Section: Obstetrics and Gynaecology

Original Research Article

COMPARISON OF PAP SMEAR WITH VISUAL INSPECTION WITH ACETIC ACID IN SCREENING OF CARCINOMA CERVIX

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Abstract

Background: Cervical cancer is the second most common among women globally. In most cases of Ca Cervix is detected late due to lack of effective screening programme. Present aim is to detecting the efficacy of visual inspection of cervix with acetic acid with Pap smear in early detection of carcinoma of cervix. **Materials and Methods:** The cross sectional study conducted in 100 women attending GYN OPD were included in the study. They were screened with Pap smear and VIA, those positive with either of the method were subjected to biopsy. The sensitivity, specificity, PPV and NPV were calculated using biopsy report as the reference standard. **Result:** The mean age of the study subjects and those with screen positivity were 39.04 yrs and 39.96yrs respectively. Multipara constituted majority of the screened positive cases. Among the study group, white discharge was the predominant complaint. Cervix was clinically healthy in (45%) of the patients and unhealthy in rest of the patients. 21.4% (3 out of14) of the cases having healthy cervix on examination had dysplasia. VIA was positive in all the 3 cases and Pap smear was positive in only one case. 25% of the patients had positive VIA. 29% of the patients had mild dysplasia, 16.1% of the patients had moderate and severe dysplasia. Pap smear missed 5 cases of dysplasia and VIA missed 1 case of dysplasia. The VIA sensitivity-92.8%, specificity-29.4%, PPV-52% and NPV-83%. In pap smear sensitivity-64.2%, specificity-76.4%, PPV-69.2% and NPV-72.2% respectively. **Conclusion:** Thus VIA was more sensitive than cytology. Whereas Pap smear was more specific.

INTRODUCTION

Cancer cervix is the second most common malignancy in females, second to breast cancer worldwide and most common malignancy in developing countries. 5, 30,000 new cases are reported annually worldwide with a death toll of 2, 75,000 every year. In India a quarter of the global burden is experienced in India. 1, 34,420 new cases occur with death toll of 72,825every year.[1] In developed countries 80% are cured because of early detection by wide spread availability screening procedure, cytology. A successful reduction of incidence by 79% and mortality by 70% has been achieved by pap smear (Novak's).

In developing countries 80% are incurable at the time of diagnosis. Screening programmes do not exist in developing countries. However in some low resource settings where cytology programme do exist they have not been effective in reducing the disease burden. Due to difficulties in ensuring high quality cytology services in many settings, there have been significant interest in new approaches of screening for precancerous lesions. Of these, visual inspection of cervix is a promising option, especially for low resource settings.

Visual inspection with acetic acid, which identifies acetowhite lesions, has now been recognized as one of the promising methods for cancer detection from Indian & African studies as compared to cytology under similar circumstances. Analysis from a growing number of studies in developing country settings indicate that the sensitivity of VIA is equivalent to or greater than Cytology, although its specificity is somewhat lower. Present aim is to detecting the efficacy of visual inspection of cervix with acetic acid with Pap smear in early detection of carcinoma of cervix.

MATERIALS AND METHODS

It is cross-sectional study done in 100 patients who were selected from Gynecology OPD of Govt.

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General Hospital, Kurnool considering the following criteria.

Inclusion Criteria

Women with history of sexual activity for more than three years with intact uterus and cervix, non pregnant, no past / present history suggestive of CIN / Cancer cervix, no bleeding P/V at the time of examination and not had any treatment for cervical lesion (like Cryo, cautery, laser etc.)

Cases referred from PHCs as a part of screening programme were also eligible.

Exclusion Criteria

Unmarried woman not exposed to sexual activity, patient in periods / bleeding PV, prior hysterectomy and obvious growth on cervix suggestive of carcinoma cervix.

An oral questionnaire was administered to all women pertaining to age, parity, education, socioeconomic status, contraception history, chief gynecologic complaints.

They were examined using an unlubricated–bivalve Cusco's speculum. The cervix was exposed properly and excessive discharge when present was gently wiped away using a saline soaked cotton swab. Cervix was closely inspected for macroscopic abnormalities such as erosion, polyp, congestion, nabothian cyst, ulceration, growth.

First Pap smear was taken using Ayer's spatula. Then visual inspection with 5% acetic acid was done, 1 minute after application. Categorization was made as VIA Positive/Negative based on the criteria laid down by IARC. VIA Positive women were subjected to cervical biopsy in the same sitting. But for Pap smear positive cases, biopsy was done in the next visit after seeing the results. Cervical biopsies were fixed in formalin. Embedded in paraffin and processed into 5µm-thick haemotoxylin /eosin-stained section for light microscopy-following the routine diagnosis. Thus, positive pap smear & VIA patients were subjected to biopsy & forwarded for Histopathology which was reviewed by Pathologists from Department of Pathology. The reports were available within two weeks of the Pap smear or biopsy being taken.

Statistical analysis: Cervical biopsy report was considered as the gold standard, mild dysplasia was considered as positive. Sensitivity, specificity, positive and negative predictive values-were calculated for all screening tests-by using the cervical biopsy reports as the gold standard.

RESULTS

Majority of patients belonged to 31-40 yrs of age (39%). Majority of patients belonged to socio economic category 4. (69%). 82% of the study group attained menarche by the age of 13-14 yrs. Mean age at marriage in the study group is 17 yrs. mean age at marriage in women with dysplasia is 14.35 yrs. The early metaplasia occurs almost exclusively in puberty, early adolescence and in the first pregnancy. Oncogenic factors are introduced through sexual intercourse. So women, who begin sexual life at an early age when the metaplastic process is more active, have greater chance of developing CIN and ca.cervix. 66% of the study population were Para 3. Multiparity with poor birth spacing between pregnancies is one of the predisposing factors for cervical cancer. Usage of OCPs over 8-year period is attributed in the development of adenocarcinoma of the endocervix.

In the study group chief complaints were white discharge (49%), menstrual disturbances (16%) and pain abdomen (13%). Of those diagnosed with dysplasia, white discharge was the predominant complaint (57% i.e. 8 out of 14 cases). 14% had post-menopausal bleeding as the chief complaint.

Table 1

Age (years)	Frequency	Percentage
21-30	25	25%
31-40	39	39%
41-50	24	24%
51-60	12	12%
Socio-economic status		
3	20	20%
4	69	69%
5	11	11%
Age at menarche		
11	3	3%
12	9	9%
13	42	42%
14	40	40%
15	12	12%
16	2	2%
Age at marriage		
11-15	27	27%
16-20	66	66%
21-25	6	6%
26-30	1	1%
Parity		
0	1	1%
1	1	1%

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2	32	32%
3	41	41%
4	21	21%
5	4	4%
Contraceptive Method		
OCP	3	3%
IUCD	4	4%
Permanent Method	81	81%
No Contraception	12	12%
Complaints		
White discharge	49	49%
Pain abdomen	13	13%
Post coital bleeding	4	4%
Post menopausal bleeding	5	5%
Menstrual disturbances	16	16%
Others	13	13%

Table 2: Clinical appearance of cervix

Appearance of cervix	No. of cases	Percentage	Dysplasia	Percentage
Normal	45	45%	3	21.4%
Erosion	31	31%	6	42.8%
Hypertrophy and congestion	20	20%	5	35.7%
Nabothian cyst	4	1%		

On examination with cuscos speculum cervix was healthy in 45% and unhealthy in 55% of cases. 78% of cases with dysplasia had erosion or hypertrophied and congested cervix.

Table 3: Results obtained by screening methods

PAP smear results	Frequency	Percentage
Normal study	25	25%
Inflammatory smear	62	62%
LSIL/Atypia	12	12%
HSIL	1	1%
VIA results		
Positive	25	25%
Negative	75	75%
Biopsy		
Cervicitis	16	51.6%
Hyperplastic squamous epithelium	1	3.2%
Mild Dysplasia	9	29%
Moderate Dysplasia	4	12.9%
Severe Dysplasia	1	3.2%

Pap smear results were positive (LSIL and HSIL) IN 13%. VIA was positive in 25% of the study group and negative in 75% of the.

Table 4: PAP smear with biopsy.

Pap smear result	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia	Hyperplasia of SCE	Cervicitis	Total
Positive (major lesions)	4	4	1		4	13
Negative (no major lesions)	5			1	12	18
Total	9	4	1	1	16	31
VIA results						
Positive	9	3	1	1	15	29
Negative		1			1	2
Total	9	4	1	1	16	31

Pap smear identified 9 of the 14 cases with dysplasia. VIA identified 13 out of 14 cases with dysplasia.

Table 5: Result of the screening tests compared with final disease status established by biopsy

	Normal	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia	Total
PAP SMEAR					
Positive	4	4	4	1	13
Negative	13	5	0	0	18
VIA					
Positive	16	9	3	1	29
Negative	1	1	0	0	2

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13 Pap smear positive and 18 negative cases were subjected biopsy. 29 VIA positive cases and 2 VIA negative cases (total 31 cases) were subjected to biopsy.

Table 6: Calculation of sensitivity, specificity, positive predictive value ad negative predictive value

	Papsmear	VIA
True positive	9	13
False positive	4	12
True negative	13	5
False negative	5	1
Sensitivity	64.2%	92.8%
Specificity	76.4%	29.4%
Positive predictive value (PPV)	69.2%	52%
Negative predictive value (NPV)	72.2%	83%

Table 7: Comparison of VIA and papsmear of present study with other studies

Comparison of VIA with other studies	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Tayyeb.R, et al3	93.9%	30.4%	60%	77.5%
A.Goel et al7	96.7%	36.4%	58%	92.3%
Siddiqui M et al6	60%	40%	65%	98%
Blumenthal Pd et al8	96%	60%	65%	92%
Singh et al-10	80%	60%	60%	90%
Malik N et al9	93%	30.4%	60%	96%
Present study results	92.8%	29.4%	52%	83%
Comparision Pap smear with other studies				
Tayyeb.R et al3	46.9%	69.5%	60%	52.8%
Sankaranarayan et al 11	62%	87%		
Denny et al 12	80%	87%		
Denny et al13	76%	95%	25%	30%
Present study results	64.2%	76.4%	69.2%	72.2%

13 Pap smear positive and 18 negative cases were subjected biopsy. The sensitivity was 64.2%, specificity was 76.4%, positive predictive value was 69.2% and negative predictive value was 72.2%. The 29 VIA positive cases and 2 VIA negative cases (total 31 cases) were subjected to biopsy. The test results were calculated and it was found as sensitivity 92.8%, specificity 29.4%, positive predictive value 52% and negative predictive value 83%.

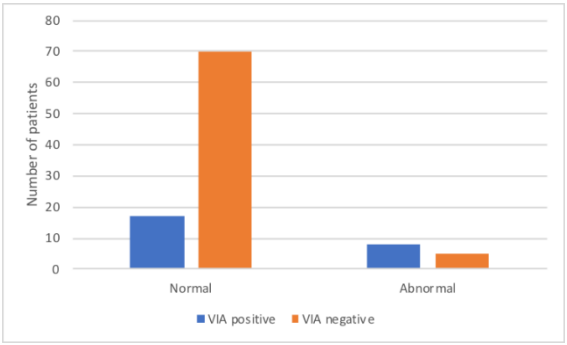

Figure 1: Correlation between Pap smear and VIA.

Of the 100 cases screened Pap smear was abnormal in 13 cases. VIA was positive in 8 cases out of 13 abnormal pap smears. 5 patients with Pap smear abnormality was negative with VIA.

Figure 2: Visual inspection with acetic acid images of positive and negative. Normal Cervix and VIA Positive.

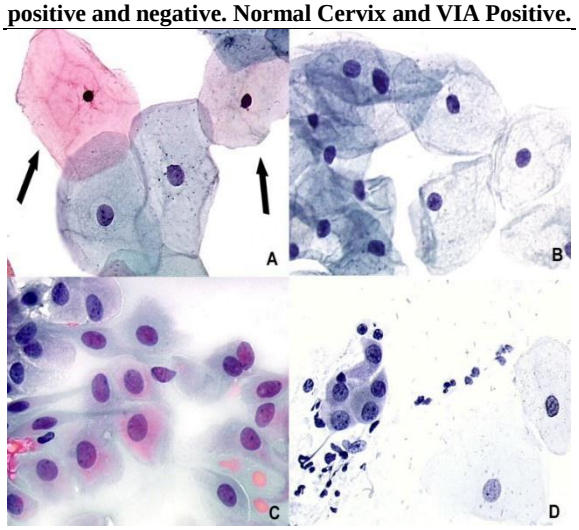

Figure 3: Different types of squamous cells - A: superficial cells (arrows); B: intermediate cells; C: parabasal cells; D: metaplastic cells. (obj. 20x)

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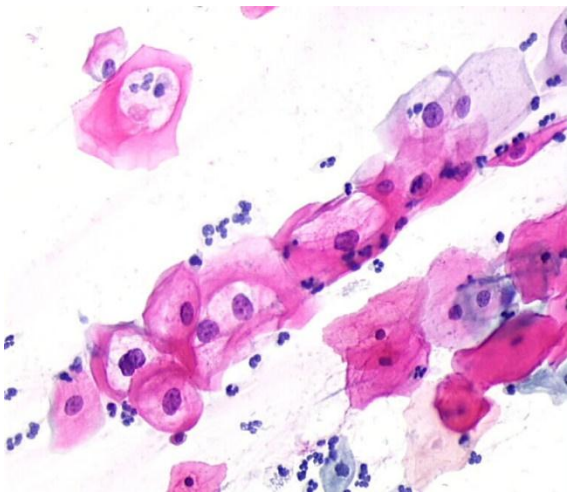

Figure 4: LSIL: eosinophilic squamous cells with a perinuclear empty cavity surrounded by cytoplasmic thickening and with moderate nuclear enlargement: typical koilocytes. (obj. 20x)

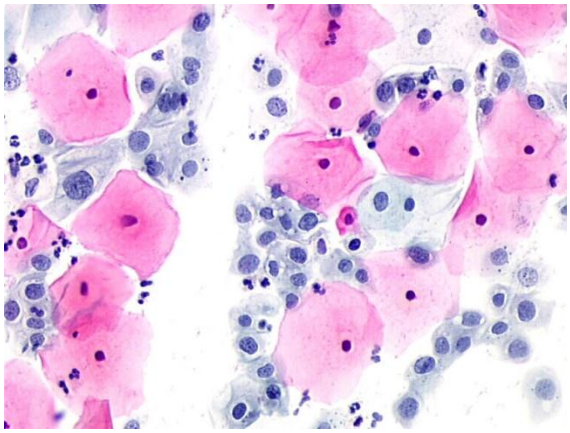

Figure 5: Parabasal cells with nuclear enlargement, irregular nuclear outlines, with anisokaryosis and anisocytosis in a homogenous cell population. HSIL. (obj. 20x)

DISCUSSION

Cervical Cancer is the second most frequent cancer worldwide in women after breast cancer. However, invasive cancer of cervix is considered to be preventable condition as it is associated with a preventive stage amenable to screening and treatment.

In present study mean age of the women screened was 39.04 years and mean age of those screened positive was 39.96years. Dysplasia was found to be more common between 35-45 yrs. (mean age of those with dysplasia was 40.64 years. Kustagi and Fernandez in their study showed the prevalence of dysplasia was higher in women over 30 years.[2] Vaidya showed in his study that CIN was more prevalent in the age group > 35 years.

Socioeconomic status had always been playing an epidemiological role in genesis of dysplasia. In our study, chronic cervicitis and dysplasia were common in low income group. Poor personal hygiene, poor living conditions and early age at first intercourse are factors associated with both low socio economic status and cervical cancer.

Regarding parity, our study showed increased incidence of dysplasia among multiparous women. 74% of screened positive cases were Para 3 and above. 78% of cases with dysplasia were Para 3 and above. The other three cases screened positive were Para 2 three had mild dysplasia. Kustagi and Fernandez showed the prevalence of CIN was significantly higher in parity of > 2.2

This might be attributed to hormonal and nutritional charges that occur in pregnancy, immunosuppression during pregnancy and cervical trauma during vaginal delivery. (Becker et al) Among the complaints, white discharge was present in majority of women with chronic cervicitis, dysplasia and metaplasia. Excessive vaginal discharge playing a role in contributing to the development of CIN was also proved to be a risk factor in the study conducted by Vaidya et al. In their study, 24% had vaginal discharge.

On examination, 55% of the patients had unhealthy cervix. In 78% of patients with severe dysplasia had eroded and congested cervix. All patients were subjected to visual inspection with acetic acid and was positive in 25 cases i.e., 25% of the study population. The above findings correlated with the study conducted by Tayyeb et al, where VIA was positive in 28.6% of the cases.[3] Also in another study by Sankara Narayanan et al, in Kolkata involving 5881 women showed VIA positive results in 30%.[4]

There were 25 cases (25%) with normal findings, 62 cases (62%) showed inflammatory findings, 12 cases (12%) showed LSIL /Atypical changes and 1case (1%) showed HSIL changes. The above findings were similar to the finding in the study conducted by Tewari R et al,[5] whose findings were with inflammatory findings (73%), HSIL (2%).

Biopsy was taken in 31 cases which were either positive in VIA or in Pap smear. It showed no evidence of atypia or dysplasia in 16 cases (51.6%), mild dysplasia in 9 cases (29.03%), moderate dysplasia in 4 cases (12.9%) and severe dysplasia in 1 case (3.2%). There were no cases of carcinoma in situ or carcinoma cervix. In the study conducted by Longatto filho et al,[6] in 2005 involving 10,000 women, the results of biopsy were 2500 normal cases (54%) 1860 inflammatory (42%), dysplasia in 80 cases (4%) (Mild dysplasia 2%) Moderate dysplasia (2%).

29 VIA positive cases and 2 VIA negative cases (total 31 cases) were subjected to biopsy. The test results were calculated and it was found as sensitivity 92.8%, specificity 29.4%, positive predictive value 52% and negative predictive value 83%. Our study is in correlation with studies of Tayyeb R. et al,[3] with sensitivity 93.9%, specificity 30.4%, positive predictive value 60%, negative predictive value 77.5%. A. Goel, et al,[7] sensitivity 96.7%, specificity 36.4%, positive predictive value 58%, negative predictive value 92.3%. Siddiqui M et al,[4]

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sensitivity 60%, specificity 40 %, positive predictive value 65%, negative predictive value 98%. Blumenthal Pd et al,[8] sensitivity 96%, specificity 60%, positive predictive value 65%, negative predictive value 92%. Singh et al,[3] sensitivity 80%, specificity 60 %, positive predictive value 60%, negative predictive value 90%. Malik N et al,[9] sensitivity 93.%, specificity 30.4 %,positive predictive value 60%, negative predictive value 96%.[10]

In a study, Sankaranarayanan et al,[11] reported equally comparable specificities for both tests, 93.2% for VIA and 92.7% for cytology which is not similar to our study. High number of false positive and consequently low specificity of VIA, could be due to large number of inflammatory lesion.

13 Pap smear positive and 18 negative cases were subjected t biopsy. The sensitivity was 64.2%, specificity was 76.4%, positive predictive value was 69.2% and negative predictive value was 72.2%. The results are comparable with other studies as Tayyeb R et al,[3] sensitivity 46.9%, specificity 69.5%, positive predictive value 60%, negative predictive value 52.8%. Sankaranarayan et al,[11] sensitivity 62%, specificity 87% Denny et al,[13] sensitivity 80%, specificity 87%. Denny et al(2002),[9] sensitivity 76%, specificity 95%, positive predictive value 25%, negative predictive value 30%.

In the recent review of the accuracy of cervical cytology based on published studies from developed countries, the average sensitivity for cytology ranged from 47% to 62% and specificity ranged from 60% to 95%. The present study also shows the same results. Finally when comparing the efficacy of VIA with pap smear cytology Sensitivity for VIA was 92.8%, Pap smear cytology 64.2%, Specificity for VIA was 29.4%, Pap smear cytology 76.4%, Positive predictive value for VIA was 52%, Pap smear cytology 69.2% and Negative predictive value for VIA was 83%, Pap smear cytology 72.2%.

Thus VIA has higher sensitivity than Pap smear and pap smear is more specific than VIA. VIA can be used as an alternative strategy to Pap smear cytology in low resource settings. The high NPV of VIA warrants particular mention. The use of VIA as a primary screening test means that women assessed as test negative would be reassured most probably that they do not have high grade CIN or Cancer cervix.

CONCLUSION

In conclusion, as a single test, cytology was associated with the best balance of sensitivity, specificity and predictive values on the basis of our findings. The significant association of abnormal VIA with cytological abnormalities suggests that both tests have potential to detect abnormal cervical lesions. The results of current study indicate that VIA is a simple objective test. The result of this procedure is available immediately, allowing an algorithm of further investigations to be carried out for the identification of cervical lesions.

VIA may find a place as an alternative low technology and low cost method of screening and case finding. Further evaluation is required to improve specificity without compromising sensitivity. As compared to Pap smear VIA has the advantage of being simple and easy-to-learn technique. Moreover VIA has low startup and ongoing costs. It integrates well with the primary health care services. VIA gives the facility of see and treat due to immediate results at one stop clinic.On the other hand VIA has the disadvantage of higher referral and potential of over-treatment due to its low specificity. To keep the quality control, the careful monitoring of this technique is required and there is clear need for training methods and quality assurance to standardize the reporting procedure.

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