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ROLE OF CYTOLOGY, COLPOSCOPY AND COLPOSCOPIC DIRECTED BIOPSIES IN THE EVALUATION OF UNHEALTHY CERVIX

Bandhavi Lagisetti Omania University Employees Colony Shaikpet,hyderabad-500008

ABSTRACT Worldwide, cervical cancer is both the fourth-most common cause of cancer and the fourth-most common cause of death from cancer in women low-income countries. Cancer cervix is the most frequent of all genital tract cancers.Invasive cancer of cervix is considered to be a preventable condition, since it is associated with long pre-invasive stage (CIN) making it amenable to screening and treatment.The Papanicolaou's (Pap) smear is the primary screening tool for Cervical Intra-epithelial Neoplasia (CIN) and for invasive cancer of the uterine cervix.The simultaneous use of cytological studies and screening colposcopy has been shown to increase the rate of the cervical cancer detection. Hence, there is an obvious need to subject the women with clinically unhealthy cervix to colposcopy and directed biopsy.

Present study correlates the findings in women with unhealthy cervix by cytology, colposcopy and colposcopic directed biopsies and to assess the utility of colposcopy in detecting the premalignant and malignant lesions of the cervix.

MATERIALS AND METHODS:

In the present study 100 women were randomly selected who were attending gynaecological OPD SVS medical college hospital, who fulfilled selection criteria.Colposcopy, papsmear and biopsy were done to all patients after proper counselling. All the patients underwent both the acetic acid and the Schiller's test before they were subjected to colposcopic directed biopsies. The biopsies were taken from the acetowhite areas and the iodine negative areas. Results were tabulated and analysed.

KEYWORDS :

INTRODUCTION

Invasive cancer of cervix has been considered a preventable cancer because it has a long pre-invasive state, cervical cytology screening programs are available and the treatment of pre-invasive lesions is effective.4 The unique accessibility of the cervix to direct visualization and the possibility of cellular and tissue sampling has permitted extensive investigations on lesions of cervix.

Pap smear has become a routine method of cervical cancer screening. Its clinical utilization is rapidly expanding due to the simplicity of the technique, cost effectiveness and less time taken to obtain the diagnosis.6

The colposcope is a low power, binocular microscope for study of surface epithelium and underlying connective tissue stroma along with vascular pattern.7Colposcopy is complementary as well as superior to cytology. It is a simple noninvasive OPD procedure. It helps in determining indications for cervical biopsy, locating sites and the extent of biopsy. It helps in avoiding traumatic diagnostic methods like cervical conization for minor lesions and at the same time significant lesions are not overlooked.

Colposcopic directed biopsy of suspicious areas provides the final diagnosis in most situations and is taken as the gold standard in diagnosis of neoplastic lesions.

OBJECTIVES

1. To correlate the findings in women with unhealthy cervix by cytology, colposcopy and colposcopic directed biopsies.
2. To critically evaluate the sensitivity and specificity of Colposcopy versus pap smear in the early detection of premalignant malignant lesions of the cervix.

REVIEW OF LITERATURE

Cervical cancer is one of the well understood human cancers and potentially the most preventable. The anatomic accessibility of the cervix to direct examination and long pre-clinical stage during which the precursor lesions can be treated conservatively and successfully make cervical cancer an ideal target for screening and treatment.

Cervical cancer is the most common neoplasm in Indian women with 1,34,420 new cases and 72,825 deaths each year(1-4p). Incidence is higher than in Eastern Asia.8 Cancer cervix accounts for 7% of all female malignancies in developed countries which is in sharp contrast to 24% in developing countries. This disparity is attributed primarily to differences in screening and treatment of precancerous lesions.9 The basic purpose of screening is to sort out from a large group of healthy persons those likely to have the disease or at increased risk of the disease under study and to bring those who are 'apparently abnormal' under medical supervision and treatment. Screening is carried out in the hope that earlier diagnosis and treatment favorably alters the natural history of the disease in a significant proportion of those who are identified as positive.

A screening test should be simple, minimally invasive, easy to perform, cost- effective and highly sensitive that can be applied to a large number of apparently healthy individuals. Participation in regular cervical screening program decreases the mortality rates of cervical cancer. The success of screening program is directly related to method used, available financial resources and is influenced by the patients cultural and educational background.

In 1986 about 50% of women in developed countries had been screened for cervical cancer compared with 5% of women in developing countries. After the introduction of regular screening, cervical cancer death rates dropped between 8% and 73%. The greatest drop occurred in Iceland and corresponded to the highest rate of participation, while in Norway, the country with the lowest participation rates, the mortality rate was almost unchanged.1

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This study was conducted in the department of obstetrics and Gynaecology at SVS medical college,in the year 2014to 2015 . 100 women were randomly selected who were attending gynaecological OPD of SVS medical college hospital, who fulfilled selection criteria.Colposcopy, papsmear and biopsy were done to all patients after proper counseling.

Inclusion criteria

1. Age: 20-60 years
2. Patients with abnormal symptoms like profuse white discharge, post coital bleeding, intermenstrual bleeding or post menopausal bleeding.
3. Patients with clinically unhealthy cervix diagnosed by speculum examination like, cervical erosion, cervicovaginitis, cervical polyp, condylomas etc.
4. Patients with pap smears showing dysplasia

Exclusion criteria

1. Women with age > 60 years and < 20 years.
2. Patients with bleeding at the time of examination.
3. Women with frank invasive cancer
4. Women who underwent total hysterectomy
5. Pregnant women,unmarried women

STATISTICALANALYSIS

The statistical analysis was done by calculating diagnostic efficacy of each test. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false positive rate, false negative rate and accuracy were calculated for Pap smear and colposcopy with colposcopy directed biopsy results as gold standard

Table 1: Visual inpection with acetic acid(VIA) results

Total	No. Of cases (n= 100)
Positive	42
Negative	58

42 women out of 100 had a positive result and 58 women had a negative result on VIA

Table 2 : Pap smear results

Outcome	Number of cases (n=100)
Normal	4
Inflammatory	77
LSIL	9
HSIL	10
Malignancy	0

Pap smear revealed that 77% had an inflammatory smear and 19% had a positive Pap smear. The result of Pap smear was considered positive if it revealed LSIL, HSIL, carcinoma in situ or invasive cancer. Among 19 positive cases, there were 9 LSIL, 10 HSIL and no case of malignancy.

Table 3 : Colposcopy results

Outcome	Number of cases
Normal	10
Inflammation/squamous metaplasia/erosion	54
Hazy/faint acetowhite areas. Fine punctations or mosaicism	12
Dense acetowhite areas. Coarse punctations or mosaicism	16
Unsatisfactory	7
Malignancy (intense acetowhite lesion, coarse irregular punctations, cork screw vessels)	1

On Colposcopy 29% women found to have a positive result. Colposcopy was considered positive if it revealed lesions of LSIL and above. Among the 29 women with abnormal colposcopies there were 12 LSIL, 16 HSIL and 1 case suspicious of malignancy. Colposcopy was unsatisfactory in 7 cases.

Table 4 : Biopsy results

Outcome	Number of cases (n=100)
Normal	03
Cervicitis/ metaplasia	60
Mild dysplasia	19
Moderate to severe dysplasia	15
Malignancy (squamous cell carcinoma)	03

The positive biopsy includes 37 cases out of 100. Biopsy was considered positive if it revealed LSIL and above. It includes 19 mild dysplasias (LSIL), 15 moderate to severe dysplasias (HSIL) and 03 malignancies. Out of 03 malignancies none had visible growth on per speculum examination.

Table 5 : Correlation between Pap smear and biopsy

Pap smear	Biopsy					Total
	Normal	Cervicitis/metaplasia	LSIL	HSIL	Malignancy	
Normal	0	4	0	0	0	4
Inflammatory	3	53	15	6	0	77
LSIL	0	3	2	3	1	9
HSIL	0	0	2	6	2	10
Total	3	60	19	15	3	100

19 cases out of 100 women were positive on Pap smear. 37 out of 100 women were positive on Biopsy. Pap smear was positive in 16 out of 37 biopsy proven positive cases. 15 cases of LSIL and 6 cases of HSIL were under reported as inflammatory on Pap smear. 3 cases of cervicitis/ metaplasia were over reported as LSIL/HSIL.

Table 6 : Correlation between colposcopy and biopsy

Colposcopy	Biopsy					Total
	Normal	Cervicitis/metaplasia	Mild dysplasia	Moderate/ Severe dysplasia	Malignancy	
Normal	2	8	0	0	0	10
Inflammatory/Squamous metaplasia/erosion	1	43	7	3	0	54
Hazy/Faint acetowhite areas, fine punctations or mosaicism	0	1	10	1	0	12
Dense acetowhite areas, coarse punctations or mosaicism	0	2	2	1	2	16
Unsatisfactory	0	6	0	1	0	7
Malignancy	0	0	0	0	1	1
Total	3	60	19	15	3	100

29 out of 100 women were positive on colposcopy. 37 out of 100 women were positive on biopsy. Colposcopy was positive in 26 out of 37 biopsy proven positive cases. Colposcopy was unsatisfactory in 7 cases. 7 cases of mild dysplasia and 3 cases of moderate/severe dysplasia were under reported as metaplasia/ erosion on colposcopy. 3 cases of cervicitis/ metaplasia were over reported as LSIL/HSIL on colposcopy.

Table 7 : Diagnostic efficacy of Pap smear

Pap smear	Biopsy		Total
	Positive	Negative	
Positive	16	3	19
Negative	21	60	81
Total	37	63	100

Sensitivity : 43.2%

Specificity : 95.2%
Positive predictive value : 84.2%
Negative predictive value : 74.1%
Accuracy : 76%

Table 8 : Diagnostic efficacy of Colposcopy

Colposcopy	Biopsy		Total
	Positive	Negative	
Positive	26	3	29
Negative	11	60	71
Total	37	63	100

Sensitivity : 70.3%
Specificity : 95.2%
Positive predictive value : 89.6%
Negative predictive value : 84.5%
Accuracy : 86%

Table 9 : Diagnostic efficacy of tests

Diagnostic efficacy	Pap smear	Colposcopy
Sensitivity	43.2%	70.3%
Specificity	95.2%	95.2%
Positive predictive value	84.2%	89.6%
Negative predictive value	74.1%	84.9%
Accuracy	76%	86%

Colposcopy has higher sensitivity (70.3%) than that of Pap smear (43.2%). Specificity of both is similar (95.2%). The positive predictive value is comparable, 84.2% and 89.6%, for Pap smear and colposcopy respectively. The accuracy of colposcopy (86%) is higher than that of Pap smear (76%).

Table 10 : False negative rate of tests

Test	False negative rate
Pap smear	56.7%
Colposcopy	29.7%

Table 11 : False positive rate of tests

Test	False positive rate
Pap smear	4.76%
Colposcopy	4.76%

DISCUSSION

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.57

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, equipments, 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.57

The present study was carried out in the OPD at Al-Ameen Medical College Hospital, Bijapur from 2008-2009. One hundred cases who fulfilled the selection criteria were recruited for the study.

Maximum number of cases was found to be in the age group 31-40 years (41%). Mean age was 37.85 years.

Majority of the study group were Para two (33%) and Para three (34%). The commonest symptom was recurrent white discharge per vagina (79%).

In our study, 42 out of 100 women showed a positive result and 58 a negative result on VIA. Various studies have shown VIA to be positive in 7-41% of cases.26,58,59 VIA positivity rate depends upon type of criteria used and population screened (high risk or general population). Our VIA positivity rate (42%) was similar to study done by Bhatla N et al.59

The positive biopsy includes 37 out of 100 cases. It includes 19 mild dysplasias (LSIL), 15 moderate to severe dysplasias (HSIL) and 3 malignancies. Out of the 3 malignancies none had visible growth on per speculum examination.

In our study, sensitivity of Pap smear was found to be 43.2%. This is because 15 cases of mild dysplasia (LSIL) and 6 cases of moderate to severe dysplasia (HSIL) were under reported as inflammatory. As a screening test, the Pap smear has been found to have a low sensitivity, between 44% and 50%, resulting in a high false negative rate of 36-40%.60The sensitivity of Pap smear has been found to be lower in developing countries because of presence of infection and inflammation.

The high specificity of Pap smear (95.2%) found in our study is similar to findings from other studies in which specificity ranges from 91-97%.60 The positive predictive value was found to be 84.2%.

A prospective study was conducted at AIIMS, New Delhi from 2003-2004. Of 133 patients included in the study, incidence on biopsy of LSIL was 6.77%, HSIL was 8.27% and carcinoma was 3%. Sensitivity and specificity of cytology for detection of HSIL and above lesions was 93.33 and 83.49 percent respectively. Of the 133 patients, 5 had unsatisfactory smears. Of the 128 satisfactory smears, 95 were negative foe intraepithelial lesions while remaining 33 showed epithelial cell abnormalities of which HSIL was seen in 16 smears and LSIL in 5.61

The sensitivity and specificity of colposcopy in our study was 70.3% and 95.2% respectively. The positive predictive value was 89.6%. Colposcopy was unsatisfactory in 7 cases of which 6 showed cervicitis/metaplasia and 1 showed moderate/severe dysplasia on histopathology. Colposcopy over reported 3 cases of cervicitis/ metaplasia as LSIL in 1 case and HSIL in 2 cases.

In a study of 268 women with unhealthy cervix, the cytology results showed 44 normal, 5 atypical squamous cells of undetermined significance, 194 (75%) inflammatory smear and 14 (5.4%) abnormal cytology. Colposcopic findings were normal in 119 and abnormal in 139 women. Four cases of invasive carcinoma, 2 of micro-invasive and 17 of high grade lesions were confirmed by colposcopic directed H/P reports. Of these, 2 cases each of invasive and micro-invasive and 11 cases of high grade lesions were missed on cytology alone. Hence CIN lesions and early invasive carcinoma were confirmed in 31.6% by colposcopy as against only 5.4% by cytology alone.1

The accuracy of colposcopy was 86% and that of cytology was 76% in our study.

It is evident that although colposcopy had higher sensitivity (70.3%) as compared to cytology (43.2%), the specificity and positive predictive value of both were comparable. Hence colposcopy is useful in detecting premalignant and malignant lesions of the cervix. Colposcopy and cytology used together in patients of cervical lesions have a relatively higher chance of detecting squamous intraepithelial lesions/malignancy as compared to either procedure when performed alone.

CONCLUSION

Following conclusions were drawn from the present study:

1. The majority of women were in the age group 31-40 years.
2. The commonest symptom was recurrent white discharge per vagina.
3. Pap smear has high specificity but low sensitivity.
4. Colposcopy has high sensitivity and specificity. Hence it is useful in detecting premalignant and malignant lesions of the cervix.
5. The specificity and positive predictive value of Pap smear and colposcopy was comparable.
6. Colposcopy has higher accuracy than Pap smear.
7. Colposcopy and cytology used together in patients of cervical lesions have arelatively higher chance of detecting squamous intraepithelial lesions/malignancy as compared to either procedure when performed alone.

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