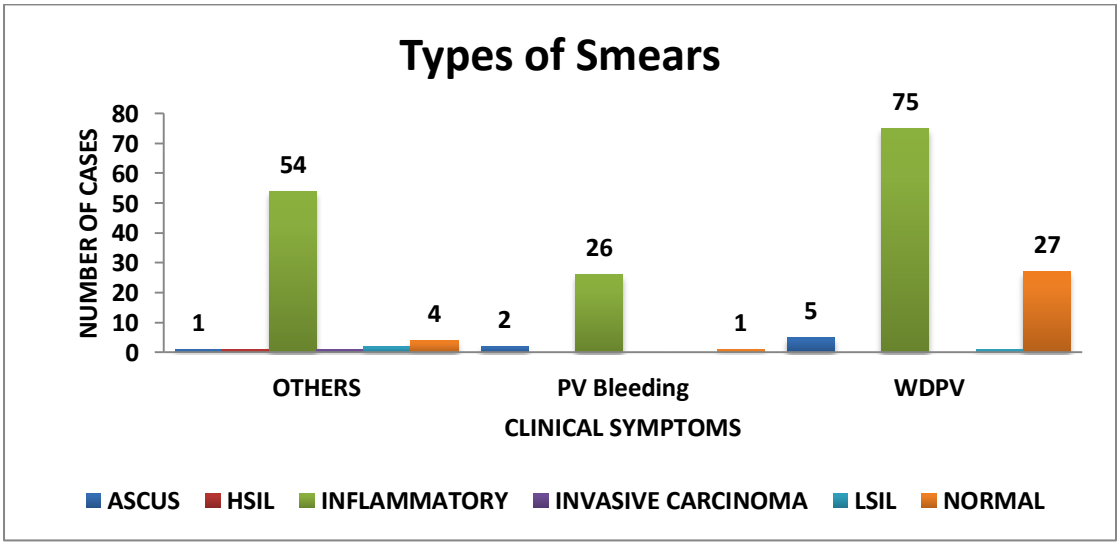
Majority of normal smears were predominant in white discharge per vagina (84.4%), Inflammatory smears mostly presented with white discharge per vaginum (48.4%), ASCUS mainly presented with white discharge per vagina in62.5%, LSIL presented with pain abdomen 66.7%. Pain abdomen was the predominant symptom in HSIL (100%) and invasive carcinoma (100%) There is significant association in type of smear with clinical symptoms in our study

TABLE:23 ASSOCIATION OF TYPE OF SMEARS AND CLINICAL SYMPTOMS

CLINICAL SYMPTOMS	Types of Smears												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
OTHERS	1	12.5	1	100.0	54	34.8	1	100.0	2	66.7	4	12.5	0.016*
PV Bleeding	2	25.0	0	0.0	26	16.8	0	0.0	0	0.0	1	3.1	
WDPV	5	62.5	0	0.0	75	48.4	0	0.0	1	33.3	27	84.4	
Total	8	100.0	1	100.0	155	100.0	1	100.0	3	100.0	32	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 18 ASSOCIATION OF TYPE OF SMEARS AND CLINICAL SYMPTOMS



19.Association of type of smears and clinical impression

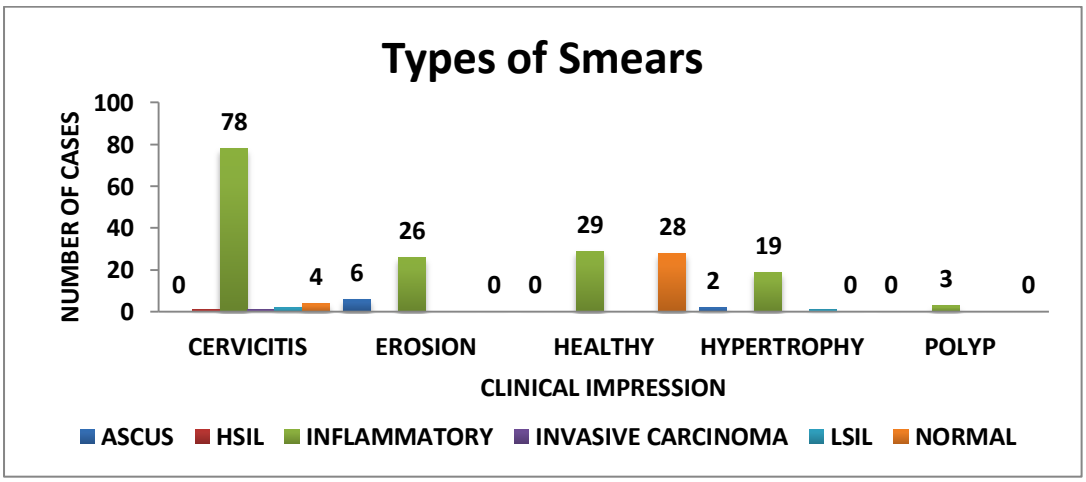
Majority of Normal smears were found to be in patients with Healthy looking cervix (87.5%). Chronic cervicitis was the most common finding in inflammatory, LSIL, HSIL and INVASIVE CARCINOMA (50.3 %, 66.67%,100 %, 100% respectively). Erosion was the main clinical finding in patients showing ASCUS (75%), and Inflammatory smears were seen with all types of cervical lesions

TABLE: 24 ASSOCIATION OF TYPE OF SMEARS AND CLINICAL IMPRESSION

CLINICAL IMPRESSION	Types of Smears												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
CERVICITIS	0	0.0	1	100.0	78	50.3	1	100.0	2	66.7	4	12.5	<0.001*
EROSION	6	75.0	0	0.0	26	16.8	0	0.0	0	0.0	0	0.0	
HEALTHY	0	0.0	0	0.0	29	18.7	0	0.0	0	0.0	28	87.5	
HYPERTROPHY	2	25.0	0	0.0	19	12.3	0	0.0	1	33.3	0	0.0	
POLYP	0	0.0	0	0.0	3	1.9	0	0.0	0	0.0	0	0.0	
Total	8	100	1	100.0	155	100.0	1	100.0	3	100.0	32	100	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 19 ASSOCIATION OF TYPE OF SMEARS AND CLINICAL IMPRESSION



20.Association of type of smears and VIA findings

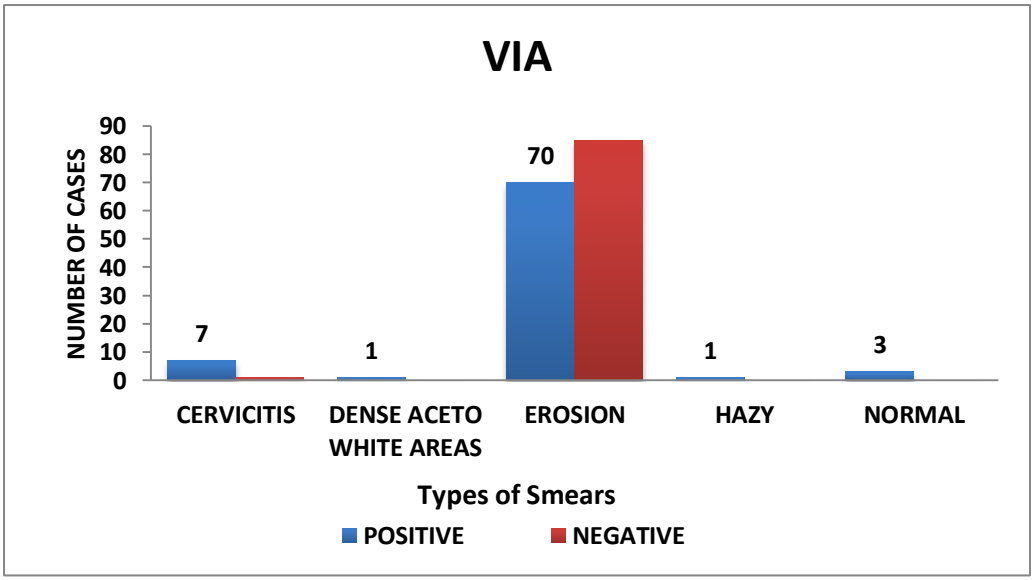
Patients who had VIA positive, among them ,7 patients had ASCUS ,1 patient had HSIL, 70 patients had Inflammatory, 1 patient had invasive carcinoma and 3 patients LSIL.

TABLE 25: ASSOCIATION OF TYPE OF SMEARS AND VIA FINDINGS

VIA	Types of Smears												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
POSITIVE	7	87.5	1	100.0	70	45.2	1	100.0	3	100.0	0	0.0	<0.001*
NEGATIVE	1	12.5	0	0.0	85	54.8	0	0.0	0	0.0	32	100.0	
Total	8	100.0	1	100.0	155	100.0	1	100.0	3	100.0	32	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 20 ASSOCIATION OF TYPE OF SMEARS AND VIA FINDINGS



21. Association of colposcopic findings and PAP smear

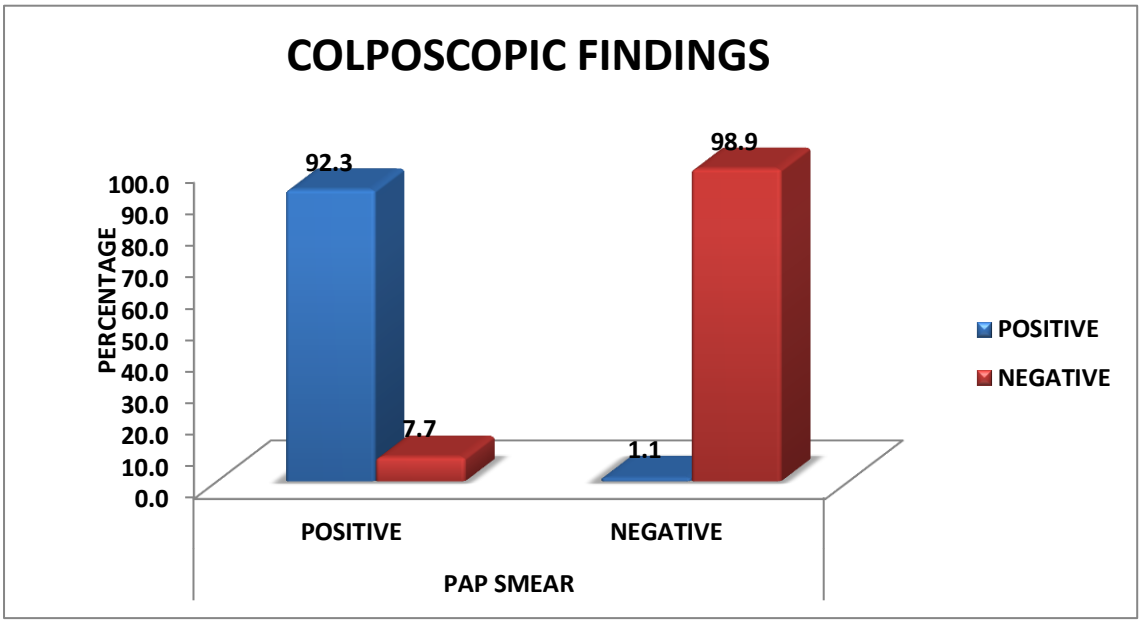
Among the patients who had PAP smear positive,92.3% showed positive colposcopic findings

TABLE: 26 ASSOCIATION OF COLPOSCOPIC FINDINGS AND PAP SMEAR

COLPOSCOPIC FINDINGS	PAP SMEAR				p value
	POSITIVE		NEGATIVE		
	N	%	N	%	
POSITIVE	12	92.3	2	1.1	<0.001*
NEGATIVE	1	7.7	185	98.9	
Total	13	100.0	187	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 21 ASSOCIATION OF COLPOSCOPIC FINDINGS AND PAP SMEAR



22. Association of type of smears and cervical biopsy

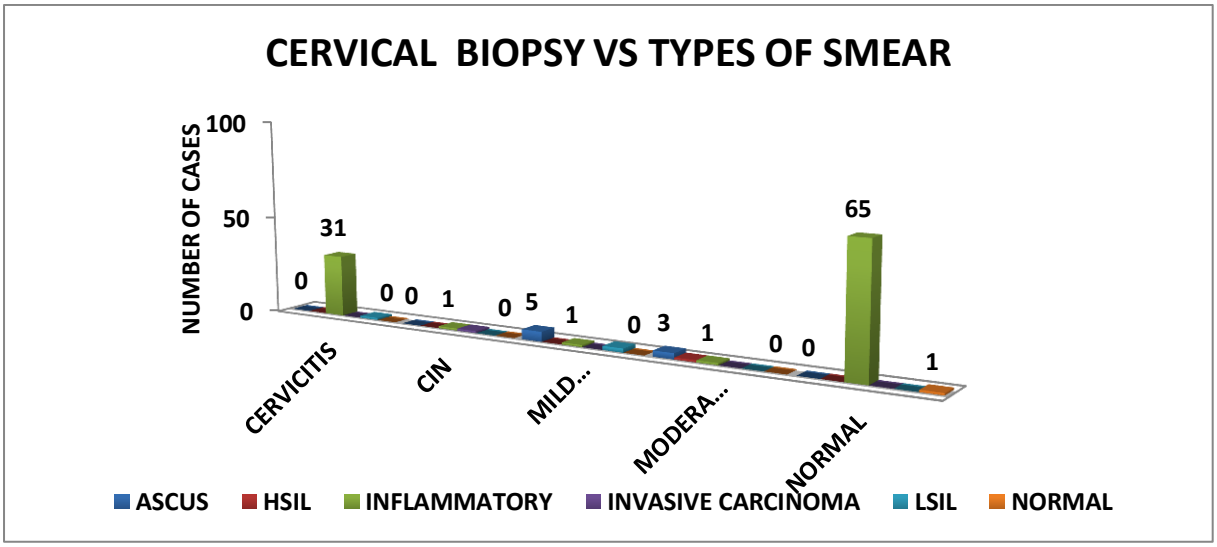
On persistence of unhealthy cervix and inflammatory smear even after a course of antibiotics- direct cervical punch biopsy was taken. Most of patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN, this stresses the importance of further screening inflammatory smear patients. Most of patients with ASCUS smear who underwent cervical biopsy had mild dysplasia and LSIL had mild dysplasia in biopsy. HSIL and Invasive carcinoma showed moderate dysplasia and CIN (severe) as their biopsy finding respectively.

TABLE: 27 ASSOCIATION OF TYPE OF SMEARS AND CERVICAL BIOPSY

CERVICAL BIOPSY	TYPES OF SMEARS												p value
	ASCUS		HSIL		INFLAMMATORY		INVASIVE CARCINOMA		LSIL		NORMAL		
	N	%	N	%	N	%	N	%	N	%	N	%	
CERVICITIS	0	0.0	0	0.0	31	31.3	0	0.0	1	33.3	0	0.0	<0.001*
CIN	0	0.0	0	0.0	1	1.0	1	100.0	0	0.0	0	0.0	
MILD DYSPLASIA	5	62.5	0	0.0	1	1.0	0	0.0	2	66.7	0	0.0	
MODERATE DYSPLASIA	3	37.5	1	100.0	1	1.0	0	0.0	0	0.0	0	0.0	
NORMAL	0	0.0	0	0.0	65	65.7	0	0.0	0	0.0	1	100.0	
Total	8	100.0	1	100.0	99	100.0	1	100.0	3	100.0	1	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 22 ASSOCIATION OF TYPE OF SMEARS AND CERVICAL BIOPSY



23. Association of type of colposcopic and VIA findings

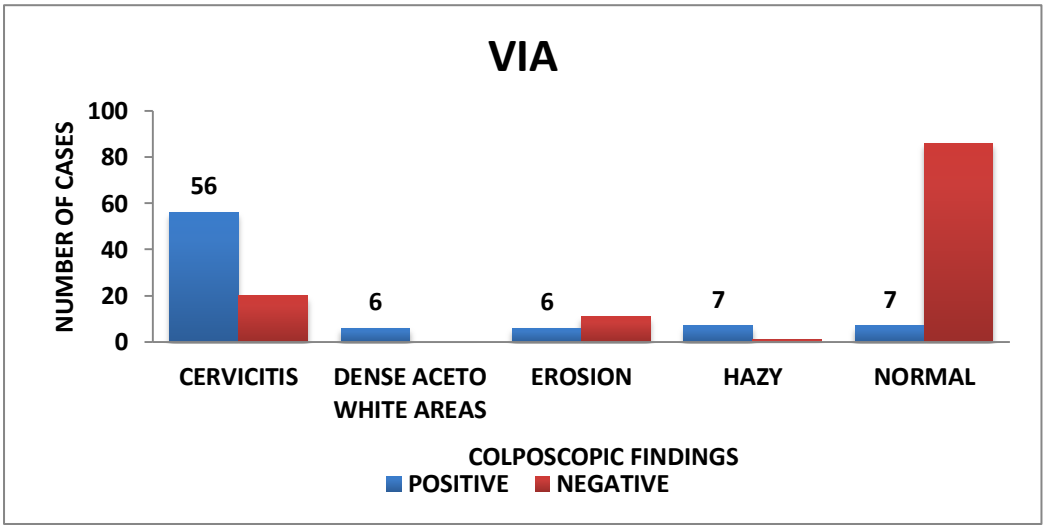
82 cases out of 200 women were positive on VIA. 14 out of 200 women were positive on colposcopy. 14 cases of VIA positive cases were also the 14colposcopy proven positive cases. 69 cases of VIA were false positive which were cases of inflammation/erosion/metaplasia. One false negative case.

TABLE: 28 ASSOCIATION OF TYPES COLPOSCOPIC FINDINGS AND VIA FINDINGS

VIA	COLPOSCOPIC FINDINGS										p value
	CERVICITIS		DENSE ACETO WHITE AREAS		EROSION		HAZY		NORMAL		
	N	%	N	%	N	%	N	%	N	%	
POSITIVE	56	73.7	6	100.0	6	35.3	7	87.5	7	7.5	<0.001*
NEGATIVE	20	26.3	0	0.0	11	64.7	1	12.5	86	92.5	
Total	76	100.0	6	100.0	17	100.0	8	100.0	93	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 23 ASSOCIATION OF COLPOSCOPIC FINDINGS AND VIA FINDINGS



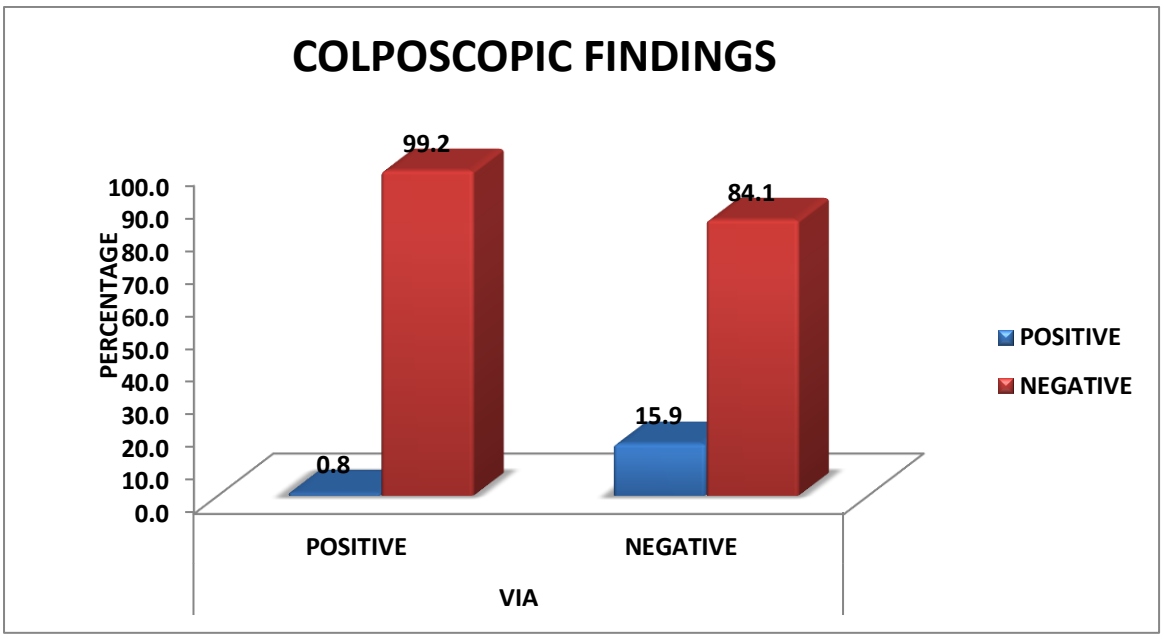
24.Asoociation of colposcopic findings and VIA

TABLE: 29 ASSOCIATION OF COLPOSCOPIC FINDINGS AND VIA

COLPOSCOPIC FINDINGS	VIA				p value
	POSITIVE		NEGATIVE		
	N	%	N	%	
POSITIVE	13	15.9	1	0.8	<0.001*
NEGATIVE	69	84.1	117	99.2	
Total	82	100.0	118	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH: 24 ASSOCIATION OF COLPOSCOPIC FINDINGS AND VIA



25. Association of Cervical biopsy vs PAP smear

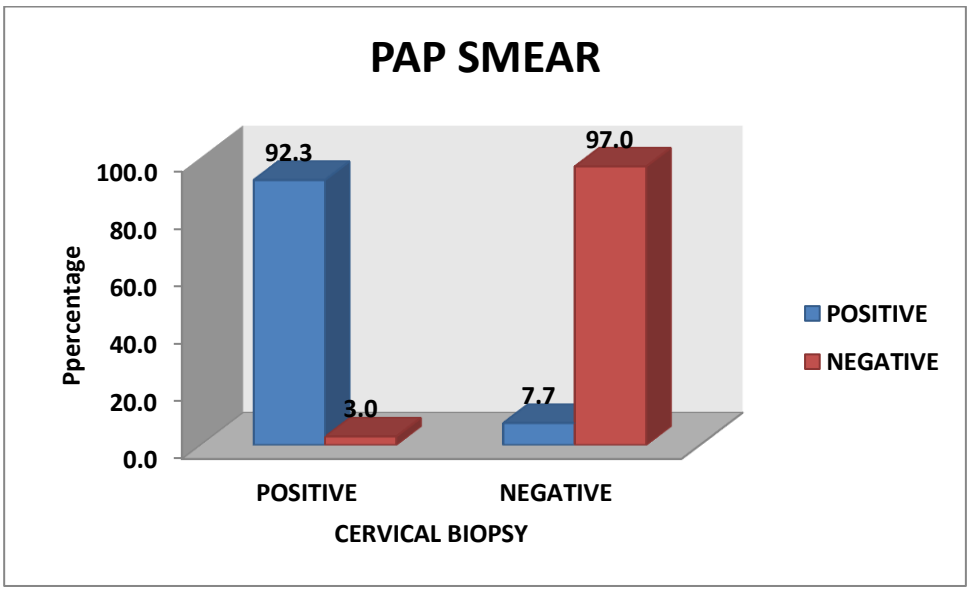
Out of 15 biopsy positive cases, 12 were positive for PAP smear and 3 were negative

TABLE 30: CERVICAL BIOPSY VS PAP SMEAR

CERVICAL BIOPSY	PAP SMEAR				p value
	POSITIVE		NEGATIVE		
	N	%	N	%	
POSITIVE	12	92.3	3	3.0	0.029*
NEGATIVE	1	7.7	97	97.0	
Total	13	100.0	100	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH 25: ASSOCIATION CERVICAL BIOPSY VS PAP SMEAR OF



26. Association of Cervical biopsy vs VIA

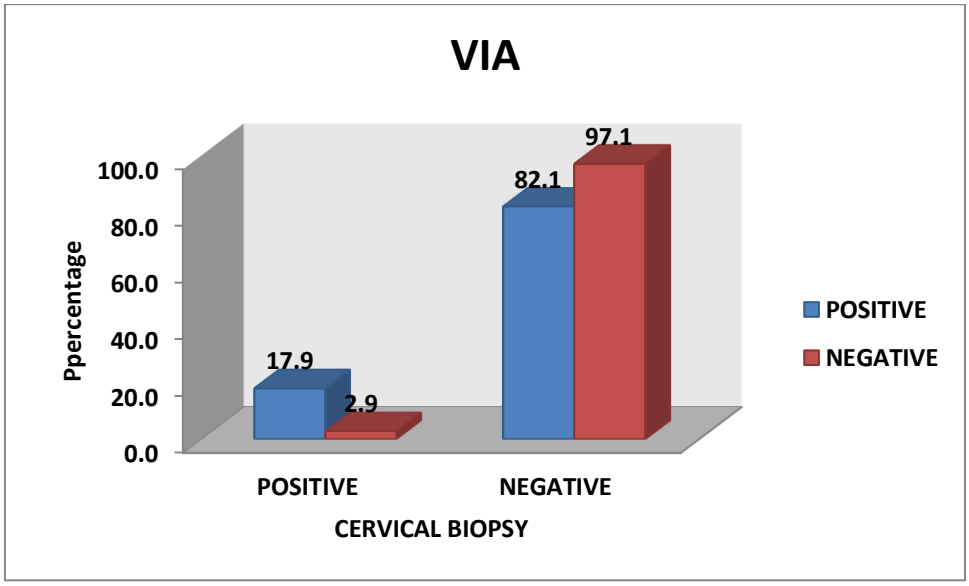
Out of 15 biopsy positive cases, 14 cases were positive for VIA and only 1 case was negative

TABLE 31: CERVICAL BIOPSY VS VIA

CERVICAL BIOPSY	VIA				p value
	POSITIVE		NEGATIVE		
	N	%	N	%	
POSITIVE	14	17.9	1	2.9	<0.001*
NEGATIVE	64	82.1	34	97.1	
Total	78	100.0	35	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH 26: ASSOCIATION OF CERVICAL BIOPSY AND VIA



27. Association of Cervical biopsy vs Colposcopic findings

Out of 15 biopsy positive cases, 14 were colposcopically positive and only 1 was negative

TABLE 32: CERVICAL BIOPSY VS COLPOSCOPIC FINDINGS

CERVICAL BIOPSY	COLPOSCOPIC FINDINGS				p value
	POSITIVE		NEGATIVE		
	N	%	N	%	
POSITIVE	14	100.0	1	1.0	<0.001*
NEGATIVE	0	0.0	98	99.0	
Total	14	100.0	99	100.0	

Note: * significant at 5% level of significance (p<0.05)

GRAPH 27: ASSOCIATION OF CERVICAL BIOPSY AND COLPOSCOPIC FINDINGS

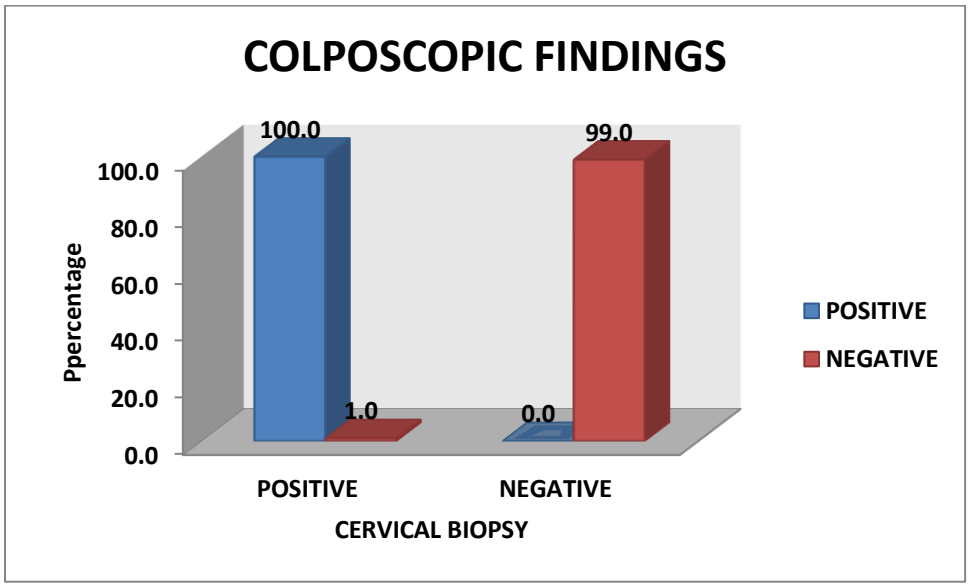


TABLE 33: COMPARISION OF DIAGNOSTIC EFFICACY OF BIOPSY, VIA AND PAP SMEAR COMPERED TO COLPOSCOPIC FINDINGS

	PAP SMEAR	VIA	CERVICAL BIOPSY
Sensitivity	85.7%	92.9%	100.00%
Specificity	99.5%	62.9%	98.99%
PPV	92.3%	15.9%	93.33%
NPV	98.9%	99.2%	100.00%
Accuracy	98.5%	65.0%	99.12%
TP (true positive)	12	13	14
FN (false negative)	2	1	0
FP (false positive)	1	69	1
TN (true negative)	185	117	98
FALSE NEGATIVE RATE	14.3%	7.1%	0.0%
FALSE POSITIVE RATE	0.5%	37.1%	1.1%

TABLE: 34 DIAGNOSTIC EFFICACY OF VIA COMPARED TO COLPOSCOPIC FINDINGS

	VIA
Sensitivity	92.9%
Specificity	62.9%
PPV	15.9%
NPV	99.2%
Accuracy	65.0%

TABLE: 35 DIAGNOSTIC EFFICACY OF PAP SMEAR COMPARED TO COLPOSCOPIC FINDINGS

	PAP SMEAR
Sensitivity	85.7%
Specificity	99.5%
PPV	92.3%
NPV	98.9%
Accuracy	98.5%

TABLE 36: DIAGNOSTIC EFFICACY OF BIOPSY

Sensitivity	100.00%
Specificity	98.99%
PPV	93.33%
NPV	100.00%
Accuracy	99.12%

TP (true positive)	14
FN (false negative)	0
FP (false positive)	1
TN (true negative)	98
FALSE POSITIVE RATE	0.0%
FALSE NEGATIVE RATE	1.1%

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office.

DISCUSSION

DISCUSSION

This is a prospective study, in which 200 women of reproductive age group who attended the Gynaecology outpatient department at Shri B.M.Patil Medical College and Hospital, Vijayapura, from October 2016 to August 2018 were studied to know the "comparison of visual inspection with acetic acid and pap smear in detecting premalignant lesions of cervix" pattern of cervical cytology by Papanicolaou smear and its incidence and correlation with various parameters.

The results are discussed as follows

Distribution of patients according to type of smears-

Only 16% reported to have normal smears. Majority had inflammatory smears (77.5%). ASCUS was seen in 4%, LSIL in 1.5%, HSIL in 0.5% and Invasive Carcinoma in 0.5% patients. The results of our study were similar to that of Gupta S et al[77] who found ASCUS in 3.6%, HSIL in 1% and Carcinoma in 0.41%.Study conducted by Ghazal et al[78] , Rao S et al[79] also showed similar results.

Distribution of patients according to Age and its cytological correlation

The age of the patients included women in reproductive age group keeping in mind the cut off of 25 years as the starting age of screening [6] we took women in the age group of 25-65years. The largest number of patients i.e. 25% belonged to the age group 35-39 years.

Similar observations were made by other authors as follows

TABLE 37: COMPARISON OF VARIOUS STUDY RESULTS (AGE/CYTOLOGICAL CORRELATION)

STUDY	
Chakravarthy et al[77]	32.09%
Prabhakar et al [78]	38.8%
V.K.Singh et al[79]	34.9%
Mukherjee et al[80]	34%
Pankaj Desai et al[81]	40.57%
Present Study	25%

Majority of normal smears were seen in 25-29 years (37.5%), 35-39 years predominantly had inflammatory smears (27.7%). ASCUS was mostly seen in 35-39 years with 62.5% and LSIL was mostly seen in 40-44years with66.7% respectively whereas HSIL was seen in 25-29years (100%) and Malignancy was found in only 30-34 years age group (100%). Study by Pankaj Desai et al [81] showed similar results with mean age of 37.5 for LSIL and 41.6 years for HSIL. Study conducted by Balaha et al[87] mean age of 45yrs for ASCUS,35.8yrs for HSIL. While Gupta et al [84] showed predominance of ASCUS, LSIL in less than 40 years and Carcinoma in >40years age group. Study by Saraiya U et al[88] found mean age of 32.5years,37.5 years and 44.2 years for mild, moderate and squamous cell carcinoma

Distribution of patients according to literacy-

Majority of women were illiterate 57% and 43% were literate.

Distribution of patients according to parity and its cytological correlation-

Most of the patients had parity ≥4 with 34% patients belonging to this group and 13% were para one. Sharma S et al[82] studied sensitivity and specificity of cytology in 50 women and it showed that majority of patients had parity more than 3

(62%).Other studies by Mukherji et al[80] showed 35%,Singh V.K[72] showed 44.1% patients having 3-5 parity which is almost similar to our study.

Abnormal Pap smear was noted in multipara with parity ≥3. Similar observations were made by Pankaj et al[81] and Susheela et al[89]where LSIL/HSIL/malignancy were seen in multiparous women.

Distribution of patients according to presenting symptom and its cytological correlation-

Majority of patients presented with white discharge per vagina i.e.54% which correlated well with study conducted by Sharma S [82] et al who reported 52% patients with white discharge per vaginum. Joshi et al [83] conducted a study on correlation of pap smear for detection of premalignant lesions found 40% patients presenting with white discharge per vaginum.

Abnormal Bleeding per vagina was seen in 14.5% which included menorrhagia, polymenorrhea, irregular cycles, oligomenorrhea, post coital bleeding. Abdominal pain was reported in 14.5%.

Mukherjee et al [80] reported abdominal pain in 19% patients and contact bleeding in 2%. Our study showed majority of normal smears were predominant in white discharge per vagina (84.375 %), Inflammatory smears mostly presented with white discharge per vaginum (48.387%), ASCUS mainly presented with white discharge per vagina in 62.5 %, LSIL presented with pain abdomen 66.67%. Pain abdomen was the predominant symptom in HSIL (100%) and invasive carcinoma (100%) There is significant association in type of smear with clinical symptoms Pankaj Desai et al [81] found leucorrhea as the most common symptom in patients with squamous intraepithelial lesions and post coital bleeding in squamous cell carcinoma. Chakravarthy et al[77] found menstrual irregularities as common symptom in dysplasia.

Distribution of patients according to clinical impression of cervix-

Majority of patients had congested cervix (cervicitis) i.e. 43% and cervical erosion was found in 16% patients. Healthy cervix was noted in 28.5% and hypertrophy was found in 11% cases whereas cervical polyp constituted 1.5%. Similar observations were made by Mukherjee et al [80], whereas Sharma S et al [82] reported hypertrophy in 52% and cervical erosion in 24% cases.

Majority of Normal smears were found to be in patients with Healthy looking cervix (87.5%). Erosion was the main clinical finding in patients showing ASCUS (75%) and hypertrophy of cervix was the second most common finding in ASCUS. Cervicitis was main clinical finding in LSIL. Inflammatory smears were seen with all types of cervical lesions.

Wahi et al found 65.5% patients with dysplasia having cervical erosion. Purandare et al found most dysplasia's in women with cervicitis and erosion. Padmanabhan et al[90] found 31.25% patients with SIL having erosion and Sunanda Rao et al showed cervical erosion and infection accounted for 40-50% of abnormalities.

Cytological correlation with VIA

Patients who had VIA positive, among them ,7 patients had ASCUS ,1 patient had HSIL, 70 patients had Inflammatory, 1 patient had invasive carcinoma and 3 patients LSIL.

Cytological correlation with colposcopy

Among the patients who had PAP smear positive,92.3% showed positive colposcopic findings

Cytological correlation with cervical biopsy finding-

Most of patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN, this stresses the importance of further screening inflammatory smear patients. Most of patients with ASCUS smear who underwent cervical biopsy had mild dysplasia and LSIL had mild dysplasia in biopsy. HSIL and Invasive carcinoma showed moderate dysplasia and CIN (severe) as their biopsy finding respectively. Massad LS et al [91] found 77% of ASCUS cases to be non-malignant.

The incidence of cervical cancer can be reduced by as much as 80% if the quality, coverage and follow- up of screening methods are of high standard [59]. Frequently repeated cytology screening programs have led to a large decline in cervical cancer incidence and mortality in developed countries.

Cytology based screening programs have achieved very limited success in developing countries like India due to lack of trained personnel, laboratory facilities, equipment's, high cost of services and poor follow-up. It has become necessary to find out alternative screening procedure to cytology which has high sensitivity and specificity [60].

The present study was carried out in the Department of Obstetrics and Gynaecology at Shri B. M. Patil Medical College & Research Hospital, Vijayapura from 2016-2018. Two hundred cases who fulfilled the selection criteria were recruited for the study.

Majority of the study group were Para three (31.5%) and Para four and above (34%).

In our study, 82 out of 200 women showed a positive result and 118 women showed negative result on VIA (visual inspection aided by acetic acid). VIA positivity rate depends upon type of criteria used and population screened (high risk or general

population). Sensitivity of VIA was 92.9% and was similar to study conducted by Bharani et. al. in their study the sensitivity of VIA was found to be 100%. The specificity and PPV of VIA were low at 62.9% and 15.9% respectively but the NPV was high at 99.2%. Accuracy of VIA is 65.0%. Of the 82 VIA positive cases and 14 cases were colposcopically proved to be positive as well, in which 8 cases of hazy acetowhite areas or fine punctuation or mosaicism, 6 cases of dense aceto white areas or coarse punctuations or mosaicism and 1 case of malignancy were found and one more malignant case was found in biopsy. The malignancy cases had no visible growth on cervix on per speculum examination. Further, among the 82 positive cases,all indicated cases were subjected to confirmatory biopsy of which 8 cases of mild dysplasia, 5 cases of moderate to severe dysplasia and 2 cases of malignancy were found.

In our study, sensitivity of Pap smear was low i.e. 85.7%. This is because 8 cases of hazy aceto white areas/ fine punctations/ mosaicism, 6 cases of dense aceto white areas /coarse punctations/ mosaicism, 2 cases of malignancy were under reported as Inflammatory/ ASCUS. As a screening test, the Pap smear has been found to have a low sensitivity and the low sensitivity rate has been attributed to the presence of infection and inflammation in high number in the developing countries. The specificity of Pap smear is high i.e. 99.5%, the PPV was 92.3% and the NPV was 98.9%. Accuracy of Pap smear was 98.5%.

In a multicentric study by Sankaranarayanan et. al. showed sensitivity of Pap smear ranging from 36.6% to 72.3% and specificity ranging from 87.2% to 98.6% [72]. In a study conducted by Goel et al[25] the sensitivity of Pap smear was found to be 50% and specificity was 97%.

In a comparative study done by Tejaswini. B. H. the Sensitivity of VIA was 95%, Specificity was 55%, PPV of 61%. Out of 210 biopsy positive patients, 100 showed cervical cytology suggestive of precancerous and cancerous lesion. The sensitivity of Pap smear was 43%, Specificity was 97%, PPV of Pap smear was 90%. The overall Accuracy of VIA was 72% and Cervical cytology was 74%. Positive cases were subjected to biopsy and majority were reported as either normal or chronic cervicitis[57].

In another study by Divya Hegde, out of 225 patients, VIA was positive in 27(12%) patients and Pap smear was abnormal in 26(11.7%). Pap smear had a sensitivity of 83%, specificity of 98%, PPV of 80 % and NPV of 97.9%. VIA had a sensitivity of 70.8%, specificity of 95%, PPV of 62.9 % and NPV of 96.5%[21].

In a study done by Afshan, the Sensitivity of Pap smear was found to be 43.2%, high Specificity of 95.2% and the PPV was 84.2%[58]. The results of various studies have been put together for comparison with our study results in the below table.

TABLE 38: COMPARISON OF VARIOUS STUDY RESULTS

Studies conducted	Sensitivity		Specificity		PPV		Accuracy	
	Pap Smear	VIA	Pap smear	VIA	Pap smear	VIA	Pap smear	VIA
Sankaranarayanan et. Al[72]	36.6% to 72.3%	-	87.2%to 98.6%	-	-	-	-	-
Goel et al[92]	50%	-	97%	-	-	-	-	-
Tejaswini. B. H.[93]	43%	95	97%	55%	90%	61%	74%	72%
Divya Hegde[94]	83%	70.8%	98%	95%	80%	62.9%	-	-
Afshan[95]	43.2%	-	95.2%	-	84.2%	-	-	-
Rana T et.al[96]	83%	93%	97%	90%	83%	62.5%	96%	90%
In our study	85.7%	92.9%	99.5%	62.9%	92.3%	15.9%	98.5%	65%

The results in various study were found to be comparable with our study. All the 13 positive cases of pap smear were subjected to biopsy on which 8 and 5 cases of mild and moderate to severe dysplasia and 1 malignancy cases were found. The high number of malignancy cases in our study is attributed to the judicious method of case selection which has made it imperative in getting high incidence of malignancy cases. In our study, out of 200 cases, 113 had abnormal cervical findings, and were subjected to punch biopsy. 58.4% were normal,28.3% had cervicitis,7.1 % had mild dysplasia,4.4 % had moderate dysplasia and 1.8 % were CIN.

Correlation of biopsy and PAP smear- Out of 15 biopsy positive cases, 12 were positive for PAP smear i.e. 92.3% and 3 were negative.

Correlation of biopsy and VIA- Out of 15 biopsy positive cases, 14 cases were positive for VIA i.e. 17.9% and 1 case was negative.

Correlation of biopsy and colposcopy- Out of 15 biopsy positive cases, 14 were colposcopically positive i.e. 100% and only 1 was negative.

The women with cervicitis/metaplasia in our study were treated with antibiotics. Women with cervical ectopy underwent cryocautery. The cases with malignancies were given option of surgery at our hospital or reference to higher center for surgery and further management. The specificity and positive predictive value of Pap smear were high at 99.5% and 92.3%, whereas the specificity of VIA was much lower at 62.9% and PPV at 15.9%, the specificity and PPV of cytology are 99.5%% and 92.3%, Hence cytology, VIA and colposcopy and confirmed by biopsy gives reliable results by which, patients of cervical lesions have a relatively higher chance of detection of pre-malignant and squamous intraepithelial lesions/malignancy as compared to any procedure when performed alone. But in rural areas, PAP smear can be used as it has got high specificity.

CONCLUSION

CONCLUSION

The VIA and Papanicolaou procedures are the most simple, safe, practical and cost-effective method for early detection of cervical cancer and its precursors which if treated, eliminates or reduces the subsequent development of invasive cancer.

Although screening with colposcopy and biopsy has been reported periodically, such an approach tends to over diagnose the immature squamous metaplasia with optimal magnification. The technique has a high false positive rate, not cost effective and therefore offers little in a screening program.

The Papanicolaou procedure is considered as a screening test, not a diagnostic test, therefore abnormalities of the smear should be confirmed histologically by biopsy. The false negative rate of Pap smear emphasizes that for its successful use it is essential that screening should be done yearly or every 2 years to reduce the chance of missing an early lesion. As the progression from pre-invasive to invasive carcinoma is slow, more frequent screening appears the gold standard for screening programs.

In developing countries like India, cytology, a low cost and easily accessible test, is the most logical screening modality although it has a very low sensitivity but has got good specificity rate and detection rates could be further improved using liquid based cytology and the use of endocervical cytobrush. And later can be referred to a higher center for biopsy which has got high sensitivity and specificity.

Hence efforts must be directed towards education of women regarding cervical cancer in order to promote awareness of malignancy and to motivate them for cytological screening in the future.

SUMMARY

SUMMARY

200 women of reproductive age group were studied to know the pattern of cervical cytology by, Papanicolaou smear, VIA, colposcopy and colposcopic biopsy wherever needed.

Maximum number of women screened were in age group of 35- 39 years (25%). 34% were of parity ≥4. 55% of women were from Low socioeconomic class and 57% were illiterate and 96.5% were Hindus while 3.5% were Muslims. 75% women had average hygiene.

The use of barrier contraception, oral contraception and intrauterine devices were practiced by 2.5%, 5% and 4% of the women respectively.24.5% women were tubectomised. This shows that majority of women didn't use contraception and lack and awareness of barrier contraception are contributing to high prevalence of epithelial neoplasia in developing countries like India.

200 cases were subjected to PAP smear, VIA and colposcopy and abnormal cases were subjected to colposcopic guided biopsy. Out of which, 13 cases were positive for PAP smear, 82(41%) cases were positive for VIA, 14(7%) were positive for colposcopy and 15(13.27%) cases were positive for biopsy.

Most common presenting complaint was discharge per vagina (54%) followed by pain abdomen (31.5%). 28.5 % of cervix were healthy,43% had cervicitis, 16% had erosion, 11% had hypertrophy.

Cervical cytology was normal in 16%, inflammatory in 77.5%, ASCUS in 4%, LSIL in 1.5%, HSIL in 0.5% and squamous cell carcinoma in 0.5%.

Maximum numbers of patients with ASCUS were in age group of 35-39 years and LSIL were in the age group of 40-44 years, HSIL were in age group of 25-29years and Squamous cell carcinoma occurred in the age group of 30-34 years.

ASCUS in parity two and ≥4 (37.5% respectively), LSIL and HSIL in parity ≥4 (66.7% and 100% respectively) and Malignancy in parity ≥4(100%).

All abnormal Pap smears (ASCUS or more) mainly presented with white discharge and pain abdomen as the second most common presentation.

Chronic cervicitis was the most common finding in inflammatory, LSIL, HSIL and INVASIVE CARCINOMA (50.32 % 66.67%,100 %, 100% respectively). Erosion was the main clinical finding in patients showing ASCUS (75%), and Inflammatory smears were seen with all types of cervical lesions. Hence no definite clinical impression is there which helps us to suspect cases of dysplasia, thus stressing the importance of cytological examination in detecting cervical intraepithelial lesions.

113 cases were subjected to biopsy. Out of which 15 were positive(i.e. mild dysplasia-8 cases, moderate dysplasia-5 cases and CIN- 2 cases).

All cases of ASCUS and LSIL had infection which showed chronic cervicitis in biopsy. HSIL and Invasive carcinoma showed CIN 2 and Carcinoma as their biopsy finding. Patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN 2, this stresses the importance of further screening inflammatory smear patients.

When positive biopsy cases were compared with PAP smear, VIA and colposcopy, the correlations were 92.3%, 17.9% and 100% respectively, this proves that screen positive(PAP smear, VIA and colposcopy)patients should further undergo biopsy.

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ANNEXURES

ANNEXURE I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-10-2016 *at* 03-pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Comparison of visual inspection with acetic acid and pap smear in detecting premalignant lesions of cervix"

Name of P.G. student Dr Nikita P. Naidu
Dept of OBG.

Name of Guide/Co-investigator Dr Dr. P.B. Jaju
Prof & HOD of OBG.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE II

SAMPLE INFORMED CONSENT FORM

TITLE OF THE TOPIC : "COMPARISON OF VISUAL INSPECTION WITH ACETIC ACID AND PAP SMEAR AS A SCREENING METHOD FOR PREMALIGNANT LESIONS OF CERVIX''.

PRINCIPAL INVESTIGATOR: Dr. Nikita P. Naidu

PG GUIDE NAME: Dr. (Prof) P.B.Jaju

RISK AND DISCOMFORTS

I understand that this procedure is not expected to aggravate any side effect or cause detrimental effect to me.

BENEFITS

As we study the cervix through PAP smear, VIA and colposcopy, it will be possible to expect the outcome and its early treatment.

CONFIDENTIALITY

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality and privacy regulation of BLDE (DEEMED TO BE UNIVERSITY)'s Shri.B. M.Patil Medical College. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a

code number. The code key connecting names to numbers will be kept in a secured location**.**

If the data are used for publication in the medical literature or for teaching purpose no names will be used**.**

I understand that the relevant designated authority and permitted to have an access to my medical record and to the data produced by the study for audit purpose. However, they are required to maintain confidentiality**.**

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Nikita P. Naidu has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience. I have been explained all the above in detail in my own language and I understand the same. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(witness to signature) Date

ANNEXURE III

PROFORMA OF THE CASE TAKEN FOR EVALUATION:

Name:	OPNo:
Age:	Case.no:
Address:	Occupation:
DOA:	DOD:
Time of admission:	IP.No:

Chief complaints:

History of present illness:

Menstrual History

PaMC :

LMP :

Obstetrics history :

Married Life :

Obstetric Score :

Past History :

Family History :

Personal History :

General Physical Examination

Build and Nourishment :

Height :

Weight :

Temp :

RR :

PR :

BP :

Breast :

Thyroid :

Spine :

Pallor / icterus / cyanosis / clubbing / edema / lymphadenopathy:

Systemic Examination

CVS :

RS :

Per Abdomen

Per speculum :

Per vaginal :

INVESTIGATIONS

Hb % **:**

Blood Grouping and Rh Typing**:**

Urine Routine **:** RBS **:**

HBs Ag **:**

RVD **:**

USG **:**

BT

CT **:**

Platelets **:**

TC **:**

DC **:**

ESR **:**

SPECIAL INVESTIGATIONS-

PAP smear-

Visual inspection with acetic acid

Colposcopy

Others

REMARKS:

KEY TO MASTER CHART

CIN	-cervical intraepithelial neoplasia
SE	-socioeconomic status
LN	- lymph nodes
H	-Hindu
M	-Muslim
Hb	- hemoglobin
VIA	- visual inspection with acetic acid
Hazy	-hazy acetowhite area
Dense	-dense acetowhite area
LSIL	-low grade squamous intraepithelial lesion
HSIL	-high grade squamous intraepithelial lesion
ASCUS	-atypical squamous cells of undetermined significance
P	-positive
N	-negative
NAD	-no abnormality detected
NR	-non-reactive
NS	-not significant
WDPV	- white discharge per vagina
OCP	-oral contraceptive pills
PV	-per vaginal
IUCD	-intrauterine contraceptive device

MASTER CHART

Sr. No	0P no.	Age	Religion	Education	SE status	Parity	Clinical Symptoms	Hygiene	Contraception	Past History	Family History	Personal	LN	Clinical Impression	HB	Urine R/m	HIV/HBsAg	VIA	colposcopic findings	Types of Smears	Cervical biopsy
1	54509	39	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	13	NAD	NR	N	Erosion	Inflammatory	not done
2	235810	42	H	Literate	High	4	WDPV	Poor	No Contraception	NS	NS	NS	N	Cervicitis	12.4	NAD	NR	P	Hazy	LSIL	Mild dysplasia
3	244193	46	H	Literate	High	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	12.8	NAD	NR	N	Normal	Normal	not done
4	318623	40	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	11.6	NAD	NR	P	Hazy	LSIL	Mild dysplasia
5	31260	45	H	Literate	middle	4	WDPV	Good	Tubectomy	NS	NS	NS	N	Cervicitis	10.4	NAD	NR	N	Normal	Inflammatory	not done
6	371346	45	H	Literate	High	1	WDPV	Good	OCP	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Normal	not done
7	383982	40	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	N	Normal	Normal	not done
8	388248	40	H	Illiterate	low	4	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.2	NAD	NR	P	Cervicitis	Inflammatory	normal
9	426831	26	H	Illiterate	low	2	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	11.8	NAD	NR	N	Normal	Normal	not done
10	3183	25	H	Literate	middle	3	WDPV	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	P	Cervicitis	Inflammatory	normal
11	40571	40	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	P	Cervicitis	Inflammatory	normal
12	3983	48	H	Illiterate	middle	6	PAIN ABDOEMN	Average	IUCD	NS	NS	NS	N	Polyp	9.5	NAD	NR	N	Normal	Inflammatory	not done
13	44519	55	H	Illiterate	low	6	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	9.6	NAD	NR	N	Normal	Inflammatory	not done
14	49095	30	H	Illiterate	low	3	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.8	NAD	NR	P	Cervicitis	Inflammatory	normal
15	50805	32	H	Illiterate	low	6	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	P	Cervicitis	Inflammatory	normal
16	52577	40	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.4	NAD	NR	P	Cervicitis	Inflammatory	normal
17	69464	27	M	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	10.1	NAD	NR	N	Normal	Normal	not done
18	76212	42	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	11	NAD	NR	P	Cervicitis	Inflammatory	normal
19	89625	30	H	Literate	middle	6	pain abdomen average	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.1	NAD	NR	N	Normal	Inflammatory	not done
20	89695	43	H	Literate	middle	3	PV Bleeding	Average	Tubectomy	DM	NS	NS	N	Cervicitis	10.4	NAD	NR	P	Cervicitis	Inflammatory	normal
21	93217	46	H	Literate	High	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	10.3	NAD	NR	N	Normal	Normal	not done
22	106696	30	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	10.4	NAD	NR	P	Cervicitis	Inflammatory	normal
23	106797	26	H	Literate	High	4	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	P	Cervicitis	Inflammatory	normal

24	134248	48	H	Illiterate	low	2	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
25	193248	31	H	Illiterate	low	4	Pain abdomen	Poor	No Contraception	NS	NS	NS	N	Cervicitis	12.7	NAD	NR	P	Normal	Inflammatory	not done
26	193137	41	H	Literate	middle	1	WDPV	Good	OCP	NS	NS	NS	N	Healthy	9.7	NAD	NR	N	Cervicitis	Normal	not done
27	199122	25	H	Illiterate	low	6	PAIN ABDOEMN	Average	No Contraception	NS	NS	NS	N	Cervicitis	12.5	NAD	NR	P	Dense aceto white areas	HSIL	Moderate dysplasia
28	18833	30	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	P	Cervicitis	Inflammatory	normal
29	203199	32	H	Illiterate	low	4	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	11.3	NAD	NR	P	Normal	Inflammatory	not done
30	241227	31	H	Illiterate	low	0	WDPV	Poor	No Contraception	NS	NS	NS	N	Healthy	13	NAD	NR	N	Normal	Inflammatory	not done
31	23552	28	H	Illiterate	low	2	WDPV	Poor	No Contraception	NS	NS	NS	N	Healthy	11.5	NAD	NR	N	Normal	Normal	not done
32	23819	28	H	Illiterate	low	0	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	12.5	NAD	NR	N	Normal	Normal	not done
33	24213	30	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.2	NAD	NR	P	Normal	Inflammatory	normal
34	254322	34	H	Literate	middle	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11.3	NAD	NR	N	Erosion	Inflammatory	normal
35	254319	25	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	13	NAD	NR	N	Erosion	Inflammatory	normal
36	262559	30	M	Literate	High	4	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.7	NAD	NR	N	Normal	Inflammatory	not done
37	25989	35	H	Illiterate	low	4	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.2	NAD	NR	P	Cervicitis	Inflammatory	normal
38	265691	48	H	Literate	middle	6	PAIN ABDOMEN	Average	IUCD	NS	NS	NS	N	Hypertrophy	12.4	NAD	NR	P	Hazy	Inflammatory	Mild dysplasia
39	270397	26	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
40	277926	32	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	12	NAD	NR	P	Normal	Inflammatory	not done
41	270629	26	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9	NAD	NR	P	Cervicitis	Inflammatory	normal
42	286786	40	H	Illiterate	middle	4	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	N	Normal	Normal	not done
43	362414	34	H	Illiterate	middle	4	WDPV	Good	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	N	Normal	Normal	not done
44	373954	30	H	Literate	High	4	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.2	NAD	NR	P	Cervicitis	Inflammatory	normal
45	373743	27	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
46	373742	25	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.6	NAD	NR	P	Erosion	Inflammatory	normal
47	373710	40	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.1	NAD	NR	N	Normal	Inflammatory	not done
48	370506	29	H	Illiterate	low	2	WDPV	Average	IUCD	NS	NS	NS	N	Erosion	9.6	NAD	NR	P	Erosion	Inflammatory	normal
49	374576	35	H	Illiterate	low	6	PAIN ABDOMEN	Good	No Contraception	NS	NS	NS	N	Hypertrophy	11.8	NAD	NR	N	Normal	Inflammatory	not done
50	378837	37	H	Literate	High	6	PAIN ABDOEMN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.1	NAD	NR	N	Normal	Inflammatory	not done

51	378821	30	H	Literate	High	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.1	NAD	NR	P	Cervicitis	Inflammatory	normal
52	378804	31	H	Illiterate	middle	4	WDPV	Good	Tubectomy	NS	NS	NS	N	Cervicitis	12.1	NAD	NR	N	Normal	Inflammatory	not done
53	378823	43	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.1	NAD	NR	P	Cervicitis	Inflammatory	normal
54	378874	38	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.6	NAD	NR	N	Normal	Inflammatory	not done
55	379072	37	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	N	Normal	Inflammatory	not done
56	378916	31	H	Illiterate	low	3	PAIN ABDOMEN	Poor	No Contraception	NS	NS	NS	N	Cervicitis	10.8	NAD	NR	N	Cervicitis	Inflammatory	normal
57	379020	38	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.6	NAD	NR	N	Normal	Normal	not done
58	374496	35	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.1	NAD	NR	P	Cervicitis	Inflammatory	normal
59	379009	36	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.5	NAD	NR	N	Cervicitis	Inflammatory	normal
60	39074	35	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.2	NAD	NR	N	Normal	Inflammatory	not done
61	381873	30	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	P	Cervicitis	Inflammatory	normal
62	38457	27	H	Literate	High	4	WDPV	Poor	OCP	NS	NS	NS	N	Cervicitis	8.6	NAD	NR	P	Cervicitis	Inflammatory	normal
63	381966	25	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Cervicitis	Inflammatory	normal
64	397121	31	H	Illiterate	low	0	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	12.8	NAD	NR	N	Normal	Inflammatory	not done
65	40790	37	H	Literate	High	1	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	9.9	NAD	NR	N	Normal	Normal	N
66	395266	50	H	Illiterate	low	2	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Healthy	10.7	NAD	NR	N	Normal	Inflammatory	N
67	395465	38	H	Literate	middle	4	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	13.3	NAD	NR	P	Cervicitis	Inflammatory	normal
68	39517	39	H	Literate	middle	4	WDPV	Average	OCP	NS	NS	NS	N	Cervicitis	12	NAD	NR	N	Normal	Inflammatory	not done
69	40706	37	H	Literate	middle	6	WDPV	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	11	NAD	NR	N	Hazy	ASCUS	Mild dysplasia
70	395918	40	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	P	Cervicitis	Inflammatory	normal
71	396407	38	H	Illiterate	low	3	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12	NAD	NR	N	Cervicitis	Inflammatory	normal
72	400648	36	H	Literate	middle	4	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	13.6	NAD	NR	N	Cervicitis	Inflammatory	normal
73	41734	35	H	Illiterate	middle	4	PV Bleeding	Poor	No Contraception	NS	NS	NS	N	Erosion	9.8	NAD	NR	P	Dense aceto white areas	ASCUS	Moderate dysplasia
74	405555	30	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	P	Normal	Inflammatory	N
75	405149	26	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	12	NAD	NR	N	Normal	Normal	not done
76	405686	30	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	13	NAD	NR	P	Dense aceto white areas	INVASIVE CARCINOMA	CIN
77	404782	34	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	12.4	NAD	NR	P	Hazy	ASCUS	Mild dysplasia

78	404817	36	H	Literate	middle	1	WDPV	Average	OCP	NS	NS	NS	N	Healthy	12.8	NAD	NR	N	Normal	Inflammatory	not done
79	399908	40	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11.6	NAD	NR	N	Erosion	Inflammatory	normal
80	405748	42	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	N	Erosion	Inflammatory	normal
81	404320	47	H	Literate	middle	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	10.4	NAD	NR	P	Cervicitis	Inflammatory	normal
82	405840	28	H	Illiterate	low	4	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	P	Cervicitis	Inflammatory	normal
83	406943	42	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.2	NAD	NR	N	Normal	Inflammatory	not done
84	404261	30	H	Literate	High	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	P	Cervicitis	LSIL	Cervicitis
85	404266	38	H	Illiterate	low	2	WDPV	Good	Tubectomy	NS	NS	NS	N	Healthy	9.8	NAD	NR	N	Normal	Inflammatory	not done
86	408961	28	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.2	NAD	NR	P	Normal	Inflammatory	N
87	409567	35	H	Illiterate	middle	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Polyp	9.5	NAD	NR	N	Normal	Inflammatory	not done
88	405477	35	H	Literate	middle	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	9.6	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
89	409599	31	H	Illiterate	low	0	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	10.8	NAD	NR	N	Normal	Normal	not done
90	409725	49	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	11	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
91	408769	55	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.4	NAD	NR	N	Normal	Inflammatory	not done
92	408772	48	H	Literate	middle	4	WDPV	Good	Tubectomy	NS	NS	NS	N	Cervicitis	10.1	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
93	408779	26	H	Literate	High	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
94	408781	37	H	Illiterate	low	1	WDPV	Average	IUCD	NS	NS	NS	N	Erosion	12.1	NAD	NR	P	Dense aceto white areas	ASCUS	Moderate dysplasia
95	414229	25	H	Literate	low	1	WDPV	Average	OCP	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Inflammatory	normal
96	412601	60	H	Illiterate	low	6	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	10.3	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
97	407980	41	H	Literate	middle	1	WDPV	Average	OCP	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Normal	not done
98	412603	38	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	9.8	NAD	NR	N	Normal	Inflammatory	N
99	412605	42	M	Literate	middle	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	11	NAD	NR	N	Cervicitis	Inflammatory	normal
100	417006	25	H	Literate	middle	4	WDPV	Good	No Contraception	NS	NS	NS	N	Cervicitis	12.7	NAD	NR	N	Cervicitis	Inflammatory	normal
101	417755	41	H	Literate	middle	1	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	9.7	NAD	NR	N	Normal	Normal	not done
102	417854	44	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	12.5	NAD	NR	N	Erosion	Inflammatory	normal
103	407892	26	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11.8	NAD	NR	N	Erosion	Inflammatory	normal
104	408005	48	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11.3	NAD	NR	N	Normal	Inflammatory	not done

105	421927	25	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	13	NAD	NR	N	Cervicitis	Inflammatory	normal
106	421680	34	H	Illiterate	low	2	WDPV	Good	Tubectomy	NS	NS	NS	N	Healthy	8.6	NAD	NR	N	Normal	Normal	not done
107	418825	55	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Erosion	Inflammatory	normal
108	418819	45	H	Illiterate	low	3	PV Bleeding	Poor	No Contraception	NS	NS	NS	N	Cervicitis	12.8	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
109	421615	30	H	Literate	middle	3	WDPV	Poor	IUCD	NS	NS	NS	N	Erosion	9.9	NAD	NR	N	Normal	Inflammatory	not done
110	417709	43	H	Literate	middle	3	PV Bleeding	Average	Tubectomy	DM	NS	NS	N	Cervicitis	10.7	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
111	431851	39	H	Illiterate	low	2	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	13.3	NAD	NR	P	Normal	Inflammatory	not done
112	431006	45	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12	NAD	NR	N	Cervicitis	Inflammatory	normal
113	430114	41	H	Literate	High	1	WDPV	Average	condom	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Inflammatory	not done
114	430117	50	H	Literate	middle	6	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	11	NAD	NR	N	Normal	Inflammatory	not done
115	430120	36	H	Illiterate	low	2	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Erosion	12	NAD	NR	P	Dense aceto white areas	ASCUS	Moderate dysplasia
116	430130	46	M	Literate	middle	4	WDPV	Average	Tubectomy	NS	NS	NS	N	Cervicitis	13.6	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
117	430131	42	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
118	430133	39	H	Literate	middle	3	WDPV	Poor	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	N	Cervicitis	Inflammatory	normal
119	430573	40	H	Illiterate	low	2	WDPV	Average	Tubectomy	NS	NS	NS	N	Erosion	12	NAD	NR	P	Erosion	Inflammatory	normal
120	435575	33	M	Illiterate	low	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	13	NAD	NR	P	Cervicitis	Inflammatory	normal
121	435382	50	H	Illiterate	low	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	12.4	NAD	NR	N	Normal	Inflammatory	not done
122	431603	26	H	Illiterate	low	2	WDPV	Average	Tubectomy	NS	NS	NS	N	Erosion	12.8	NAD	NR	N	Normal	Inflammatory	not done
123	435386	34	H	Illiterate	low	0	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.6	NAD	NR	N	Normal	Normal	not done
124	435390	36	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
125	431714	42	H	Literate	middle	1	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Hazy	ASCUS	Mild dysplasia
126	431894	32	H	Illiterate	low	0	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	11.8	NAD	NR	N	Normal	Normal	not done
127	431222	36	H	Illiterate	middle	4	WDPV	Average	Tubectomy	NS	NS	NS	N	Cervicitis	10.2	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
128	431692	38	M	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.8	NAD	NR	N	Normal	Inflammatory	not done
129	431638	40	H	Illiterate	low	2	WDPV	Average	condom	NS	NS	NS	N	Erosion	9.8	NAD	NR	N	Erosion	Inflammatory	normal
130	431509	53	H	Literate	middle	4	WDPV	Good	Tubectomy	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	N	Cervicitis	Inflammatory	normal
131	4588	27	H	Illiterate	low	3	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Healthy	9.5	NAD	NR	N	Normal	Normal	not done

132	12180	37	H	Illiterate	low	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	9.6	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
133	12894	50	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.8	NAD	NR	N	Erosion	Inflammatory	normal
134	12948	32	H	Literate	middle	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
135	13228	27	H	Literate	middle	1	WDPV	Poor	OCP	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Normal	not done
136	2796	27	H	Illiterate	low	4	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.1	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
137	26591	29	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
138	35169	40	H	Illiterate	low	3	PAIN ABDOMEN	Good	No Contraception	NS	NS	NS	N	Cervicitis	12.1	NAD	NR	N	Cervicitis	Inflammatory	normal
139	35179	33	H	Literate	middle	3	WDPV	Average	Tubectomy	NS	NS	NS	N	Cervicitis	10.4	NAD	NR	N	Cervicitis	Inflammatory	normal
140	35173	45	H	Literate	middle	4	WDPV	Average	Tubectomy	NS	NS	NS	N	Cervicitis	10.3	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
141	3499	40	H	Illiterate	low	2	WDPV	Poor	OCP	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Normal	not done
142	54063	56	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	N	Cervicitis	Inflammatory	normal
143	57946	37	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11	NAD	NR	P	Erosion	Inflammatory	normal
144	116828	43	H	Illiterate	low	3	PV Bleeding	Good	No Contraception	NS	NS	NS	N	Cervicitis	12.7	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
145	117130	35	H	Illiterate	low	3	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9.7	NAD	NR	N	Cervicitis	Inflammatory	normal
146	126246	45	H	Illiterate	low	2	WDPV	Poor	condom	NS	NS	NS	N	Healthy	12.5	NAD	NR	N	Normal	Normal	not done
147	11817	60	H	Illiterate	low	6	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	11.8	NAD	NR	N	Normal	Inflammatory	not done
148	143734	35	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	11.3	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
149	138275	38	M	Illiterate	low	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	13	NAD	NR	N	Normal	Inflammatory	not done
150	146468	45	H	Literate	middle	3	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.2	NAD	NR	N	Normal	Inflammatory	normal
151	150022	31	H	Literate	middle	4	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Normal	not done
152	150008	26	H	Literate	High	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	12	NAD	NR	N	Normal	Normal	not done
153	16275	46	H	Illiterate	low	2	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Hazy	ASCUS	Mild dysplasia
154	170390	32	H	Literate	low	1	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	10.6	NAD	NR	N	Normal	Inflammatory	not done
155	169762	30	H	Literate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	11	NAD	NR	N	Normal	Inflammatory	not done
156	170789	36	H	Illiterate	low	4	WDPV	Poor	No Contraception	NS	NS	NS	N	Hypertrophy	12.6	NAD	NR	P	Hazy	ASCUS	Mild dysplasia
157	169762	30	H	Illiterate	low	0	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	13	NAD	NR	N	Normal	Inflammatory	not done
158	170305	30	H	Literate	middle	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.4	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis

159	166577	35	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.8	NAD	NR	N	Normal	Inflammatory	not done
160	21714	30	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.6	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
161	222471	52	H	Literate	middle	4	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Normal	not done
162	221475	50	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	10.4	NAD	NR	N	Normal	Inflammatory	not done
163	221482	60	H	Literate	middle	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	P	Dense aceto white areas	Inflammatory	Moderate dysplasia
164	221470	31	H	Literate	middle	3	WDPV	Average	Tubectomy	NS	NS	NS	N	Erosion	10.2	NAD	NR	N	Erosion	Inflammatory	Cervicitis
165	21224	36	H	Literate	middle	3	Pain abdomen	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.8	NAD	NR	N	Cervicitis	Inflammatory	Cervicitis
166	221996	55	H	Literate	middle	4	WDPV	Average	IUCD	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
167	222010	56	H	Literate	High	1	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	11.2	NAD	NR	N	Normal	Inflammatory	not done
168	222072	46	H	Literate	middle	3	WDPV	Average	Tubectomy	NS	NS	NS	N	Erosion	9.5	NAD	NR	N	Normal	Inflammatory	not done
169	246039	40	H	Literate	middle	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	9.6	NAD	NR	P	Erosion	Inflammatory	normal
170	244146	26	H	Literate	middle	1	WDPV	Poor	OCP	NS	NS	NS	N	Healthy	10.8	NAD	NR	N	Normal	Inflammatory	not done
171	246328	35	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Inflammatory	not done
172	246568	40	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	10.4	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
173	244147	25	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	10.1	NAD	NR	N	Normal	Inflammatory	not done
174	246785	44	H	Illiterate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Hypertrophy	11	NAD	NR	N	Normal	Inflammatory	not done
175	246824	35	H	Literate	middle	3	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.1	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
176	249974	35	H	Illiterate	middle	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Polyp	10.4	NAD	NR	N	Normal	Inflammatory	not done
177	250443	38	H	Illiterate	low	2	WDPV	Poor	No Contraception	NS	NS	NS	N	Healthy	10.3	NAD	NR	N	Normal	Inflammatory	not done
178	249959	25	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	10.4	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
179	250615	40	H	Illiterate	low	4	Pain abdomen	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9.8	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
180	246328	40	H	Illiterate	low	3	PV Bleeding	Poor	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	N	Normal	Inflammatory	not done
181	246565	43	H	Illiterate	low	6	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Hypertrophy	12.7	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
182	251309	38	H	Illiterate	low	3	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9.7	NAD	NR	N	Cervicitis	Inflammatory	normal
183	251343	38	H	Illiterate	low	2	WDPV	Poor	IUCD	NS	NS	NS	N	Erosion	12.5	NAD	NR	N	Erosion	Inflammatory	normal
184	251348	26	H	Illiterate	low	1	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11.8	NAD	NR	N	Normal	Inflammatory	not done
185	247438	26	H	Illiterate	low	2	WDPV	Poor	IUCD	NS	NS	NS	N	Healthy	11.3	NAD	NR	N	Normal	Inflammatory	not done

186	247448	36	H	Literate	middle	4	WDPV	Good	No Contraception	NS	NS	NS	N	Cervicitis	13	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
187	256259	25	H	Literate	middle	3	WDPV	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.5	NAD	NR	N	Cervicitis	Inflammatory	normal
188	256320	38	H	Illiterate	low	4	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.5	NAD	NR	N	Normal	Inflammatory	not done
189	256638	42	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
190	256804	38	H	Illiterate	low	2	WDPV	Good	No Contraception	NS	NS	NS	N	Healthy	11.3	NAD	NR	N	Normal	Inflammatory	not done
191	252788	40	H	Illiterate	low	3	PV Bleeding	Poor	No Contraception	NS	NS	NS	N	Cervicitis	13	NAD	NR	P	Cervicitis	Inflammatory	CIN
192	256865	35	H	Illiterate	low	2	WDPV	Good	condom	NS	NS	NS	N	Healthy	12.7	NAD	NR	N	Normal	Inflammatory	not done
193	256897	40	H	Literate	middle	3	PV Bleeding	Average	Tubectomy	NS	NS	NS	N	Cervicitis	12.2	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
194	257253	30	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Erosion	12.4	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
195	256203	40	H	Illiterate	low	4	Pain abdomen	Poor	No Contraception	NS	NS	NS	N	Cervicitis	11	NAD	NR	N	Normal	Inflammatory	not done
196	257911	45	H	Illiterate	low	4	PAIN ABDOMEN	Average	No Contraception	NS	NS	NS	N	Cervicitis	12	NAD	NR	P	Cervicitis	Inflammatory	Cervicitis
197	253302	35	H	Literate	low	6	PAIN ABDOMEN	Average	Tubectomy	NS	NS	NS	N	Cervicitis	9	NAD	NR	N	Cervicitis	Inflammatory	normal
198	253243	25	H	Illiterate	low	2	WDPV	Average	No Contraception	NS	NS	NS	N	Healthy	11	NAD	NR	N	Normal	Inflammatory	not done
199	253261	35	H	Illiterate	low	3	PV Bleeding	Average	No Contraception	NS	NS	NS	N	Cervicitis	11.2	NAD	NR	N	Cervicitis	Inflammatory	normal
200	253874	37	H	Literate	middle	1	WDPV	Good	condom	NS	NS	NS	N	Healthy	10.2	NAD	NR	N	Normal	Inflammatory	not done