

Opportunistic Colposcopic Evaluation of Cervical Lesions for Detecting Early Malignancy

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DOI: 10.29322/IJSRP.9.05.2019.p8933

<http://dx.doi.org/10.29322/IJSRP.9.05.2019.p8933>

Abstract- Background: Cervical cancer is very frequent, being the second most common in women worldwide and the second most common of genital tract cancers in India. Around 80% of Carcinoma cervix incidence is in developing countries. **Aim:** To inspect the squamo-columnar junction of the cervix and identify suspicious areas by using colposcope for early detection of cervical cancer. **Objectives:** Through colposcopic screening, carcinoma cervix can be detected at an earlier stage. Appropriate measures can be taken for early and correct management at the right time. These measures will ultimately contribute to early diagnosis and better prognosis of carcinoma cervix. **Material & methods:** The study is an opportunistic study consisting of 100 women of age group between 30-50 yrs with clinically suspicious cervix, discharge per vaginum, inter menstrual bleeding or contact bleeding attending outpatient section in Dept of Obstetrics & Gynaecology at a tertiary care centre in eastern India from June 2012 to October 2014. All these patients were examined and findings noted using Colposcope & 5% acetic acid. The colposcope used in this study was BPL stereo-photo-colposcope model No. DVC-6000 with magnification of 15-30x. **Results:** We registered 43 cases, in which the diagnosis was made by colposcopy. 27% of the women among the study group had hypertrophy of cervix with congestion, 12% had erosion. Majority of CIN occurred in the age group, 30-40 yrs. Incidence of CIN is found more in women of high parity (p3 or more). Among the CIN; 11 cases had CIN1, 7 cases had CIN 2, and 3 cases had CIN 3. 6 cases were diagnosed to have invasive carcinoma. Colposcopy showed sensitivity of 91%, specificity of 74%. Positive predictive value and negative predictive value of colposcopy were found to be 60% and 85% respectively. Accuracy of colposcopy was found to be 87% which is comparatively more than pap smear. Accuracy is high with high grade lesions than with low grade lesions. **Conclusion:** This study demonstrated high accuracy and correlation between colposcopy and histology comparable with similar studies in the literature. We also demonstrated the usefulness of colposcopy as a screening test in preclinical cervical carcinoma, the main goal being- the identification of high grade lesions which are true precursors of invasive carcinoma and require treatment.

Index Terms- CIN, Carcinoma cervix, Colposcope, Acetic acid, High grade lesion, Low grade lesion

I. INTRODUCTION

Cervical cancer is very frequent, being the second most common cancer in women worldwide and the second most

common of genital tract cancers in India and also worldwide (WHO 2009).

Around 80% of Ca cervix incidence is in developing countries (1). In India it is 20-35/one lakh women between 35 to 64 yrs (2) and in developed countries – 1-8/ one lakh women (2). India accounts for one fifth of the world's burden of carcinoma cervix (3).

Age standardized mortality rate for Carcinoma cervix in India is 17.4/ one lakh- highest in south Asia (4). Recent studies clearly substantiate the view that Carcinoma cervix develops from well defined precursor lesions over a variable period of time and that it is preventable and curable if detected in early or pre-invasive stage. The detection of these precancerous lesions is of utmost importance. Premalignant lesions are characterized by abnormal cellular/ epithelial architecture in the areas surrounding the SCJ of uterine cervix (7), and are microscopically characterized as a spectrum of events progressing from cellular atypia to various grades of dysplasia and finally to cancer.

II. IMPORTANCE OF COLPOSCOPY

The unique accessibility of uterine cervix to direct visualization and the possibility of cellular and tissue sampling has permitted intensive investigation on cervical lesions. Since early detection predicts better prognosis, one of the most effective ways of preventing and controlling cervical cancer is, by regular screening & early diagnosis.

Measures of prevention are crucial, given the fact that only 11.62% of women of developing countries have ever been screened for cervical abnormalities (9). Studies showed existing screening services cannot effectively cover the female population at risk, in rural areas of India (10). Colposcopy is the examination of cervix and vagina with an instrument designed to study epithelium of cervix and vagina in vivo under adequate illumination and magnification

The value of colposcopy has been recognized mainly in the evaluation of abnormal smears. In the presence of an abnormal cytological smear, a tissue diagnosis is essential before proceeding with definitive treatment. Colposcopy is more than a simple intermediate link between cytologic screening and histologic diagnosis (11)

Cytology (pap smear) is the laboratory method, while Colposcopy is the clinical method, the two complementing each other.

The main purpose of Colposcopy is to detect intraepithelial neoplasia and early neoplasia of the cervix. It is also used to diagnose lesions due to HPV infection, as these are now regarded as precursor lesions of

cervical neoplasia, and also because they can coexist with areas of CIN. Premalignant lesions of Carcinoma cervix are..ASCUS, LSIL and HSIL according to BETHESDA system of classification.

Colposcopy with directed biopsy is described as the reference investigation or ‘gold standard’ for the diagnosis of cervical precancer(12). Precancerous lesions include various grades of dysplasia or CIN before progression to Carcinoma.

Aims & objectives

To inspect the squamo columnar junction of cervix and identify suspicious areas by using colposcope, for early detection of cervical cancer as an opportunity for our out patients.

- Carcinoma cervix can be detected at an earliest possible stage.
- So that, appropriate measures can be taken for early and correct management at the right time.
- These measures will ultimately contribute to early diagnosis and better prognosis of Carcinoma cervix. Introduction of new colposcopic classification and grading system makes interpretation of colposcopic findings easier and simpler(14).

III. MATERIAL & METHODS

The study is an opportunistic study consisting of 100 women of age group between 30-50 yrs attending outpatient department in a tertiary care centre from June 2012 to October 2014 including patients with clinically suspicious cervixes, discharge per vaginum, intermenstrual bleeding and patients with contact bleeding.

Colposcope & 5% Acetic acid are used for the examination of the cervix.

The COLPOSCOPE used in this study was BPL stereo photo colposcope model no DVC-6000. An informed consent was taken. Patients were asked to empty the bladder and were put in dorsal position. Cervix was exposed using ausco’s speculum and examined under illumination through the colposcope with focal length adjusted to 22-25 cm.

Normal saline was used to remove the mucus, then cervix is examined with green filter and saline application, for better visualisation of blood vessels. Then examination of cervix for 2 minutes after applying 5% acetic acid visualizing Squamo Columnar Junction (for any lesions, acetowhite areas and vascular changes).

Patients’ characteristics such as age, menstrual history, parity, presenting complaints, clinical appearance of cervix, and colposcopic findings were recorded. Statistical analysis was carried out by calculating sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for colposcopy.

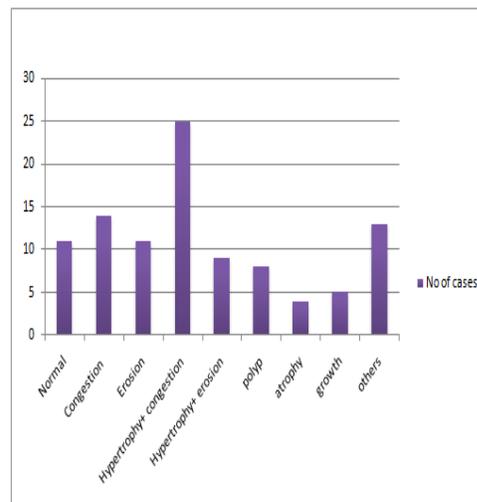
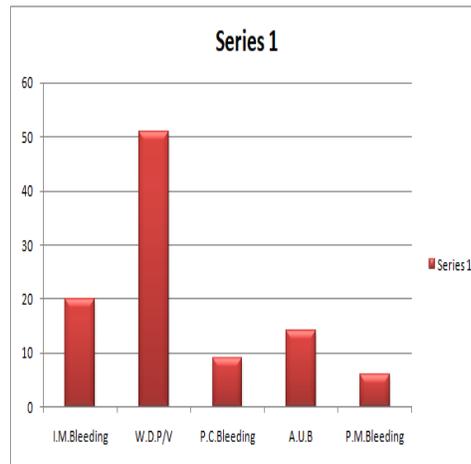
IV. OBSERVATIONS & RESULTS

From the 100 patients examined, 10 patients demonstrated no abnormal findings on colposcopic visualization, that did not

require biopsy for Histopathological examination. Remaining 90 patients underwent colposcopic examination followed by biopsy. These patients represent our study group. Mean age-36.3 yrs, mean parity-3.3. Most common symptom was white discharge p/v followed by intermenstrual bleeding. Most common colposcopic finding was acetowhite patch.

Most common symptoms appearance of cervix
Chart No.2

Chart No.1

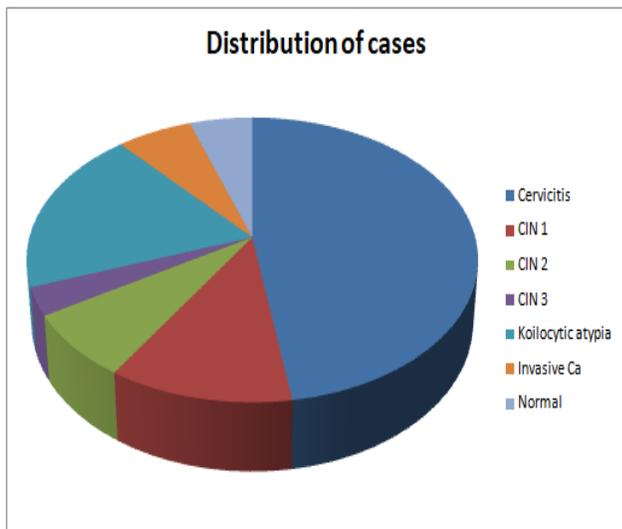


COLPOSCOPIC FEATURES among study group
Table No.5

Colposcopic features	No. of cases	Percentage
<i>Normal</i>	10	10%
<i>Erosion cervix</i>	16	16%
<i>Acetowhite areas</i>	33	33%
<i>Inflammatory changes</i>	15	15%
<i>Polyp</i>	8	8%
<i>Atypical vessels</i>	5	5%
<i>Punctations</i>	3	3%
<i>Mosaic patterns</i>	2	2%
<i>Leukoplakia (keratosis)</i>	5	5%
<i>Others</i>	6	6%

Distribution of cases(n=100)		
Age	30-40yrs	70
	40-50yrs	30
Parity	P2or less	33
	P3or more	67
AW area within TZ (n=33)	Flat aceto White area	27
	Dense aceto white area	6

Distribution of cases based on HPE findings



Statistical analysis

This study was an opportunistic study conducted in the department of obstetrics and gynaecology on 100 women who came to out patient department with various symptoms, 100 women were randomly selected from the patients attending gynaecology out patient section. Colposcopy and biopsy were done for all cases who needed the same. The results were tabulated and analysed.

Statistical analysis

True positives	27
True negatives	63
False positives	13
False negatives	3
Sensitivity	91%
Specificity	74%
PPV	60%
NPV	85%
Accuracy	87%

In our study it is demonstrated that, colposcopy performed equally good in predicting both low grade and high grade lesions.

Positive predictive value of colposcopic impression is better as the cervical lesion is more severe.

We registered 43 cases in which, the diagnosis was made by colposcopy which include acetowhite area, abnormal vessels, punctations & mosaic pattern. Out of these 43 cases, 27 patients showed abnormal HPE findings. Among them, 11 cases were diagnosed as CIN1, 7 cases as CIN2, 3 cases as CIN3 out of 90 cases in the study group. In low grade lesions positive predictive value is poor because biopsy was done only in selective cases.

All these patients were asked to come for follow up, but only 9 of them have come back for follow up. CIN 1 cases were advised follow up every 3-6 months for periodic pap smear and repeat biopsy if the smear is abnormal. CIN 2 & 3 cases were advised repeat biopsy and if repeat biopsy confirmed the diagnosis, were advised locally destructive procedures like Cautery and/or Cryo. If the family is completed, they were advised hysterectomy depending upon the needs of the patient and availability of resources. The patients with microinvasive or invasive carcinoma were advised hysterectomy or referred for radiotherapy.

Colposcopic findings and correlation.

Colposcopic aspects of the selected cases showed a variety of issues that can be found isolated, or associated with other findings.

1) Acetowhite patch 2) Punctations 3) Mosaic pattern 4) Leukoplakia(keratoses)

5) Abnormal vessels

1) acetowhite patch- Epithelium which looks normal, but turns acetowhite after application of 5% acetic acid within 1-2 minutes. These can be differentiated into 2 categories a) LSIL- CIN1 and condylomas. b) HSIL- CIN2, CIN3 and CIS.

LSIL – Elements suggestive of LSIL- Acetowhite epithelium which appears slowly and disappears slowly, has shiny irregular outline (geographical), and feathery borders sometimes accompanied by satellite lesions. Vessels are fine, uniform, separated and arranged in vertical or horizontal network.

HSIL- Elements suggestive of HSIL- Acetowhite epithelium develops rapidly and disappears slowly with net limits and dirty white colour. Vessels have an irregular design with increased intercapillary distance.

The most significant association between colposcopic changes and histological grading was thick acetowhite epithelium with colour variations (internal border). Other changes seen were coarse mosaic and fragility of the tissues.

Invasive cancer- Invasive cancer of cervix is the result of progressive development over a long time of precursor lesions that begin at the squamo columnar junction. Invasive carcinoma was diagnosed on colposcopic examination at the pre-cinical stage at which, genital symptoms and clinical examination are unable to suggest the diagnosis.

Whereas in clinical stage (Frank cancer)- gynaecological examination is sufficient, colposcopy is unnecessary, punch biopsy being carried out directly.

2) Punctations- Thick acetowhite epithelium with vascular spots on surface with variable distribution and site. Corresponds to simple dysplasia and CIN1. (fig.4)

3) Mosaic pattern- Looks like pavement areas composed of rectangular fields-square or polygonal blocks of tissue separated by dilated vessel lines. (fig 2,3)

4) Keratosis(leukoplakia)- Simple shape, hypertrophied or warty raised lesion. Colposcopic appearance is pearly white, irregular surface, single or multiple plaques corresponds to CIN1, CIN2 or CIN3.

CIN may be suspected after colposcopic examination. The final diagnosis (CIN, and respective degree) is made on the cervical tissue specimen, depending on the histological features concerned with differentiation, maturation and stratification of cells and nuclear abnormalities.

5) Abnormal vessels- These show haphazard shapes, great variation in caliber with abrupt changes in direction and caliber, often forming acute angles also with increased and variable intercapillary distance. (fig 3)

Clinically, features suggestive of invasion- Fragile tissue, irregular contour, ulcerated areas, atypical vessels, spotting on touch and monstrous ectopy etc. Colposcopic features suggestive of invasive cancer(18) are:1)Irregular surface contour,erosion ,or ulceration 2)Dense acetowhite change 3)Coarse mosaic and punctuations 4)Atypical vessels

Fig.2 coarsemosaic,punctuations&abnormal vessels

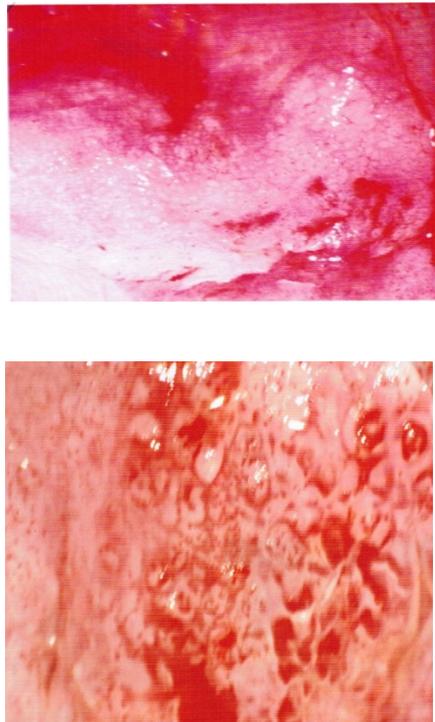
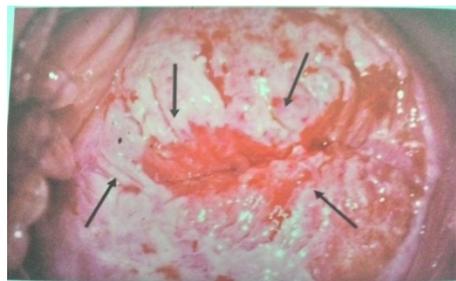
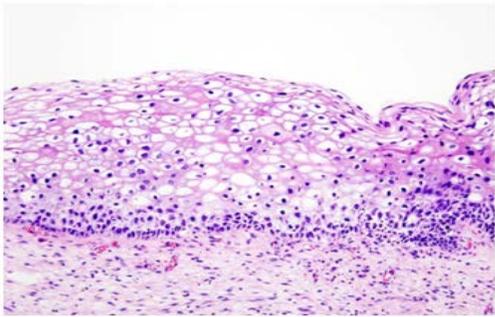


FIG 3.Dense acetowhite areas suggestive of high grade lesion

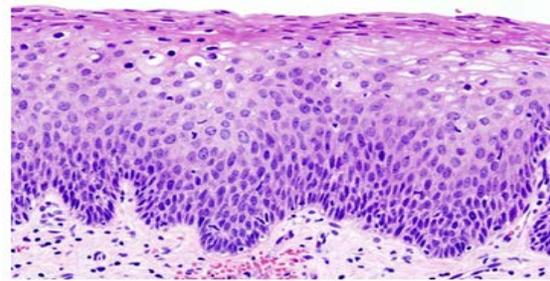


Histological changes



CIN-1 with koilocytic Changes

Fig.4



CIN-2

Fig.5

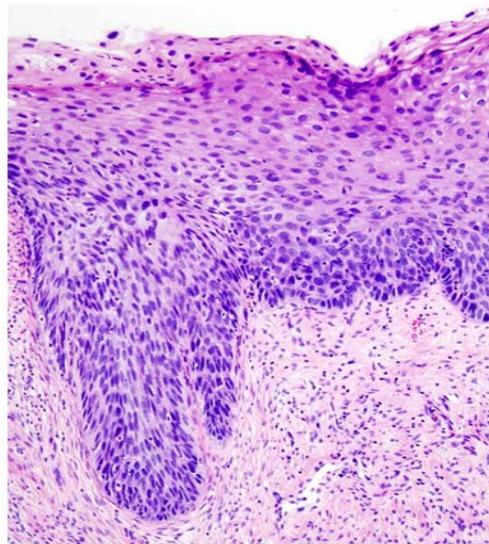


Fig.8-CIN-3

CIN-1- there is good maturation with minimal nuclear abnormalities and few mitotic figures. Undifferentiated cells are confined to the deeper layers(lower one third) of the epithelium(fig 4)

CIN-2- Is differentiated by dysplastic cellular changes mostly restricted to the lower half or lower two thirds of epithelium with more marked nuclear abnormalities than in CIN1. Mitotic figures may be seen throughout the lower half of the epithelium. (fig 5)

CIN-3- Differentiation and stratification may be totally absent or present only in the superficial quarter of the epithelium with numerous mitotic figures. Nuclear abnormalities extend throughout the epithelium. Many mitotic figures have abnormal forms.(Fig.6)

V. DISCUSSION

In our study it is demonstrated that, colposcopy performed equally good in predicting both low grade and high grade lesions. Positive predictive value of colposcopic impression is better as the cervical lesion gets more severe. We registered 43 cases in which, the diagnosis was made by colposcopy.

Out of these 43 cases who also underwent biopsy from the abnormal area, 27 patients showed abnormal HPE findings. Among them,11 cases were diagnosed as CIN1, 7 cases as CIN2, 3 cases as CIN3 out of 90 cases in the study group.6 cases were diagnosed to have invasive carcinoma. In low grade lesions positive predictive value is poor because biopsy was done only in selective cases. All these patients were asked to come for follow up, but only 9 of them have come back for follow up.

CIN 1 cases were advised follow up every 3-6 months for pap smear and repeat biopsy if the smear is abnormal.

CIN 2 & 3 cases were advised repeat biopsy and if repeat biopsy confirmed the diagnosis, were advised locally destructive procedures like Cautery and/or Cryo. If the family is completed, they were advised hysterectomy depending upon the needs of the patient and availability of facilities.

The patients with microinvasive or invasive carcinoma were advised hysterectomy or referred for radiotherapy. Colposcopy incurred fewer false negatives(3 patients), giving a general accuracy rate of 87%.

Out of the 100 women, 90% of them had never been screened for carcinoma cervix. Similarly one study reported that despite the fact that more than 80% of cervical cancer cases are in developing countries, only 5% of women had ever been screened

for cervical abnormalities. It is predicted that figures are expected to be double by 2020, if no action is taken.

Age above 36 yrs and parity above 3, was significantly related to positive biopsy results. Thus patients age and parity may be helpful for selecting them for colposcopy. Low socioeconomic status had a definitive role on the development of dyskaryosis as demonstrated by Vaidya (26).

STUDY	SENSITIVITY	SPECIFICITY
Sankaranarayanan et al(VIA)	96%	65%
Ghaemmaghami et al	91%	13%
Present study	91%	74%

STUDY	ACCURACY
Massad et al	80%
Stafi.A et al	80%
Present study	87%

Sankaranarayanan et al(4) have shown specificity of VIA and cytology 65% vs 90% respectively; sensitivity estimate was 96% vs 62%. Considering false negative pap smears, and the failure of patients to have routine pap test repeated every 4-6 months, it is a weak diagnostic method .

In a study of ASCUS pap smears performed at the Imam Khomeini hospital, biopsy and endocervical curettage showed LSIL in 14 cases, HSIL in 16 and invasive carcinoma and endometrial carcinoma in one case each(Melnikow et al 1995)

In a study of 86 patients with abnormal colposcopy, Allameh et al reported that 83.7% were normal ,7% had LSIL, 5.8% had HSIL and 3.5% had cancer of cervix(Allameh et al 2009). In a similar study conducted in Iran, Ghaemmaghami et al 2005 reported a sensitivity of 91%, specificity of 13% based on ASCUS results.

Singh et al had reported visual inspection after acetic acid application being highly sensitive 93.1% but less specific(35). Oleniyan et al did a meta analysis of 8 longitudinal studies and compared the correlation of colposcopic impression with biopsy results(26).

In our study regarding the clinical appearance of cervix, most common finding was hypertrophy of cervix with congestion 27% (25/90), followed by erosion 12%(11/90). CIN was found in 23% of cases (21/90), among them 14%(3/21) were CIN3. Microinvasive/invasive carcinoma was evident in 18% of cases among acetowhite positive cases (6/33).

Adams et al noticed in their study that the true sensitivity of the whole diagnostic process of colposcopy + biopsy is low because biopsies were not performed in all cases(27).

Stafi A and Mattingly RF prospectively evaluated the colposcopic impression in 282 patients and compared from the histology, then subsequently recommended a minimal proficiency level of 80% for colposcopic accuracy to show proof of colposcopic competency (28).

In present study sensitivity is 91%, specificity is 74%, Positive predictive value-60%, negative predictive value-85% and overall accuracy is noted to be 87%.Massad et al reported accuracy of 80%. M.GOPAL et al demonstrated that PPV & NPV of colposcopy were found to be 48% and 96% respectively.

When interpreting values from different studies we might take into consideration that the performance and accuracy of colposcopy depends largely on the training, expertise and skills of the colposcopist and that accuracy of cytology requires laboratory services and skilled cytologists.

When deciding which test to use for screening, specificity must be taken into account because, tests with low specificity when applied to a healthy population with a very low prevalence of disease, will result in a high proportion of false positive test results(29).

The most important role of these tests is to identify the women with HSIL lesions that require treatment, because the low grade lesions are frequently regressive(30).

Summary

Present study was an opportunistic study on 100 symptomatic women. We registered 43 cases, showing significant changes on colposcopy.

27% of the women among the study group had hypertrophy of cervix with congestion, 12% had erosion.

Majority of CIN occurred in the age group 30-40 yrs. Incidence of CIN is found to be more in high parity women (p3 or more).

Among the CIN; 11 cases had CIN1, 7 cases had CIN 2, and 3 cases had CIN 3. 6 cases were diagnosed to have invasive carcinoma. Colposcopy showed sensitivity of 91%, specificity 74%. Positive predictive value and negative predictive value of colposcopy were found to be 60% and 85% respectively. Accuracy of colposcopy was found to be 87% which is comparatively more than with pap smear. Accuracy is good with both high grade & low grade lesions

VI. CONCLUSION

This study demonstrated high accuracy and correlation between colposcopy and histology comparable with similar studies in the literature.

Specificity is low in our study probably because all symptomatic women were made to undergo biopsy, except for the few women who did not show any abnormal colposcopic findings.

We also demonstrated the usefulness of colposcopy as a screening test in preclinical cervical carcinoma, the main goal being- the identification of high grade lesions which are true precursors of invasive carcinoma and require treatment.

Advantages of colposcopy

- 1) Localizes lesion.
- 2) Evaluates the extent of lesion.
- 3) Differentiates between inflammatory atypia and neoplasm.
- 4) Differentiates between non invasive/invasive lesions.
- 5) Enables follow up.

Disadvantages of colposcopy

- 1) Inadequate for detection of endocervical lesions and needs endocervical curettage.
- 2) Needs more expertise.
- 3) More expensive.

Given the high accuracy(87%) demonstrated in present study, we strongly recommend colposcopy as a screening test for women in child bearing age group, regardless of their previous screening status. Colposcopy is useful in estimating lesion grade, and management decisions for the same require biopsy.

List of abbreviations

CA – carcinoma
TZ- transformation zone
AW area- Acetowhite area
SCJ- squamo columnar junction
LSIL – low grade squamous intraepithelial lesions
HSIL – high grade squamous intraepithelial lesions
CIN – cervical intraepithelial neoplasia
PAP smear – papanicolaou smear
HPE – histopathological examination
LBC – liquid based cytology
ECC - endocervical curettage
PPV – positive predictive value
NPV – negative predictive value

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