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Original Research Article

Efficacy of VIA Test (Visual Inspection of Cervix with Acetic Acid) As an Alternative to Cytology and Colposcopy in Early Screening of Cervical Cancer: A Study in Tertiary Care Centre in Jaipur, Rajasthan

Mohan Meena[1], Rima Biswas[2], Seema Dhami[3], Himanshi Gangwal[4*], Divya Saini[5], Hina Chaturvedi[6]

[1]Senior Professor & Unit Head, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

[2]Junior Resident 3rd Year, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

[3]Junior Resident 2nd Year, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

[4]Assistant Professor, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

[5]Junior Resident 3rd Year, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

[6]Medical Officer, Department of Obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan

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Corresponding Author: Dr. Himanshi Gangwal

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Abstract:

Introduction: Cervical cancer is major health problem in women worldwide. Cervical cancer is the only female genital tract cancer which can be diagnosed and treated in precancerous state by simple screening techniques. VIA/VILI are cheap and noninvasive methods and can be done in a low-level health facility. More importantly, VIA and VILI provide instant results, and those eligible for treatment of the precancerous lesions can be treated immediately. Various studies suggested that VIA and VILI test closely match the Pap smear in its performance in detecting cervical cancer precursor and with combination of colposcopy it has more effective in detecting cervical cancer in early precancerous stages .Studies have demonstrated that VIA or VILI are alternative screening methods.

Material And Methods: This retrospective study was carried out at Department of Obstetrics & Gynecology SMS Medical College, Jaipur, from period of June 2023 to Dec 2023. 200 patients were studied. A relevant history regarding Obstetrical & Gynecological history, previous history of intake of oral contraceptive pills, IUCD insertion, of any treatment for white discharge, and other high-risk factors were taken. Patients were explained the procedure to be performed, written informed consent was taken, with the patient being reassured that the procedure was painless. Per speculum & a per vaginal examination was done. After taking pap smear, the same patients were subjected to visual inspection of the cervix with acetic acid. Using a cotton swab soaked in acetic acid, 5% acetic acid was applied for 1-2 minutes and then the cervix was carefully inspected for any acetowhite lesions, particularly in the transformation zone. VILI test was performed by application of Lugol's Iodine and results were noted. Colposcopy was done in all patients in our study. All findings of VIA, VILI test ,pap smear and colposcopy findings were noted.

Observation & Results: In our study we found that out of 200 patients who had Pap smear done 50 cases shows inflammatory smear, 33 patients had positive and normal pap smear results seen in 112 women. Out of positive pap smear CIN1, CIN 2 and CIN 3 were seen in 21[63.63%], [9.09%], 1[3.03%] patients respectively. One patient had carcinoma in situ in pap smear. VIA results were positive in 31[%] patients and 169 [84.5%] patients had negative VIA test result. VILI test was positive in 22[11%] patients and negative VILI seen in 178 [89%] patients. On Colposcopy 65 cases[32.4%] has low grade lesion.12 [6%] patients shows high grade lesion noninvasive and 8 [4%] patients shows high grade /invasive lesion. In our study, out of the total 200 patients who have undergone all three screening tests (Pap+VIA+VILI), 42 patients were showed positive results by a combination of these tests and undergone biopsy. Of these 42 positive cases, 22 (i.e., 52.38%) had CIN on histopathological examination This thus proved the adjunctive role of VIA and VILI to Pap smear in diagnosing premalignant and malignant lesions of the cervix, and so increasing the sensitivity of combination tests to 100% but specificity of theses combined tests are only 25.92%. Sensitivity of VILI test is 94.44, specificity of VILI test is 82.75%, PPV of VILI test 72.27%, NPV of VILI test is 96.0%. Number of false positive cases in VILI test 17.24 % and number of false negative cases in VILI test is 5.56 %. Sensitivity of combination tests (Pap +VIA+VILI) is 100.00%, specificity of combination tests is 25.92%, PPV of combination tests are 55.0%, NPV of combination tests are

100.00%. Number of false positive cases in combination test are 74.07% and number of false negative cases are 00%.

Conclusion: Our study showed that VIA and VILI had sensitivity comparable to Pap smear and can thus be a suitable potential alternative/adjunctive screening test not only in a resource-poor setting but in well-equipped centres also. And, use of a combination of tests (Pap+VIA+VILI) had 100% sensitivity but at cost of low specificity and more false-positive results. VIA and VILI can be adopted as screening tools for the diagnosis of cervical lesions. Result and follow-up treatment can be provided in a single sitting hence fewer women are lost to follow-up.

Keywords: Cervical Cancer, Pap Smear, Visual Inspection With Acetic Acid, Visual Inspection with Lugol's Iodine, Colposcopy.

Introduction

Cervical cancer is a major health problem worldwide. Cervical malignancy is the most common malignancy among Indian women.[1] In Indian women, cervical malignancy accounts for 26.1%–43.8% of all cancers.[2] Cervical cancer is preceded by a long phase of premalignant cytological change. Cervical cancer can be prevented if cellular changes are detected and treated in early stage. In developed countries, the incidence of cervical cancer has decreased, due to screening, early detection, and early treatment of precancerous lesions.

The reasons for the higher prevalence of cervical cancer in developing countries are a lack of resources, lack of awareness, lack of effective screening programs, and poorly organized health system aimed for detecting precancerous condition. In developing countries, 80% of cervical cancers are incurable at the time of detection due to the advanced stage.[3]

Hence, there is a need for low-cost, mass approach for effective cervical cancer screening programs.[4] Although cytology (Pap smear) is reliable, the laboratory infrastructure, counselling, follow-up, and logistics including technical expertise may not be available in low-resource settings.[5] Newer approaches such as automated Pap, liquid-based Pap and HPV DNA testing using hybrid capture II (HC II) are time consuming, expensive and not widely available.

The accuracy of a traditional Pap smear could be easily affected by the following factors: the facilities in the cytological room, professional technicians, sampling method, slide quality, dyeing skills, and cytological personnel experience. Prompted by the need for optimal strategies for cervical cancer screening in low-resource settings, the role of visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) has been widely studied in several recent studies, which suggest that VIA and VILI closely match the Pap smear in its performance in detecting cervical cancer precursor.[6]

Studies have demonstrated that VIA or VILI are alternative screening methods. These methods are cheap and noninvasive and moreover they can be done in a low-level health facility. Most importantly, VIA and VILI provide instant results, and those eligible for treatment of the precancerous lesions can be treated immediately. This see-and-treat method ensures adherence to treatment soon after diagnosis, hence emanate from the problem of default to appointments and referrals.[6,7]

Visual inspection with acetic acid is a naked-eye examination of the uterine cervix, after applying 5% acetic acid and interpreting the result after 1 minute. This is a simple and inexpensive test for the detection of cervical precancerous lesions and early invasive cancer. The results of the VIA test are immediately available and do not require any laboratory support.

Acetic acid application on the cervical epithelium causes reversible intracellular dehydration and coagulation of protein within the cervical cells. The intensity of coagulation is dependent on the amount of protein in the cell. As the dysplastic cells have more chromatin content, the coagulation is intense and cells turn white after the application of acetic acid. The VIA test can be categorized as VIA positive or VIA negative. A test is considered positive if there is the detection of well-defined, densely opaque dull acetowhite lesions in the TZ of the cervix. The test is said to be negative in the case of faint, ill-defined, translucent acetowhite areas, faint acetowhitening of endocervical polyps, nabothian cysts, dot-like acetowhite appearance, and prominent SCJ. Naked eye visual inspection of the uterine cervix, after the application of Lugol's iodine as an adjunct to the VIA test, to confirm and delineate the abnormal lesion is called visual inspection with Lugol's iodine. It works on the principle that the squamous epithelium contains glycogen. Since iodine is glycophillic, when applied to normal squamous epithelium, it turns mahogany brown or black. Columnar epithelium and immature metaplastic cells do not contain glycogen, so they do not stain after the application of Lugol's iodine. The

inflammatory cells either stain partially or do not stain. The abnormal cells contain either less glycogen or no glycogen depending upon the degree of the lesion. So these lesions do not stain brown after the application of iodine and become mustard yellow. Various studies indicate that VIA more or less is as effective as conventional cytology in diagnosing high-grade lesions.

Both VIA and VILI appear to be the most promising technology which can successfully serve as an alternative to cytology when these techniques are combined and correlated with colposcopy their efficacy doubles for screening purposes. These tests can be performed at primary and secondary health centres. In countries where resources are limited and HPV test is not feasible, WHO recommends that screening should be done with VIA and VILI procedures.[13]

So to prevent the occurrence of cervical cancer in India an early screening is needed. VIA and VILI serve as important and inexpensive screening tests that need to be incorporated into our healthcare systems to prevent the untimely deaths of women in the country.

Material and Methods

This retrospective study was carried out at department of obstetrics & gynecology SMS Medical College Jaipur, from period of June 2023 to Dec 2023. 200 patients were studied. A relevant history regarding obstetrical & gynecological history, previous history of intake of oral contraceptive pills, IUCD insertion, of any treatment for white discharge, and other high-risk factors were taken.

Patients were explained the procedure to be performed, written informed consent was taken, with the patient being reassured that the procedure was painless. Per speculum & a per vaginal examination was done. After taking pap smear, the same patients were subjected to visual inspection of the cervix with acetic acid. Using a cotton swab soaked in acetic acid 5% acetic acid was applied for 1-2 minutes and then the cervix was carefully inspected for any acetowhite lesions, particularly in the transformation zone. VILI test was performed by application of Lugol's Iodine and results were noted. Colposcopy was done in all patients in our study

Inclusion Criteria: All women about 25 years of age or more or marital life more than 3 years were subjected for screening irrespective of the purpose of GOPD visit.

Exclusion Criteria: Unmarried women, women with frank invasive cancer cervix (with visible growth on cervix), women with bleeding per vagina and pregnancy were excluded.

Reporting: Pap smear reporting was done according to the Bethesda classification.

The outcome of VIA test was considered positive on the basis of the following criteria

1. Intensity of the white color of acetowhite lesion.
2. Borders and demarcation of the white lesion.
3. Whether the lesion is uniformly white in color or the color intensity varies across the lesion.
4. Location of the lesion.
5. Size and number of the lesion.

Positive test: Visualization of the dense acetowhite lesion with sharp margins located in the transformation zone, close to SCJ.

Negative test: If no acetowhite lesions were observed on the cervix polyps protruding from cervix, bluish white in colour, nabothian cysts which appear as button like areas as whitish area or pimples, dot like areas present in the endocervix which were due to grape like columnar epithelium staining with acetic acid; if there were shiny pinkish white, cloudy white or bluish white, faint patchy or doubtful lesions with ill defined, indefinite margins or irregular, acetowhite lesions resembling geographical lesions away from the SCJ.

Inconclusive test: No distinct acetowhite lesion or somewhat doubtful lesions or when the cervix could not be adequately assessed.

If VIA turns out to be positive the patient was subjected to further investigations such as colposcopy and guided biopsy.

Grading of lesion was done according to the Swede colposcopic index.

Sewede score

Overall Swede Score	Colposcopic prediction of probable histology
0-4	Low grade /normal CIN 1
5-6	High grade /non-invasive cancer CIN-2
7-10	High grade /suspected invasive cancer CIN -3

Biopsy was done for confirmation of lesion if either of the three screening tests or colposcopy had a positive finding or if the Pap smear reported ASCUS, for confirmation of lesion.

Collected data was statistically analysed. All the data were analysed using IBM SPSS Ver.20 software. Data are expressed as numbers, percentages, and means .The patients who reported normal on all screening tests and colposcopy were called for annual follow-up.

Patients who were positive at either of the screening tests or colposcopy underwent biopsy and were treated according to the grade of the lesion (6-monthly follow-up and repeat Pap, Cryo /Thermal coagulation of leisons loop electrode excision procedure (LEEP), hysterectomy). Approval from ethical committee of our institute was taken before commencing the study.

Results & observations

We observe in our study that most of the women came with complaints of excessive vaginal discharge 44% [table1]. Abnormal uterine bleeding follows next in form of intermenstrual bleeding, postcoital bleeding 22.5% & 13.5% respectively. 10% women had complains of low backache and 4% patients had dyspareunia.

Table 1: Distribution of cases according to complaints

Complaints	Number of cases	Percentage
Excessive vaginal discharge	88	44 %
Intermenstrual bleeding	45	22.5 %
Postcoital bleeding	27	13.5 %
Post-menopausal bleeding	12	6 %
Dyspareunia	8	4 %
Low backache	20	10 %
Total	200	100 %

Table 2: Result of Pap smear, VIA, VILI and colposcopy examination

Pap smear	Number of women	percentage
Normal	112	61 %
Inflammatory	50	22.5 %
ASCUS	7	21.21 %
LSIL - CIN1	21	63.63 %
HSIL		
CIN2	3	9.09 %
CIN3	1	3.03 %
CIS	1	3.03 %
VIA		
Positive	15	7.5 %
Strong positive	16	8 %
Negative	169	84.5 %
VILI		
Positive	22	11 %
Negative	178	89 %
Colposcopy- Swede Score		
0-4	65	32.5 %
5-6	12	6 %
7-10	8	4 %
Normal	115	57.5 %

VIA – Visual inspection with acetic acid; VILI – Visual inspection with Lugol's iodine; CIN – Cervical intraepithelial neoplasia

Table no.2 shows that out of 200 patients who had Pap smear done 50 cases [22.5%] shows inflammatory smear, Positive pap smear seen in 33 patients [16.6%] and normal pap smear results seen in 112 women [61%]. Out of positive pap smear CIN1, CIN 2 and CIN 3 were seen in 21[63.63%], [9.09%], 1[3.03%] patients respectively. One patient had carcinoma in situ in pap smear cytology report. VIA results were positive in 31[%] patients and 169 [84.5%] patients had negative VIA test result. VILI test was positive in 22[11%] patients and negative VILI seen in 178[89%] patients. All patients who are studied in our study had colposcopy done after the pap smear and VIA,VILI examinations. Colposcopic grading done by Swede Score. Normal colposcopic findings were seen in 115 [57.5%] patients and 65[32.4%] patients' shows score 0-4, which is considered as low grade lesion.12[6%] patients shows score 5-6 i.e. high grade lesion noninvasive and 8 [4%] patients shows high grade /invasive lesion.

Table 3: Correlation of Pap smear, VIA and VILI with histopathological examination

	Histopathological finding			
	Positive	**Negative**	**Total**	**Pearson Chi-Square test X2 & P value**
Pap smear				X2-10.770 P -0.0010
Positive	16	10	26	
Negative	3	18	21	
Total	19	28	47	
VIA				X2-8.038 P-0.0046
Positive	16	15	31	
Negative	2	16	18	
Total	18	31	49	
VILI				X2-26.587 P-0.0001
Positive	17	5	22	
Negative	1	24	25	
Total	18	29	47	
VIA+VILI				X2-7.853 P-0.0051
Positive	15	13	28	
Negative	1	12	13	
Total	16	25	41	
PAP+VIA+VILI				X2-6.654 P-0.0099
Positive	22	20	42	
Negative	0	7	7	
Total	22	27	49	

Table 4: Tests and their characteristic in diagnosing CIN

Screening test	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Pap smear	84.21 %	64.28 %	61.53	85.71
VIA	88.88	51.61	51.61.	88.88
VILI	94.44	82.75	77.27	96
VIA +VILI	93.75	48	53.57	92.30
VIA+VILI+Pap	100	25.92	55	92.30

As shown in Table 3 in our study, out of the total 200 patients who have undergone all three screening tests (Pap+VIA+VILI), 42 patients were showed positive results by a combination of these tests; of these 42 positive cases, 22 (i.e., 52.38%) had CIN on histopathological examination and no cases were missed by using a combination of these tests.

This thus proved the adjunctive role of VIA and VILI to Pap smear in diagnosing premalignant and malignant lesions of the cervix, and so increasing the sensitivity of combination tests to 100% but specificity of theses combined tests are only 25.92%. In patients in whom VIA+VILI both were performed, 28 had positive results. Of these 28 cases, 15 (i.e., 53.57%) showed CIN on histopathological examination, one case (6.26%) was missed on a combination of tests (VIA+VILI), that had showed positive for CIN on histopathological examination. This thus proved the role of VILI as a parallel screening test to VIA.

The sensitivity, specificity, NPV and PPV of different screening tests or their combinations are shown in Table 4. Sensitivity of Pap smear 84.21%, specificity of Pap smear 64.28%, PPV of Pap smear 61.53%, NPV of Pap smear85.71%. Number of false positive in Pap smear are 34.72% and of false-negative 15.79%.

Sensitivity of VIA test is 88.88%, Specificity of VIA test is 51.61%, PPV of VIA test is 51.61%, and NPV of VIA test is 88.88%.

Number of false positive cases in VIA test is 48.39% and Number of false negative are 15.79%.

Sensitivity of VILI test is 94.44, specificity of VILI test is 82.75%, PPV of VILI test 72.27%, NPV of VILI test is 96.0%. Number of false positive cases in VILI test 17.24 % and number of false negative cases in VILI test is 5.56%. Sensitivity of combination tests (Pap +VIA+VILI) is 100.00%, specificity of combination tests is 25.92%, PPV of combination tests are 55.0%, NPV of combination tests are 100.00%. Number of false positive cases in combination test are 74.07% and number of false negative cases are 00%. Sensitivity of combination tests (VIA+VILI) is 93.75%, specificity of combination tests (VIA +VILI) is 48.00%, PPV of combination tests (VIA+VILI) is 53.57%, NPV of combination tests (VIA+VILI) is 92.30%. Number of false positive cases in combination test (VIA+VILI) are 52% and of false negative are 6.25%.

Table 5: Intervention done in patients on the basis of screening test results and positive histopatholgical findings

Intervention	Number of women	Percentage
Yearly F/U	110	55
6 monthly F/U with repeat Pap Smear /VIA	28	14
LEEP	25	12.5
Pan hystrectomy	1	0.5
Cryo/thermal cauterization	36	18

Patients in whom pap smear shows ASCUS and on colposcopy shows CIN, that was confirmed in histopathological report histopathological were called after 6 months for follow-up and repeat Pap smear. 25 patients who reported CIN-1 (who had no complaints and had associated risk factors) and patients with CIN-2 underwent LEEP. 1 patients who had CIN-3 and CIS (with superficially invasive cancer with negative margins) underwent Pan hysterectomy. Cryo /Thermal ablation of cervical lesion were done in 36 patients who had CIN1/CIN2 with complaints.

Conclusion

There is no perfect screening tests available till now that have 100% sensitivity and good specificity. Therefore, in the present study, an attempt has been made to analyse Pap smear, VIA and VILI as standalone tests and when used in combination. We found that the combination tests had 100% sensitivity but at the cost of low specificity and more false-positive results. Our study showed that VIA and VILI had sensitivity comparable to Pap smear and can therefore be a suitable potential alternative/adjunctive screening test not only in resource-poor settings but also in well-equipped centres. In developing countries, where cervical cytology screening is not possible due to limited resources (lack of infrastructure and trained health staff and financial limitations), visual inspection of the cervix can be used as a primary screening method for a diagnosed premalignant lesion of the cervix because it is very simple inexpensive, easy and low learning curve method. As fewer specialized personnel, less infrastructure, training, and equipment are required hence VIA screening can be implemented in remote public healthcare settings with more coverage.

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