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Original Research Article

## A comparative study to see the effectiveness of Pap smear, visual inspection with 3-5% acetic acid and its confirmation by cervical biopsy

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### ABSTRACT

**Background:** Cancer of the cervix is a leading cause of morbidity and mortality among women worldwide. The present study was undertaken to compare the effectiveness of Pap smear and visual inspection with 3-5% acetic acid (VIA) in screening carcinoma cervix followed by its confirmation by cervical biopsy.

**Methods:** A total of 100 patients with abnormal looking cervixes or symptomatic patients having age beyond 30 years, attending the obstetrics and gynaecology OPD at Naval Hospital Powai, Mumbai from 31<sup>st</sup> December 2015 to 31<sup>st</sup> December 2017 were selected for the study. Pap smear and VIA was done on consecutive days. In positive cases cervical biopsy were done to confirm the result.

**Results:** The sensitivity of VIA was 100% but at the same time specificity was 41% there will be unnecessary investigation and biopsy in false positive cases. The sensitivity of cytology was 75% and specificity was 97%. Not a single case was missed by Pap smear only one case of severe dysplasia on cytology had squamous cell carcinoma on HPE which was done after 90 days because of delay in patients follow up.

**Conclusions:** Both the Pap smears and VIA is very effective screening tool for cervical cancer and histopathological examination remains the mainstay. But VIA is very cost effective and easy procedure, though it gives false positive reports but is not going to miss any case, rather leads to over diagnosis of the cases with cervicitis and hence treatment starts early and thus the progress of disease can be slowed down or even stopped.

**Keywords:** Acetic acid, Biopsy, Cancer, Cervix, Dysplasia, Mainstay, Pap smear, Squamous cell carcinoma

### INTRODUCTION

Worldwide cancer accounts for 9% of deaths. In developed countries cancer is the leading cause of death next to cardiovascular disease but in developing countries it ranks fourth as a cause of death.<sup>1,2</sup> Approximately half a million women are diagnosed with cervical cancer each year making it the second most common malignancy in women globally.<sup>3,4</sup> In India among all type of genital cancer, carcinoma cervix accounts for 80%, ovary 10%,

and uterine body 4-5%.<sup>5</sup> Carcinoma cervix does not arise de novo but follows a spectrum of premalignant epithelial abnormalities in the form of dysplasia or CIS. Since cervix is a readily accessible organ for examination, it is considered as an unique malignancy that can be prevented.<sup>6</sup> In India cervical cancer is the most common women related cancer killing one woman every 8 minutes according to National Cancer registry program by Indian Council of Medical Research (ICMR) in the year 2007, about 1,32,082 are affected by cancer cervix every year in

India and 74,118 die of the disease.<sup>7</sup> In view of natural history of disease cervical cytology screening continues to be the main stay in diagnosis of cervical cancer.<sup>8</sup>

In developing countries due to lack of resources, primary health care, literacy and lack of follow up the screening programmes are only institution based and caters a limited group of population. Hence there is a need to look at alternate strategies for mass screening. Practically the procedure should be easy, simple, effective, inexpensive, less time consuming and should be acceptable to the female population.<sup>9</sup> In the present era in addition to exfoliative cytology, researchers are finding many alternative screening procedures like visual inspection, visual inspection with acetic acid, schillers test, cervicospoty, gynospoty, colposcopy, HPV typing etc. In the present study only symptomatic patients coming to OPD and abnormal looking cervixes were chosen as study group. A comparison was made between findings of exfoliative cytology and visual inspection with acetic acid in order to see the effectiveness of procedure and in positive cases cervical biopsy being done in order to find the sensitivity and specificity of all procedures.

## METHODS

The present study was carried out in the department of obstetrics and gynaecology, at Naval Hospital Powai, Mumbai during a period of 2 years from 31<sup>st</sup> December 2015 to 31<sup>st</sup> December 2017. A total of 100 women with abnormal looking cervixes or symptomatic patients (e.g. vaginal discharge, itching vulva, postmenopausal bleeding etc.) attending obstetrics and gynaecology OPD and family welfare centre of NH Powai were chosen as the cases for the study. The inclusion criteria were women between 30 to 75 years of age, irrespective of parity, parity of one or more irrespective of age, women having cervical erosion, cervicitis, hypertrophied cervix, cervical polyp, uterine prolapse with ulceration, vaginal discharge, postmenopausal, bleeding and post coital bleeding were considered as unhealthy cervixes, women using contraceptives. Clinically diagnosed advance cases and cancer cervix were excluded from the study.

A detailed clinical history including age, age of marriage, first child birth, number of children, socioeconomic status, number of partners and a proforma was made for each of the hundred cases. Detailed history of their husband, socioeconomic status, coital practices, obstetrics history, menstrual history, present complaints was noted. Personal history, past history, general, systemic, local, bimanual and rectal examination records were kept. These ladies were subjected to routine blood, urine examination, VDRL, HIV < iii random blood sugar along with papnicolaou's stain, VIA with 3-5% acetic acid and finally histopathological examination. All the cases were subjected to exfoliative cytology i.e., pap smear, without waiting for its report they were all subjected to staining with 3-5% acetic acid within two or three days. Then the positive cases were subjected to

histopathological examination. The reports of Pap smear, VIA and cervical biopsy were compared and were followed up for subsequent management. The findings were then compared to find the effectiveness of the screening procedures. All the data were presented in number of patients.

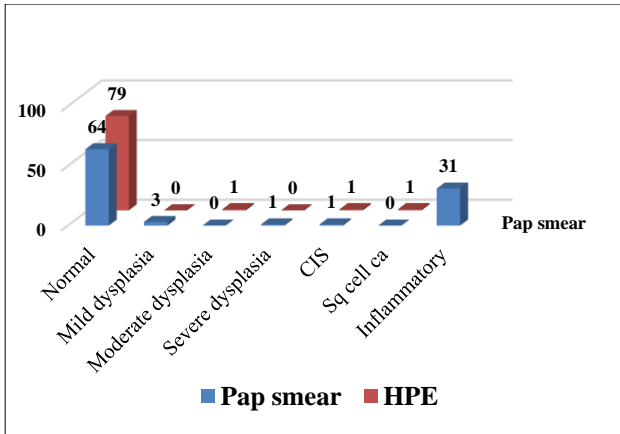
## RESULTS

Out of 100 patients enrolled in the study, 3 cases had Mild dysplasia, 1 case had severe dysplasia, 1 case had carcinoma in situ (CIS) and 31 patients had chronic inflammation smear and 64 had normal smear. However, we found 58 cases with acetowhite area, 1 case with white gland opening and 1 case with polyp turning white arising from the anterior lip of cervix and 40 cases without any change on application of 3-5% acetic acid and had normal findings. Histopathological report shows 1 case each of moderate dysplasia, carcinoma in situ and squamous cell carcinoma and all the observations are shown in (Table 1).

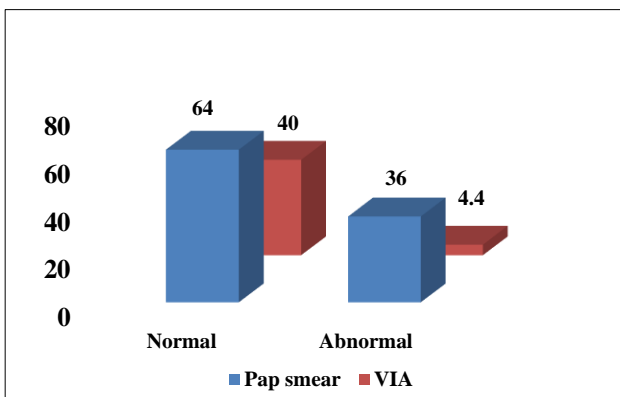
**Table 1: Result of Papnicolaou's stain, VIA with 3-5% acetic acid and histopathological examination among the study group.**

PAP Smear	No. of cases
Mild dysplasia	03
Moderate dysplasia	00
Severe dysplasia	01
Carcinoma in Situ	01
inflammation	31
Normal findings	64
<b>VIA with 3-5% acetic acid</b>	
Leukoplakia	00
Aceto white area	58
White gland opening	01
Mosaic punctate	00
Miscellaneous	01 (polyp)
Normal findings	40
<b>HPE report</b>	
Moderate dysplasia	01
Severe dysplasia	00
Carcinoma in Situ	01
Squamous cell carcinoma	01
Inflammatory	18
Normal findings	79

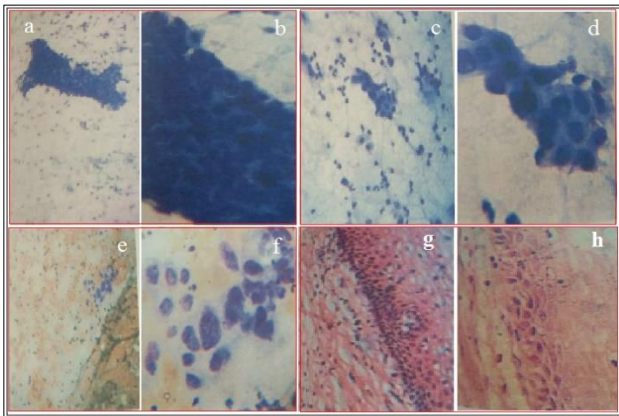
Summarising the result from the (Figure 1), we find cytology more or less correlating with HPE report. On cytology 03 cases had mild dysplasia out of which only 01 case had moderate dysplasia on HPE and other 02 cases were inflammatory. 01 case had severe dysplasia on cytology which on HPE showed squamous cell carcinoma where time period (since the time on which biopsy was taken about 90 days later from the date when Pap smear was done) may be one of the cause for the mismatching of the reports. Rest all the cases tallied.



**Figure 1: Comparative results between Pap smear and histopathology.**



**Figure 2: Correlation of VIA report with cytology.**



**Figure 3: Pap smear - a) low and b) high power mild dysplasia, c) low and d) high power moderate dysplasia, e) low and f) high power severe dysplasia, HPE g) low and high-power moderate dysplasia.**

Comparing the VIA report with cytology and HPE it is found that it has not missed a single positive case but at the same time it is positive in many inflammatory and normal cases too, (Figure 2).

The relationship between Pap smear, VIA and HPE Report being the standard for comparison is shown in (Table 2).

**Table 2: Relationship between Pap smear, VIA and HPE report.**

Particulars	PAP	VIA	HPE report
Mild dysplasia	3	3 (acetowhite)	-
Moderate dysplasia	-	-	1
Severe dysplasia	1	1 (white gland)	0
Carcinoma in situ	1	1 (acetowhite)	1
Squamous cell carcinoma	-	1 (polypoid)	1
Inflammation	31	54 (acetowhite)	18
Normal	64	40	79

## DISCUSSION

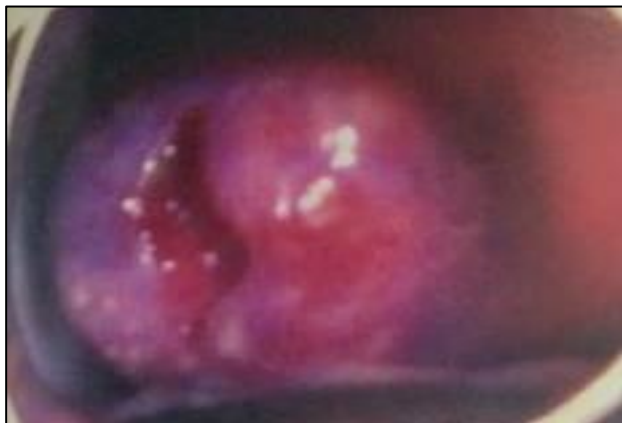
Carcinoma cervix is the second most common cancer in developing countries like India it is most important cancer among the women in past two decades by now it is known that the accessibility of uterine cervix, propensity of cells to exfoliate from precancerous lesion, the evidence from pathological studies of existence of histological changes from mild atypia through premalignancy to the frank malignancy, the apparently prolonged natural history the long premalignant phase and the ability for detecting changes using potential for control of cervical cancer.<sup>10-12</sup> It is assured that cervical intraepithelial neoplasia (CIN) acts as a premalignant disease and progress slowly over a period of 15-20 years to invasive cancer. Immense attention has been paid to natural history of cancer cervix and it has been proved beyond doubt that during the course of development of the disease there is sufficiently large period in which it is absolutely curable. Much of the recent increase in cancer incidence can be explained by known risk factors and improved detection rate and this justifies the importance of earliest possible diagnosis in premalignant and preclinical stages.

Keeping in mind the present study was carried out to compare the effectiveness of various screening procedures in 100 symptomatic women of age 30 years or more attending the gynaecological OPD of NH Powai during the period of 2015-2017.

Amongst various modalities for control of cancer cervix, screening to diagnose preinvasive lesions remain the only means to curb the disease. Screening of cancer cervix causes a dramatic reduction in mortality (50 to 70%).<sup>13,14</sup> The appropriateness of a screening test depends not only on its accuracy, as measured mainly by sensitivity and specificity but also on its simplicity and safety.<sup>15</sup> Alternative methods for cervical cancer screening have been sought. One method, direct visualization with acetic acid has gained popularity and proven itself in many

clinical trials as an adequate alternative to PAP smears in developing countries.<sup>16</sup>

Naked eye visual inspection of the cervix after application of 3 to 5% acetic acid causes a reversible coagulation or precipitation of the cellular proteins. Areas with dysplasia or invasive cancer have large number of undifferentiated cells in the epithelium and hence undergo maximal coagulation because of higher content of nuclear protein and prevent light from passing through the epithelium, hence these areas appear acetowhite (Figure 4).



**Figure 4: Visual inspection after the application of acetic acid (VIA) - positive lesion.**

Most studies compared VIA with PAP, looking at sensitivities and specificities of both, while comparing them to colposcopy with biopsy as the gold standard with varying results. Comparing with the previous study we find that our result of cytology i.e. sensitivity was 75% where as in previous study it was 62%.<sup>17</sup> The specificity was 97% in our study and 89% in previous study.<sup>17</sup> The reason for such a high sensitivity may be due to smear collection and preparation of the slide and its interpretation. Consul, et al reported the sensitivity of Pap smear was 84.20% and the specificity was 62.10%.<sup>18</sup>

The sensitivity of VIA in current study was 100% and specificity was 41%. Thus, VIA showed higher sensitivity compared to Pap smear, whereas VIA had lower specificity compared to Pap smear. In Shankarnarayan et al, study the sensitivity and specificity of VIA being 95.8% and 68%.<sup>17</sup> Consul, et al found sensitivity of VIA was 84.20% and specificity of 55.20%.<sup>18</sup> The result of present study more or less correlates with the previous study and the reason for 100% sensitivity may be due to the fact that 54% of patients have chronic cervicitis and hence have positive results falsely. Because of the high number of false-positive cases and low specificity of VIA, the usefulness of this procedure is limited. But, due to the high sensitivity of VIA, it is still used as primary screening in some developing countries for early detection of cervical carcinoma.<sup>18</sup>

Among 100 total cases, 61 cases were from Hindu religion and 38 were Muslim and 1 case was from other religion. The incidence of abnormal smear was more in Hindu religion. CIN were present more in Hindu religion i.e. 5 out of total 8 positive cases and only 3 cases in Muslim community. This finding correlated with the previous studies.<sup>19,20</sup> The dysplastic lesions were more common in 30-39 years age group. The grade of lesion increases as the age increases. Similar results were obtained by Upreti and Rohtage.<sup>21</sup> The average age for mild to moderate dysplasia was 32.5 years (37 patients) and average age for severe dysplasia was 37 years (38 cases). The mean age for CIS and invasive cancer was 38.5 years (41 cases) and 42 years (46 cases) respectively. These findings are compared with the Saraiya and Lula.<sup>22</sup>

Duration of marriage and duration of exposure to sexual intercourse has an important role in the genesis of cervical dysplasia. In present study, 8 cases were married at the age of 15 years or less and 63 cases were married between 16-20 years age group and 29 cases were married at more than 20 years of age. The development of CIN were more in 16-20 years age group of marriage i.e. 6 out of total 8 positive cases and development of CIN in 1 case each of < 15 years and > 20 years age group of marriage. These results are corresponded with the study done by Bhattacharyya et al.<sup>23</sup>

## CONCLUSION

Both the Pap smears and VIA is very effective screening tool for cervical cancer and histopathological examination remains the mainstay but, in a resource, poor country VIA can be implemented which is very cost effective and easy procedure. Though it gives false positive reports but is not going to miss any case, rather will over diagnose the cases with inflammation and hence treatment can be started early and the progress of the disease can be slowed down or even stopped.

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