

# Effectiveness of Colposcopy in the Detection of Cervical Intraepithelial Neoplasias and its Correlation with a Histopathological Examination Report

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## ABSTRACT

**Objectives:** The objectives of the study were to screen women who have an unhealthy cervix by cytology and correlate the findings with colposcopy, and colposcopic-directed biopsies.

**Materials and methods:** This is a prospective study conducted in the Department of Obstetrics and Gynecology in Mamata Medical College, Khammam, from October 2011 to June 2013. A total of 100 cases who fulfilled the selection criteria were included in the study. All the women enrolled in the study underwent a pap smear, colposcopy, and a colposcopic-directed biopsy. The sensitivity, specificity, positive predictive value, negative predictive value, false-positive rate, false-negative rate, and accuracy were calculated for the Pap smear and colposcopy, with the colposcopic-directed biopsy taken as the gold standard.

**Results:** The sensitivity and specificity of the Pap smear were found to be 54.3% and 96.2%, respectively, and those of the colposcopy were 76.1% and 96.2%, respectively. The colposcopy showed a higher sensitivity than did the Pap smear. The specificity and positive predictive value of the Pap smear and colposcopy was comparable, whereas the accuracy of the colposcopy was higher than that of the Pap smear.

**Conclusion:** Most of the women were in the age group of 31–40 years. The most common symptom was a recurrent white discharge per vagina. Colposcopy was useful in detecting cervical intraepithelial neoplasias. Colposcopy and cytology used together in patients with cervical lesions have a higher chance of detecting squamous intraepithelial lesions/malignancy than when either procedure used alone.

**Keywords:** Cervical biopsy, Colposcopy, Histopathological examination, Inflammatory cervical smears.

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## INTRODUCTION

Globally, cervical carcinoma continues to be a significant healthcare problem. In developing countries, where healthcare resources are limited, cervical carcinoma is the second most frequent cause of death in women.<sup>1</sup> India, which accounts for one-sixth of the world's population, also bears one-fifth of the world's burden of cervical carcinoma. There are approximately 130,000 new cases of a cervical cancer diagnosed in India every year and the disease is responsible for almost 20% of all deaths in women. Age-standardized incidence rate (30.7 per 100,000) and age-standardized mortality rate (17.4 per 100,000) of cervical cancer in India are the highest in South Central Asia.<sup>2</sup>

## ETIOPATHOGENESIS

An invasive cancer of the cervix has two peaks, one at about 35 years and another at about 50–55 years. CIN occurs at a much lower age, one-third of cases are found in women less than 30 years. Sexually active women are two to four times more likely to develop cancer than sexually inactive women. Young age at the first intercourse, multiple sexual partners, and high parity have been implicated as the risk factors for the CIN and cervical cancer.<sup>3</sup> The women of certain races (notably orthodox Jews) are almost immune to cervical cancers. Carcinoma cervix is unusually common in Africans. The disease is more prevalent in women living in poor conditions. An invasive carcinoma of the cervix is 20 times more common amongst the wives of unskilled laborers than in those of the professional men. The practice of coitus is now being established as a prime cause of the cervical malignant

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disease. It is almost unknown in groups of nuns and virgins. Early age at the first intercourse and multiple sexual partners are associated with a higher risk of developing cervical cancers.<sup>4</sup> HPV infection has been detected in up to 99% of women with a squamous cervical carcinoma. Specific HPV types are associated with cervical cancer. Low-risk strains include types 6, 11, 42 and 44 and high-risk strains include types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56 and 58. HPV subtypes 16 and 18 are found in 62% of cervical carcinomas. The mechanism by which HPV affects cellular growth and differentiation is through the interaction of viral E6 and E7 proteins with tumor suppressor genes p53 and Rb, respectively. Inhibition of p53 prevents cell cycle arrest and cellular apoptosis, which normally occurs when damaged DNA is present, whereas inhibition of Rb disrupts transcription factor E2F, resulting in unregulated cellular proliferation.<sup>1</sup>

Lower cancer survival and higher mortality rates partly result from higher rates of late-stage cancer diagnosis among women in developing countries, which is largely due to the lack of effective cervical cancer screening programs in most developing countries. Detection of cancer at an early stage may be considered a marker for access to health care and preventive health services, including cervical cancer screening. Screening can reduce rates of both cervical cancer incidence and mortality by detecting precancerous lesions and invasive cervical cancers at an early stage, thereby increasing patient survival. About 81% of cervical cancer patients in Singapore are diagnosed at an early, localized stage, compared with only 7% in India. The high rate of early-stage diagnosis in Singapore is higher than the rate for many industrialized countries, including the United States, where only 52% of invasive cervical cancers in 2008 were diagnosed at the localized stage. According to a recent study, only 19% of women in developing countries use cervical cancer screening compared with 63% in developed countries. An invasive cancer of cervix has been considered a preventable cancer because it has a long preinvasive state. This is characterized microscopically as a spectrum of events progressing from a cellular atypia to various grades of a dysplasia or a cervical intraepithelial neoplasia (CIN) before progression to an invasive carcinoma.<sup>5</sup> The anatomical accessibility of the cervix to direct examination, with a long preclinical stage during which precursor lesions can be treated conservatively and successfully (~95%), make cervical neoplasia ideal for screening.<sup>6</sup>

Pap smear has become a routine method of cervical cancer screening. Its clinical utilization is rapidly expanding owing to the simplicity of the technique, cost-effectiveness, and less time taken to obtain the diagnosis. Cytology has got certain limitations such as low sensitivity of 51% and a false-negative rate of 49%.<sup>7</sup> As a screening test, the role of cervical cytology is to identify patients who have a cervical neoplasia so that they may be directed to a diagnostic procedure. An abnormal Pap smear serves as the initial warning sign that neoplasia may be present. A colposcopic examination involves the systematic evaluation of the lower genital tract, with a special emphasis on the superficial epithelium and blood vessels of the underlying connective tissue stroma. Colposcopy allows the examiner to identify specific colposcopic features that distinguish normal from abnormal findings and to form an impression as to whether the features are benign or the hallmarks of a preinvasive or an invasive disease. The primary goal of a colposcopist is to ensure that invasive disease is not missed. If the colposcopic examination is performed according to acceptable protocols and is guided by a colposcopic assessment method that allows the grading of epithelial findings, an accurate diagnosis can be made.<sup>8</sup> Colposcopy is complementary as well as superior to cytology. It is a simple and noninvasive OPD procedure. It helps in determining indications for a cervical biopsy, locating sites, and the extent of biopsy. It helps in avoiding traumatic diagnostic methods such as 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.<sup>9</sup> Colposcopy is practiced in two ways: (1) referral colposcopy—to assess women with abnormal screening findings and/or clinically suspicious cervix; (2) routine colposcopy—to assess women as part of a routine gynecological examination.<sup>10</sup>

## OBJECTIVES

To screen women who have abnormal symptoms with Pap smear and colposcopy, to screen women who have an unhealthy cervix

on visual inspection and women with dysplastic smears with colposcopy, to do histopathological analysis of colposcopically directed biopsies, to compare and correlate colposcopy and cytology with a histopathological diagnosis, to critically evaluate the sensitivity and specificity of colposcopy vs pap smear in the early detection of CIN. Patients with symptoms such as recurrent white discharge, post coital bleeding, intermenstrual bleeding, or post menopausal bleeding were included. Patients with a clinically unhealthy cervix diagnosed by speculum examination were included. Patients with Pap smears showing a dysplasia were included. Women with a frank invasive cancer and women who underwent a hysterectomy and pregnant women were excluded.

## Pap Smear

After the preliminary inspection of the cervix, a Pap smear was taken using an Ayre's spatula. The squamocolumnar junction was scraped with the Ayre's spatula by rotating it to a full 360 degrees. The scrapings were evenly spread on a glass slide and immediately fixed by dipping it in the jar containing equal parts of 95% ethyl alcohol and ether and transported to the cytopathological laboratory. Smears were analyzed by a senior pathologist. Revised Bethesda System 36 was used for describing Pap smear results.

## Colposcopy

Colposcopy was performed in all women using normal saline, green filter, acetic acid, and Lugol's iodine. Findings were recorded and a colposcopy diagnosis was made based on the modified Reid colposcopic index (RCI).

Reid et al. defined three objective categories based on the colposcopic index using four colposcopic signs, i.e., color, margin (including surface contour), vascular pattern, and iodine response. Each category is offered scores of 0–2 and summation of these scores is done—scores of 0–2: low grade disease (CIN 1 or HPV), scores of 3–4: intermediate grade disease (CIN 1 and 2), and scores of 5–8: high-grade disease (CIN 2 and 3). A correlation between the Pap smear and biopsy: 27 cases out of 100 women were positive on the Pap smear, whereas 46 of 100 women were positive on Biopsy. Pap smear was positive in 27 of 46 biopsy-proven positive cases. Totally, 16 cases of CIN1 and 5 cases of CIN 2/3 were underreported as inflammatory on Pap smear. An estimated 2 cases of cervicitis/metaplasia were overdiagnosed as CIN 1 (Table 1).

## 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 a high standard. Cytology-based screening programs have achieved a very limited success in developing countries such as India owing to a lack of trained personnel, laboratory facilities, equipment, a high cost of services, and poor follow-up. It has become necessary to find out a screening procedure alternative to cytology, which has high sensitivity and specificity. Pap smear has the disadvantage of having a low sensitivity, often less than 50%. On the other hand, a sensitivity of conventional colposcopy was found to be high (64–99%) but specificity was found to be low (30–93%). Adjunctive testing using both these tests in sequential combination assists in improving the sensitivity of the test without compromising its specificity. Colposcopy is a simple OPD procedure having an advantage of being more sensitive than Pap smear in diagnosing precancerous lesions. The present study was carried out in the gynecology opd at Mamata General Hospital,

**Table 1:** Correlation between colposcopy and biopsy

Colposcopy	Biopsy				Total
	Normal	Cervicitis / metaplasia	CIN 1 (mild dysplasia)	CIN 2/3 (moderate/ severe dysplasia)	
Normal	2	8	0	0	10
Inflammation/erosion	1	39	8	2	50
Hazy/faint acetowhite areas, fine punctations or mosaicism, iodine partially positive epithelium	0	1	13	1	15
Dense acetowhite areas, coarse punctations or mosaicism, iodine negative epithelium	0	1	3	18	32
Unsatisfactory	0	2	1	0	3
Total	3	55	25	21	100

Khammam from October 2011 to June 2013. One-hundred cases who fulfilled the selection criteria were recruited for the study. In the present study, colposcopy and Pap smear evaluation were done in a sequential manner correlating with histopathology findings as the reference standard.

A maximum number of cases were found to be in the age group 31–40 years (46%). Majority (93.4% (i.e., 43/46)) of CIN occurred in the age group of >30 years. Majority of the study group were para two (34%) and para three (35%). In our study, multiparous women were at a high risk for developing carcinoma cervix, i.e., 97.8% (45/46) of CIN cases were  $\geq$  para 2, which was comparable to the findings of Gopal et al. and Kushtagi and Fernandez et al. studies.

### Complaint

The most common symptom was recurrent white discharge per vagina (WDPV) (81%). Among them CIN was found in 69.5% (32/46).

### Pap Smear

In our study, sensitivity of the Pap smear was found to be 54.3%. This is because 16 cases of mild dysplasia (LSIL) and 5 cases of moderate to severe dysplasia (HSIL) were underreported as inflammatory. The positive predictive value and negative predictive value was found to be 92.5% and 71.2%, respectively. A literature review of cervical cytology testing techniques was conducted by agency for healthcare research and quality. The conclusion was that as a screening test, the Pap smear has been found to have a sensitivity of 51%, with an estimated false-negative rate of 49%. In three reviews of the accuracy of cervical cytology assessment, the sensitivity of the Pap test in detecting CIN 2 or 3 ranged from 47 to 62%. The sensitivity of the Pap smear has been found to be lower in developing countries because of the presence of infection and inflammation.

### Colposcopy

The sensitivity and specificity of colposcopy in our study was 76.1% and 96.2%, respectively. The positive predictive value and negative predictive value were found to be 94.6% and 82.5%. Colposcopy was unsatisfactory in 3 cases, of which 2 showed cervicitis/metaplasia and 1 showed mild dysplasia on histopathology. Colposcopy overdiagnosed 2 cases of cervicitis/metaplasia as LSIL in 1 case and as HSIL in the other case. The positive predictive value of colposcopy was high in our study when compared with that of other studies. In relation to the negative predictive value of colposcopy, Malur et al. and Ramesh et al. studies were comparable with our study. The accuracy of colposcopy was 87% and that of cytology was 77% in our study. The women with cervicitis/metaplasia in our study were treated with antibiotics. Women with CIN 1 were advised follow

up. In women with CIN 2/3 who were not willing for follow up, a hysterectomy was done. It is evident that although colposcopy had a higher sensitivity (76.1%) when compared to cytology (54.3%), the specificity and positive predictive value of both were comparable. Hence, colposcopy is useful in detecting premalignant and malignant lesions of the cervix effectively.

### CONCLUSION

The majority of women were in the age group of 31–40 years. The commonest symptom was recurrent white discharge per vagina. Pap smear had a high specificity but low sensitivity. Colposcopy had a high sensitivity and specificity. Hence it is useful in detecting premalignant and malignant lesions of the cervix effectively. The specificity and positive predictive value of Pap smear and colposcopy were comparable. Colposcopy had a higher accuracy than Pap smear. Colposcopy and cytology used together in patients with cervical lesions had a relatively higher chance of detecting squamous intraepithelial lesions/malignancy when compared to either procedure when performed alone.

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