ORIGINAL RESEARCH

Evaluation of Visual Inspection after Acetic Acid/ Cervicography as an Alternative to Colposcopy for Detection of Cervical Intraepithelial Neoplasia

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Abstract

Objective: The study was conducted to (1) find out if visual inspection after acetic acid (VIA)/cervicogram can be used as an alternative to colposcopy and (2) compare the sensitivity and specificity of VIA/cervicogram with conventional Pap smear.

Methods: A total of 540 sexually active women aged between 20 and 60 years attending gynecology outpatient (OPD) treatment were included in the study. After the complete evaluation and informed consent, the patients were subjected to the following tests: Pap smear, visual inspection after acetic acid (VIA) application, cervicography, and finally colposcopy. Cervical biopsy was done (a) in women with any of these three tests positive and (b) in patients with unsatisfactory colposcopy. Cervical tissue was obtained with the help of loop electrosurgical excision procedure (LEEP). Biopsies revealing mild dysplasia or worse lesions on histopathology were considered as true positive cases. Biopsies showing chronic cervicitis were considered negative. All results were compiled and subjected to statistical analysis.

Results: Our study revealed sensitivity, specificity, positive predictive value, negative predictive value of Pap smear for LSIL or above as 28, 99.7, 25, and 97.9. Sensitivity, specificity, positive predictive value, negative, predictive value of VIA was 71.4, 92, 20, and 99.1. The sensitivity, specificity, positive predictive value, negative predictive value of cervicography in our study was 71.4, 93.9, 23, and 99%. The sensitivity of colposcopy was 78 and specificity 56.66%.

Conclusion: Results of VIA and cervicography are quite promising and can be considered as primary screening in low-resource settings.

Keywords: Cervicography, Cervical biopsy, Colposcopy, Pap smear, Visual inspection after acetic acid.

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Introduction

Globally, cervical malignancy is the fourth most common and comprises almost 7.9% of all female cancers. Out of which 90% occurs in poor countries.[1] In Iran, this is the second most common after ovarian malignancy and included 32.5% of all women's carcinomas.[2] Over the last five decades, deaths from cervical carcinoma have decreased largely because of Pap smear screening.[3,4]

In comparison to many malignancies, cervical carcinoma is preventable through various screening tests that can identify and treat premalignant states.

Globally, the well-known Pap smear examination is considered as the standard screening method. Colposcopy (the visualization of cervix and vagina under bright light with magnification) entails the use of a field microscope to examine the cervix after the application of acetic acid and Schiller's Iodine. It has a sensitivity ranging 64–97%, considered as the gold standard, but requires a costly instrument and training.

Another popular method used in the developing countries is VIA application. In various see-and-treat programs, females with cervical lesions, which are identified by VIA, are immediately treated with cautery or cryotherapy.

Cervicography as a means of screening was introduced by Adolf Stafl at the beginning of 1908. In many studies, cervicography is shown to be a reliable method for the identification of precancerous cervical lesions. After acetic acid application, a photograph is taken by a good resolution camera, and the picture is assessed after projection on a large screen and interpreted by an expert. Also, these images can be used later on as a permanent record of the assessment. Because of the complementary nature of cervicography and visual inspection of acetic acid, this study was conducted to see if VIA with cervicography as an adjunct can be used as an alternative to colposcopy for the detection of cervical intraepithelial neoplasia (CIN).

The aim of this study was to find out if VIA with cervicogram can be used as an alternative to colposcopy, and the objectives of the study were (a) to know the prevalence of CIN, (b) to find out the sensitivity and specificity of VIA/cervicogram and conventional Pap smear, and (c) to compare the sensitivity and specificity of VIA/cervicogram with conventional Pap smear.

Materials and Methods

This is a prospective cohort study that was conducted in the Department of Obstetrics and Gynecology in collaboration with the Department of Pathology, LLRM Medical College, and associated

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SVBP Hospital, Meerut, Uttar Pradesh, India for a duration of 1 year. The sampling method was of convenience sampling and the sample size was 540 women fulfilling the inclusion criteria. Ethical committee approval was taken from the institutional ethical committee.

Inclusion and Exclusion Criteria

A total of 540 sexually active women aged between 20 and 60 years attending gynecology OPD treatment were included in the study. Among them, pregnant woman, women who were menstruating during a clinical examination, women who currently using vaginal pessaries, and women who were of in the age more than 60 years and less than 20 years, and women with frank cervical cancer at the time of evaluation were excluded from the study.

Methods

After taking a thorough history, women were subjected to complete physical and pelvic evaluation. The patient, after informed consent, was subjected to the following tests:

Pap's Smear

After explaining the procedure, the patient was laid comfortably on the examination table in a dorsal position. The light was positioned to visualize the cervix clearly. The vaginal speculum was inserted and the cervix was brought into view by the gentle movement of the speculum encouraging the patient to relax. The appearance of the cervix was noted. Pap smear was taken by a conventional method using Ayer's spatula and Cytobrush. The smear was then immediately fixed with 95% ethanol to prevent air drying and cellular distortion.

The reporting was done by the Modified Bethesda system (2001). The following is Bethesda system of classification: (a) Within normal limits; (b) Infection (organism specified); (c) Reactive and reparative changes; (d) Squamous cell abnormalities. Atypical squamous cells (d.1) of undetermined significance (ASC-US), and (d.2) exclude high-grade lesions (ASC-H); (e) Low-grade squamous intraepithelial lesion (LSIL); (f) High-grade squamous intraepithelial lesion (HSIL); (g) Squamous cell carcinoma (SCC).

Visual Inspection after Acetic Acid Application

Freshly made 5% acetic acid was gently applied to the endocervix and ectocervix (to involve the transformation zone) using a piece of cotton. After 1–2 min, a naked eye evaluation was done with the naked eye in good light. If acetowhite areas were present within the transformation zone the VIA was considered positive.

Low-grade CIN on the Application of 5% Acetic Acid

Low-grade CIN presented as thin, smooth, less dense acetowhite lesions with feathery, irregular, angular, or geographic margins and with punctuation and/or mosaicism. Sometimes, low-grade lesions are seen away from the squamocolumnar junction and termed as "satellite" lesions.

High-grade CIN on the Application of 5% Acetic Acid

High-grade CIN was seen as thick, opaque, dense, acetowhite areas with coarse punctuation, and/or mosaicism and had well-demarcated and regular borders close to or touching the transformation zone. These lesions often involved both lips and sometimes had atypical blood vessels.

The acetowhite pictures were not specific to precancerous lesions and early carcinoma. It was also seen in other conditions where the increased nuclear protein was present; for example, congenital transformation zone, immature squamous metaplasia, regenerating and healing epithelium, leucoplakia, and condyloma.

The acetowhite areas associated with regenerating epithelium and immature squamous metaplasia were thin, pale, often translucent, and patchily distributed without well-defined margins. Acetowhite areas due to healing and inflammation were widely distributed in the cervix and not limited to the squamocolumnar junction, disappeared rapidly, within 45–60 s.

Cervicography

These are replicate photographs of the cervix, after 5% acetic acid application, using a special camera called a cervicoscope. The images are projected onto a screen and are interpreted by a trained evaluator. The cervicoscope used was a 13.6 MP Sony cyber shot camera. In all VIA-positive patients, a photograph of the cervix was taken and was evaluated for acetowhite areas. Cervicograms were then labeled as positive and negative.

If any lesion positive on VIA (an acetowhite area) and cervicography were identified, the patient was informed and a detailed colposcopic examination and directed biopsy were carried out as and when indicated. The findings of VIA, cervicography, and colposcopy were recorded in the predefined proforma.

Women with negative VIA were asked to attend OPD, with Pap results, and colposcopy was done if Pap was positive. A colposcopic-directed biopsy if necessary was taken and fixed in 10% buffered formalin.

Women with negative Pap smear reports and negative findings on VIA and cervicography were considered to be normal. Of these, 100 normal women were randomly subjected to colposcopy and if found to be positive on colposcopic examination subjected to biopsy.

The colposcopy/histodiagnosis was taken as the gold standard against which the specificity and sensitivity of cytology, VIA, and cervicography as screening tests were evaluated using standard statistical methods.

A report of colposcopy was prepared using Reid's classification; Reid's classification of coloscopy findings (1985) is listed as follows:

Coloscopic sign	*Zero*	*One*	*Two*
Margin	Condylomatous or micropapillary contour. Flocculated or feathered, angular, jagged lesions. Satellite lesions and acetowhitening beyond the transformation zone	Regular lesions with smooth indistinct borders	Rolled, peeling edges. Sharp margins
Color	Shiny, snow–white, semi-transparent, opaque	Shiny, grey–white, intermediate white	Dull, oyster grey
Vessels	Uniform, fine caliber non-dilated capillary loops, fine punctuations or mosaic	Absence of surface vessels	Definite punctuation or mosaic Individual vessels dilated
Iodine	Positive iodine uptake	Partial iodine uptake	Yellow staining of lesion

The predictive value of the following scoring was used for documenting the colposcopy findings:

Score	*Predictive lesion*
0–2	Minor grade lesion: HPV infection, CIN I
3–5	Middle-grade lesion: CIN I or CIN II
6–8	Significant lesion: CIN II or CIN III

Cervical Biopsy

Cervical biopsy was performed (a) in women with any of the above three tests positive and (b) in patients with unsatisfactory colposcopy. Cervical tissue was obtained from the abnormal areas with the help of LEEP. Biopsies reported as mild dysplasia or advanced lesions on histopathology were considered as true positives. The chronic cervicitis was considered a true negative.

Analysis

All results were analyzed by using appropriate statistical methods. The prevalence of CIN was evaluated for the screened population.

A study of the various risk factors in the study population and the positive cases was done, a comparison was made, and the inference was drawn based on sensitivity, specificity, negative predictive value, and positive predictive value of the tests.

Observations and Results

It was seen that in the age group more than 45 years, the incidence of dysplasia was significantly higher. The maximum number of patients of CIN were in the age group 25–35 years (52.59%). One patient was below the age of 25 years. She was 22-year-old and was presented to our OPD as a case of primary infertility. Pap's smear was reported as LSIL and histopathology report was mild dysplasia. Six women out of 14 positive on histopathology were multiparous with parity more than 4. The prevalence of dysplasia was significantly higher in subjects with parity more than 4. Almost all women with dysplasia had first coitus before the age of 20 years. Only two cases of dysplasia were detected among women who had first coitus between 21–22 years. The incidence of dysplasia was higher proportion wise 14.25% among smokers as compared to non-smokers (2.43%). The proportion of dysplasia was slightly higher among Muslims (3.13%) as compared to Hindus (2.5%) and others (0%). Among the various contraceptive methods used, the oral pills were found to be significantly associated with higher positivity (3.73%) (Table 1).

A high incidence of dysplasia was found among patients attending OPD for the purpose of lap ligation. Since these patients were multiparous, in the age group of 25–35 years' cervical cancer screening can be effectively used in these patients. Among the various complaints postmenopausal bleeding (25%) and bleeding after intercourse (13.33%) were associated with a significantly higher proportion of dysplasia. Cervical ectopy/erosion was significantly associated with CIN (Table 2).

On Pap's smear examination, 8 patients had missing data and 32 patients had unsatisfactory colposcopy. Inflammation was the most common cytological finding (79.13%). Out of 540 patients, 9.07% patients were positive on VIA application. Cervicography was done only in VIA-positive cases. Out of the 49 patients screened, 6 cervicography tests were of poor quality due to shadow, unclear picture, inadequate exposure, etc. and no conclusion could be drawn. Colposcopy was done in the following cases:

Table 1: Distribution of dysplasia cases according to demography

	Total cases (n = 540)		*Dysplasia cases (n = 14)*	
Parameters	*Number*	*Percentage*	*Number*	*Percentage*
Age				
<25	96	17.77	01	1.04
25–34	274	52.59	08	2.91
35–44	112	20.74	03	2.67
45–55	54	10.00	02	3.70
>55	04	0.74	00	00
Parity				
Nullipara	21	3.88	01	4.76
1–2	83	33.88	03	1.63
3–4	252	46.66	04	1.58
>4	84	15.50	06	7.14
Age at first coitus				
<18	26	4.81	02	7.60
18–20	406	75.81	10	2.46
21–22	98	18.15	02	2.04
23–24	10	1.85	00	00
>24	00	00	00	00
Smoking				
Yes	533	98.71	13	2.43
No	07	1.29	01	14.28
Religion				
Hindu	440	81.48	11	2.50
Muslim	96	17.70	03	3.12
Others	04	0.74	00	00
Contraceptive used				
Barrier	136	25.18	02	1.47
None	242	44.81	09	3.17
Tubectomy	64	11.85	01	1.56
IUCD	44	8.14	00	00
OCPs	54	10.00	02	3.73

IUCD, intra-uterine contraceptive device; OCPs, oral contraceptive pills

- Any of the above-mentioned three tests are positive.
- In randomly picked 25 negative-tested patients.

Colposcopy findings were revealed to be normal in 51.35%. In 5.41%, there was found to be unsatisfactory. In 43.13% of subjects, the colposcopy showed positive results (Table 3).

Biopsy was done with the help of LEEP. Mild dysplasia or worse was considered true positive. Fourteen out of 74 women (18.91%) were positive on biopsy. Sixty (81.08%) were negative on biopsy (histopathological reported as normal or chronic cervicitis). Fourteen biopsies included 10 mild dysplasia, 3 moderate-to-severe dysplasia, and 1 carcinoma *in situ* (Table 4).

The most sensitive diagnostic test is colposcopy (78.57%). The specificity of Pap's smear test is highest, but the negative predictive value of VIA and cervicography was maximum (99.1%) (Table 5).

Table 2: Distribution of dysplasia cases according to presentation and examination findings

	Total cases (n = 540)		*Dysplasia cases (n = 14)*	
Parameters	*Number*	*Percentage*	*Number*	*Percentage*
Presentation in OPD				
For lap ligation	146	27.03	04	2.73
For gynecological complaints	354	65.55	10	2.82
Presenting symptoms				
Excessive vaginal discharge	232	42.96	08	3.44
Vulvovaginal itching	24	4.40	00	00
Lower abdominal pain	342	63.33	05	1.46
Dyspareunia	21	3.88	01	4.76
Postcoital bleeding	15	2.77	02	13.33
Intermenstrual bleeding	114	21.11	01	0.87
Postmenopausal bleeding	04	0.74	01	25.00
Examination findings				
Healthy cervix	184	34.07	02	1.09
Nabothian cyst	112	20.74	00	00
Cervical hypertrophy	132	24.44	02	1.51
Cervicitis	306	56.66	05	1.63
Cervical erosion	198	36.66	05	2.52
Cervical polyp	04	0.74	00	00

Table 3: Results of various screening tests

		Total cases	
Screening test	*Findings*	*Number*	*Percentage*
Pap smear (*n* = 540)	Normal	74	13.90
	Inflammatory	421	79.13
	ASC-US	00	00
	LSIL	04	0.75
	HSIL	01	0.18
	AGUS	00	00
	Unsatisfactory	32	6.01
	Missing data	08	1.5
VIA (n = 540)	Positive	49	9.08
	Negative	491	90.92
Cervicography (n = 49)	Positive	42	85.71
	Negative	7	14.29
Colposcopy (n = 74)	Reid's = 0	33	51.35
	Reid's = 1–8	37	43.13
	Unsatisfactory	04	5.41

AGUS, atypical glandular cells of undetermined significance

Table 4: Results of biopsy reports

Histopathological diagnosis	*Number of subjects (n = 74)*	*Percentage*
Normal	26	35.13
Chronic cervicitis	34	45.94
Mild dysplasia	10	13.51
Moderate/severe dysplasia	03	4.05
Carcinoma *in situ* (CIS)	01	1.35
Squamous cell carcinoma (SCC)	00	00
Total	74	100

Table 5: Diagnostic efficacy of various screening tests

Test	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
Pap's smear	28	99.7	25	97.9
VIA	71.42	92	20	99.1
Cervicography	71.42	93.62	23.8	99.1
Colposcopy	78.57	56.66	29.78	97.89

Discussion

On the global scale, Asian countries including India are among those with high mortality rates in patients with cervical cancer. Despite some local efforts to establish cervical cancer screening, no organized national screening programs exist.

These conditions prompted us to design the present study to test different screening tools.

In this study, a detailed history and examination of all patients were done according to a working proforma, and then all patients were subjected to a Pap smear, VIA, and cervicography and if any of the above three tests were positive and 25 negative-tested patients were subjected to colposcopy examination.

All patients with any of the above three tests positive and positive colposcopy findings were subjected to biopsy using LEEP.

Patients who had a positive histopathological report were taken as positive.

A study of the demographic features and sensitivity, specificity, positive predictive value, the negative predictive value of the above-mentioned tests, Pap smear, VIA, cervicography, and colposcopy was done in comparison to the gold standard of biopsy.

In our study, 6.9% of patients had abnormal Pap tests (other than inflammatory smear, 79. 13%). In one study,[5] 53.5% of patients had abnormal Pap tests that were higher than the present study, and the reason being was that inflammatory reports were also documented abnormal in that study. Among the cases with abnormal Pap smear, most cases reported as ASC-US with 17% and LSIL, HSIL, ASC-H with 2.7, 0.5, and 0.2%, respectively, that are more (13.5%) in comparison to the present study.

We found abnormal colposcopy (Reid's Index 1–8) in 43.13% of cases. In a recent study,[6] normal colposcopic findings were seen in 38% of cases and CIN1, CIN2, CIN3, and SCC were seen in 28, 19, 10, and 5%, respectively.

In our study, Pap smear had less sensitivity but its specificity was much higher than some studies, in a study[7] specificity of Pap smear was reported more than VIA. Overall, it was seen that in the current study, VIA has a higher sensitivity than Pap smear, but its specificity is less than Pap smear. The reason behind this is that all acetowhite areas were considered positive and that the presence of metaplasia, cervical polyps, and inflammation, could also result in false-positive VIA.

Zahra Vahedpoor et al.[8] (2019) found the sensitivity, specificity, NPV and PPV of Pap smear 29.7, 85.5, 59.8, and 62.6%, and these values for VIA was 94.6, 81.6, 78.8, 95.4%, respectively. These findings were nearly similar to our study.

Three observers,[9] blinded to each other's interpretations, evaluated 540 DC photographs. Interobserver agreement of DC interpretations was moderate among the three observers, between them and histopathology, and no significant difference was noted among other visual-based screening methods, that is, VIA, cytology, or colposcopy.

Kamal Patil et al.[10] did a study, named, "Evaluation of down-staging, visual inspection with acetic acid and Lugol's Iodine in screening of cervical cancer" and found that the sensitivities of downstaging, VIA, and VILI were 54.55, 63.64, and 90.91% and specificities were 93.42, 95.07, and 97.46%, respectively. The positive predictive value of downstaging, VIA, and VILI were 12.01, 17.5, and 35.7% and negative predictive values were 99.2, 99.37, and 98.85%, respectively. Also, he did another study[11] to compare the diagnostic efficacy of visual inspection of cervix with acetic acid and Pap smear for prevention of cervical cancer and observed that sensitivity and specificity of VIA were 86.95 and 72.51%, respectively, and that of Pap smear 37.68 and 92.36%, respectively. Colposcopy showed higher sensitivity (94.20%) and specificity (94.65%).

In many clinical settings, cervicography is thought to be an adjunct to cytology rather than an initial screening tool. Some clinics use standardized digital cameras, or even cell phone cameras, to photograph the cervix, which allows for review of the images at a later time or by a remote expert.[12]

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