

STUDY OF COMPARISON OF VISUAL INSPECTION WITH LUGOL'S IODINE TEST AND COLPOSCOPY IN CERVICAL CANCER SCREENING

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INTRODUCTION

Cervical cancer is one of the most common cancers in India. Carcinoma cervix basically affects the lower part of the uterus which is connected to the vagina. It is most commonly caused by human papilloma virus. Gynaecologists receive various cases from tertiary care centres with diagnosis of various patients as “unhealthy cervix”.

Symptoms include

1. Vaginal bleeding after intercourse.
2. Bleeding between periods or after menopause.
3. Pelvic pain.
4. Pain at the time of intercourse.

It is basically divided into two types

- A. Squamous cell carcinoma
- B. Adenocarcinoma

RISK FACTORS INCLUDE

- Multiple sexual partners
- Early sexual activity
- Presence of other sexually transmitted infections which increases the risk of HPV
- Weak immune system
- Smoking

Women immune system generally prevents the virus from doing any harm. But in some women with low immunity, virus survives for many years leading to cancer. But this can be prevented by having screening test and by receiving a vaccine against Human papilloma virus.^[1]

Most common complaint of which the patient come to the gynaecological OPD is various types of vaginal discharges and examination of such patients is very important to look for the changes in the epithelium of cervix and further to rule out any STDS.

Poor vaginal hygiene in Indian women is responsible for excessive vaginal discharge.

The cervix can be infected by both upper genital tract infection and also by viral or chemical carcinogens.^[2]

Since last 40 years deaths from cervical cancer has been reduced greatly. This decrease is basically because of awareness created among the women regarding PAP smear which can detect cervical cancer in early stages. 12,109 women were diagnosed with cervical cancer and only 4092 women died with it.^[3]

Cervical cancer is the fourth most common cancer affecting women worldwide after breast, colorectal and lung cancers.^[4]

Infection of vaginal mucosa by Trichomoniasis vaginalis and Candida is one of the most common causes of leucorrhoea. These are treatable as well as preventable causes as both of them are transmitted sexually. Although 25% of both the infections are asymptomatic^[5], chronic inflammation may progress to dysplasia if it is not treated.^[6,7]

Cancer cervix is the most common genital cancer seen in India accounting for 80% of all female genital tract cancers. Early detection of preinvasive disease and treatment of cervical intraepithelial lesion (CIN) is the main aim to improve the outcome of the patient.^[8]

There are various screening tests for cervical cancer, of which PAP smear, is the primary screening tool for carcinoma of cervix.

Many studies have raised questions against the accuracy of PAP smear which was predicted to be around 80% to 95% for detecting cervical carcinoma in early stages.

Combine use of PAP smear along with colposcopy has been shown to increase the rate of cervical cancer detection.

The most common screening test used in India for screening of cervical carcinoma is PAP smear.

Recently the accuracy of pap smear, which was found to be 80% to 95% for detecting CIN and early invasive cancer, was questioned.

Conversely, a false negative rate of the Pap smear had been reposted under carefully controlled conditions.

Also because of various screening programs running in different developed countries, has led to reduction of cervical carcinoma.

The combine use of screening colposcopy and cytological studies has been shown to increase the rate of the cervical cancer detection.^[9]

Conventional cervical cytology or pap smear is the most widely used cervical cancer screening test in the world.

Cytology screening programs in developed countries have been associated with high reduction in cervical cancer.^[10,11]

Cancer cervix is still the single largest cause of deaths in developing countries. This is due to almost nonexistent and ineffective cytology based screening test. Though pap smear is reliable, the laboratory infrastructure, counselling, follow up may not be available in low resource setting.^[12]

Colposcopy has been incorporated in almost every part of the world for detection of early stages of cervical cancer.^[13]

The best diagnostic step for detecting the unhealthy cervix is colposcopy with cervical biopsy.

Visual inspection with lugol's iodine (VILI) is the primary screening test which is used to detect early stages of carcinoma of cervix.

It has got high sensitivity and has low false negative rates. and also doesn't require much training. The women who test positive with VILI can be treated on the same setting.

VILI is based on the ability of the colors taken up by the transformation zone of the cervix. In experimental settings VILI is considered as an alternative to cervical cytology.

Columnar epithelium does not take up iodine while squamous epithelium takes up iodine. Similarly precancerous areas and early stages of carcinoma of cervix do not take up iodine as they lack glycogen.

Precancerous lesions and invasive cancer do not take up iodine (as they lack glycogen) and appear as well-defined, thick, mustard or saffron yellow areas.^[14]

This discussion tells us about the role of VILI in detection of early stages of carcinoma of cervix and further the role of colposcopy for early screening of carcinoma of cervix.

I have selected this topic for my study so that I can screen all women in the society for early cervical cancers and a curative treatment can be given to reduce the burden of invasive cancer from society.

Research question

What is the best method for screening carcinoma cervix in females (18 – 75 yrs) whether visual inspection with lugol's iodine or colposcopy and to confirm the findings with biopsy.

Rationale

Visual inspection with lugol's iodine (VILI) gives a rough idea about unhealthy cervix. Colposcopy has best sensitivity and specificity.

AIM AND OBJECTIVES

AIM

To compare Visual inspection with lugol's iodine and colposcopy as screening tool for carcinoma cervix.

OBJECTIVES

1. To study about the efficacy of visual inspection with lugol's iodine as screening tool in tertiary care center
2. To study the role of colposcopy in the evaluation of unhealthy cervix.

3. Screening of the women for detection of early neoplastic lesion of the cervix using Visual inspection with lugols iodine and Colposcopy and final confirmation with biopsy.

REVIEW OF LITERATURE

- **Anatomy Of Cervix**

- ✓ Cervix is the lower most portion of the uterus which extends from the histological internal os to external os and opens in to the vagina.
- ✓ It is cylindrical in shape and measures 2.5cm in length and diameter.
- ✓ It is divided into supravaginal part i.e. the part above the vagina measuring about 1.25cm and the vaginal part.
- ✓ In nulliparous women the vaginal part of the cervix is conical with external os being circular. In parous women it is cylindrical with external os having bilateral slit.

- **HISTOLOGY**

- ✓ **Epithelial lining of the cervix**

1. Endocervical canal and glands- the canal is lined by single layer of tall columnar epithelium with basal nuclei. Those folds at the top are ciliated.

There are patches of cubical basal or reserve cells below the columnar epithelium which may under go squamous metaplasia.

The glands are lined by secretory columnar epithelium.

2. Portio vaginalis- covered by stratified squamous epithelium and extends upto the external os where it is columnar type.

- **The Squamo-Columnar Junction-(Scj)**

The SQUAMO-COLUMNAR JUNCTION-(SCJ) is the point at which the squamous and columnar cells meet. It is typically found between the central ectocervix and the lower cervical canal, but location varies through out the womens life, from foetal development to menopause.

- In reproductive aged women, the original SCJ moves out into the portio of the cervix with hormonal influence. thus acidic vaginal pH plus mechanical irritation likely induces the process of squamous metaplasia, resulting in a new SCJ.
- The area between the original and new SCJ is now referred to as the transformation zone.
- immature squamous metaplastic cells in this transformation zone are theoretically the most vulnerable to neoplasia.^[15]

- **Transformation Zone**

- ✓ 1-10 mm width and is covered by squamous epithelium.
- ✓ The zone is not static and changes with level of oestrogen and is also irritated by infection and trauma.
- ✓ Thus is more chances of severe dysplasia, CIN or invasive carcinoma at this zone.

- **Development of The Cervix**

- ✓ The cervix is the narrowed caudal part which forms the distal 2/3rd part of uterus.
- ✓ it is of paramesonephric origin.^[16]
- ✓ its mucous membrane is derived from urogenital sinus.

- **Cervical Secretion**

- ✓ The endometrial secretion is scanty and watery.
- ✓ The physical and chemical properties of cervical secretion changes with menstrual cycle and also with pregnancy.
- ✓ It secretes an alkaline mucous with pH of 7.8 and this mucous is rich in fructose, glycoprotein and mucopolysaccharides. It also contain sodium chloride.
- ✓ The fructose provides nutritive function to the spermatozoa.
- ✓ Under oestrogenic stimulation glycoprotein network is arranged in a parallel fashion facilitating sperm ascent.
- ✓ Progesterone provides interlacing bridges preventing sperm penetration.
- ✓ Cervical mucous contributes significantly to the normal vaginal discharge.

- **Blood Supply**

- ✓ Cervix is supplied by descending branch of Uterine artery.

- **Venous Supply**

- ✓ Drains in to Uterine vein.

- **Nerve Supply**

- ✓ Pelvic splanchnic nerves S2-S3.

- **Lymphatic Supply**

- ✓ External iliac, obturator lymph nodes either directly or through para cervical lymph nodes.

- ✓ Internal iliac
- ✓ Sacral

Cervical Carcinoma

It is a cancer arising from the cervix which is due to abnormal growth of the cells that has the ability to spread to other parts of the body. In early stages no symptoms are visible but later on abnormal vaginal bleeding, pelvic pain or pain during sexual intercourse may be seen.

Most common cause is human papilloma virus but other causes include smoking, weak immune system, birth control pills and having multiple sexual partners.

About 90% of it are squamous cell carcinoma, 10% are adenocarcinoma.

Diagnosis is done by cervical screening and biopsy.

It can be prevented by HPV vaccines. Other method of prevention include single or no sexual partners or use of condom.

Cervical cancer screening is done by PAP test or VILI or colposcopy.

World wide it is the 4th most common type of cancer. About 70% of the cervical cancer in occur in developing countries.

Treatment

1. Microinvasive cancer (stage 1A) may be treated by hysterectomy (removal of whole uterus and part of vagina).
2. Fertility preserving surgery is trachelectomy in which we remove the cancer and preserve uterus and ovaries.
3. Early stage (IB1 and IIA <4cm) can be treated by radical hysterectomy with removal of lymph node and radiation therapy.
4. Large early stage (IB2 and IIA >4cm) may be treated with radiation therapy and cisplatin based chemotherapy which may be followed by hysterectomy.
5. Advanced stage tumors(IIB-IVA) are treated radiation therapy and cisplatin based chemotherapy.

Cervical Carcinoma Screening

It is used to find changes in the cervix which can lead to cancer.

The cervix is the opening to the uterus and is located at the top of the vagina.

It usually takes 3-7 years for the high grade changes in cells to become cancer.

History of Pap Smear

George Nicholas Papanicolaou was a pioneer in elucidating the physiology and cytologic characteristics of the female reproductive system. He is best known for creating the Papanicolaou test, commonly known as the Pap smear, which revolutionised the early detection of cervical cancer.

Pap Smear

- It is a screening test used to examine cells from vagina and cervix.
- Collection of samples – an optimal gynaecologic cytology sample should contain appropriate representative cells from the transformation zone. If the Pap smear does not contain appropriate representative cells from the transformation zone and the endocervical canal, the ability to detect the test is very low. In order to prepare an adequate pap smear test, the smears must be accurately labelled, the cells must be spread in a thin layer over a slide, without any thick areas or mechanical distortion, they should be distributed over the central areas of the slide, sparing the ends of the slides. The smears should be made rapidly and fixed quickly, to avoid air drying.

Procedure of Collection of Samples

- According to American cancer society, the ideal time for collection of a pap smear is five days after menstrual period has ended. It should not be performed during the menstruation period except in cases when the patient is experiencing abnormal vaginal bleeding. The patient should be instructed not to use a vaginal douche or any type of lubricant or spermicide for 24 hours prior to having a cytological specimen obtained. Cytological specimens should be obtained with a non lubricant speculum prior to the pelvic examination.

Instruments Used

- 1) Plastic or wooden ayers spatula – The ayers spatula is used to sample the ectocervix. The contoured endofayers spatula which best fits the anatomy of ecto cervix and its

transformation zone is selected. The spatula is rotated 360 degree around the entire ectocervix while maintaining tight contact the ectocervical surface.

- 2) Koplins Jar
- 3) Fixative - cytospray or the solutions (95 % ethanol and ether in equal proportions)
- 4) Glass marking pencil
- 5) Wooden layers spatula
- 6) Endocervical brush

Fixation of Slides and Staining

The slides are fixed immediately using 95% alcohol or spray. 95% alcohol is generally accepted as the optimal fixative for cytology smears. 80% isopropanol may be used as a substitute. The freshly fixed material is placed in a container with 95% ethanol and material is usually fixed after 15 – 20 minutes

Papanicolaou classification

- Class 1: Negative absence of atypical or abnormal cells
- Class 2: Negative atypical cells present but without abnormal features
- Class 3: Suspicious cells with abnormal features suggestive but not conclusive of malignancy.
- Class 4: Positive cells and cell clusters fairly conclusive for malignancy
- Class 5: Positive cells and cell clusters conclusive for malignancy

Colposcopy

HISTORY

- Currently, colposcopy is recommended for women with low-grade squamous intraepithelial lesion (LSIL) or worse cytology, or atypical squamous cells of undetermined significance (ASC-US) that persists or is associated with high-risk human papillomavirus (HPV) infection. Colposcopy is an endoscopic instrument that is used to study the epithelium of the vagina and cervix in vivo under adequate illumination and magnification.^[17-19]
- Colposcopy was first developed by Hinselmann, a gynaecologist in collaboration with his physicist colleagues in December, 1924. He believed that cervical cancer must originate as a small dot invisible to naked eye. He devised a series of magnifying lenses which would make the dot visible and this originated the clinical investigation called colposcopy.

- The Second World War was great setback to its development. When cytology screening programs were taken up all over the world in 1950s and 1960s many cases with abnormal cytology by detected and all these cases had to be further investigated by colposcopy. Hence in 1970s saw the renaissance of colposcopy and its popularity increased. This was further aided by the manufacture of this instrument in all parts of world.
- Colposcopy introduced by Prof. Hinselmann (1925) is an optical method for visualizing the lower female genital tract with bright illumination using stereoscopic vision, at a magnification between 4 and 40 fold.
- It has many advantages over cytology. It permits the topographical study of lesion during clinical examination. It is an important tool which complements cytology and histopathology in early detection various cervical lesions.
- Thus, colposcopy is the traditional method for evaluation of abnormal Pap smears and today colposcopy has a central role in the cervical screening programs. Initially, colposcopy was used to identify asymptomatic early invasive disease, thereby improving patient survival. Subsequently, it helped in diagnosing pre-invasive lesions, with resultant reduction in the incidence of cervical cancer and significant drop in the number of diagnostic conisation.
- Colposcopy remains the bestavailable tool to assess women considered at high risk forhaving or developing cervical cancer.^[20]

In 1990, De pale (Italy) published a manual on colposcopy and treatment of lower genital tract. Mitchel et al in 1998, did a meta analysis in the role of colposcopy for the diagnosis of CR4 and found that average weighted sensitivity of diagnostic colposcopy.^[21]

Colposcopy is a clinical method which evaluates changes in the terminal vascular network of cervix that reflects the biochemical and metabolic changes in the tissue. It consist of examination of connective tissue of the cervix, across mucosa using stereoscopic vision.

The following factors are assessed

1. Colour, tone and opacity of the mucosa
2. Surface contour
3. Transformation zone must be seen clearly as most cancers originate from there
4. Presence or absence of abnormal vessels on the surface
5. Acetic acid application

The objectives of colposcopy assessment are

- 1) To further assess abnormalities detected on cervical smear
- 2) To confirm diagnosis by directed biopsy
- 3) To exclude invasive disease

INSTRUMENTATION

Acolposcope is a low power, stereoscopic, binocular, field microscope with a powerful variable intensity light source that illuminate the area being examined. The head of the colposcope, also called the “optics carrier” contains the objective lens, a light source, a light source, green filters to be interposed between the light source and objective lens, a knob to introduce the filter, a knob to change the magnification of the objective. The filter is used to remove the red light, to facilitate the visualization of blood vessels by making them appear dark. Modern colposcope usually permit magnification of 6X to 40 X usually. It may have electrical zoom capability to alter the magnification. Most simple colposcope have a single field magnification level such as Modern light source usually either on tungsten or halogen 6 x, 9x, 10 x, 12 x or 15 x Lower magnification yields a wider view and greater depth of field for examination of cervix.

In 1989, first computer aided colposcope was introduced. Recently, Crisp et al, Mikhail described a system of digital imaging as applied to Colposcopic assessment. The system provide digital image capture and processing.

Modern Colposcope consists of following main parts

- Binocular magnification system
- Illumination system
- Articulated and mobile system
- Video camera

The performance and accuracy of colposcopy depends on the training, experience and skills of the colposcopist. Hence accuracy of colposcopy varies widely among studies in different parts of the world.

In developing countries including India it is not possible to launch cytology based or colposcopy based screening programmes for cervical cancer.

INDICATION OF COLPOSCOPY

The most common indication is positive screening test. Screening may be by cytology, visual inspection with lugols iodine.

- 1) Evaluation of the women with squamous or glandular cell abnormalities on pap smear, with no gross lesion on the cervix or vagina
- 2) Persistence of inflammatory cells despite adequate treatment
- 3) Presence of keratinized cells
- 4) Women with postcoital bleeding, metrorrhagia and postmenopausal bleeding
- 5) Naked eye examination reveals an unhealthy cervix or vagina suspicious of malignancy, especially one with significant aceto whitening after acetic acid wash.
- 6) Evaluation of women with a positive screening high risk HPV, DNA test including those with negative PAP smear
- 7) Evaluation of women with anogenitalcondylomas
- 8) Persistently abnormal PAP smear – Colposcopy is a universally accepted method for studying physiology and pathology of the lower genital tract
- 9) Suspicious looking cervix
- 10) Low grade or high grade lesion
- 11) H/o persistent vaginal discharge
- 12) Positive on visual inspection with lugol's iodine

Normal Transformation Zone

Area between the original SCJ and the new squamo columnar junction in which metaplastic epithelium has replaced the preexisting columnar epithelium.

Coppleson and Reid in 1967, described the features of immature metaplasia in three stages after acetic acid application.

Stage I: Individual VILI assume opaque white appearance.

Stage II: Individual VILI retain their density, but fuse so that intervening spaces are filled.

Stage III: Villus configuration is lost and the new epithelium has a homogenous glass pattern.

Care should be taken, not to configure this immature metaplasia with dysplasia.

COMPONENTS OF TRANSFORMATION ZONE

- 1) Branching vessels – Large capillaries showing tree like branching pattern found only in transformation zone in the walls of retention cyst.
- 2) Nabothian follicles – Mucous filled retention cyst.

- 3) **Gland opening** – Small holes from which mucous seems to pour, representing areas where the new squamous epithelium has covered incompletely and underlying columnar cleft is in continuity with the surface.

Cervical cancers are potentially the most preventable. The anatomical accessibility of cervix to direct examination and long preclinical stage during which 95% of precursor lesion can be treated conservatively and successfully. The basic purpose of screening is to sort out from large group of healthy person those likely to have disease or at increased risk of disease under study and to bring those who are apparently abnormal under medical supervision, perform, cost, effective and highly sensitive. Screening test should be simple, minimally invasive and criteria for participation in cervical screening program should be easy. This will decrease mortality rate of cervical cancer.

ABNORMAL COLPOSCOPIC FINDINGS

- 1) **Acetowhite epithelium** – Flat acetowhite epithelium. These are the areas of high nuclear activity which appears white. A mild degree of acetowhiteness occurs in areas of immature metaplasia
- 2) **Dense aceto white epithelium** - Severe lesions is generally associated with a dense acetowhite change that appears fast and persists longer. Dense acetowhite change within columnar epithelium may indicate glandular disease

PUNCTATION

Fine punctuation– This is a focal area with the capillaries appearing in a stippled pattern like dots. The finer the punctuation, the more likely the lesion is of low grade or metaplasia or inflammation.

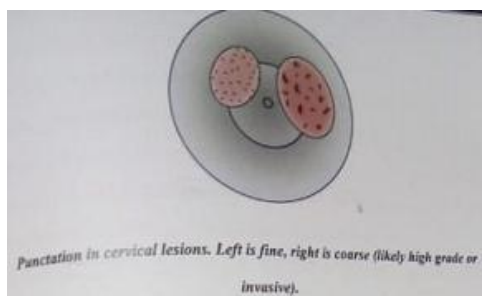


Figure 1- Punctuation.

Coarse punctuation – The coarser the punctuation, the more likely the lesion is of severe or major grade.

MOSAIC

Fine mosaic: Focalcolposcopic appearance in which the capillaries appear to surround abnormal areas appearing as tiles. The smaller, smoother/finer the mosaic, the more likely the lesions is of low grade.

Coarse mosaic: The coarser, wider more irregular the mosaic the more likely the lesion is of major grade.



Figure 1: Mosaicism.

In the year 2005 a study by Sarian LO et al^[22], reported that overall test positivity was 23.0% for VILI. Both the sensitivity, specificity and positive predictive value of VILI in detecting CIN 2 or CIN 3 could be significantly improved.

In the year 2006 a study by Ghislain Sangwa-Lugomo et al^[23], did visual inspection as a cancer screening method which showed that VIA and VILI performed are slightly more sensitive but less specific than Pap cytology across multiple combinations of test and lesion thresholds. Given their lower cost and easy deployment, visual inspection methods merit further assessment as cervical cancer screening methods.

In a study done by Lynette Denny et al^[24] in the year 2006, found that the pooled sensitivity and specificity to detect high-grade CIN were 92 and 85%, respectively by VILI.

In year 2009 a study by Sukhpreet L Singh^[25] compared the PAP smear with the colposcopic findings in ring for cervical intraepithelial neoplasia and cervical cancer. Patients between the ages of 18 and 63 years who had symptoms such as chronic leucorrhoea, postcoital bleeding, intermenstrual bleeding or the findings of erosion, an unhealthy cervix, a lesion bleeding on touch, or an abnormal or suspicious PAP smear were included in this study. Colposcopy was

performed using the Leisgang model. All patients underwent both acetic acid and Sciller's test before subjecting them to colposcopic directed biopsy. It suggests that colposcopy detected 4.75 times more cervical intraepithelial neoplasia lesions than by the PAP smear.

In year 2011, a study by Bahar Kohli^[5] showed that the PAP smear had a sensitivity of 80% and a specificity of 64.29% with positive predictive value of 48.98% and negative predictive value of 88.24% while sensitivity and specificity of colposcopy were 100% and 57.14% respectively and positive predictive value and negative predictive value of colposcopy were found to be 50% and 100% respectively.

A study done by Bhatla N et al^[26] in 2009, in which they evaluated 5050 women in 17 villages, found that 15.6% were positive by VILI. And hence concluded that VILI was accurate screening test and the cure rates for CIN were satisfactory.

In a study, done by Consul S et al^[27] in 2012, showed that VIA and VILI had sensitivity comparable to Pap smear and can thus be a suitable potential alternative screening test in a resource-poor setting. And, use of a combination of tests (Pap+VIA+VILI) had 100% sensitivity but at cost of low specificity and more false positive results.

In a study done by P Ghosh et al^[28] in the year 2012, concluded that cervical cancer screening by Pap smear can be replaced by visual methods like VILI, which has the highest sensitivity (100%) to detect any grade of dysplasia, and a good specificity (93.3%).

In the study done by A. Longatto-Filho et al^[29] in 2012, compared the performance of different screening tests and their feasibility in a cohort of over 12,000 women: conventional Pap smear, liquid-based cytology, visual inspection with acetic acid (VIA), visual inspection with Iodine solution (VILI), cervicography, screening colposcopy, and high risk human papillomavirus (HPV) testing (HR-HPV) collected by physician and by self-sampling. HR-HPV assay collected by the physician has the highest sensitivity (80%), but high unnecessary referrals to colposcopy (15.1%). HR-HPV test in self-sampling had a markedly lower (57.1%) sensitivity. VIA, VILI, and cervicography had a poor sensitivity (47.4, 55, and 28.6%, respectively). Colposcopy presented with sensitivity of 100% in detecting CIN2+, but the lowest specificity (66.9%). Co-testing with VIA and VILI Pap test increased the sensitivity of stand-alone Pap test from 71.6 to 87.1% and 71.6 to 95%, respectively, but with high number of unnecessary colposcopies.

In year 2014, a study by Penagaluru Radha^[30] resulted that majority (70.5%) of CIN occurred in the age group of 30-49 years. Among them 9 women who took OCP, 12% had CIN. Incidence of CIN in the permanently sterilized group was 59% and among IUCD user was 5.9%. Among women who were diagnosed to have CIN, 70.5% complained of excessive vaginal discharge and 11.7% of women had post coital bleeding. PAP smear had a sensitivity of 29% and a specificity of 88% which was attributed to higher number of false negative smears. Colposcopy showed a sensitivity of 82% and specificity of 81% Sensitivity was more then the PAP smear but specificity was less then the PAP smear. Accuracy of colposcopy was found to be 82% which was comparatively more accurate then PAP smear (78%) and hence it concludes Colposcopy offers an excellent tool in evaluating cervical lesions. It is an easy and perspective method and its importance lies in and its importance lies in teaching, diagnosis and management of cervical lesions both neoplastic and non neoplastic.

In the year 2013, a study by DrNavya BN^[31] included Diagnostic accuracy of colposcopic findings Using Modified Reid Colposcopic Index with histopathology in Cervical lesions resulted as according to Reid colposcopic index, there were 54% benign cases, 18% women were diagnosed as CIN 1, CIN2, CIN3 respectively The general accuracy rate was 92 % and specificity of colposcopic examination was was 90.48% The kappa value was 0.903(p = 0.00<= 0.05) The study concluded high accuracy and correlation between colposcopy and histopathology.

In a study done by Richa D. Chaudhary et al^[32] in the year 2014, concluded that The sensitivity of colposcopy was 79.37%, specificity 81.02%, positive predictive value 65.79%, negative predictive value 89.52% respectively and accuracy was 80.5%.

Pap smear had a sensitivity of 25.4%, specificity of 99.27%, positive predictive value of 94.12%, negative predictive value of 74.32%, and accuracy of 76.0% respectively. Pap smear had a poorer sensitivity compared to Colposcopy but a better specificity than colposcopy.

In a study done by Nikila P^[33] in 2015, showed that Colposcopy is the best screening tool with highest sensitivity. But need for expert made it difficult to implement in low resource settings. Hence, the emphasis was shifted to visual inspection methods with acetic and Lugol's iodine. This method could sustain due to its simplicity and ease of performing in mass programmes. Moreover the specificity and sensitivity of these visual inspection based

tests were also equally good 78% and 93% respectively. Hence for resource restricted settings, VIA/VILI followed by colposcopy gives a much better results.

In year 2015, A study by Chandrakala Joshi^[34] included Care centre results cytology correlation of Pap smear and colposcopy in relation to hpe findings in detection of Premalignant lesions of cervix in A tertiary Care centre resulted that colposcopy directed biopsy sensitivity is 65.38% specificity is 95.83%. Positive predictive value 94.4%, negative predictive value 71.8% and accuracy as 80% concluded that incidence of cervical intraepithelial neoplasia 1 was 28%, squamous cell carcinoma 5% and adenocarcinoma 2% This emphasizes the use of all 3 methods PAP cytology, colposcopy, and histology is complementary to each other and helps to reduce false negative cases.

In the year 2015, a study by Zainab S Nayani^[35] on comparison and correlation of PAP smear with colposcopy and histopathology in evaluation of cervix resulted sensitivity of pap smear to be 31.25% which was very low compared to its specificity which was 94.44% which means pap smear shows higher number of false negative smears. Colposcopy showed a high sensitivity of 96.57% and a good specificity of 88.55% compared to pap smear. the study concluded that colposcopy is definitely more sensitive and accurate than pap smear. By combining pap smear with colposcopy we can maximize the sensitivity and specificity of cancer screening.

In a study by Saurabh Bobdey et al^[36] in the year 2016, concluded that, the pooled estimates of sensitivity and specificity of with visual inspection with Lugol's iodine (VILI), were found to be 78.27% and 87.10% respectively. In developing countries because of lack of necessary infrastructure and quality control, high-quality cytology screening may not be feasible for wide-scale implementation.

In a study by K Rama et al^[37] in 2016, the sensitivity was higher for VIA/VILI(94.55%). However the specificity was higher for Pap smear (94.55%). The positive predictive value and the percentage of false negatives were higher with Conventional Pap smear whereas the negative predictive value and the percentage of false positives were higher with VIA/VILI. VIA/VILI can be used as an initial screening test for cervical cancer. Conventional Pap smear is a specific test for diagnosis of pre-invasive lesions of cervix.

In a study by Richa Garg et al^[38], in 2017, Commonest complaint was white discharge per vaginum in 58.5% followed by pelvic pain in 24% women. 8% women had abnormal pap smear findings with 4% of women had ASCUS, 0.5% had ASC-H, 3% had LSIL and 0.5% had HSIL, 73% had inflammatory and 19% with normal smear. 38.5% had abnormal colposcopy with maximum 28% women had aceto white lesions. Sensitivity of pap smear was 44.44% while sensitivity of colposcopy was 88.88%. Pap smear had poor sensitivity as compared to colposcopy. Hence simultaneous use of colposcopy has shown to increase in the rate of carcinoma cervix detection in symptomatic women.

In a study done by Shashwat Vidyadhar et al^[39] in the year 2017, concluded that Pap smear had a poor sensitivity compared to colposcopy but a better specificity than colposcopy. Hence, it may be better to utilize it in screening of premalignant lesions of cervix.

MATERIAL AND METHODS

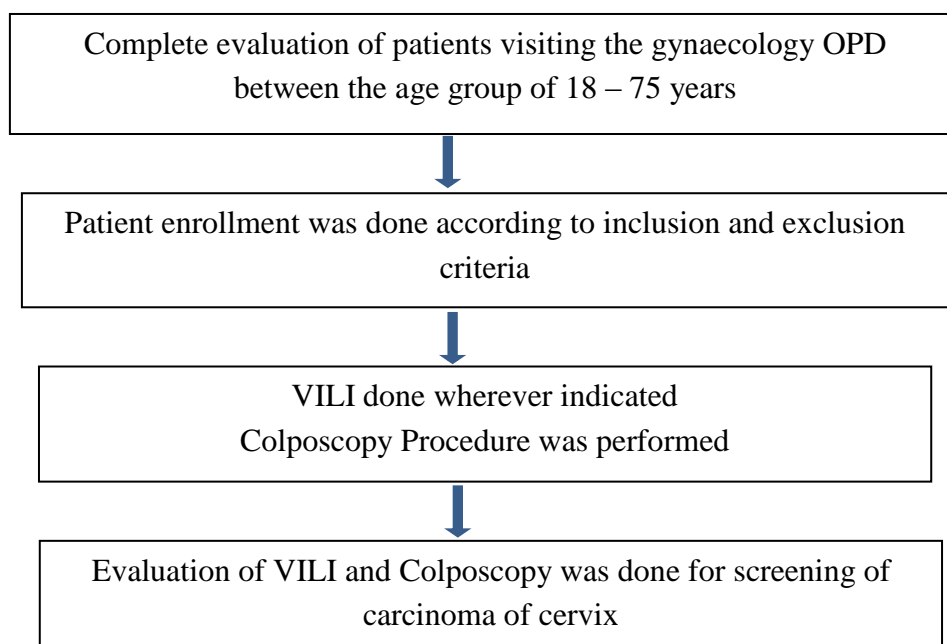
Study Setting

The study has been carried out in Department of Obstetrics and Gynaecology in our hospital.

Participants

Patients who will be visiting the gynaecology OPD between the age group of 18 – 75 years.

Flow chart



IEC clearance : Approval from institutional ethical committee has been taken

Inclusion criteria

1. Women (in the age group of 18-75years) attending Gynaecology OPD
2. Those who are ready to participate in study

Exclusion criteria

1. Allergy from iodine
2. Excessive cervical and vaginal discharge
3. History of hysterectomy
4. Actively bleeding per vagina
5. Any past surgery of the cervix
6. Pregnant women

METHODOLOGY**SAMPLE SIZE**

Estimated sample size for study is 100 patients

Formula

SENSITIVITY = 91.3%

SPECIFICITY = 96.2%

$n_{se} = Z\alpha/2$

$(1.96)^2 * 0.913 * 0.09$

$(0.10)^2 * 0.32$

$98.32 = 100$

Design

Prospective cross sectional study.

Study Duration

This study was performed for 1 year. Informed consent was included for the women who fulfilled the inclusion criteria and enrolled in the study.

Procedure Study

The detailed history of the patient including demographic data like age, education level, age at which first coitus was done, parity, age at the time of marriage and age at the time of enrolment was noted on a structured questionnaire.

Documentation

Colposcopic findings of the patient is documented carefully on the paper immediately after the examination. The report of colposcopy is given to the patient on the same day. Hence colposcopy is very feasible.

The procedure to be performed was clearly explained to the patients and the written consent was taken along with the relevant history, and also complete reassurance was given to the patient that the procedure is painless.

After taking the PAP smear with the help of Ayers spatula results were evaluated according to the Bethesda system. Following this Visual inspection with lugol's iodine test was done (VILI). Results of VILI were recorded as positive or negative.

All patients in the study underwent colposcopy. Colposcopy inspection of the cervix was done after seeing the cervix with naked eyes.

After taking the Pap smear, cleaning of the cervix was done with normal saline and visualized, followed by VILI and colposcopy.

Confirmation of lesion was done with help of biopsy if colposcopy showed positive finding or if VILI had positive findings. Statistical analyzation of the collected data was done and then sensitivity, specificity, Negative predictive value and Positive predictive value of VILI and colposcopy are compared.

COLPOSCOPY**Instruments required for colposcopy are**

1. Examination table
2. Cuscos speculum
3. Reagents
4. Normal saline
5. Acetic acid – 1%, 3%, 5%
6. Cotton swabs
7. Punch biopsy forceps
8. Colposcope



Figure 3: Dr. Camscope colposcope.

All patients underwent colposcopy using the Dr Camscope Colposcope model no. 150 FC with magnification between 10X to 12.5 X. While performing colposcopy surface was first cleaned with normal saline and then assessment of all the lesions including vascular lesions were done. Via green filter abnormal vessels were examined. Then According to the REID'S index colposcopy findings were noted.

The report of colposcopy was considered as positive if REID'S index was less than 3 and it was considered as abnormal if REID'S index was more than 3.

Before performing colposcopy well informed valid consent was taken from the patient and the procedure was well explained to her and then she was given lithotomy position. Under all aseptic precaution, a double bladed sim's speculum was placed in the vagina and. 3% of acetic acid was applied over to cervix.

Aceto white areas implies high nuclear density. Development of precancerous lesions over the transformation zone is basically to be noted.

The part of the cervix which turn white on applying acetic acid or shows some abnormal vascular pattern was further taken up for biopsy.

Swede Score For Interpretation of Colposcopic Findings^[40]

Grades	0	1	2
Lesion size	<5mm	5-15 mm	>15 mm
Vessels	Diffuse	Absent	Atypical course
Acetic acid uptake	Transparent	Milky,shady	Distinct
Surface and margins	Diffuse	Sharp and irregular, geographical areas	Sharp with difference in surface levels
Staining with iodine	Brownish	Faint yellow	Distinctly yellow

Interpretation According To Swede Score

The total SWEDE score ranges between 0 and 10. A score of

>8 - REQUIRES EXCISION

5-7 - REQUIRES BIOPSY

>5 - HIGH GRADE LESIONS

< 5 - DOESN'T REQUIRE BIOPSY

Complication of Colposcopy

- Local bleeding
- Infection

Pap Smear

After explaining the procedure to the patient, they are placed in lithotomy position with the help of sister and per speculum examination is done of cervix and vagina Then the squamo columnar junction is identified carefully, and Ayers spatula is inserted and scraping done along the whole circumference. Then the scraping was evenly spread on a glass slide and fixed immediately with 95% alcohol and ether by dipping in Kopliks jar and then transported to cytopathological laboratory. The result of Pap smear (cytology) was done according to Revised Bethesda System.

If cytology report was ASCUS (Atypical Squamous Cell of Undetermined Significance) and above then PAP smear was considered positive or abnormal.

If cytology report was NLIM (Negative for intraepithelial lesion or Malignancy) or inflammatory smear then the PAP smear was considered as negative.

Cervical Biopsy (Histopathology)

The patients who came out to be positive on any of the screening tests underwent biopsy. Punch biopsy was taken from abnormal areas and the excised tissue, obtained was fixed in 10% formalin and sent to the pathology department of our hospital.

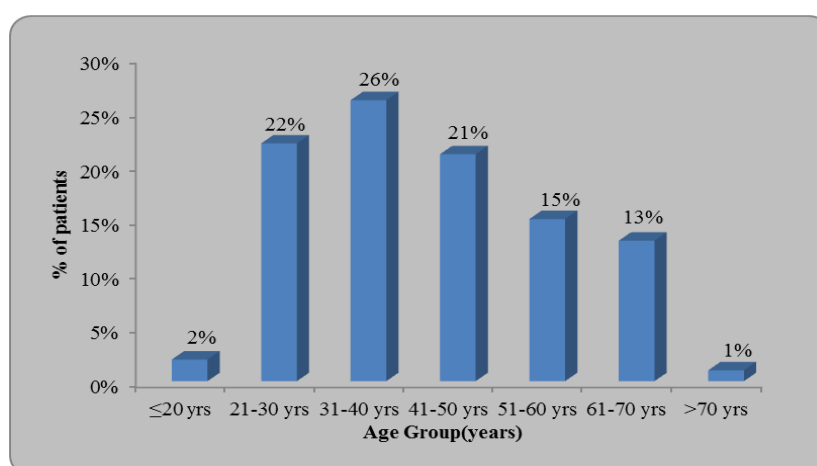
Statiscal Analysis

Descriptive and inferential statistics were used to analyze the data which was done using chi square test, sensitivity, specificity, PPV, NPV and diagnostic accuracy The software used in the analysis was SPSS 22.0 version and Graph Pad Prism 6.0 version and $p < 0.05$ is considered as level of significance.

OBSERVATIONS AND RESULTS

Table 1: Age wise distribution of patients.

Age(years)	No of patients	Percentage
≤20 yrs	2	2
21-30 yrs	22	22
31-40 yrs	26	26
41-50 yrs	21	21
51-60 yrs	15	15
61-70 yrs	13	13
>70 yrs	1	1
Total	100	100
Mean ±SD	43.23±13.92(17-75 years)	



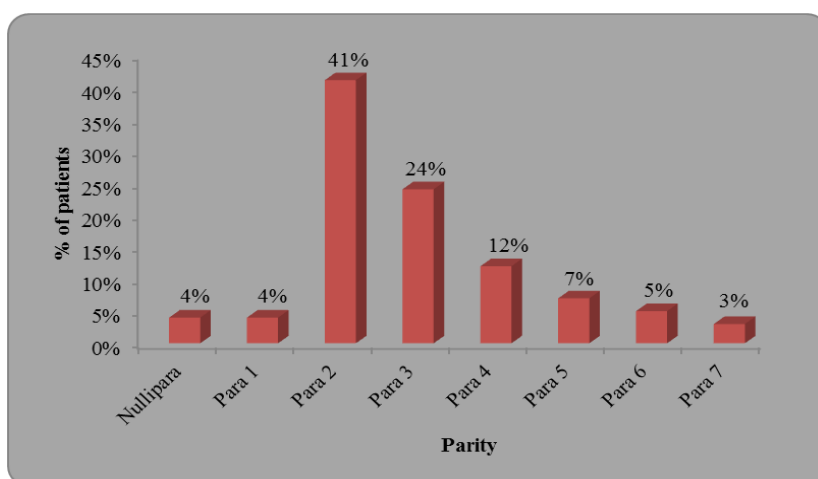
Graph 1: Age wise distribution of patients.

Table 1 and graph 1 shows age wise distribution of 100 cases out of which 26 patients were in the age group of 31- 40 years, 21 patients were in the age group of 41 to 50 years, 15

patients were in the age group of 51 to 60 years, 13 patients were in the age group of 61- 70 years. Mean age was 43.23 years with range from 17 to 75 years of age.

Table 2: Parity wise distribution of cases.

Parity	No of patients	Percentage
Nullipara	4	4
Para 1	4	4
Para 2	41	41
Para 3	24	24
Para 4	12	12
Para 5	7	7
Para 6	5	5
Para 7	3	3
Total	100	100

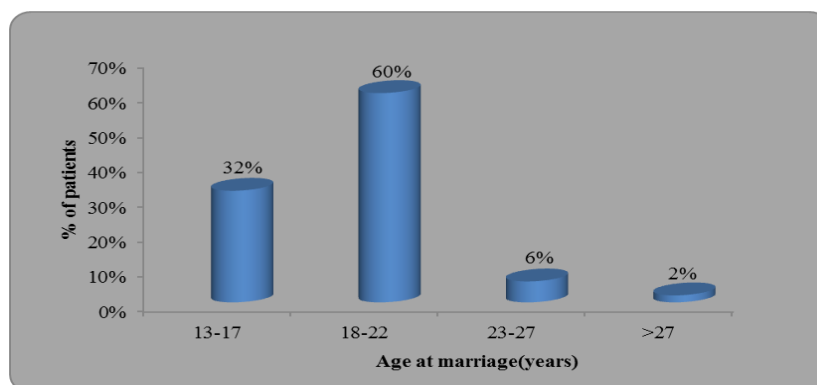


Graph 2: Parity wise distribution of cases.

Table 2 and graph 2 shows parity wise distribution of 100 cases out of which 4 were nulliparous, 41 patients were para2, 24 patients were para 3, 12 patients were para 4, 7 patients were para 5, 5 were para 6, and 3 were para 7.

Table 3: Distribution of Cases According To Age of Marriage.

Age At Marriage(Years)	Number Of patients	Percentage
13-17	32	32
18-22	60	60
23-27	6	6
>27	2	2
Total	100	100
Mean \pm SD	19.14 \pm 3.12(13-30 years)	

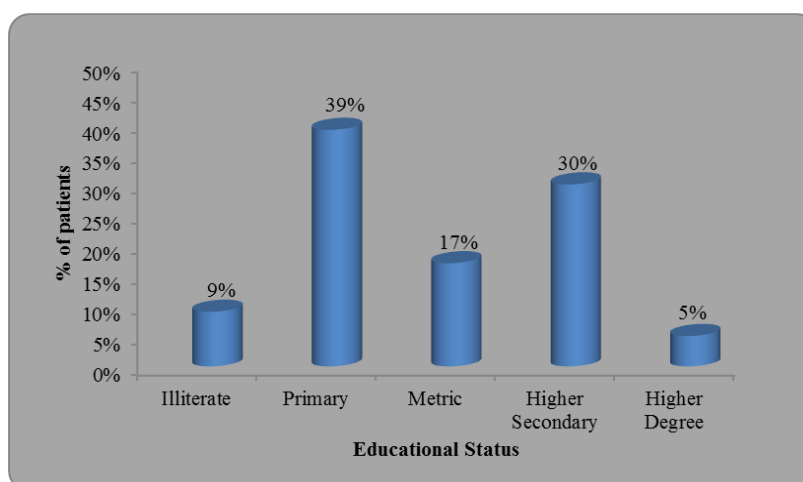


Graph 3: Distribution of Cases According To Age of Marriage.

Table 3 and graph 3 shows distribution of cases revealed that out of 100 patients 60% of the patients were married between the age group of 18 – 22 years, 32% were married between the age group of 13-17 years of age and 2% of the patients were married after 27 years of age. Mean age of marriage was 19.14 years.

Table 4: Distribution of Cases According To Educational Status.

Educational Status	Number Of patients	Percentage
Illiterate	9	9
Primary	39	39
Metric	17	17
Higher Secondary	30	30
Higher Degree	5	5
Total	100	100



Graph 4: Distribution of Cases According To Educational Status.

Table 4 and graph 4 shows educational status of 100 patients out of which 39 patients received primary education, 9 were illiterate and 35 patients received higher degree.

Table 5: According To Presenting Complaints distribution of cases.

Presenting Complaints	Number Of patients	Percentage
White Discharge	42	42
Curdy White Discharge	5	5
White Discharge With Itching Over Vulva	7	7
Itching Over Vulva	6	6
Burning Micturition With Itching	3	3
Yellowish White Discharge	5	5
Something Coming Out Of Vagina	5	5
Postmenopausal Bleeding	6	6
Pain in abdomen	21	21
Total	100	100

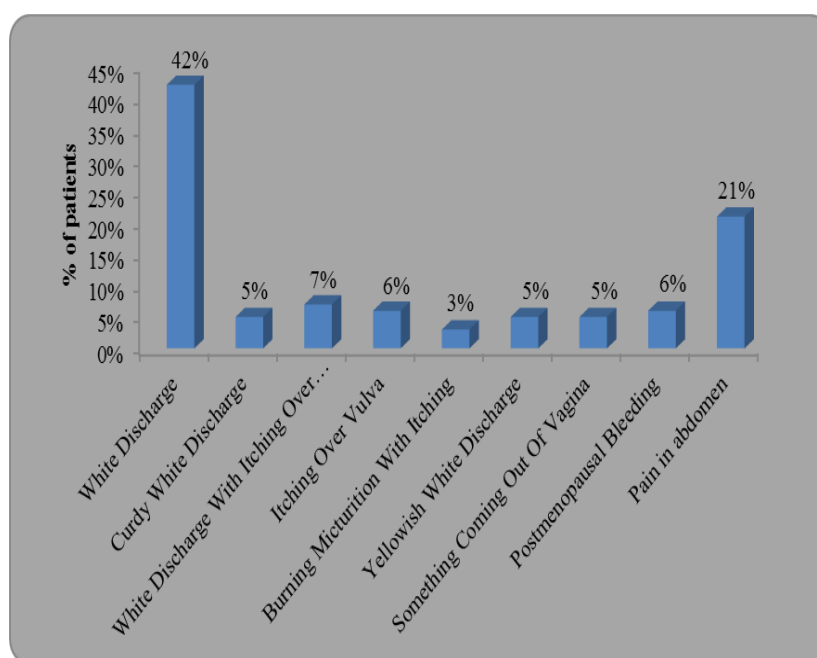
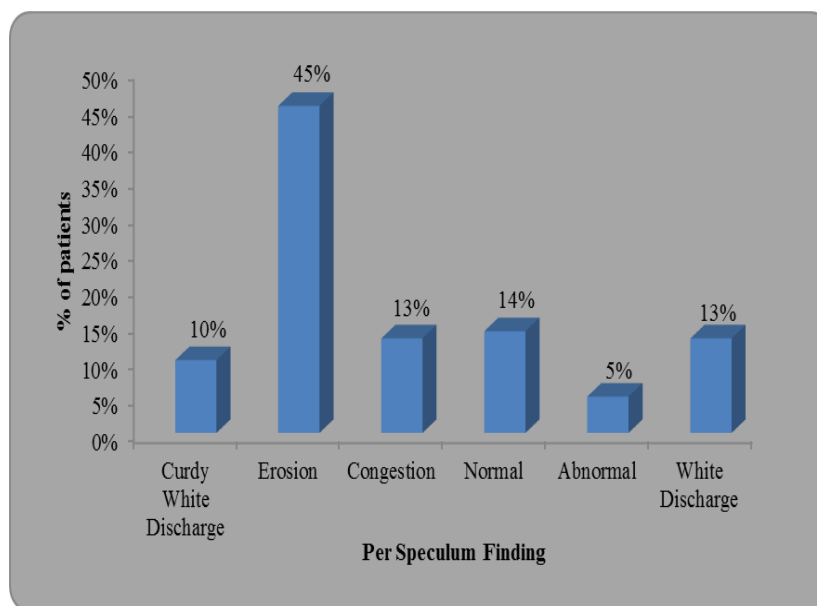
**Graph 5: According To Presenting Complaints distribution of cases.**

Table 5 and graph 5 shows presenting complaint was white discharge in 42 % of the cases with various other complaints as discussed.

Table 6: According To Per Speculum Findings distribution of cases.

Per Speculum Findings	Number Of Cases	Percentage
Curdy White Discharge	10	10
Erosion	45	45
Congestion	13	13
Normal	14	14
Abnormal	5	5
White Discharge	13	13

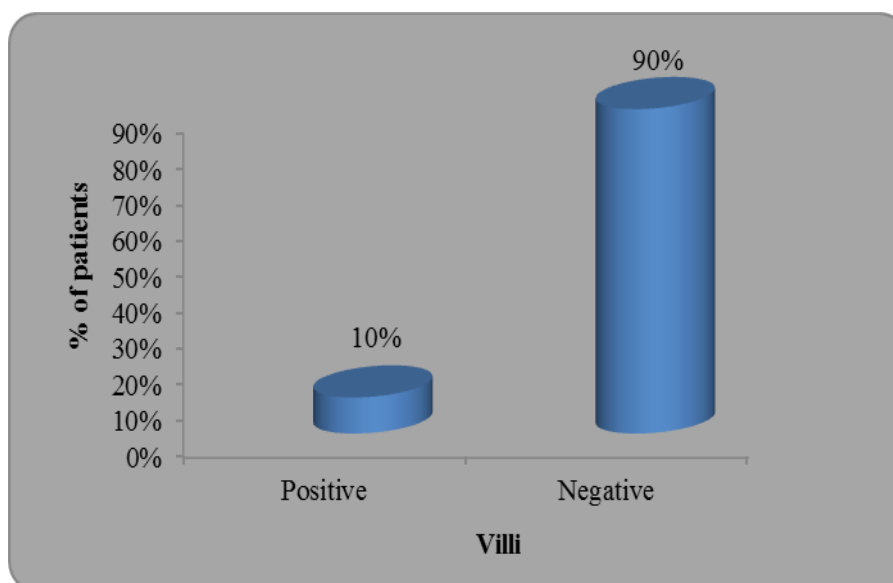


Graph 6: According To Per Speculum Findings distribution of cases.

Table 6 and graph 6 shows per speculum examination done in all 100 cases, on examination it was found that 45% of the cases had cervical erosion, 14% had normal findings and 5% had abnormal findings.

Table 7: Distribution of Cases According To VILI.

VILI	Number Of Cases	Percentage
Positive	10	10
Negative	90	90
Total	100	100

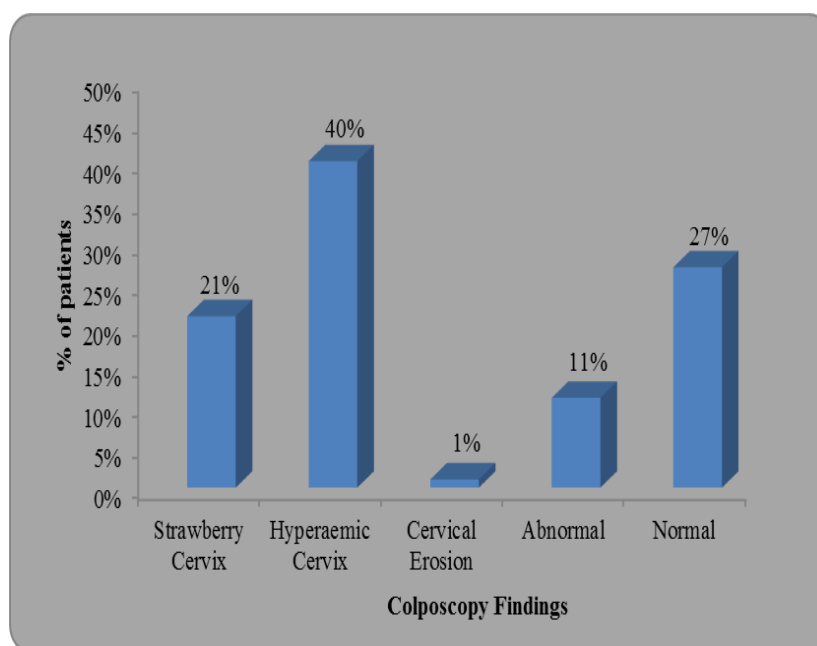


Graph 7: Distribution of Cases According To VILI.

Table 7 and graph 7 showed distribution of cases according to positive and negative findings of VILI, out of which 10 patients had positive findings and rest have negative findings.

Table 8: Distribution of Cases According To Colposcopy Findings.

Colposcopy Findings	Number Of Cases	Percentage
Strawberry Cervix	21	21
Hyperaemic Cervix	40	40
Cervical Erosion	1	1
Abnormal	11	11
Normal	27	27
Total	100	100

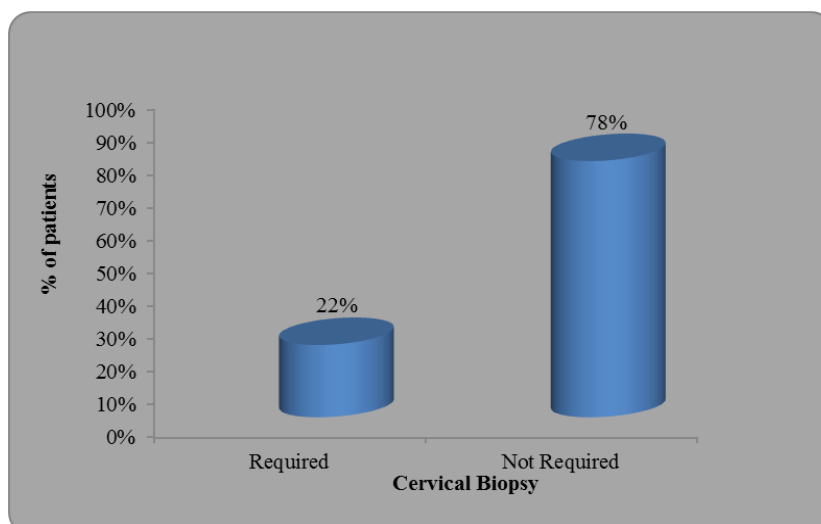


Graph 8: Distribution of Cases According To Colposcopy Findings.

Table 8 and graph 8 showed distribution of cases according to colposcopy findings out of which 11 patients had abnormal findings and 27 patients had normal findings and rest findings as above.

Table 9: Distribution Of Cases According To Cervical Biopsy.

Cervical Biopsy	Number Of Cases	Percentage
Required	22	22
Not Required	78	78
Total	100	100

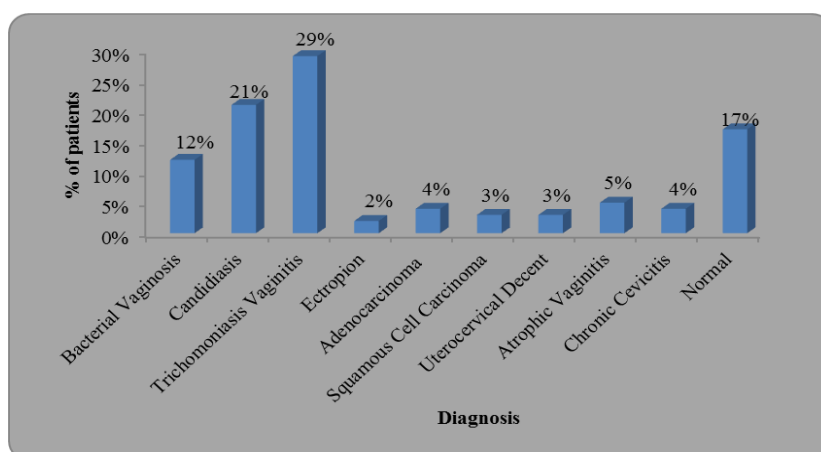


Graph 9: Distribution of Cases According To Cervical Biopsy.

Table 9 and graph 9 showed distribution of cases according to requirement of cervical biopsy, out of 100 patients, 22 patients required biopsy rest did not require biopsy.

Table 10: Distribution Of Cases According To Diagnosis.

Diagnosis	Number Of Cases	Percentage
Bacterial Vaginosis	12	12
Candidiasis	21	21
Trichomoniasis Vaginitis	29	29
Ectropion	2	2
Adenocarcinoma	4	4
Squamous Cell Carcinoma	3	3
Uterocervical Decent	3	3
Atrophic Vaginitis	5	5
Chronic Cevicitis	4	4
Normal	17	17
Total	100	100

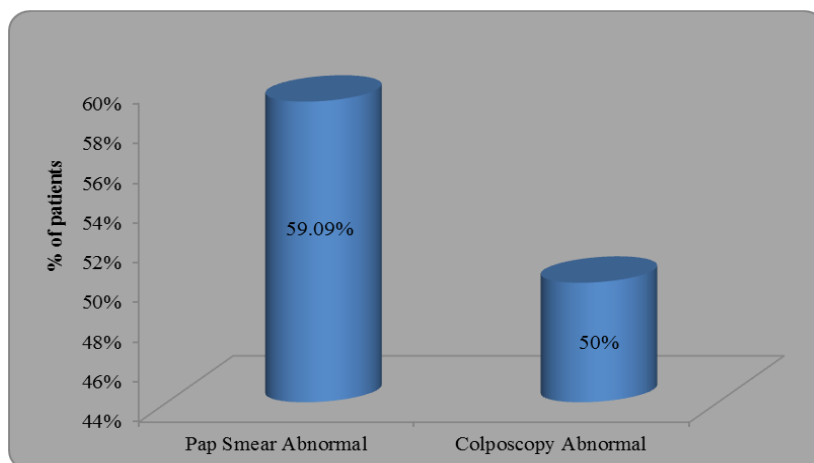


Graph 10: Distribution of Cases According To Diagnosis.

Table 10 and graph 10 shows distribution of cases according to diagnosis, trichomoniasis vaginitis were present in 29% of cases, candidiasis seen in 21% of the cases, 12% of the cases had bacterial vaginosis. and 17% had normal findings.

Table 11: Distribution of Cases Who Required Cervical Biopsy.

	Pap Smear Abnormal	Colposcopy Abnormal
Number	13	11
Percentage	59.09%	50%

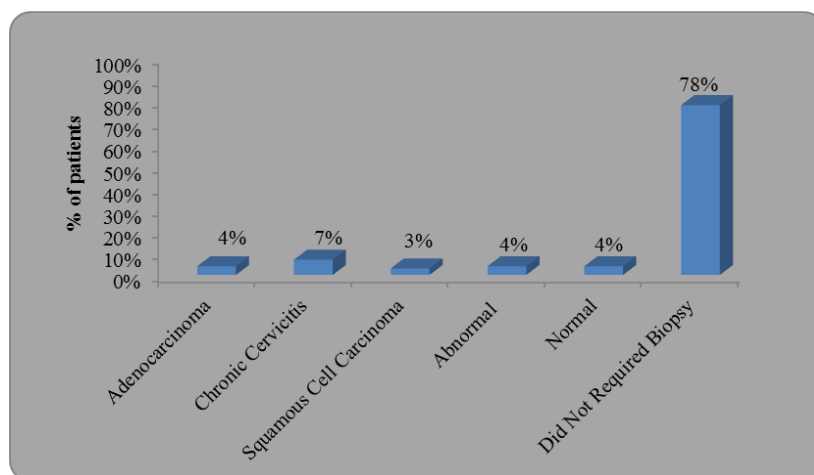


Graph 11: Distribution of Cases Who Required Cervical Biopsy.

Table 11 and graph 11 shows distribution of cases who require cervical biopsy out of which 13 had abnormal pap smear and 11 had abnormal colposcopy findings.

Table 12: Distribution of Cases According To Cervical Biopsy Reports.

Cervical Biopsy Reports	Number Of Cases	Percentage
Adenocarcinoma	4	4
Chronic Cervicitis	7	7
Squamous Cell Carcinoma	3	3
Abnormal	4	4
Normal	4	4
Did Not Required Biopsy	78	78
Total	100	100



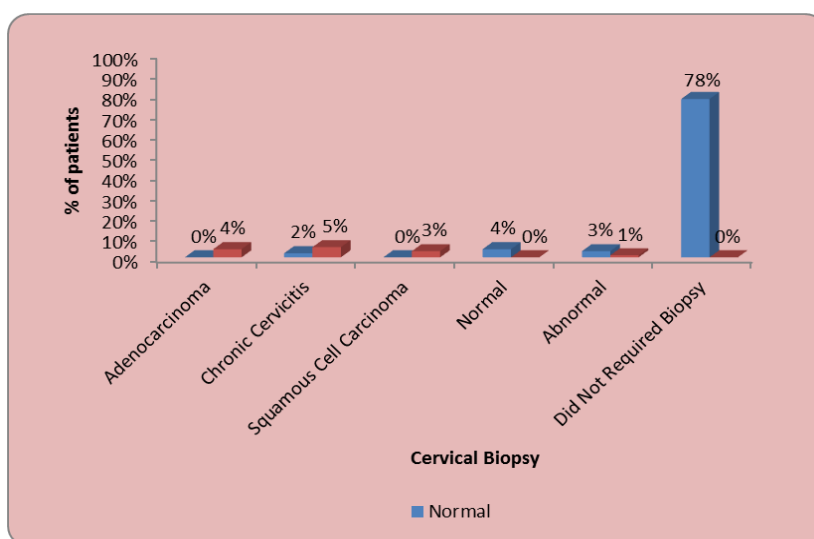
Graph 12: Distribution of Cases According To Cervical Biopsy Reports.

Table 12 and graph 12 shows out of 22 cases who underwent cervical biopsy 4 cases had adenocarcinoma, 7 cases had chronic cervicitis and 3 cases had squamous cell carcinoma.

Table 13: Agreement Between Abnormal Pap Smear And Cervical Biopsy.

Pap Findings	Number Of Cases	Adenocarcinoma	Chronic Cervicitis	Squamous Cell Carcinoma	Normal	Abnormal	Did Not Required Biopsy
Normal	87	0(0%)	2(2%)	0(0%)	4(4%)	3(3%)	78(78%)
Abnormal	13	4(4%)	5(5%)	3(3%)	0(0%)	1(1%)	0(0%)
Total	100	4(4%)	7(7%)	3(3%)	4(4%)	4(4%)	78(78%)

χ^2 -value=80.73, p-value=0.0001, Significant



Graph 13: Agreement Between Pap Smear And Cervical Biopsy.

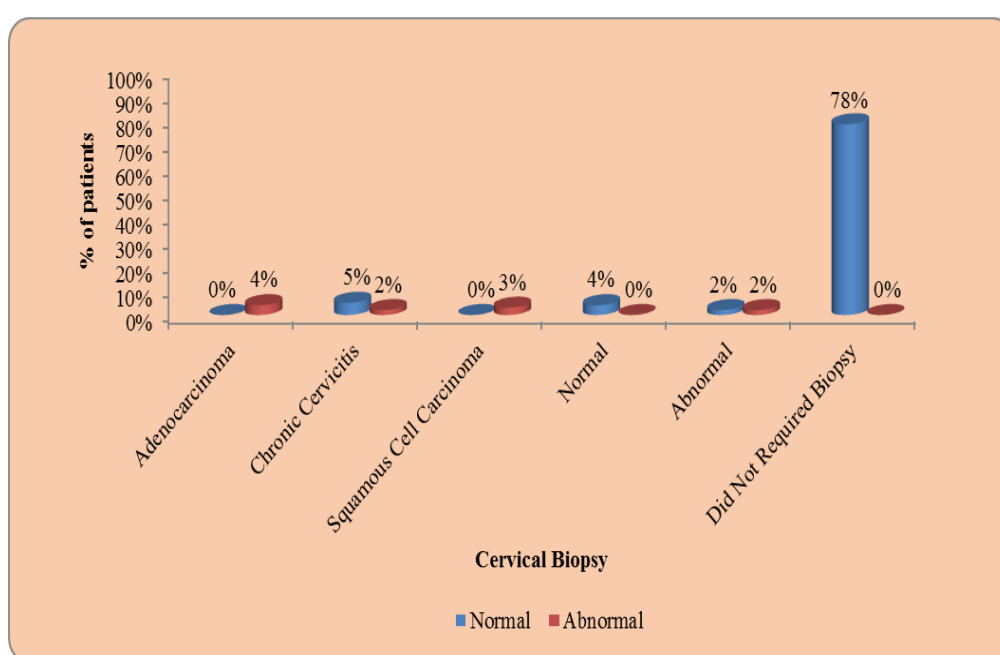
Table 13 and graph 13 shows agreement between pap smear and cervical biopsy out of which 4 cases were diagnosed as adenocarcinoma out of which 4 cases had abnormal pap findings. 7

Cases of chronic cervicitis were observed out of which 5 were abnormal. 3 Cases of squamous cell carcinoma were seen, all three had abnormal pap findings.

Table 14: Agreement Between Colposcopy And Cervical Biopsy.

Colposcopy Findings	Number Of Cases	Adenocarcinoma	Chronic Cervicitis	Squamous Cell Carcinoma	Normal	Abnormal	Did Not Required Biopsy
Normal	89	0(0%)	5(5%)	0(0%)	4(4%)	2(2%)	78(78%)
Abnormal	11	4(4%)	2(2%)	3(3%)	0(0%)	2(2%)	0(0%)
Total	100	4(4%)	7(7%)	3(3%)	4(4%)	4(4%)	78(78%)

χ^2 -value=75.19, p-value=0.0001, Significant

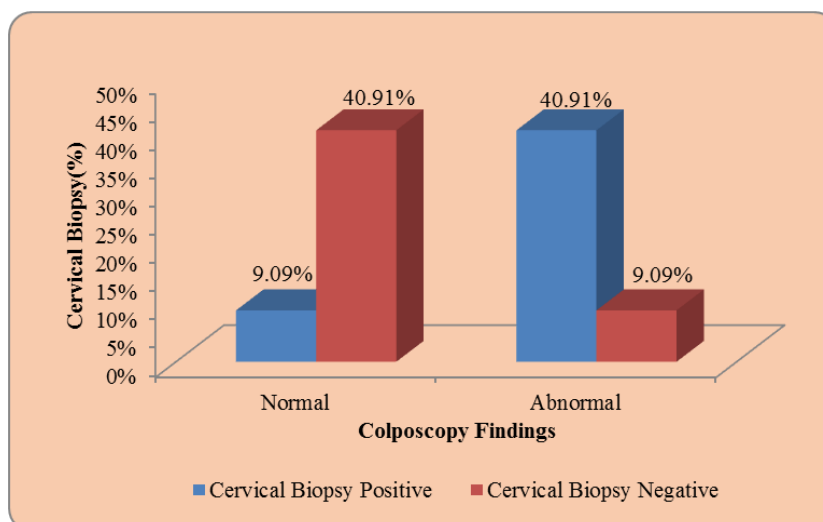


Graph 14: Agreement Between Colposcopy And Cervical Biopsy.

Table 14 and graph 14 shows agreement between colposcopy and cervical biopsy, 11 cases had abnormal colposcopy findings out of which 4 patients were diagnosed as adenocarcinoma, 2 were diagnosed as chronic cervicitis, 3 were diagnosed as squamous cell carcinoma and 2 had abnormal findings.

Table 15: Accuracy of Colposcopy With Cervical Biopsy.

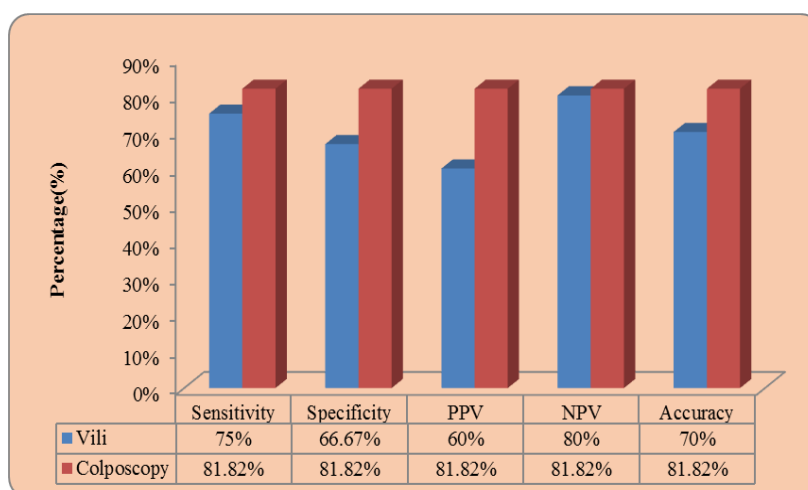
Colposcopy Findings	Cervical Biopsy Positive	Cervical Biopsy Negative
Normal	2(9.09%)	9(40.91%)
Abnormal	9(40.91%)	2(9.09%)
Total	11	11(50%)



Graph 15: Accuracy of Colposcopy With Cervical Biopsy.

Table 16: Statistical Comparison of Screening Test.

	VILI	Colposcopy
Sensitivity	75%	81.82%
Specificity	66.67%	81.82%
PPV	60%	81.82%
NPV	80%	81.82%
Accuracy	70%	81.82%
P Value	0.0001,S	0.003,S



Graph 16: Statistical Comparison of Screening Test.

Table 16 and graph 16 shows statistical comparison of, VILI and Colposcopy, the sensitivity of VILI is 75%, and that of colposcopy is 81.82%. Specificity of VILI is 66.67% and of Colposcopy is 81.82%. Positive predictivevalue of VILI is 60% and that of colposcopy is 81.82% Negative predictive value of VILI is 80% and that of colposcopy is 81.82%. Accuracy of VILI is 70% and that of colposcopy is 81.82%.

DISCUSSION

In the study all the patients were evaluated on the basis of inclusion and exclusion criteria and who attended the gynaecology OPD in our hospital,. 100 patients were enrolled as cases for study and consent was taken. The cases were subjected to Per speculum examination, VILI and colposcopy. Confirmatory biopsy were taken if required

Age

In this study, the age range taken was 17 years to 75 years. This consideration was taken because the prevalence of carcinoma of cervix is maximum in sexually active group.

According to age wise distribution of 100 patients, 26 patients were in the age group of 31-40 years, 21 patients were in the age group of 41 to 50 years, 15 patients were in the age group of 51 to 60 years, 13 patients were in the age group of 61- 70 years. Mean age was 43.23 years with range from 17 to 75 years of age.

Parity

In the present study, parity range was from nulliparous to para 7.

Age At Marriage

The mean age of marriage in the present day study was 19.14 years Goel et al^[41] and Jeronimo J et al^[42] reported mean age at marriage 21 and 20 years respectively. Bhatia N et al^[43] had noted the age at marriage in their study to be 19 years.

Study Process

In the present study, we screened patients using per speculum examination, VILI and colposcopy. All the cases underwent screening tests. Positive cases on any of the following screening test underwent cervical biopsy. Cervical biopsy was taken as gold standard.

Colposcopy Findings

In the present study, the sensitivity, specificity, NPV and PPV of colposcopy is 81.82% respectively The accuracy of colposcopy to cervical biopsy is 81.82%.

The wide range of statistical difference was seen at the interpretation. Also the study populations were different. Some studies were done hospital based populations who had symptoms and others as a mass screening test. So the difference is due to the observer's bias So colposcopy can be a better alternarnative to VILI as specificity of colposcopy is 81.82%

as compared to that of VIL which is 66.67% Also the sensitivity and positive predictive value is more for colposcopy as compared to VILI So, colposcopy is better then VILI.

Summary

The present study “Study of comparison of Visual inspection with lugol’s iodine test and colposcopy in cervical cancer screening” was conducted in dept of Obstetrics and Gynaecology. The patients enrolled in the study mainly belonged to rural areas of our district.

Colposcopy performs a better diagnostic test as compared to VILI The sensitivity as well as specificity of colposcopy was more then that of VILI.

Colposcopy can be used not only as a screening test for cervical cancer but can also be used to diagnose various infective cause of cervical infections.

Patients of low socio economic status can’t afford repeated follow up hence colposcopy can be used as a investigation to rule out cervical cancer lesions and also as a diagnostic test for various cervical infections.

CONCLUSION

It is evident that colposcopy is definitely more accurate and sensitive then VILI. By combining both we can increase the sensitivity and specificity of screening of cervical cancer.

RECOMMENDATIONS

Colposcopy is a promising, practical alternative, to cytology in screening of cervical cancer in low resource set up

- Integrate colposcopy based screening programme at primary level, tertiary hospitals and rural health posts in order to downstage cancer cervix in our country.
- We need more population based study to validate the results.
- Training to the medical officers, nurses and paramedical staff to enhance the effectiveness of colposcopy as screening test.
- Expansion of colposcopy and VILI based screening programmes by organizing more workshop for health workers and recruitment of more trained staff for mass screening programmes.
- In low resource setup colposcopy can be used as a complementary test with VILI for universal screening.

LIMITATIONS

Limitations in our study are

1. Our study is hospital based which is located in Central India. Considering whole of India population our study is definitely not typical.
2. Small sample size is and further larger studies are required for confirmation of results
3. Difficult to detect recurrence due to small follow up period of 6 months
4. Colposcopy is a visual evaluation test, so liable for observer bias
5. The study is liable to verification bias, as only those cases which tested positive on screening were subjected to biopsy confirmation

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