Original Article

Comparison of Pap smear with visual inspection of cervix with acetic acid test in screening for cervical cancer

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Abstract

Background: Cervical cancer is the second most common among women globally. It is a unique malignancy that can be prevented by proper screening methods. Pap smear is presently considered to be the gold standard screening test, but has some inherent limitations. VIA can be a possible and promising screening test with similar efficacy of detecting Ca cervix. This study was undertaken to assess the sensitivity and specificity of VIA and compare the test characteristics with those of Pap smear. **Material and Methods:** In this prospective study 100 women, aged up to 70 years, who fulfill selection criteria were enrolled. The pap smear and VIA were done in these cases. The sensitivity and specificity of each test were determined and compared. **Results:** Out of 100 women screened, VIA tested positive in 21 patients (21%) and Pap smear positive in 14 patients (14%).The sensitivity of VIA was 100% as compared to Pap smear which was 66.67%. But the specificity of VIA was 91.86% Vs Pap smear was 100%. **Discussion:** VIA was found to be more effective in screening the true positives (14%). The percentage of false negatives with VIA was lower than with Pap smear (0% Vs 33.33%) which indicates that VIA has less chance of missing cancerous or precancerous lesions of the cervix. Use of both VIA and Pap smear simultaneously, appears to detect more cases of cancerous and pre-cancerous lesions of the cervix.

Keywords: Carcinoma of cervix, Pap smear, VIA test, screening.

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INTRODUCTION

Cancer of the uterine cervix is the second most common cancer in women worldwide and is the leading cause of cancer deaths among women. 80% of cervical cancers occur in developing countries, which emphasizes the importance of socioeconomic factors in the progression of disease[1]. 80% of these cases are at an advanced stage at the time of diagnosis. India has one sixth of the world's total population and one third of the world's cervical cancer burden[2]. Cervical cancer is a unique malignancy that can be prevented as the process typically starts from the cervical epithelium and the cervix is readily amenable for examination and treatment. Thus, screening of cervix can prevent development of cancer and even if it has developed, can be diagnosed and treated at an early stage[3]. Cervical cytology – Pap smear is presently considered to be the gold standard screening test, known to reduce cervical cancer incidence in organized screening program in developed countries. However, an organized screening programme is difficult to implement in developing countries where resources are scarce[1,4]. Given this difficulty of ensuring high quality cytology based services and the error rate inherent to cytology, there is significant interest in new, simpler approaches for cervical cancer screening. These non-cytological methods may be used in low resource settings

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where cytology is not available and in developed countries, where it is hoped that this combining cytological screening methods with visual screening methods may reduce error rate. Visual inspection of the cervix after application of acetic acid (VIA) appears to be a promising approach for cervical cancer screening.VIA involves the application of acetic acid in dilution of 3-5 % to the cervix and visualization with the naked eye without magnification. Abnormal areas appear as acetowhite patches due to osmotic dehydration and protein denaturation. VIA appears to be less expensive than cytological screening tests and paramedical workers too can be trained easily to perform the test with good results[5]. Additional advantage is that there is immediate feedback of test result to the patient and treatment can be immediately started after the test – at the same setting. Thus it may be possible to "see and treat" at the same visit. Various studies conducted worldwide indicate that VIA has a high sensitivity[6] in detection of cancerous and pre-cancerous lesions. VIA also has a positive predictive value comparable to Pap smear. Its main limitation noted is a high rate of false positive results [6].Combining visual screening methods with an inexpensive outpatient treatment could put cost effective cervical cancer prevention programme within much of even the poorest countries.VIA done in concurrence with Pap smear may also prove to reduce the high false negative rate attributed to Pap smear. Considering the potential significance of VIA, this study was undertaken to assess the sensitivity and specificity of VIA and compare the test characteristics with those of Pap smear.

MATERIAL AND METHODS

In this prospective clinical comparative study 100 women, aged up to 70 years, attending the Gynecology OPD at Tertiary care hospital in Maharashtra from February 2010 to May 2011 were included. All women who fulfill the selection criteria enrolled in the study gave informed consent. They came presenting with history of any or all of the following; post coital bleeding, intermenstrual bleeding, chronic white discharge, erosion, hypertrophied, irregular cervix on per-speculum examination. Women with frank invasive cervical cancer, continuous per vaginal bleeding, during menstruation and pregnancy were excluded from the study. Patients to be screened were explained the procedure to be performed, the relevant obstetrical and gynecological history was taken. Firstly, the patient was put in lithotomy or dorsal position and the genital area was inspected with a properly directed light source. Cervix was visualized with speculum and the findings of cervix prior to application of acetic acid were noted. Pap smear was taken using the Ayre's Spatula on clean glass slide (the broad end of a sterilized Ayre's spatula was used to collect cells from transformation zone by rotating it through 360 degrees and fix the smear with fixative and stained with Papanicolaou staining technique (labeled as slide A from transformation zone and slide B from endocervical region). The excess mucus was cleaned with a cotton swab soaked in normal saline and the cervix was washed with a cotton swab soaked in acetic acid. Squamo-columnar junction was identified entirely
and rapidity of appearance and disappearance of lesion was noted. After 1 minute, the cervix was inspected for changes, with adequate lighting. The smear from the acetowhite area is taken (labeled as slide C). Pap smear positive cases and cases with abnormal findings following application of acetic acid were referred for colposcopy and biopsy if necessary.

RESULTS

Most of the women who screened were in the age group of 30-39 yrs.Out of 100 women screened, VIA tested positive in 21 patients (21%) and Pap smear positive in 14 patients (14%). The maximum number of Pap smear positive and VIA positive was detected in the age group of 30- 39yrs. Most of the positive cases were housewives (78%), uneducated (58%), belonged to low socioeconomic status (74%) andmultiparous (36%). There was no statistically significant association between Pap smear and VIA positive cases in these clinico-demographic data (Table 1).

There was no any association of carcinoma of cervix with menstrual irregularities found. But maximum number of patient with VIA positive and Pap smear positive had regular menses. There were 10 menopausal patients, in which 4 patients were VIA and Pap smear positive.

The average at marriage was less than 19 years (86%) and most of VIA positive and Pap smear positive patients got married before 20 years of age. So, carcinoma of cervix was associated with earlier marriage and most of the patients gave history of first sexual contact before age of 20 years. All patients were in monogamous relation.

Mean age of menarche was 13.26 years in this study. Maximum number of VIA and Pap smear positive cases with age of menarche was 13 to 14 years.

Commonest symptom was white discharge per vagina which accounted for an overall of 92%. Most complaint overlapped although white discharge per vagina predominated. Maximum number of VIA positive and Pap smear positive cases had moderate type of anaemia.

Table 1: Clinico-demographic data

Data	Pap smear	VIA test	Significance
Age groups (years)			
20-29 (n=15)	00	01	
30-39 (n=54)	08	13	
40-49 (n=17)	03	04	$\chi^2 = 0.97$;
50-59 (n=02)	01	01	p> 0.91;
60-69 (n=09)	02	02	Not significant
70-79 (n=03)	00	00	
Education			$\chi^2 = 0.00$;
Educated (n=42)	10	15	p > 0.8703;
Uneducated (n=58)	04	06	Not significant
Occupation			
Housewife(n=78)	10	14	$\chi^2 = 0.277$;
Laborer(n=6)	00	00	p> 0.8703;
Farmer(n=15)	03	06	Not significant
Others(n=1)	01	01	
Socio-economic status			
Low (n=74)	12	16	$\chi^2 = 0.476$;
Middle (n=26)	02	05	p > 0.49;
High (n=0)	00	00	Not significant
Parity			
Nullipara(n=0)	0	0	
Para 1(n=2)	0	0	$\chi^2 = 3.06$;
Para 2(n=28)	0	4	p> 0.215;
Para 3(n=36)	6	8	Not significant
Multipara(n=34)	8	9	

In VIA test, dense white areas present in 21 (21%)out of 100 patients. From these 21 patients, only 14 patients had positive Pap smear results, remaining 7 patients had inflammatory result on Pap smear. VIA guided cytology taken from dense white area in which 11 patients had positive cytology report.

Table 2: VIA result

VIA Result	No. of Patients	Percentage %	Pap Smear Positive
Pale White	79	79%	0
Dense White	21	21%	14

In Pap smear, 1 patient had VIA positive and Pap smear result as ASCUS. 11 patients had VIA positive result and Pap smear result as HSIL. 2 patients had VIA positive and Pap smear results as carcinoma of cervix. 86 patients had Pap smear result as inflammatory in which 7 patient had VIA positive result.

Table 3: Pap smear result

Pap Smear Result	No. of Patients	Percentage %	VIA positive	PAP Smear positive
Normal	0	0%	0	0
Inflammatory	86	86%	7	0
ASCUS	1	1%	1	1
L-SIL	0	0%	0	0
H-SIL	11	11%	11	11
Carcinoma	2	2%	2	2

(ASCUS - Atypical cells of undetermined significance; L-SIL – Low grade Squamous Intraepithelial Lesion; H-SIL - High grade Squamous Intraepithelial Lesion)

Table 4: Comparison of VIA and Pap Smear

VIA	Pap Smear		Total
	Positive	Negative	
Positive	14	7	21
Negative	0	79	79
Total	**14**	**86**	**100**

The sensitivity of VIA was 100% as compared to Pap smear which was 66.67%. But the specificity of VIA was 91.86% Vs Pap smear was 100%. Hence VIA was found to be more effective in screening the true positives (14%).Thus study VIA had a higher detection rate of true positives cases than cytology.

DISCUSSION

Screening for cervical cancer, forms an important part of early detection and prevention of carcinoma cervix. Pap smear has been considered as the gold standard screening test, but requires laboratory infrastructure and logistics in addition to technical expertise. Hence, alternative screening methods such as VIA may be considered. The maximum number of Pap smear positive and VIA positive was detected in the age group of 30- 39yrs. There was no statistically significant association between Pap smear and VIA positive cases with age. This study was comparable to Basu *et al*[7] where mean age was 35 -39 yrs and in Megev and *et al*[8] mean age was 31yrs for cytology and VIA positive. Most of the patients were uneducated, multiparous, had first sexual contact or age at marriage less than 19 years and belongs to low socioeconomic status in this study. The factors responsible for higher incidence of CIN and ca cervix in lower economic group include poor personal hygiene, poor living condition, illiteracy, multiparity and early age at first intercourse. These findings were similar in other studies[5,9-12]. The most common complaint with which the women had attended the hospital was white discharge per vaginum (92 out of 100) which was comparable to Singh *et al*[13]. VIA was considered positive if acetowhite areas with sharp well defined, borders within the transformation zone were identified. These lesions appeared to change color faster and remain white for a longer time. Abnormal result was reported if the cervix appeared congested, hypertrophied, discharge was present or if there was erosion. Pap smear report was considered positive if the result was ASCUS, LSIL, HSIL or Carcinoma. VIA alone detected 21 neoplastic lesions whereas Pap smear alone detected 14 neoplastic lesions.The sensitivity of VIA in our study was 100%, which was comparable to studies conducted by Singh V

et al[13] and Sankaranarayanan *et al*[14] - 81.6- 86.7% and 82.6% respectively. The specificity of VIA in the present study was 91.86%. This was comparable to other studies conducted by Sankaranarayanan *et al*[15] and Basu *et al*[7] where the specificity of VIA was 86.5% and 82.1% respectively and Singh Kavita *et al*[16] where specificity of VIA was 86.8%. The positive predictive value of VIA was 66.67% in our study, which was higher than a study conducted by Sankaranarayanan *et al*[14] where the PPV was 9.4% and in a study of Singh Kavita *et al*[16] where PPV was 22.1%. These values indicate the high number of false positive cases reported by VIA. The negative predictive value of VIA was 100% which was comparable to studies conducted by Sankaranarayanan *et al*[14] and Juneja *et al*[17] who reported NPV of 99.5% and 95.5- 99% respectively. Basu *et al*[7] in a study in Kolkata, India reported an NPV >98%. And also Singh kavita *et al*[16] in a study in Jabalpur, reported NPV of VIA 99%. Thus the VIA is quite reliable in ruling out false negative cases.

The percentage of false negatives in our study was 0% which was less than to the study of Londhe *et al*[18] where the value was 15.2%. The percentage of false positive was 8.13% which cause increased number of cases referred to colposcopy, thus increasing the cost incurred. The sensitivity of Pap smear in our study was 66.67% which was comparable to values obtained in studies performed by Singh *et al*[13] - 73.3-75.3% and Sankaranarayanan *et al*[14] – 72.1%. But the value was higher than those obtained in other studies, such as the study by Chirenje *et al*[19]– 44.3%, probably because our study was performed by a single examiner and the study by Chirenje *et al*[19] was performed by six different trained midwives. And in Singh Kavita *et al*[16] study conducted at Jabalpur, which shows sensitivity of Pap smear was 70.02%. The PPV in our study was 100% which was higher than reported by Jeronimo *et al*[20]. The NPV of Pap smear in our study was 91.86% which was comparable to the value reported by Basu *et al*[7] i.e. >98%. The percentage of false negatives in our study was 33.33%, which was comparable to that reported by Londhe *et al*[18]- 24.4%.The percentage of false positives with the Pap smear in our study was 0%, which was lesser than that reported by Singh V *et al*[13] -1%. This was probably because; most of the women who were screened in our study were in the reproductive age group between 18-39 years of age and are more susceptible to genital tract infections which may cause inflammatory changes and dysplasia. Comparing the results of VIA and Pap smear in our study, it appears that VIA has a higher sensitivity (100% Vs 66.67%), hence it is more effective in screening the true positives, has a lower specificity (91.86% VS 100%) to detect cancerous and precancerous lesions of the cervix in comparison to Pap smear. This result is comparable to that reported by other studies.

These results also indicate that there is a higher false positive rate (8.13% vs. 0%) of VIA compared to Pap smear. This leads to more number of cases referred for diagnostic testing – colposcopy and biopsy. This increases the amount of money spent to detect each case of cancerous and precancerous lesions.

The PPV of Pap smear was higher than that of VIA (100% Vs 66.66%) indicating the higher number of true positives with Pap smear. The percentage of false negatives with VIA was lower than with Pap smear (0% Vs 33.33%) which indicates that VIA has less chance of missing cancerous or precancerous lesions of the cervix. The negative predictive value of both tests – VIA and Pap smear (100% Vs 91.86%) were comparable in our study indicating that both tests were reliable in ruling out false negative cases.

The attractive features of VIA include low cost, simple administration, real-time screening of results and accuracy comparable to good quality PAP smears. In developing nations, resources are limited so, VIA as a visual screening test would be a possible and promising alternative screening tool for early detection of cervical cancer. Use of both VIA and Pap smear simultaneously, appears to detect more cases of cancerous and pre-cancerous lesions of the cervix.

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