

Comparison of colposcopic directed biopsy and cytology in screening of pre invasive lesions and early detection of Cervical Cancer

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Abstract

Introduction: Cancer cervix is the most common malignancy in the developing world and second most common in the world amongst women. The easy accessibility of cervix with newer screening and diagnostic procedures has rendered it a preventable disease. Colposcopic evaluation and guided biopsy is an important diagnostic step and standard of management for abnormal cytological smear. **Methods:** A cross sectional study of a total of 50 patients attending gynecology OPD in Gauhati Medical College and Hospital was conducted between July 2013 & June 2014. Patients between 20-60 years were included. PAP smear, Colposcopy and Colposcopic directed Biopsy were taken from the suspicious areas. **Results:** On cytology 24% cases (12/50) were neoplastic. On colposcopy 28% cases (14/50) were neoplastic though on histopathology 50% cases (25/50) were neoplastic. Sensitivity, specificity, positive predictive value and negative predictive value for PAP smear was 24%, 76%, 50% and 50% respectively. Sensitivity, specificity, positive predictive value and negative predictive value for colposcopy was 40%, 84%, 71% and 58% respectively. **Conclusion:** For screening and detection of cervical lesions combination of various methods should be employed which will increase diagnostic accuracy.

Key words: Cervical cancer, Pap Smear, Colposcopy, Biopsy, pre-invasive lesion.

Introduction

Cervical cancer has surpassed incidence of all the other cancers globally. The toll of death reaches 2,86,823 amongst the 5,50,700 cases identified every year. In India cancer cervix remains the most common (80%) cancer of all the genital tract malignancies accounting for one-fourth of the burden of the world [1]. According to Indian Council of Medical Research (ICMR), in the Hospital Based Cancer Registries (HBCRs) ,Dibrugarh is the third leading site in India [2]. The report of the North Eastern Population Based Cancer Registries (PBCRs) indicates an age Standardized Incidence Rates (AIR) of 25.4 per 100,000 in Aizawal district of Mizoram state followed by AIRs in Imphal West District (20.5) and Kamrup Urban District (17.3) [3].

Dr. Papanicolaou, in his paper, New Cancer Diagnosis in Jan 1928, recognized the importance of wet fixation of cytological specimen [4]. In 1927-28 Dr. Aurel described appearance of cells of squamous cell carcinoma in scrapings from uterine cervix [5]. Since then PAP smear has become the best modality for screening of cancer cervix worldwide. It has got certain limitations such as low sensitivity (19-51%), high false negative rate (49-

71%) & an expert cytopathologist is required for interpretation of the results. It becomes important to use an adjunctive screening method like Colposcopy which has high sensitivity (40-85%). It further helps to execute guided biopsies which serve as the gold standard in detecting pre invasive and invasive lesions of cervix. Present study is undertaken to screen high risk population with abnormal cytology and subjecting them to colposcopy and directed biopsies so that adequate and timely intervention can be instituted.

Aims and Objectives

- To screen high risk patients coming to gynecology OPD at the age of 20-60 years by performing Pap smear.
- To screen those high risk cases further by doing colposcopy.
- To detect all the cases of cervical intraepithelial neoplasia(CIN) and early cases of cancer cervix using colposcopy directed biopsy.
- To find out the correlation between colposcopy and pap smear findings and to take necessary steps for further management.

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- To critically evaluate the sensitivity and specificity of colposcopy versus pap smear in the screening and early detection of cancer cervix.

Methods and Materials

A cross sectional study was conducted in the department of Obstetrics and Gynecology, Gauhati Medical College and Hospital, Guwahati from July 2013- to June 2014 on patients attending Gynaecology OPD in the age group of 20-60 years.

Inclusion Criteria

- Patients with symptoms like persistent vaginal discharge, post coital bleeding, post menopausal bleeding, inter menstrual bleeding, persistent leucorrhoea not responding to antibiotics
- Normal looking cervix with symptoms or unhealthy cervix on per speculum examination.
- Women with cervical lesions like polyps, erosion, hypertrophied cervix, cervix with nabothian cyst.
- Women with clinical evidence of acute pelvic infection.

Exclusion Criteria

- Women with bleeding at the time of examination.
- Women who had been previously treated for carcinoma cervix
- Pregnant women.
- Women with frank lesions.
- Women with previous cervical surgery
- Women with normal looking cervix but asymptomatic

Patients were clinically examined after eliciting detailed history and then subjected to PAP smear and Colposcopic directed biopsy. PAP smear was obtained by using Ayre's spatula (ane cytobrush) by rotating it 360 degree clockwise at the transformation zone. The scrapings were evenly distributed on a glass slide which was fixed in 95% alcohol. Interpretation of PAP smear was done by using Bethesda classification.(2001) [6].

Table 1: correlation of cytology with histopathology findings

| Cytology | Normal | Cervicitis | CIN -1 | CIN -2-3 | SCC | Adeno carcinoma | Metaplasia | Leukoplakia | Total |
|------------------------------|--------|------------|--------|----------|------|-----------------|------------|-------------|-------|
| Normal | | 1 | | 1 | | | 2 | 1 | 5 |
| Inflammatory | 1 | 10 | 7 | 5 | 5 | 1 | 0 | 1 | 30 |
| Ascus | | 3 | | | | | | | 3 |
| LSIL | | 2 | | 2 | | | | | 4 |
| HSIL | 1 | 2 | 1 | 2 | | | 1 | | 7 |
| SCC | | | | | 1 | | | | 1 |
| Adeno carcinoma | | | | | | 0 | | | 0 |
| Total | 2 | 18 | 8 | 10 | 6 | 1 | 3 | 2 | 50 |
| Percentage of cytology cases | 0.04 | 0.36 | 0.16 | 0.2 | 0.12 | 0.02 | 0.06 | 0.04 | |

After taking PAP smear, visualization of cervix was done by Colposcopy using normal saline, green filter, acetic acid and lugol's iodine. Results were interpreted using modified Reid's Colposcopic Index [7]. Colposcopic directed Biopsy was obtained from acetowhite areas. Tissue obtained was fixed in formalin solution and histopathological results were noted.

Statistical Analysis

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 comparing colposcopic directed biopsy results as gold standard.

Results

A total of 50 cases of cervical smears were studied using the Bethesda System of classification and the cytological findings were compared with the corresponding histopathological findings in all the cases.

In the present study, maximum number of cases fell in the age group of 31-40 years. CIN amongst them were 14%. All the patients were married. CIN after 20 years of married life was 14%. Multiparous patients (more than 1 child) had high incidence of CIN. Majority of patients had low socioeconomic status with CIN in 24% cases. Chief complaint was white discharge (38%) with CIN in 14% cases.

Per speculum findings- maximum patients had hypertrophied cervix or cervix with erosions (62%) In all 50 cases, results of PAP smear, colposcopy and directed biopsy were compared. Biopsy confirmed CIN-1 lesions were 16%, CIN-2/3 lesions were 20%, Squamous cell carcinoma were 12% and adenocarcinoma in 2%.

SCC- squamous cell carcinoma. LSIL- low squamous cell carcinoma, HSIL- high squamous cell carcinoma

Retrospective analysis of biopsy confirmed cases and pap smear results were compared as shown in table-1. Results can be interpreted as:

| Diseases | Histopathology | Cytology |
|-------------------------|----------------|----------|
| CIN-1 | 8 | 2 |
| CIN-2/3 | 10 | 2 |
| Squamous Cell Carcinoma | 6 | 1 |
| Adenocarcinoma | 1 | Nil |

Table 2: Diagnostic efficacy of PAP smear

| Cytology | HPE | | Total |
|----------------|------------|----------------|-------|
| | Neoplastic | Non Neoplastic | |
| Neoplastic | 6 | 6 | 12 |
| Non neoplastic | 19 | 19 | 38 |
| Total | 25 | 25 | 50 |

In present study Pap smear has 24% Sensitivity, 76% Specificity, 50% positive predictive value, 50% negative predictive value and 50% accuracy in diagnosing pre malignant and malignant lesions.(CIN-1 or LSIL and CIN 2/3 or HSIL are considered premalignant)

Table 3: correlation of colposcopy and colposcopy directed biopsy (hitopathology)

| Colposcopy | Normal/ inflammatory | Cervicitis/ metaplasia | CIN-1/ mild dysplasia | CIN 2- 3/moderate/ severe dysplasia | Malignant | Leukoplakia | Total |
|--|-------------------------|---------------------------|-----------------------------|--|-----------|-------------|-------|
| Normal | 1 | 3 | 1 | | | | 5 |
| Inflammation/erosions/squamous metaplasia | 1 | 13 | 6 | 6 | 1 | | 27 |
| Hazy/fine punctations/faint aw areas | | 3 | | 3 | | | 6 |
| Dense aw/coarse punctuation/mosaic pattern | | 1 | | 1 | 6 | | 8 |
| Polyps | | 1 | 1 | | | | 2 |
| Leucoplakia | | | | | | 2 | 2 |
| Total | 2 | 21 | 8 | 10 | 7 | 2 | 50 |

Colposcopic diagnosis of CIN-1 and above lesions was made in 14/50 cases. The results are interpreted as following:

| Colposcopy | Biopsy |
|------------------|--|
| 6 fine AW areas | 3 cases of CIN2/3 |
| 8 dense AW areas | 1 case of CIN2/3, 6 cases of malignancy |
| 27 erosions | 6 cases of CIN- 1, 6 cases of CIN2/3, 1 case malignant |

Table 4: Diagnostic efficacy of colposcopy

| Colposcopy | HPE | | Total |
|--------------|--------------|--------------|-------|
| | Positive (+) | Negative (-) | |
| Positive (+) | 10 | 4 | 14 |
| Negative (-) | 15 | 21 | 36 |
| Total | 25 | 25 | 50 |

In the present study colposcopy has 40% Sensitivity, 84% Specificity, 71% positive predictive value, 58% negative predictive value and 62% accuracy. (Fine Acetowhite areas on colposcopy indicate CIN-1 or LSIL. Dense Acetowhite areas on colposcopy indicate CIN-2/3 or HSIL.)

Discussion

Globally cancer cervix accounts for the second most common type of cancer in the world. The high incidence of cancer cervix is attributed to lack of awareness of the disease amongst the people due to their education status (most of them are illiterate) and low socio economic status [8]. The blessing in disguise for this slow progressive disease lies in the fact that it has got a long pre invasive period and if detected early in this phase, will bring down the incidence of CIN and frank cancer cervix.

Effective screening programme at the grass root level should begin as Pap smear and pap positive and all high risk patients should be further evaluated with colposcopy and directed biopsies. Pap along with colposcopy can detect the lesions early in its pre invasive phase and can prevent deadly consequences [9].

The mean age in the present study was 37 years which is comparable to other studies [8,10,11]. Mean age in other studies were slightly lower i.e. Tuon FF et al (30.2years) & Vaishali et al (32.6years) [12, 13]. Higher mean age group was seen in Karimi Zarchi study (42.9years) [14].

In the present study, maximum numbers of CIN cases were illiterate (64%). Once duration of marriage increases the risk of sexual exposure increases many folds and this leads to development of dysplasias contributing to premalignant and malignant conditions of the cervix. In the present study maximum number (20%) of CIN cases were married for 20 years or more. Saha Thapa showed mean age of marriage was 21 years [8]. Ashmita et al showed higher prevalence of CIN in cases of early marriage <18years) [15]. Increasing the number of sexual partners has the effect on increasing incidence of CIN and invasive diseases.

In the present study it was found that cases of CIN were high with the increasing parity (>2). With repeated pregnancies and trauma of cervical dilatation the connective tissue of cervical epithelium become less effective in preventing cancer cell invasion. Higher parity means more number of coitus starting at young age predisposing to CIN and carcinoma cervix. In studies conducted by S Sharma et al [10] Ashmita et al [15], Malur et al [9] as well as present study pre invasive lesions were seen in women having more than 2 children.

Socioeconomic status has always played a major epidemiological role in the genesis of dysplasia. The factors contributing to higher incidence are poor personal hygiene, poor living conditions, unstable marriages, lack of awareness and early age at first sexual intercourse. In the present study, majority of CIN cases belonged to low socio economic status which is comparable to studies conducted by Saha Thapa et al [8] & El Moss et al [16].

In the present study majority of cases attending OPD and those who are CIN positive have chief complaints of white discharge per vaginum. The incidence of CIN is 14% amongst patients having white discharge. In other studies conducted by Saha Thapa et al [8], Malur et al [9] and Ashmita et al [15] white discharge was the presenting complaint of the patient.

Regarding the clinical appearances of cervix, the most common finding was erosion of cervix where the squamous epithelium of ectocervix was replaced by the columnar epithelium of endocervix. Erosion was seen in 62% cases out of which 24% had CIN.

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In our study sensitivity of Pap smear was 21% as 2 cases of LSIL were reported as inflammatory and 3 cases of HSIL were reported as 1 normal and 2 inflammatory respectively. This shows high false negative smear. Specificity of Pap is 74% showing low false positive smears in the present study.

Table 5: Comparison of different studies for Pap smear sensitivity and specificity

| Studies | Sensitivity | Specificity |
|----------------------------|-------------|-------------|
| Karimi zarchi et al [14] | 51% | 66.6% |
| Ashmita et al [15] | 19.5% | 83.33% |
| Sukhpreet singh et al [17] | 20% | 91.25% |
| Tata Memorial study [11] | 57.4% | 99.4% |
| Malur et al [9] | 41.66% | 96.92% |
| Present study | 24% | 76% |

In all the studies, Pap smear as a screening test, has been found to have a low sensitivity varies between 19-57% to 57.4%. The sensitivity of Pap smear has been found to be lower in developing countries because of presence of infection and inflammation.

In our study sensitivity and specificity of colposcopy was 40% and 84% respectively. Our study showed low sensitivity of colposcopy as 6 cases of CIN-1, 6 cases of CIN-2 and 1 malignant case were picked up as inflammatory or having erosions on colposcopy

Table 6: Comparison of different studies for colposcopy sensitivity and specificity

| Studies | Sensitivity | Specificity |
|----------------------------|-------------|-------------|
| Karimi zarchi et al [14] | 70.9% | 44.4% |
| Ashmita et al [15] | 90.24% | 72.73% |
| Sukhpreet singh et al [17] | 95% | 63.75% |
| Tata Memorial study [11] | 64-99% | 30-93% |
| Ramesh G et al [18] | 83.33% | 46.42% |
| Malur et al [9] | 80% | 81.54% |
| Present study | 40% | 84% |

Sensitivity of colposcopy was found to be 40% and specificity was 84%. This showed a high sensitivity and a high specificity when compared to Pap smear. The accuracy of Pap smear and colposcopy is 54% and 62% respectively. Expertise and experience is necessary for proper interpretation of colposcopy. With the passage of time sensitivity of colposcopy shall increase when more training will be provided to health personals regarding colposcopy and related studies.

In our study all 50 cases were subjected to colposcopically directed biopsy after performing Pap tests and colposcopy for each patient. Majority of patients showed inflammations or erosions or metaplasia having cryptic openings or doughnut appearance on colposcopy. (54%) . Colposcopy was able to pick 28% cases as pre malignant (CIN) which showed hazy or dense aceto white areas or fine or coarse punctuations whereas on colposcopically directed biopsy 36% cases were picked up as CIN and 14% were malignant (squamous cell carcinoma and adeno carcinoma)

Histopathology is considered as gold standard in our study. Sensitivity and specificity of Pap smear and colposcopy is compared to the colposcopic directed biopsy positive cases.

| Diagnostic Efficacy | Pap Smear | Colposcopy |
|------------------------------|-----------|------------|
| Sensitivity | 24% | 40% |
| Specificity | 76% | 84% |
| Positive predictive value | 50% | 71% |
| Negative predictive value | 50% | 58% |
| Percentage of false negative | 76% | 60% |
| Percentage of false positive | 24% | 16% |
| Accuracy | 50% | 62% |

It is evident that although colposcopy had higher sensitivity and specificity as compared to cytology. Positive predictive value is also high for colposcopy. 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. Also colposcopic directed biopsy is much more reliable in picking up true positive cases as compared to biopsy through visual inspection procedures

Conclusion

Thus colposcopy offers an excellent tool in evaluating cervical lesions. It is easy and cost effective and its importance lies in teaching, diagnosis and management of pre invasive and invasive diseases. There is a need to encourage and practice sequential use of Pap smear and colposcopy along with colposcopy directed biopsy which is the gold standard in early detection and management of Cervical Intraepithelial Neoplasm (CIN) and Cancer Cervix in all the medical colleges and institutions to prevent this disease from stepping up to number one position amongst cancers in the world.

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