A Comparative study of visual inspection with acetic acid versus PAP smear in detection of cervical dysplastic lesions in ante–natal women

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Abstract:
Aim Of The Study: To Compare the method of visual inspection with acetic acid(VIA) with pap smear in detection of cervical dysplastic lesions in ante–natal women.
Materials And Method: It was a prospective study performed in 113 antenatal patients between 16-28 weeks of gestation. The pap smear and VIA performed for all patients in the study group. Positive screens were classified as atypical squamous cells of undetermined significance; low-grade or high-grade squamous intraepithelial lesion, including those showing atypia, cervical intraepithelial neoplasia, or carcinoma-in-situ. All patients with positive pap screens or positive for aceto white lesions were subjected to colposcopy.
Results: Out of the 113 patients screened 10 patients were VIA positive, among them 3 were found to be colposcopically positive. one patient found to be pap smear positive, and subsequently found to be positive. In our study the detection rate of VIA was 2.65%, and pap smear was 0.88%. In our study the ratio of detection rate between VIA/PAP smear 3.01. Specificity for VIA in our study is 93.6% and for pap smear sensitivity is 100%.
Conclusion: We conclude that VIA is more specific than PAP smear in detection of cervical dysplastic lesions among ante-natal women.
Key words: Acetowhite, Cervical dysplasia, Colposcopy, PAP smear, VIA

I. Introduction
It has been well established that organized cytology screening programs can substantially reduce the incidence of mortality from cervical carcinoma.
This study was taken up because screening during pregnancy in our setup provides an excellent opportunity for opportunistic screening as women in our population hardly ever voluntarily come for screening. Physiological changes during pregnancy further help in performing VIA as there was a physiological ectropion and the transformation zone was visualized better for VIA.
When a pap smear was taken women usually do not come back for follow up to view her pap results but during pregnancy she will definitely come back for here next ante-natal visit and hence the rationale for screening during pregnancy.
This study was undertaken to analyze if VIA is better than pap smear in picking up cervical dysplastic changes by conforming the test result with colposcopy.

II. Objectives
1. To compare the effectiveness of VIA and pap smear as a screening tool in ante-natal patients for cervical dysplasia.
2. To evaluate VIA as an alternative or adjunct to the Papanicolaou (pap) smear.
3. As an opportunistic screening because most of the women in our setup hardly ever voluntarily come for screening.

III. Materials and method
After obtaining ethical committee approval and informed consent, the prospective study was carried out amongst the antenatal women attending the obstetric out patient at Coimbatore medical college hospital between January 2015 and January 2016.
Inclusion criteria
1. All antenatal women in the gestational period between 16 and 28 weeks.
2. Any parity.

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Exclusion criteria
Women who had a history of abnormal cytology or previously treated for cervical intraepithelial neoplasia (CIN) or cancer cervix.

3.1. Pap smear
In the pap smear sample of cells is taken from the uterine cervix using Ayers spatula and onto a slide and examined under a microscope for abnormal cells (pre – cancer or cancer). When a pap smear shows abnormal cells i.e. LSIL and higher it is reported as positive

Visual inspection with acetic acid (VIA)
After taking the pap smear VIA is done by applying 4% acetic acid to the cervix and we have to wait for 1 minute to observe any aceto-white lesions. If positive then patients is referred for colposcopy.

3.2. Colposcopy
The cervix was inspected at low-power magnification (5x to 10x), looking for any obvious areas of abnormality (e.g., leukoplakia). Visibility of entire transformation zone was checked. Following which normal saline was applied and viewed through green filter to check for abnormal vasculature. Followed by application of 4% acetic acid and looked for any aceto-white areas. Then Lugol’s iodine was applied and areas which do not take up iodine were termed positive.

The pap smears of all the patients in the study group were evaluated by cytology laboratory using the Bethesda system for reporting results; all pap smears were run in regular clinical pap smear batches and were reviewed by cyto-pathologists. Pap smears characterized as negative and smears characterized by inflammatory changes without condylomatous features were considered to be negative screens. Smears classified as atypical squamous cells of undetermined significance; low-grade squamous intraepithelial lesion; or high-grade squamous intraepithelial lesion, including those showing atypia, cervical intraepithelial neoplasia, or carcinoma-in-situ, were classified as positive screens. All patients with positive pap screens or positive for aceto white lesions were subjected to colposcopy.

IV. Results and analysis
All our patients were categorized according to the age distribution which shows that nearly 49.55% were within 18 to 24 age group. Out of the 113 patients 86 patients had 1 to 4 years of sexual intercourse. Out of the 113 patients screened 10 patients were VIA positive and one patient found to be pap smear positive. Out of the 10 VIA positive patients 3 were true colposcopically positive. And the only one pap smear positive patient also true colposcopically positive.

The detection rate of moderate dysplasia (true positive) was calculated by dividing the number of screened women with these lesions by total number of screened women. In our study the detection rate of VIA 2.65% for pap smear it is 0.88%.

The ratio of sensitivity between these two tests was calculated by dividing the detection rate of VIA by the detection rate cervical cytology. In our study the ratio of detection rate 3.01. Specificity for VIA in our study is 93.6% and for pap smear sensitivity is 100%.

5. Tables and Figures

<table>
<thead>
<tr>
<th>Table 1 Age wise distribution</th>
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<tbody>
<tr>
<td>Age</td>
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<tr>
<td>18-24</td>
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<td>25-28</td>
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<td>29-32</td>
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<td>33-36</td>
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<th>Table 2 Distribution based on years of sexual intercourse</th>
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<tr>
<td>No. of years of sexual intercourse</td>
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<td>1-4 years</td>
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<td>5-8 years</td>
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<td>9-12 years</td>
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<th>Table 3 Screen positives</th>
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<td>Table no. screened</td>
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<td>113</td>
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Table 4 Age wise distribution of cases

<table>
<thead>
<tr>
<th>Age</th>
<th>No.of cases</th>
<th>VIA +</th>
<th>Pap +</th>
<th>Colposcopy positive</th>
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</thead>
<tbody>
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<td>18-24</td>
<td>56</td>
<td>0</td>
<td>0</td>
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<tr>
<td>25-28</td>
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<td>29-32</td>
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<td>7</td>
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<td>33-36</td>
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Table 5 PAP smear results

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<th>Pap smear</th>
<th>Inflammatory</th>
<th>Normal</th>
<th>B12/folate</th>
<th>HSIL</th>
<th>No. of patients</th>
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<td></td>
<td></td>
<td></td>
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Table 6 Distribution of colposcopy positive cases

<table>
<thead>
<tr>
<th>Colposcopy positive</th>
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<tbody>
<tr>
<td>VIA</td>
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<td>Pap smear</td>
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Table 7 Correlation between VIA, pap and colposcopy

<table>
<thead>
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<th>Patient number</th>
<th>VIA</th>
<th>Pap smear</th>
<th>Colposcopy findings</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Squamous metaplasia</td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>HSIL</td>
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<tr>
<td>10</td>
<td>+</td>
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V. Analysis

Total number of patients = 113
Total screen positive for VIA = 10, for which colposcopy positive =3 (1 HSIL and 2 LSIL)
Total screen positive for pap = 1 (HSIL), for which colposcopy Positive = 1 (HSIL on biopsy)

As shown in TABLE 6, patient no1 had was positive for VIA and on pap showed HSIL. This patient was 25 years of age and was married for 2 years only. She had complaints of excessive white discharge. On colposcopy she had a cluster of grape like lesion extending all over the posterior lip of the cervix. On green filter bizarre patterns lesion and bled on touch. The whole lesion was acetowhite. On lugols iodine whole lesions was iodine negative. The biopsy revealed HSIL.

Patient no 2 she was a 32 year of age, VIA positive and on pap revealed B12/Folate deficiency but by our criteria was pap negative. Colposcopy revealed a small aceto white area at 12 o clock and multiple acetowhite lesions studded around the cervix – leopard skin appearance. The same areas were negative by iodine. Hence it appeared LSIL hence did not biopsy it.

Patient number three, 32 years of age, was VIA positive and on pap showed similar B12/Folate deficiency. Colposcopy revealed acetowhite areas with faint mosaic pattern at 4 o clock position. This was designated LSIL and no biopsy was taken.

Patient no 4, she was 25 years of age, was positive on VIA and negative on pap. On colposcopy she had squamous metaplasia hence was designated colposcopy negative.

6.1 Statistical analysis

Sensitivity and specificity of the screening tests could not be calculated directly, as the reference test was not applied to all women who were negative on screening. The performances of two tests (VIA and cytology) can nevertheless be compared by means of the following parameters.

1. The detection rate of moderate dysplasia or worse lesion (true positives): this was calculated by dividing the number of screened women with these lesions by the total number of screened women.
2. The ratio of sensitivities between the two tests: this was calculated by dividing the detection rate of VIA by the detection rate of cervical cytology; a ration of more than unity indicated that the first test was more sensitive.
3. The approximate specificity of each screening test was calculated by dividing the number of women with negative screening tests by the total number of screened subjects minus the number of true-positive cases detected by the test.

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1) Detection rate for a test = total no of screened women with the lesions (ie positive on colposcopy)/total no of screened women
   Hence for VIA = 3/113 = 2.65%, in Sankararayanan et al study 1.57%
   For pap = 1/113 = .88% in Sankararayanan et al study 1.5%

2) Ratio of detection rates
   = 2.65/ .88
   =3.01 (if the ration is more than utility then the first test was more sensitive)
   Hence VIA is more sensitive

3) Specificity
   = -VE BY SCREENING / TOTAL NO. SCREENED – TRUE +VE BY THE TEST
   Hence for VIA
   = 103/113-3=103/110
   =93.6 , 92.2% by Sankararayanan et al
   Hence for pap
   1112/113-1
   =100%,  92.7% Sankararayanan et al

VI. Discussion

Total number of patient = 113, total screen positive for VIA = 10, for which colposcopy positive = 3 (1 HSIL and 2 LSIL), total screen positive for pap = 1 (HSIL), for which colposcopy positive = 1 (HSIL on biopsy). The rest of the cases on pap smear, 106 cases came as inflammatory smear, 4 cases were normal smears, 2 cases were B12/ folate deficiency.

Out of the ten screened positive by VIA 3 were positive for colposcopy and out of those three one was positive for pap too. VIA picked up more cases probably because of the physiological changes in pregnancy i.e., high estrogenic milieu of pregnancy causes an increase in cervical volume through hypertrophy of the fibromuscular stroma, an increase in the vascularity of the entire lower genital tract, more prominent gland opening with tenaciousmucus production, and an increase in stromal edema. The endocervical canal also frequently everts onto the ectocervix. The endocervical canal also frequently everts onto the ectocervix. The vagina becomes more acidic as a result of higher estrogen levels, and the decidual cells of the cervix show an increase in the nuclear-to-cytoplasmic ratio, together with more prominent nucleoli. Because of these expected changes inflammatory responses sometimes ensue, with a concomitant increase in the percentage of suboptimal pap smears in pregnancy and an increase in the via screen positive.

Another reason for the low screen positives could be because our study involved a younger population of 49.5% being younger than 24yrs of age and most of them had a short period of exposure to sexual intercourse 86 patients out 113 had less or equal to a 4 year exposure. There were 2 other interesting cases which revealed folate/B12 deficiency. The 2 cases of folate/B12 deficiency was not considered as a positive screen by pap because our criteria for a positive pap was LSIL and higher.

Visual inspection with acetic acid is a new screening adjunct that is noninvasive and can provide visualization of the cervix and detection of cervical lesions without the need for tissue damage, Insofar as the pap smear remains a mainstay of for screening purpose regardless of pregnancy status, the combination of the via examination and the pap smear allows for immediate screening results.

Our preliminary study shows visual inspection with acetic acid to be atraumatic and well-tolerated. Results from this study support the general finding that visual inspection with acetic acid increases the sensitivity of cervical cytology screening, especially cervical cancer precursor lesions. Further study is needed to determine the overall sensitivity and specificity of visual inspection with acetic acid in screening gravid patient for cervical cancer and its precursors, as well as the improvement, if any, in the detection and treatment of patients with cervical cancer when visual inspection with acetic acid is used. In addition, studies show that economic impact of visual inspection with acetic acid makes it an effective adjunctive protocol or solitary cervical cancer screening procedure. Although initial studies than pap smear alone,” a study by massed et al showed a cost saving of 24% when speculoscopy was added to the cervical screening protocol. Finally, visual inspection with acetic acid may eventually have a definite role in screening pregnant patients in geographic locations that do not have access to a cytology laboratory.

Ibrahim et al, 2015 emphasized that VIA has higher sensitivity and lower specificity compared to Pap smear, but a combination of both tests has greater sensitivity and specificity than each test independently. Shastri et al, 2014 stated that VIA screening by primary health workers statistically significantly reduced cervical cancer mortality.

VII. Summary

1. The detection rate of VIA is more than that of PAP smear

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2. According to the ratio of detection rates, VIA was more sensitive than PAP
3. The specificity of VIA is more than that of Pap smear

Overall, the findings show that visual inspection with acetic acid is “a simple, feasible and effective method for cervical cancer screening during pregnancy” in developing countries. Moreover pregnancy provides an excellent opportunity for screening as it may be the only point in a woman’s life in our setup when she is screened. Researchers believe that visual inspection screening “should be established in routine health service in India” and other low-resource countries, as the implementation of such screening programs will not only reduce the disease burden but will create the infrastructure that will eventually be needed to administer HPV screening efforts.

VIII. Conclusion

We conclude that VIA is more specific than Pap smear in detection of cervical dysplastic lesions among ante-natal women.

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