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## A study of cytology and colposcopy in correlation with histopathology report in women with gynaecological complaints

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### Abstract

The Carcinoma of cervix is commonly seen in fifth decade of life though it is initiated almost 8 to 10 years earlier. This is a crucial period with wide span in which if we act appropriately, we can avoid the disease or cure it completely. There are many screening methods which have different sensitivity and specificity. This study is intended to search out suitable and easy method of cervical carcinoma screening.

**Aims and Objectives:** To evaluate the patients having white discharge or other genitourinary complaints by cytology, colposcopy and histopathology. 2) To find the individual efficacy of cytology, colposcopy in correlation with histopathology and combined correlation of these modalities.

**Materials and methods:** Following study was conducted on 100 patients coming to Gynaecology OPD with gynaecological complaints after obtaining consent.

**Results:** In present study, the positive predictive value (PPV) of cytology as well as colposcopy was high for detection of malignancy than benign lesions and LSIL. The negative predictive value of cytology for CIN 3 was high (95.92%) as compared to CIN 1(81.63%). Specificity was found low in colposcopy for CIN1 (95.06%) as compared to PAP smear (98.77%).

**Conclusion:** Cytology and colposcopy combined can become a better method for screening in perspective of high sensitivity, specificity and positive predictive value.

**Keywords:** Colposcopy, cytology, cervical carcinoma, HSIL, LSIL, and ASCUS

### Introduction

Cervical carcinoma is remained to be second most common malignancy amongst women, all over world according to the World Health Organization (WHO). Cervical screening programmes have been implemented so vigorously that down staging the disease and reduction in morbidity and mortality have been achieved to some extent in developed countries <sup>[1]</sup>. In India still, it is number one malignancy. In a developing country like India, cytology based screening programs are difficult to organize because of absence of trained manpower, infrastructure, logistics, quality assurance, frequency of screening and costs involved <sup>[2, 3]</sup>. The importance of screening programme has to be emphasised preinvasive on general population such that each and every carcinoma should be picked up in their stage. This is slow growing malignancy. Almost 8 to 10 years is the breathing period to act before conversion to invasive carcinoma. This crucial period should be picked up with all screening methods. The purpose of the study is to understand better screening method which is cost effective, less time consuming, technically simple and having availability of resources at remote places with high sensitivity and specificity, and easy to counsel and motivate the patients for early screening.

**Aims and Objectives:** To evaluate the Patients complaining of white discharge or other genitourinary complaints by cytology, colposcopy and histopathology. 2) To find the individual efficacy of cytology, Colposcopy in correlation with histopathology and combined correlation of these screening modalities.

**Materials and methods:** Following study was conducted in Dr. D.Y Patil Hospital Kolhapur from January 2018 to December 2019 on the patients coming to Gynaecology OPD with gynaecological complaints.

**Inclusion Criteria:** The current study is conducted on patients of age group between 20 to 60 years having gynaecological complaints.

**Exclusion Criteria:** Patients with pregnancy and puerperium, previous surgery on Cervix, cauterisation on cervix cervical cerclage, amputation of cervix, utero-vaginal prolapse and clinically visible cervical growth. Written consent was obtained.

100 patients were selected. All were subjected to Pap smear and colposcopy and biopsy from suspicious area. We have used conventional method of taking Pap smear with spatula. Two samples, one from squamocolumnar junction rotating 360 degree and from posterior fornix were taken.

### Observation

**Table 1:** Chief complaints, and its correlation with cytology, colposcopy, and histopathology

| Chief Complaints                | Total | Cytology positive | Colposcopy positive | Histopathology Positive |
|---------------------------------|-------|-------------------|---------------------|-------------------------|
| White discharge                 | 54    | 0                 | 9                   | 4                       |
| Blood stained white discharge   | 0     | 0                 | 0                   | 0                       |
| Postictal bleeding              | 3     | 2                 | 2                   | 2                       |
| Menorrhagia                     | 2     | 0                 | 0                   | 0                       |
| Polymenorrhagia                 | 4     | 0                 | 0                   | 0                       |
| Abdominal Pain                  | 27    | 0                 | 6                   | 6                       |
| Burning                         | 4     | 0                 | 2                   | 1                       |
| Dyspareunia                     | 1     | 0                 | 0                   | 0                       |
| Bleeding/history of weight loss | 1     | 0                 | 0                   | 1                       |

A total of 54 patients out of 100 had complaints of PV white discharge. Of them 9 had abnormal Colposcopy and 4 had abnormal HPR. Out of 3 patients complaining postictal bleeding 2 had squamous cell carcinoma. Total 6 patients had

menorrhagia and polymenorrhea but did not have any abnormality in cervix. Total 6 patients of 34 abnormal HPR had abdominal pain and one had urinary complaints. One patient had dyspareunia which had no connection with cervical abnormality.

**Table 2:** Correlation of Speculum Examination findings with Cytology, Colposcopy, and Histopathology

| Speculum                | Total | Cytology | Colposcopy | Histopathology |
|-------------------------|-------|----------|------------|----------------|
| Bleeds on touch         | 13    | 2        | 6          | 1              |
| Irregular mass          | 3     | 1        | 1          | 1              |
| Cervical ulceration     | 1     | 0        | 0          | 1              |
| Erosion                 | 5     | 0        | 2          | 0              |
| With Cherry red spot on | 1     | 0        | 0          | 0              |

Total of 13 patients had bleeds on touch, out of them only 2 had abnormal cytology, 6 had abnormal Colposcopy and only one had abnormal HPR. Out of 3 patients of cervical mass, 1 patient had abnormal findings in all screening methods. Out of 5 patients of erosion, 2 had abnormal Colposcopy. Only one patient had cherry red spot on cervix.

Out of 100 patients 13 had abnormal findings. Out of them only 3 patients were of HSIL and 1 patient of ASCUS. Atrophic changes were in 6 patients, while remaining 3 were suggestive of infective pathology.

**Table 3:** Abnormal Pap smear Findings

| Abnormal Pap smear findings | Number |
|-----------------------------|--------|
| BV*                         | 1      |
| Candidiasis                 | 1      |
| ASCUS                       | 1      |
| HSIL                        | 3      |
| Trichomoniasis              | 1      |
| Atrophic                    | 6      |
|                             | 13     |

BV\*: bacterial vaginosis

**Table 4:** Colposcopy Findings

| Colposcopy Findings                         | Number |
|---|--------|
| Normal                                      | 82     |
| Abnormal :                                  | 18     |
| Atypical vessel                             | 13     |
| Course Mosaic                               | 2      |
| Ace to white with mosaic coarse punctuation | 12     |
| Gland Openings crypts with cuffs            | 2      |

Out of 100 colposcopy, 82 were having normal findings. Out of 18, about 13 showed atypical vessels, of which 2 had invasive carcinoma, 16 had high grade features.

**Table 5:** Correlation of HPR with Colposcopy and Pap smear

|                         | HPR | Positive Colposcopy | Positive PAP |
|-------------------------|-----|---------------------|--------------|
| Inflammatory smear      | 72  | 3                   | 1            |
| CIN 1                   | 19  | 6                   | 1            |
| CIN 2                   | 2   | 0                   | 0            |
| CIN 3                   | 6   | 6                   | 2            |
| Squamous cell Carcinoma | 2   | 2                   | 2            |
| Squamous Metaplasia     | 1   | 0                   | 0            |
| Koilocytic Changes      | 4   | 2                   | 0            |

In present study, 3 patients of abnormal colposcopy and 1 of abnormal Pap smear had reported to be inflammatory smear. Out of 19 CIN 1, 6 patients had abnormal colposcopy. Only 2

patients had CIN2 which were not picked up by colposcopy. All 6 patients of CIN3 were detected by colposcopy, but of them only 2 had abnormal Pap smear.

**Table 6:** Comparison of colposcopy and Pap smear sensitivity and specificity with Histopathology.

|            | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|------------|-----------------|-----------------|---------|---------|--------------|
| Cytology   | 14.71%          | 98.48           | 0.83    | 0.69    | 70%          |
| Colposcopy | 47%             | 95.31%          | 0.84    | 0.77    | 78.56%       |

Above table shows that colposcopy has high sensitivity (47%) as compared to cytology (14.71%), but the specificity of cytology is more (98.48%) than that of colposcopy (95.31%) with accuracy of 70% and 78.56% respectively.

**Table 7:** Treatment Modalities

| Treatment Modality      | Numbers |
|-------------------------|---------|
| Antibiotics             | 100     |
| Cryosurgery             | 60      |
| TAH, TAH+BSO            | 11      |
| Wertheim's Hysterectomy | 2       |

Above table shows about treatment modalities that we offered to the patients. All patients were treated with antibiotics only or along with cryotherapy or hysterectomies. Total 13 patients had undergone hysterectomies of which 2 had Wertheim's hysterectomies and 11 had total and pan hysterectomies.

**Discussion**

Awareness and willingness in participating the screening programme is still low in our set up. Females strongly resist to get examined per vaginally as it makes them feel like breaching their privacy. Patient seeks medical advice only if they have some complaints like commonly PV white discharge, abdominal pain or urinary and menstrual complaints. That was the reason; the patients who underwent screening were having some genitourinary symptoms that are included in the study. This scenario has to be changed when we want to reduce morbidity and mortality due to malignancy of cervix.

Out of 100, 54 patients had complaints of PV white discharge and 13 patients had abnormal findings on Pap smear. Out of 13 only 3 patients were of HSIL and 1 patient of ASCUS and in 6 women atrophic changes were found, while remaining 3 were suggestive of infective pathology. The common infections are trichomonas, candidiasis and bacterial vaginosis. In most of patients the cause for white discharge was local inflammation. Out of 100 patients, 60 had Histopathology of inflammatory smear. The 2 cases of invasive carcinomas detected on Histopathology, both had a complaints of postictal bleeding. Cervical carcinoma does not have any symptoms unless advanced stage occurs. So there comes a role of having screening in early stages.

An ideal indicator of screening methods is one which has good sensitivity and specificity and much concern has arisen recently to develop a better screening test for the disease prevention. Specificity of cytology in our study was very high 98.8% - Shastri *et al.* also reported high specificity of cytology from Tata Memorial Mumbai [2].

In present study, the overall positive predictive value for CIN was high in cytology in correlation with histopathology (95.92% for CIN 3 and 81.63% for CIN 1). This correlates with the findings of Bendet who reported statistically significant agreement between cytology and histology in one grade of disease. CIOCAM also reported overall concordance of 86.9% between histopathology and Pap smear in their series of 3,229 women [18]. Then reported sensitivity to 77% PPV and non-positive predictive value (NPPV) of 45% of Pap smear. In statistical analysis report of 2001 PPV of CIN III was 80%.

[14]. In present study the sensitivity of cytology is very low especially for CIN1 (5.26%) and 33.33% for CIN3. In recent years, a large number studies have found addition of HPV test along with liquid based cytology improves sensitivity of Pap [4-5], Liquid based cytology reduces sampling error and inclusion of endocervical cells with the use of endocervical brush. Doing alone HPV testing has greater sensitivity (approximately 90%) and reproducibility [6]. However, it has slightly decreased specificity for cervical intraepithelial neoplasia (CIN) 2 and 3 when compared with cytology [7]. Besides, this test in women less than 30 years has no value as these women have a high prevalence of transient infection and a low prevalence of underlying high-grade lesions [8,9]. However, studies concerning the diagnostic value of comparison with HPV testing plus cytology with isolated cytology have been rarely reported. Systematic review and meta-analysis by Tong Li, Yan Li *et al* de menstruate that combination of HPV testing and cytology method in screening cervical cancer was superior to isolated cytology method in sensitivity, while was inferior in specificity [10]. The another advantage of combining Pap and HPV testing may help us to triage ASCUS and HSIL so that in selective patients can be subjected for colposcopy.

Some studies have found high sensitivity of colposcopy up to 100% [11, 12, 13]. In present study we found sensitivity of colposcopy was only 47%. It may be due to intraobserver differences, presence of keratosis, and the high incidence of ace to white epithelium. Acetowhite area due to immature squamous cell metaplasia & inflammatory lesion seem to be responsible for large number of false positive findings. In present study we have found: out of 12 colposcopy showing acetowhite area, 2 patients had only ace to white area without other changes & had normal HPR. Remaining 10 patients had either atypical vessels / negative iodine uptake & coarse punctuation which showed association with CIN changes.

Specificity of colposcopy in our study was measured for CIN 1 and CIN3 separately. Low specificity of colposcopy for CIN1 (95.06%) compared to Pap smear (98.77%). When thinking of low specificity, appearance of ace to white area like faint, dense with sharp/diffuse margin, rapidly appearing and persisting as it changes the grading from low to high grade which have a subjective variability and have an impact on interpreting the findings. Sometimes latent HPV infection and sub mucosal vessels are misinterpreted as atypical vessels. Use of Reid Index is advised by Ferris DG *et al* to reduce intraobserver variability. The Reid Index considers 4 Colposcopic signs which include lesion margins, colour of ace to white, blood vessels & Iodine staining. It is said that Reid score is 90% accurate in predicting histological findings as grading system rasion on critical analysis trivial findings will not be over interpreted [15]. Need for interpretation with Reid's scores to be evaluated further to improve the predictability and accuracy of the method. In present study cytology has low Sensitivity (5.26%) as compared to colposcopy (33.33%) for CIN1.

In present study Koilocytic changes are seen in 4 patients who indicate HPV infection. Of them only 2 had abnormal colposcopy changes & only 1 patient out of 4 had abnormal Pap smear. Koilocytic changes have no much significance as below 30 years it may come which will get cleared eventually. Seckin reported a very high incidence of HPV-related lesions (64.5%)

whereas Frisch reported an incidence of only 8%.<sup>[16]</sup> High-grade lesions have high chances of malignancies<sup>[14]</sup>. Total 34 patients had abnormal HPR in which only 2 had invasive carcinoma picked up in both colposcopy and Pap smear. In present study, the Positive predictive value (PPV) of cytology as well as colposcopy was highest for malignancy followed by benign lesions and LSIL; this correlates with Bendet in which PPV was 91.8% for malignancy and 35% for benign lesions<sup>[17]</sup>. In present study, positive predictive value for invasive lesions and CIN3 was 100% for both Pap as well as colposcopy as compared to CIN1 (50 and 60% respectively). Similar finding shown by Geeta *et al* states that the predictive value of colposcopy was also shown to be better with increasing grades of neoplasia. This implies that colposcopy performs better in the diagnosis of high grade lesions<sup>[14]</sup>.

In treatment, all patients are offered antibiotics. Of them 27 were given only antibiotics and followed. In remaining 73 patients, 60 underwent cryotherapy. Advantage of cryotherapy is that being an OPD procedure patient's compliance is good and it conserves the uterus and further complications of hysterectomies. And 13 landed up with hysterectomies in which 2 were modified radical hysterectomies for invasive carcinomas.

### Conclusion

Colposcopy is found to be a better method for screening in perspective of high sensitivity, specificity and positive predictive value. But it is more time consuming. Colposcopy is a visual technique that requires extensive training and experience. Role of proper training and certification of colposcopists have to be evaluated, burdening over health personal, and less specific due to intraobserver variations. Colposcopy with cytology gives a satisfactory level of accuracy. Combining it with HPV testing and collection method by liquid base cytology may improve the further accuracy. Screening in asymptomatic patients has to be emphasised on general population by social media and awareness should be created about screening to downstage the disease and to reduce morbidity and mortality. Use of Reid index, application of acetic acid and Lugol's iodine are the areas needs to be worked upon to find out better screening method. In present study have not discussed about role of high risk factors such as young age at first intercourse (less than 16) years of age, multiple sexual partners, cigarette smoking, race, high parity, low socioeconomic status, and chronic immune suppression as well place for HPV vaccination as initiating event in cervical dysplasia and carcinogenesis is infection with HPV.

Studies on larger scale are required to define accurate screening method.

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