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A Comparison of 3 ways of conventional pap smear, liquid- based cytology and colposcopy vs cervical biopsy for early diagnosis of premalignant lesions or cervical cancer in women with abnormal conventional pap test

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Abstract

A prospective comparative study of conventional pap smear, liquid based cytology and colposcopy guided biopsy as a screening method for early detection of precursor lesion of ca cervix in 70 women attending OPD at SMSMC Jaipur. Pap smear, liquid based cytology taken and patient subjected to colposcopy guided biopsy. Out of 28 patients positive on pap's test, only 17 (24.2%) were positive on histopathology whereas out of 45 patients positive on liquid based cytology only 38(54.2%) patients were positive on histopathology. Colposcopy report was positive for 48 patients but histology was positive for 46(65.7%) patients only. Sensitivity of pap smear was found to be 35.4% with high false negative but high specificity. Colposcopy has 90.9% specificity but high sensitivity (95.8%). This study demonstrate that colposcopy has higher sensitivity in diagnosis of any cervical lesions compared to the pap smear and liquid-based cytology and also statistically significant relationship was found between them.

Keywords: Cervical cancer, papanicolaou test, liquid based cytology, colposcopy

Introduction

Cervical cancer is the second most common gynecological cancer in women ^[1]. Due to lack of infrastructure and trained personnel, the incidence of cervical cancer has remained as high as 80% in developing nations India alone accounts 18% cases. According to Program for Appropriate Technology (PATH), an international nongovernmental organisation "an important reason for high incidence in developing countries is lack of effective screening program to detect precancerous condition and treat them before they progress to cancer". Based on the experience of the countries with mass screening programs, International Agency of Research on cancer (IARC) reported 93% reduction in cervical cancer incidence when women aged 35 to 64 years were screened 1 to 3 yearly; 84% reduction when screened 5 yearly and 64% reduction when screened 10 yearly ^[2].

For the last 60 years, the mainstay of cervical cancer screening is Papanicolaou test (pap test). It involves the examination of exfoliating cells from the transformation zone and detects cancerous or precancerous lesion. The test can be performed by traditional method or liquid-based cytology. In liquid- based cytology, collected cells are released into a vial of liquid preservative that is then used for microscopic evaluation of the cells. Traditional pap test involves direct transfer of the cervical cells to a microscope slide for evaluation. When abnormal cells are detected on the pap test, colposcopy is indicated ^[3].

The traditional pap's smear has a significant false negative rate of 15 to 40% where absolute sensitivity for CIN (cervical intraepithelial neoplasia) II-III is 50-89% ^[4-6]. The main factors for false negative rate are: specimen collection, smear formation, false error, deficiency of consistent sufficient number of cytotechnician.

There are two limitations of pap's smear which are false negative result and cost of the test ^[7].

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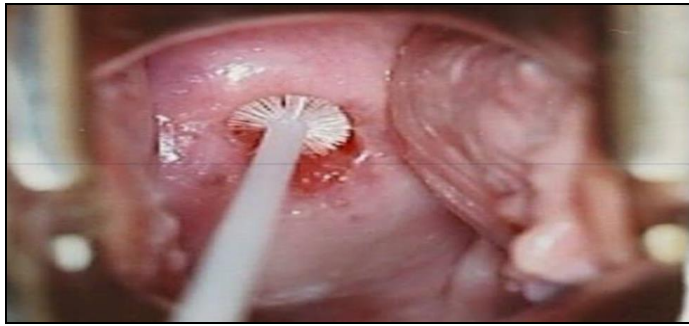


Fig 1: Pap smear of a healthy cervix

Liquid-based cytology has been associated with the reduction of unsatisfactory rate [8]. It has been suggested that the sensitivity of liquid-based cytology for the detection of CIN I-II is same as conventional cytology but its sensitivity for detection of CIN II-III is lower. Comparative performance of liquid-based cytology has suggested that sensitivity for detection of CIN II-III is similar to that of conventional cytology but specificity is lower [9]. Another study showed that liquid-based cytology does perform better than conventional cytology in term of positive predictive value for detection of CIN -II or CIN- III [10]. Liquid-based cytology is found to be cost effective [11] and this test is important for detection of HPV-DNA testing. It is known that screening test has a higher sensitivity but conventional pap's test has long been known for its low sensitivity because of inadequate sample collection and interpretation difficulties [12]. Liquid-based cytology has been well documented for its higher sensitivity [13-15].

Colposcopy remains the gold standard for evaluation of patients with abnormal cytology. Colposcopy has the best efficacy in detecting any cervical lesion in compared with any other diagnostic technique. Its primary goal is to identify invasive and preinvasive neoplastic lesions for directed biopsy and subsequent management. However its sensitivity, interobserver agreement and reproducibility are less than previously thought. Sensitivity estimates range between 50 and 80% [16]. This highlights the need for further evaluation or surveillance when initial colposcopy fails to reveal high grade neoplasia. Lesion grading is done based on margin, acetowhite coloring, vessels pattern and Iodine staining also known as Reid Colposcopy Index [17].



Fig 2: Colposcopy of a healthy cervix with cervical ectropion

Materials and methods

This prospective study was conducted in a tertiary care obstetrics and gynecology hospital at Jaipur. Study was approved by the Institutional Ethics Committee. Data was

collected from March 2019 to February 2020. Patients who attended gynecology OPD with chief complaint of (Inclusion criteria)

1. Persistent vaginal discharge
2. Post coital bleeding
3. Abnormal vaginal bleeding or irregular menstrual cycle
4. Pain in lower abdomen
5. Any abnormal finding on per speculum examination
6. Women who has undergone supracervical hysterectomy

Exclusion criteria were

1. Women above the age of 65 years who have been previously screened completely.
2. Women who have already undergone total hysterectomy
3. All women with normal histology on cervical biopsy.

Sample size is calculated as 70 subject with an alpha error 0.05 and power assuming proportion satisfactory for evaluation of cervical cancer screening by pap smear and liquid based cytology 50% and 13% respectively with drop out rate of 10%.

After obtaining proper consent, detailed history was taken with physical examination. Pap smear was taken by ayers spatula and endocervical cytobrush. Slides were made and the residual material on both cytobrush and spatula were rinsed in 10-15ml of pap spin collection, a buffered methanol preservative solution in vial and sent for cytology. Colposcopy will be done in same patient after pap smear reporting using acetic acid. Biopsy is taken from suspicious area.

Results and discussion

Results were compiled and manually analyzed. Total number of patients is 70 with average age of 42 ± 9.94 years, and range of 21 to 65years of age. Thirty (42.8%) patients came to the clinic with pain, 22 patients (31.4%) with bleeding and 18 patients (12.6%) with a complaint of vaginal discharge.

Regarding the report of cervical cancer screening tests, conventional pap's test, liquid based cytology, colposcopy guided biopsy were done from 70 patients, findings are listed in Table 1.

Table 1: Result of Pap Smear, LBC, Colposcopy

	Pap smear	Liquid based cytology	Colposcopy
Positive	28	45	48
Negative	42	25	22
Total	70	70	70

On assessment of the distribution of the relative frequency of Atypical findings including ASCUS, ASC-H, AGC), 10 (14.2%) cases were reported on conventional pap smear and 6 (8.5%) cases were positive for LSIL, 12 (17.1%) cases were positive on HSIL and no case of carcinoma was noted.

On the other hand, liquid based cytology 19 (13.7%) were positive for Atypical cells, 15 (21.4%) were positive for LSIL, 13 (18.5%) were positive for HSIL and 5 (7.14%) cases were positive for carcinoma.

Colposcopy findings were positive for 32 (45.7%) for low grade lesion as per Reid index and 16 (22.8%) cases were positive for high grade lesion. Biopsy taken at time of colposcopy was suggestive of 32 (45.7) cases of ≤CIN1, 10 (14.2%) cases were of CIN2/CIN3, and 6 (8.5%) cases were of Carcinoma.

On comparing pap smear, liquid based cytology and colposcopy results with biopsy, finding are listed in Table 2,3 and 4 respectively.

Table 2: Comparison of Pap result with histopathology

Biopsy	Atypical	LSIL	HSIL	Carcinoma	negative
CIN 1	4	3	1	0	24
CIN2/3	2	1	4	0	3
Carcinoma	0	0	2	0	4
Negative	4	2	5	0	11
Total	10	6	12	0	42

Table 3: comparison of Liquid Based cytology result with histopathology

Biopsy	Atypical	LSIL	HSIL	Carcinoma	Negative
CIN1	9	10	6	0	7
CIN2/3	1	1	4	2	2
Carcinoma	0	0	2	3	1
Negative	2	4	1	1	15
Total	12	15	13	6	25

Table 4: comparison of Colposcopy result with histopathology

Biopsy	Low grade	High grade	Negative
CIN1	26	4	2
CIN2/3	3	7	0
Carcinoma	1	5	0
Negative	2	0	20
Total	32	16	22

Based on the above data, the sensitivity. Specificity of Pap smear, Liquid based cytology and colposcopy is listed in table 5

Table 5: Statistical analysis of pap smear, liquid based cytology and colposcopy

	Pap smear	Liquid Based Cytology	Colposcopy
Sensitivity	35.4%	79.2%	95.8%
Specificity	50%	68.2%	90.9%
Positive Predictive Value	60.7%	84.4%	95.8%
Negative Predictive Value	26.2%	60%	90.9%
Accuracy	40%	75.7%	94.2%

Colposcopy clinical impression has the highest agreement with colposcopy biopsy. It is a diagnostic test and not a screening test. Liquid based cytology showed better performance as a screening test compared to conventional Pap smear due to its high specificity.

Although the pap smear has been utilised for cervical cancer screening for more than 50 years, despite being credited with a 70% reduction in mortality for cervical cancer, the false negative rate is still a cause for concern.

Setzu akamatsu and his colleagues in a study published in 2012 concluded that LBC technique has significantly lower percentage of unsatisfactory samples than conventional pap smear method [18].

In a study done in 2010 by Doctor Karimi and her colleagues comparing the colposcopy and conventional pap smear with biopsy standard diagnostic showed that the colposcopy method has higher sensitivity and specificity compared to the conventional pap smear [19]. In another study performed by Doctor Karimi and her colleagues in 2011, sensitivity and specificity of repeated pap smears for ASCUS was reported to be 15% and 93%, respectively, while the sensitivity and specificity of colposcopy in diagnosis of cervical cancer was 80% and 80%, respectively. Considering the fact that the low accuracy of pap smear in India as a developing country and the need for early detection of cervical cancer, cervical biopsy and colposcopy is recommended for patients.

Conclusion

From the result of the present study, of various method of screening, colposcopy and colposcopy guided biopsy was definitely found to be more sensitive. Several limitation of other screening method were identified. For conventional pap smear limitations identified were inadequate transfer of cells to slide, in homogenous distribution of abnormal cells, presence of obscuring blood, inflammation or thick areas of overlapping epithelial cells. These are overcome by liquid based cytology which showed a better performance as a screening test as compared to Pap smear.

But LBC also has few limitations, high cost, commercial systems required of cytotechnologists and pathologists in order to interpret the thin prep slides, which has led to development and evaluation of alternative.

Colposcopy guided biopsy was also found to be useful in understanding the morphology of the cervical lesion, both of neoplastic and the non-neoplastic ones and was very helpful in planning their management.

Hence colposcopy when used with cytology together in patients of cervical lesions, has a relatively higher chance of detecting premalignant and malignant lesions as compared to either procedure when performed alone. Other screen tests when performed well are viable alternatives for consideration as screening options in different settings based on the availability of resources and technical capacity.

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