

Comparison of Visual Inspection with Acetic Acid and Pap Smear in Detecting Premalignant Lesions of Cervix

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Abstract

Background: Worldwide cervical cancer comprises approximately 12% of all cancers in women with 122,844 new cases reported annually in India. Cervical cancer progresses slowly for a decade as it is preceded by intraepithelial histological changes, visual inspection aided by acetic acid test (VIA), Pap smear, and colposcopy can be utilized as a tool for cytological analysis of cervix, early identification of risk factors and preinvasive lesions of cervix and hence early diagnosis and treatment of cervical cancer even in rural areas.

Objectives: The objectives are as follows: (1) To compare VIA with Pap smear in detecting premalignant lesions of cervix, (2) to correlate VIA and Pap smear findings with colposcopic findings, and (3) to localize the lesion by colposcopy and obtain biopsy wherever necessary.

Materials and Methods: A prospective study of 200 women attending the Gynecology Outpatient Department at BLDE (deemed to be university) Shri B. M. Patil Medical College Hospital and Research Center, Vijayapura, between October 2016 and August 2018 was included in the study.

Results: The incidence of premalignant and malignant lesions of the cervix was 7%. Cervical cytology was normal in 16%, inflammatory in 77.5%, ASCUS in 4%, LSIL in 1.5%, HSIL in 0.5%, and squamous cell carcinoma in 0.5%. Maximum number of patients with ASCUS and LSIL was in the age group of 35–39 years and 40–44 years and HSIL and squamous cell carcinoma occurred in the age group of 25–29 years and 30–34 years, respectively. ASCUS, LSIL, and HSIL were seen in parity 3–5 and malignancy in parity >3 observed mostly in low socioeconomic status. All abnormal Pap smears mainly presented with white discharge PV, pain abdomen and with irregular PV bleeding as the second most common and erosion and cervicitis as the most common clinical picture. Cervical biopsy confirmed HSIL and invasive carcinoma cytology.

Conclusion: In India, cytology, a low cost and easily accessible test, is the most logical screening modality although it has very low sensitivity, detection rates could be further improved using liquid-based cytology and the use of endocervical cytobrush.

Key words: Biopsy Screening XIII, Cervix, Colposcopy, Pap smear, Visual inspection aided by acetic acid test

INTRODUCTION

Worldwide cervical cancer comprises approximately 12% of all cancers in women with an incidence of 5 lakh new cases reported each year of which almost one-fourth of it

occurs in India.^[1] About 122,844 new cervical cancer cases are diagnosed annually in India, and 67,477 cervical cancer deaths have been reported annually in India.^[2] It is the second most common cancer in women worldwide but the most common in developing countries like India. It accounts for 80% of cervical cancer deaths in developing countries like India.^[3]

The dramatic reduction in the incidence of cervical cancer in developed countries is due to the widespread use of an effective cytological screening test, i.e., Papanicolaou Smear, which can identify the premalignant and malignant lesions of the uterine cervix, which cannot be detected or even suspected by history and clinical examination.^[4-6]

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Various screening methods are available such as cytology by Pap smear, visual inspection of cervix with acetic acid and/or Lugol's iodine, HPV-DNA test, and liquid-based cytology.

1. Screening by Papanicolaou test (Pap) should not be used for women aged <21 years, regardless of initiation of sexual activity.
2. A screening interval of 3 years should be maintained by Pap smear for women aged 21–30 years. HPV test is not recommended.
3. Women aged 30–65 years should have a Pap test and a HPV test (cotesting) every 5 years or are even acceptable to have a Pap test alone every 3 years.

MATERIALS AND METHODS

Methods of Collection of Data

Source of data

A prospective study of 200 women attending the Gynecology Outpatient Department at BLDE (deemed to be university), Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura was included in the study.

Period of the study

The period of the study was from October 2016 to August 2018.

Sample size calculation

Using the formula:

$$n = z^2 p(1-p)$$

$$d_2$$

Where

Z = z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate

A sample size of 185 (~200) was allowed for the comparison of visual inspection with acetic acid and pap smear as screening methods for premalignant lesions of the cervix with a 95% confidence level and margin of error of $\pm 7\%$ with finite population correction.

Statistical Analysis

Data were represented using Mean \pm SD and analyzed by Chi-square test for association, comparison of means using *t*-test, ANOVA for comparison, sensitivity, specificity, positive predictive value, and negative predictive values.

Methods of Collection of Data

Informed consent was taken from each woman. Relevant obstetrics and gynecology history were taken and recorded.

Inclusion Criteria

The following criteria were included in the study:

1. Age between 25 and 65 years
2. Chronic cervicitis
3. Symptoms such as vaginal discharge, postcoital bleeding, postmenopausal bleeding, intermenstrual bleeding, and persistent leukorrhea not responding to antibiotics
4. Normal looking cervix but symptomatic.

Exclusion Criteria

The following criteria were excluded from the study:

1. Menstrual bleeding at the time of examination
2. Cancer cervix
3. Clinical evidence of acute pelvic infection
4. Pregnancy.

Methodology in Brief

Method

A total of 200 patients as per the inclusion and exclusion criteria attending the Gynecology Outpatient Department, BLDE (deemed to be university), Shri. B. M. Patil Medical College and Hospital were considered for the study and patients were subjected to visual inspection aided by acetic acid test (VIA) and PAP smear and colposcopy and colposcopy assisted biopsy if necessary after taking informed consent.

RESULTS

The study was performed on 200 women who attended the Department of Obstetrics and Gynaecology at Shri B. M. Patil Medical College and Research Hospital, Vijayapura. The objectives of the study were to correlate the findings in women using, PAP smear, VIA, colposcopy, and colposcopic directed biopsies wherever necessary, in detecting the premalignant lesions of the cervix and to find the efficacy of individual tests. The detailed analysis of the study conducted, and the results are computed together after all the tests were employed to arrive at a conclusion [Tables 1-9].

Association of the Type of Smears and VIA Findings

Patients who had VIA positive, among them, 7 patients had ASCUS, 1 patient had HSIL, 70 patients had inflammatory, 1 patient had invasive carcinoma, and 3 patients had LSIL.

Association of Colposcopic Findings and Pap Smear

Among the patients who had PAP smear positive, 92.3% showed positive colposcopic findings.

Association of the Type of Smears and Cervical Biopsy

On the persistence of unhealthy cervix and inflammatory smear even after a course of antibiotics direct cervical punch

Table 1: Association of the type of smears and VIA findings

VIA	Types of smears						P value
	ASCUS	HSIL	Inflammatory	Invasive carcinoma	LSIL	Normal	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Positive	7 (87.5)	1 (100.0)	70 (45.2)	1 (100.0)	3 (100.0)	0 (0.0)	<0.001*
Negative	1 (12.5)	0 (0.0)	85 (54.8)	0 (0.0)	0 (0.0)	32 (100.0)	
Total	8 (100.0)	1 (100.0)	155 (100.0)	1 (100.0)	3 (100.0)	32 (100.0)	

*Significant at 5% level of significance (p<0.05)

Table 2: Association of colposcopic findings and pap smear

Colposcopic findings	Pap smear		P value
	Positive	Negative	
	n (%)	n (%)	
Positive	12 (92.3)	2 (1.1)	<0.001*
Negative	1 (7.7)	185 (98.9)	
Total	13 (100.0)	187 (100.0)	

*Significant at 5% level of significance (P<0.05)

biopsy was taken. Most of patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN; this stresses the importance of further screening inflammatory smear patients. Most of patients with ASCUS smear who underwent cervical biopsy had mild dysplasia and LSIL had mild dysplasia in biopsy. HSIL and invasive carcinoma showed moderate dysplasia and CIN (severe) as their biopsy finding, respectively.

Association of the Type of Colposcopic and VIA Findings

A total of 82 cases out of 200 women were positive on VIA. 14 out of 200 women were positive on colposcopy. 14 cases of VIA positive cases were also the 14 colposcopy proven positive cases. 69 cases of VIA were false positive which were cases of inflammation/erosion/metaplasia. There was one false-negative case.

Association of Cervical Biopsy versus Pap Smear

Out of 15 biopsy positive cases, 12 were positive for PAP smear and 3 were negative.

Association of Cervical Biopsy versus VIA

Out of 15 biopsy positive cases, 14 cases were positive for VIA and only 1 case was negative.

Association of Cervical Biopsy versus Colposcopic Findings

Out of 15 biopsy positive cases, 14 were colposcopically positive and only 1 was negative.

DISCUSSION

This is a prospective study, in which 200 women of reproductive age group who attended the Gynaecology

Outpatient Department at Shri B. M. Patil Medical College and Hospital, Vijayapura, from October 2016 to August 2018 were studied to know the “comparison of visual inspection with acetic acid and Pap smear in detecting premalignant lesions of cervix” pattern of cervical cytology by Papanicolaou smear and its incidence and correlation with various parameters [Figures 1-6].

The results are discussed as follows.

Association of the Type of Smears and VIA Findings

Patients who had VIA positive, among them, 7 patients had ASCUS, 1 patient had HSIL, 70 patients had inflammatory, 1 patient had invasive carcinoma, and 3 patients had LSIL.

Association of Colposcopic Findings and Pap Smear

Among the patients who had Pap smear positive, 92.3% showed positive colposcopic findings.

Association of the Type of Smears and Cervical Biopsy

On persistence of unhealthy cervix and inflammatory smear even after a course of antibiotics direct cervical punch biopsy was taken. Most of the patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN; this stresses the importance of further screening inflammatory smear patients. Most of the patients with ASCUS smear who underwent cervical biopsy had mild dysplasia and LSIL had mild dysplasia in biopsy. HSIL and invasive carcinoma showed moderate dysplasia and CIN (severe) as their biopsy finding, respectively.

Association of the Type of Colposcopic and VIA Findings

A total of 82 cases out of 200 women were positive on VIA. 14 out of 200 women were positive on colposcopy. 14 cases of VIA positive cases were also the 14 colposcopy proven positive cases. 69 cases of VIA were false positive which were cases of inflammation/erosion/metaplasia. There was a one false-negative case.

Association of Cervical Biopsy versus Pap Smear

Out of 15 biopsy positive cases, 12 were positive for PAP smear and 3 were negative.

Table 3: Association of the type of smears and cervical biopsy

Cervical biopsy	Types of smears						P value
	ASCUS	HSIL	Inflammatory	Invasive carcinoma	LSIL	Normal	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Cervicitis	0 (0.0)	0 (0.0)	31 (31.3)	0 (0.0)	1 (33.3)	0 (0.0)	<0.001*
CIN	0 (0.0)	0 (0.0)	1 (1.0)	1 (100.0)	0 (0.0)	0 (0.0)	
Mild dysplasia	5 (62.5)	0 (0.0)	1 (1.0)	0 (0.0)	2 (66.7)	0 (0.0)	
Moderate dysplasia	3 (37.5)	1 (100.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Normal	0 (0.0)	0 (0.0)	65 (65.7)	0 (0.0)	0 (0.0)	1 (100.0)	
Total	8 (100.0)	1 (100.0)	99 (100.0)	1 (100.0)	3 (100.0)	1 (100.0)	

*Significant at 5% level of significance (P<0.05)

Table 4: Association of types colposcopic findings and VIA findings

VIA	Colposcopic findings					P value
	Cervicitis	Dense acetowhite areas	Erosion	Hazy	Normal	
	n (%)	n (%)	n (%)	n (%)	n (%)	
Positive	56 (73.7)	6 (100.0)	6 (35.3)	7 (87.5)	7 (7.5)	<0.001*
Negative	20 (26.3)	0 (0.0)	11 (64.7)	1 (12.5)	86 (92.5)	
Total	76 (100.0)	6 (100.0)	17 (100.0)	8 (100.0)	93 (100.0)	

*Significant at 5% level of significance (P<0.05)

Table 5: Association of colposcopic findings and VIA

Colposcopic findings	VIA		P value
	Positive	Negative	
	n (%)	n (%)	
Positive	13 (15.9)	1 (0.8)	<0.001*
Negative	69 (84.1)	117 (99.2)	
Total	82 (100.0)	118 (100.0)	

*Significant at 5% level of significance (P<0.05)

Table 6: Cervical biopsy versus pap smear

Cervical biopsy	Pap smear		P value
	Positive	Negative	
	n (%)	n (%)	
Positive	12 (92.3)	3 (3.0)	0.029*
Negative	1 (7.7)	97 (97.0)	
Total	13 (100.0)	100 (100.0)	

*Significant at 5% level of significance (P<0.05)

Table 7: Cervical biopsy versus VIA

Cervical biopsy	VIA		P value
	Positive	Negative	
	n (%)	n (%)	
Positive	14 (17.9)	1 (2.9)	<0.001*
Negative	64 (82.1)	34 (97.1)	
Total	78 (100.0)	35 (100.0)	

*Significant at 5% level of significance (P<0.05)

Association of Cervical Biopsy versus VIA

Out of 15 biopsy positive cases, 14 cases were positive for VIA and only 1 case was negative.

Table 8: Cervical biopsy versus colposcopic findings

Cervical biopsy	Colposcopic findings		P value
	Positive	Negative	
	n (%)	n (%)	
Positive	14 (100.0)	1 (1.0)	<0.001*
Negative	0 (0.0)	98 (99.0)	
Total	14 (100.0)	99 (100.0)	

*Significant at 5% level of significance (P<0.05)

Table 9: Comparison of diagnostic efficacy of biopsy, VIA, and pap smear compared to colposcopic findings

	Pap smear	VIA	Cervical biopsy
Sensitivity (%)	85.7	92.9	100.00
Specificity (%)	99.5	62.9	98.99
PPV (%)	92.3	15.9	93.33
NPV (%)	98.9	99.2	100.00
Accuracy (%)	98.5	65.0	99.12
TP	12	13	14
FN	2	1	0
FP	1	69	1
TN	185	117	98
False-negative rate (%)	14.3	7.1	0.0
False-positive rate (%)	0.5	37.1	1.1

TP: True positive, FN: False negative, FP: False positive, TN: True negative

Association of Cervical Biopsy versus Colposcopic Findings

Out of 15 biopsy positive cases, 14 were colposcopically positive and only 1 was negative. The sensitivity of VIA was 95%, specificity was 55%, and PPV was 61%.

The sensitivity of Pap smear was 43%, specificity was 97%, and PPV of Pap smear was 90%. The overall accuracy of



Figure 1: Abnormal colposcopic images

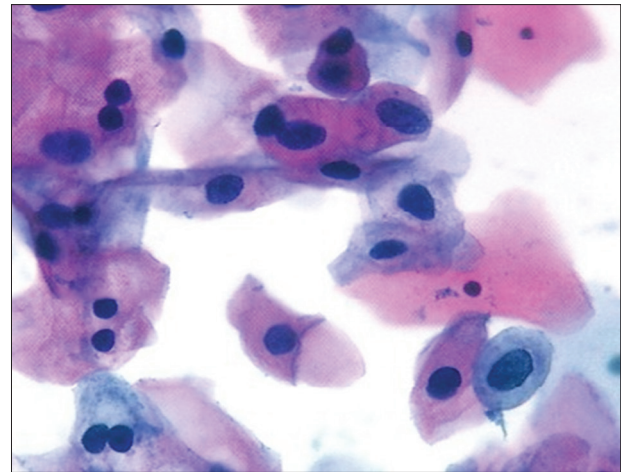


Figure 4: Pap smear showing LSIL

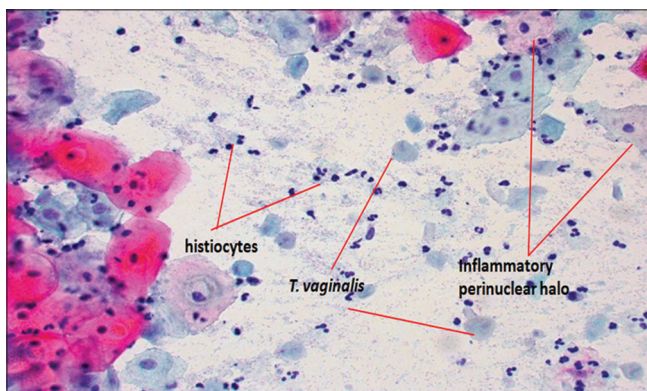


Figure 2: Pap smear showing inflammatory changes

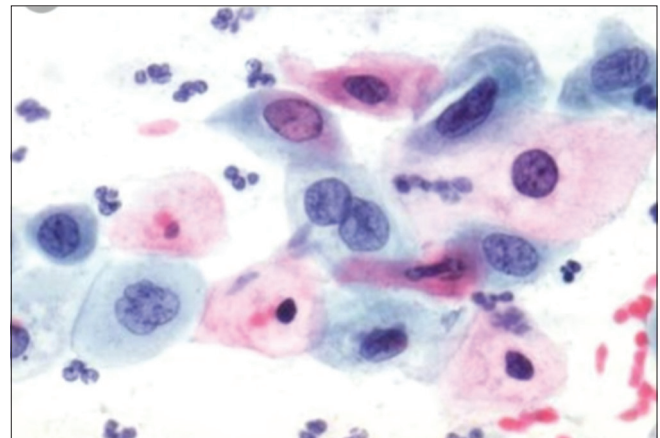


Figure 5: Pap smear showing HSIL

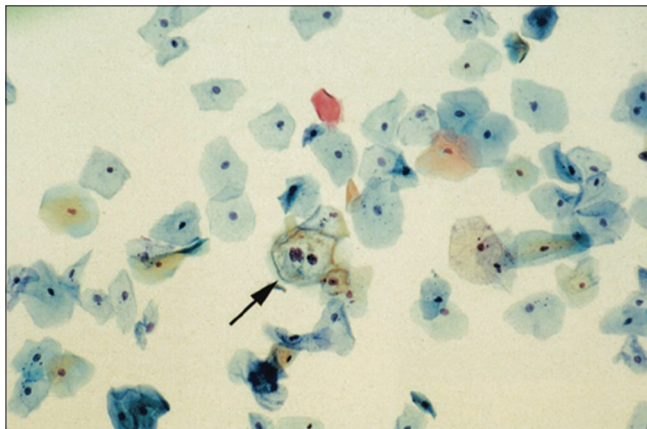


Figure 3: Pap smear showing ASCUS changes

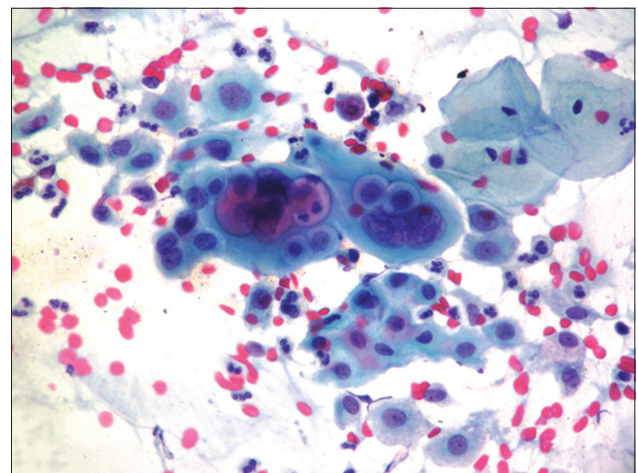


Figure 6: Pap smear showing squamous cell carcinoma

VIA was 72% and cervical cytology was 74%. Positive cases were subjected to biopsy and majority was reported as either normal or chronic cervicitis.^[7]

Most of the patients with inflammatory smear who underwent cervical biopsy had cervicitis 28.3% and 1.8% showed CIN; this stresses the importance of further screening inflammatory smear patients. Most of patients with ASCUS smear who underwent cervical

biopsy had mild dysplasia and LSIL had mild dysplasia in biopsy. HSIL and invasive carcinoma showed moderate dysplasia and CIN (severe) as their biopsy finding, respectively. Massad *et al.*^[8] found 77% of ASCUS cases to be nonmalignant.

In another study by Divya Hegde, out of 225 patients, VIA was positive in 27(12%) patients and Pap smear was abnormal in 26(11.7%). Pap smear had a sensitivity of 83%, specificity of 98%, PPV of 80%, and NPV of 97.9%. VIA had a sensitivity of 70.8%, specificity of 95%, PPV of 62.9%, and NPV of 96.5%.^[8]

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.^[9] 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 such as India due to lack of trained personnel, laboratory facilities, equipment's, 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.^[10]

In a multicentric study by Sankaranarayanan *et al.* showed sensitivity of Pap smear ranging from 36.6% to 72.3% and specificity ranging from 87.2% to 98.6%.^[11] In a study conducted by Goel *et al.*,^[12] the sensitivity of Pap smear was found to be 50% and specificity was 97%.

Wahi *et al.* found 65.5% patients with dysplasia having cervical erosion. Purandare *et al.* found most dysplasia's in women with cervicitis and erosion. Padmanabhan *et al.*^[13] found 31.25% patients with SIL having erosion and Sunanda Rao *et al.* showed cervical erosion and infection accounted for 40–50% of abnormalities.

CONCLUSION

The VIA and Papanicolaou procedures are the most simple, safe, practical, and cost-effective method for early detection of cervical cancer and its precursors to prevent invasive cancer.

Although screening with colposcopy and biopsy tend to over-diagnose the immature squamous metaplasia with optimal magnification. The technique has a high false-positive rate, not cost effective, and therefore, offers little in a screening program.

The Papanicolaou procedure is considered as a screening test, not a diagnostic test; therefore, abnormalities of the smear should be confirmed histologically by biopsy. Screening with PAP smear should be done yearly or every 2 years to reduce the chance of missing an early lesion. As the progression from pre-invasive to invasive carcinoma is slow, more frequent screening appears the gold standard for screening programs.

In developing countries like India, cytology, a low cost and easily accessible test, is the most logical screening modality although it has a very low sensitivity but has got good specificity rate and detection rates could be further improved using liquid-based cytology and the use of endocervical cytobrush and later can be referred to a higher center for biopsy which has got high sensitivity and specificity.

Hence, efforts must be directed toward education of women regarding cervical cancer to promote awareness of malignancy and to motivate them for cytological screening in the future.

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