

# Visual Inspection of Cervix with Acetic Acid (VIA): An Effective Method of Screening for Cervical Cancer

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## Abstract

**Objective:** To assess diagnostic accuracy of visual inspection of cervix with 3-5% acetic acid(VIA) as a screening method for early detection of cervical intraepithelial neoplasia and early cervical cancer.

**Method:** This cross-sectional study was conducted at Gynecology & Obstetrics Department Unit-1, Abbasi Shaheed Hospital, Karachi, from April 2017 to September 2018. Participants were included in the study through non-probability convenience sampling technique. Married, non-pregnant and sexually active women aged between 21-50 years were included in the study. Demographic information and relevant history was taken followed by the procedure for VIA. Acetowhite changes were noted after application of 5% acetic acid on the cervix. The result of the test was documented as positive or negative. Colposcopy was done in all VIA positive cases and suspicious cases with abnormal looking cervix. Biopsy of the cervix was taken for histopathology to assess the results of VIA. SPSS version-20 was used for statistical analysis.

**Results:** There were 323 subjects with a mean age of  $35.5 \pm 7.6$ . Out of 323 participants only 6 were found VIA positive (1.86). On histopathology, only two cases were found positive (0.62%), one early invasive cervical cancer and one CIN1. Sensitivity, specificity, positive predictive value and negative predictive value of visual inspection of cervix after acetic acid application was 100%, 57%, 40%, 100% respectively and the diagnostic accuracy was 66.7%.

**Conclusion:** Visual inspection of cervix with 3-5% acetic acid is highly sensitive, screening method for cervical cancer. It is quite simple, affordable and better screening modality for detecting cervical cancer at an early stage.

**Keywords:** Visual Inspection, Acetic Acid, Colposcopy, Cervical biopsy.

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## Introduction

Cervical cancer is the fourth most common cancer in women and second most common cancer living in less developed regions. There were 569,847 new cases and 311,365 deaths recorded globally in 2018. According to globocan 2018, the incidence rate of cervical cancer is 13.1 per

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100,000 population with a mortality rate of 6.9 per 100,000 population and a five year survival rate of 38.98%. Almost 85% of these deaths occur in low- and middle - income countries<sup>1</sup>. Cervical Intraepithelial Neoplasia (CIN) is a premalignant lesion of the cervical cancer that takes around 10-15 years to develop into an invasive cancer. Thus cervical cancer can be prevented if screened and diagnosed in this period and significant reduction can occur in morbidity and mortality<sup>2</sup>.

In low resource setting, it has been estimated that in women, life time risk of having cervical cancer varies between 21% to 41%<sup>3</sup>. In Asia, death rate due to cervical cancer is 6.4 per 100,000

women but this rate vary largely among different sub-regions<sup>4</sup>. Bangladesh and India have an annual incidence of 11,956 and 125,952 patients of cervical cancer, respectively<sup>5</sup>. In Pakistan about 5,601 cases of cervical cancer are reported each year and around 3,861 deaths occur from the disease. In females of aged between 15-44 years, cervical cancer is found second common cancer<sup>6</sup>. According to the statistics, the occurrence of cervical cancer in Pakistan is reported as 3.6%<sup>7</sup>. In the developed countries, highly organized screening programs have lessened the rate of cervical cancer by 50% in the past forty years<sup>8</sup>. On the other hand, developing countries are deficient in resources to implement these screening programs and only 20% cases are detected at early stages whereas other 80% are detected at last stages where management becomes very challenging. There are different methods recommended for cervical cancer screening including HPV test, visual inspection of cervix with acetic acid (VIA), and cytology (Pap smear)<sup>9</sup>. Colposcopy is a worldwide-accepted method for detection of early cervical cancer. It is a diagnostic procedure in which colposcope is used to provide a magnified view of the cervix. The most frequent indication of colposcopy is positive cervical screening test. Colposcope aids in detecting the abnormal area on the cervix for biopsy. In developed countries, liquid based cytology and HPV testing have been superseded by Pap smear for detection of cervical cancer whereas in developing countries these tests are expensive for cervical cancer screening<sup>4</sup>. These tests require laboratory setup, skills and entail follow up of women, which diminish the screening coverage in developing countries for cervical cancer.

World Health Organization has developed a screening program for cervical cancer known as the visual inspection of cervix with 3-5% acetic acid (VIA) to detect cervical cancer at an early stage. VIA is an alternative sensitive screening method to Papanicolaou smear test in developing countries. It is cheap, non-invasive and can be done in a low level health facility<sup>9</sup>. In the VIA screening method, 3-5% acetic acid is applied for the inspection of cervix. The presence of dull, well defined aceto white

lesion on the cervix indicates a positive test. Higher protein content is found in the premalignant lesion in contrast to normal epithelium and it becomes white after application of acetic acid. VIA does not require laboratory setup and the results are prompt. Several studies have been conducted to validate accuracy of VIA and reported that it is more sensitive but usually less specific than cytology. Due to higher resources in developed countries, 85% women have undergone screening for cervical cancer in comparison with developing countries that is only 5%. Pakistan has reported only 1.9% screening coverage for cervical cancer<sup>10</sup>.

Pakistan is a developing country and lacks in facilities and number of well-trained cytopathologist. Therefore, screening with cytology is a challenging issue in Pakistan leading to choose VIA as a screening method. VIA is not expensive and easily affordable for patients as a part of initial screening. Therefore, VIA is important in enhancing screening coverage and plays a major role in early diagnosis of cervical intraepithelial neoplasia and cervical cancer.

The aim of our study was to evaluate the diagnostic accuracy of VIA in detecting cervical intraepithelial neoplasia and cervical cancer at an early stage with less expenses to improve our screening coverage especially in resource poor areas of Pakistan to prevent adverse prognosis and mortality related with cervical cancer.

## Methods

This cross-sectional study was conducted at Gynecology and Obstetrics department unit 1of Abbasi Shaheed Hospital from April 2017 to September 2018 after getting approval from Ethical & Scientific Review Committee of Karachi Medical and Dental College. Sample size of at least 291 cases was calculated by using sample size calculator for sensitivity and specificity. Taking statistics of sensitivity of VIA 90.74% and specificity 80.99% and disease prevalence 43.20% at margin of error 6% with confidence interval 95%. In this study, 323 subjects were included. Participants were included in the study through non-probability convenience sampling tech-

nique. Women attending outpatient department of Gynae Unit 1 Abbasi Shaheed Hospital aged between 21 and 50 years, married, non-pregnant, sexually active women were included, while those women with pelvic inflammatory disease (PID), trichomoniasis or candida infections were included in the study after treatment. Women who were treated for CIN and diagnosed cases of cervical cancer were excluded. All those women who have had a pap smear in the past 3 years which was found negative were also excluded. After taking informed consent data was collected through proforma. Demographic information and relevant history was taken followed by the procedure for VIA. After explaining the procedure, women were placed in lithotomy position. Cusco's speculum was introduced into the vagina under good light source to assess cervix. Cervix was examined grossly for its size and shape, ectropion, cervical polyp, Nabothian cyst, healed laceration of the cervical lips, and signs of cervicitis. Squamocolumnar junction and transformation zone was identified. Bleeding from cervix, especially on touch and ulcerative or proliferative growth was also noted. Secretions wiped off gently. 5% acetic acid then applied on the cervix with the help of cotton swab, left for one minute for acetowhite changes. After removing the swab, cervix was examined for any white lesions, especially in the transformation zone near to the squamocolumnar junction, or dense, or non-removable acetowhite areas in the columnar epithelium. Timing of appearance of acetowhite lesion was also noted. The acetowhite lesion was also assessed for intensity of white color (shiny white, cloudy white, pale white or dull white), borders and demarcation (regular or irregular margins), uniformity of white color, location, size and number of the lesions. VIA was considered positive if definite acetowhite lesion visualized close to the squamocolumnar junction (SCJ) or if entire cervix or any growth on cervix turned out to be acetowhite, while faint or doubtful acetowhite areas were considered negative. Details were documented on the proforma. Outcome of the test results was explained to the participants, and any further need of follow-up actions. In those test was found negative, the woman was reassured and repeat testing was ad-

vised after 5 years. Colposcopy was done in all VIA positive patients and those who were VIA negative with abnormal looking cervix, bleed on touch and VIA test was found suspicious. Biopsies were taken and sent for histopathology. Histopathology was taken as reference standard for VIA results. Statistical analysis was performed by using statistical software SPSS version-20. Frequencies and percentages were calculated by all categorical variables. Mean and standard deviation (SD) was calculated for quantitative variables and sensitivity, specificity, predictive values and accuracy of VIA was calculated using standard statistical formulas.

## **Results**

In our study total no of participants were 323. Mean age of the women was  $35.1 \pm 7.6$  (range:21-50) years. Mean age at the time of marriage was  $20.7 \pm 3.4$  years. Among the participants, 177 (54.7%) were married between 15-20 years and only 1 (0.3%) was married before 15 years. Mean age at the time of first pregnancy was  $20.2 \pm 6.0$ . Out of 323 participants, 315 (97.5%) were married once while only 8 (2.47%) were married twice. Those married for more than 20 years were 74 (22.9%) and 126 (39%) were married for 11-20 years. About 19 (5.88%) had no children, 156 (48.2%) were multipara while 94 (29.1%) were grand multipara. Among presenting complains, vaginal discharge was found in 81 (25%), lower abdominal pain in 47 (14%), intermenstrual bleeding in 14 (4.3%) and postcoital bleeding in 8 (2.47%) participants. Family history of cancer was found in 12 (3.7%) including blood cancer, breast, ovarian and gastrointestinal cancer but no one had history of cervical cancer. No one was found smoker. Barrier contraception was used by 74 (22.9%), intrauterine contraceptive device (IUCD) used by 9 (2.7%) and various hormonal contraceptive methods were used by 16 (5%) of the participants. Rest of the participants either used withdrawal or no method. On examination healthy looking cervix was observed in 236 (73%) participants, in rest of the 82 (25%) cervical lesions were observed including erosion or ec-

**Table 1.** Study Characteristics (n=323)

Variables	Mean ± SD / n (n%)
Age of Patient; mean	35.1 ±7.6
21 - 30yrs	111 (34.4%)
31 - 40yrs	135 (41.8%)
41 - 50yrs	77 (23.8%)
Age the time of Marriage	20.7 ±3.4
< 15yrs	1 (0.3%)
15 - 20yrs	177 (54.79%)
21 - 25yrs	122 (37.77%)
> 25yrs	23 (7.12%)
Duration of Marriage	14.5 ±8.0
?5yrs	49 (15.2%)
6 - 10 yrs	74 (22.9%)
11 - 20yrs	126 (39%)
> 20yrs	74 (22.9%)
Age at the time of First Pregnancy	20.2 ±6.0
15 - 20yrs	155 (48%)
21 - 25yrs	133 (41.2%)
> 25yrs	35 (10.8%)
Parity No children	19(5.88%)
Primipara	54(16.7%)
Multipara	156(48.2%)
Grand-multipara	94(29.1%)
Lower Abdominal Pain	47 (14%)
Vaginal discharge	81(25%)
Inter-menstrual bleeding	14 (4.3%)
Post coital bleeding	8 (2.4%)
Married; Once	315(97.5%)
Twice	8(2.47%)
Religion; Muslim	321 (99.4%)
Non-Muslim	2 (0.6%)

**Table 2.** Outcome of VIA and Histopathology.

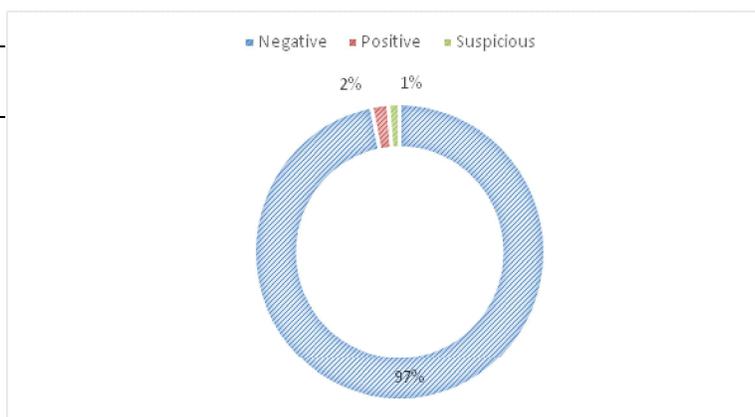
VIA (n= 323)	HISTOPATHOLOGY		
	Positive	Negative	Total
VIA	2	3	5
*Suspicious	0	4	4
TOTAL	2	7	9

VIA-Visual inspection of cervix with acetic acid.  
\*VIA negative but abnormal cervix and suspicious.

**Table 3.** Sensitivity, Specificity, PPV, NPV & Predicted Diagnostic Accuracy of VIA procedure (n=9).

Results	Value	95% C.I
Sensitivity	100%	15.81% - 100%
Specificity	57%	18.41% - 90.10%
PPV	40%	22.08% - 61.06%
NPV	100%	-
Diagnostic Accuracy	66.67%	29.93% - 92.51%

PPV=Positive Predictive Value, NPV=Negative Predictive Value.



**Fig. 1** Relative Frequency of Patients with Positive & Suspicious VIA Findings (n=323).

tropon, polyp, Nabothian cyst, 1 with irregular growth and 4 were abnormal looking cervix Table 1.

Out of 323, six cases (1.86%) were found VIA positive in which one was lost to follow up. VIA negative were 313 (96.9%) and suspicious with abnormal looking cervix were 4 (1.24%) showed in Fig.1 Colposcopy was performed in all cases of VIA positive and cases of VIA negative but abnormal looking cervix and suspicious except the case with irregular growth on cervix and bleed heavily on touch so biopsy was performed directly. Biopsy was performed in total of 9 cases including VIA positive and suspicious with abnormal looking cervix Table 2. Out of 9 biopsies, two (0.62%) were found positive while seven (2.17%) were found negative. On histopathology six cases were of chronic cervicitis, one with metaplasia and benign endocervical tissue, one CIN1 and one early invasive cervical cancer. Out of 6 VIA positive cases, 5 were multipara and only one with low parity.

Sensitivity, specificity, positive predictive value and negative predictive value of visual inspection of cervix after acetic acid application was 100%, 57%, 40%, 100% respectively and the diagnostic accuracy was 66.7% Table 3. Relative frequency of VIA positive and suspicious cases is shown in Fig 1.

## Discussion

This study was conducted to evaluate the diagnostic accuracy of visual inspection of cervix with 3-5% acetic acid (VIA) as a screening method for early detection of precancerous or cancerous lesions of the cervix.

In our study, although the sample size is not very large but out of 323 women, 6 women (1.86%) had a positive result. VIA positive rate in our study is much lower which is close to study in Nepal in 2008 where VIA positive result was 2.86% whereas it extends from 3.13% in a study by Megev et al to 41% by Ngelangel et al<sup>11</sup>. In a study in Ethiopia in 2018, the VIA positivity rate was 10.3%. The study showed that this higher rate was due to having multiple sexual partners and early age at first sexual intercourse<sup>12</sup>. In study in Vietnam, VIA test was found positive in 7.7% of cases<sup>13</sup>. In a recent study in Nepal in 2019, the VIA positive result was 20%. In this study out of forty patients 35 with abnormal cervix and 5 with abnormal pap smear so rate of VIA positivity was found higher with sensitivity of 80% and specificity of 88.5%<sup>14</sup>.

In two studies conducted in India and Bangladesh in 2017, the VIA positive results were 22% and 14% respectively<sup>5,15</sup>. The annual rate of cervical cancer is higher in India and Bangladesh as compared to Pakistan<sup>5,6</sup>. In India, VIA has been successful in preventing 22000 deaths annually due to cervical cancer (Kay, 2013)<sup>4</sup>. The prevalence of VIA positive cases is between 12.5 to 53.0%<sup>16</sup>. This large variation is because of different criteria used for test positivity along with observer training, inter observer variation, light source, presence of infection, inflammation and metaplasia. Acetowhite areas described on VIA may also represent cervicitis and HPV infection along with premalignant and malignant lesions. In two studies conducted in civil hospital, Karachi, the positive results were 8.67%<sup>17</sup> and 15.2%<sup>18</sup> respectively, while another study conducted in Lahore, VIA positive result was 23.1%<sup>19</sup>. This wide variation in VIA positive result is due to difference in interpretation. We had taken VIA positive to those with distinct well defined dense

acetowhite area. In some studies, they had taken all grades of acetowhite as positive while in study in 2015 in Karachi, they screened symptomatic population<sup>18</sup>.

The accuracy of both VIA and cytology for detecting cervical intraepithelial neoplasia varies from one setting to another. Sensitivity of VIA in previous studies ranged from 60-100% and specificity from 36.4-99%<sup>20</sup>. It is observed in many studies that VIA has higher sensitivity and higher negative predictive value than cytology but its specificity is lower for detecting cervical intraepithelial neoplasia leading to more false positive results<sup>4,16,21</sup>. In our study, sensitivity of VIA was found 100% and specificity was 57% which is consistent with study conducted in India in 2017 in which the sensitivity was 95.24% and specificity was 44.19% while in the same study sensitivity and specificity of pap smear was 90.48% and 81.40% showing VIA more sensitive but less specific for cervical cancer screening than pap<sup>15</sup>. In study in civil hospital, Karachi, 2015 where sensitivity and specificity of VIA was 81% and 92% respectively<sup>18</sup>, while study in Lahore in 2018 sensitivity and specificity of VIA was 97.67% and 84.29% respectively<sup>22</sup>. The positive predictive value (PPV) in our study was only 40% which is consistent with study in India in 2017, where PPV was 45.45%<sup>15</sup> while in previous studies it ranged from 38-90%<sup>19,2</sup>. In one study, carried out by Ardahan and Temel, in the year 2011, demonstrated 67.64% positive predictive value of VIA<sup>24</sup>, while study conducted in civil hospital, Karachi, 2015 and in Lahore 2018, it was 76.3%<sup>18</sup> and 38.18%<sup>22</sup> respectively. In present study, reason for false positive cases were chronic cervicitis and metaplasia, similar reasons were found for false positive results in other studies<sup>11,1</sup>. In study in Nepal 2008, out of 350 cases, 10 cases were found VIA positive and on biopsy chronic cervicitis was found in six cases and acute cervicitis in one case<sup>11</sup>. In study in Vietnam, the positive predictive value of VIA was 50%<sup>13</sup>, while in a recent study in Nepal in 2019, it was 51.2%<sup>14</sup> which is comparable to our study. In study in India 2017, the VIA positivity was 22% and out of 44 positive cases, 22 cases came as chronic cervicitis

on cervical biopsy<sup>15</sup>. In study in Iran in 2019, the false positive rate of VIA was 21.2% and its false negative was 4.6%. The false positive rate of VIA is increased by up to two times because of inflammation and infection. Presence of cervical polyps can also affect the positivity of VIA<sup>25</sup>.

In our study, negative predictive value (NPV) and diagnostic accuracy was 100% and 66.67% respectively which is consistent with the study in India in 2017 where NPV was 95% and overall diagnostic accuracy was 60.93%<sup>15</sup>. The negative predictive value was also found higher in other studies and it was 97.1%<sup>3</sup>, 99%<sup>18</sup> and 99.7%<sup>2</sup>. In study in Vietnam and Nepal the negative predictive values were 83.3%<sup>13</sup> and 96.87%<sup>14</sup>. The high NPV of VIA can reassure the women that they are not likely to have cervical precancerous or cancerous lesions of the cervix. In study in Vietnam, the diagnostic accuracy was 63.4% which is close to our study showing VIA has higher sensitivity but its diagnostic accuracy is still limited in cervical cancer screening.

Many trials conducted on VIA all over the world and proved this test a better alternative to cytology because it is very easy to perform, no specific equipment required, no special skill or extensive training is required. WHO recommends screen with VIA and treat with cryotherapy, or LEEP when not eligible for cryotherapy, or when feasible HPV testing followed by treatment. In Pakistan HPV testing is now available but still there is affordability issue for both cytology and HPV testing. According to WHO guidelines 2013, it has been advised to provide management instantly after positive screening. So WHO recommends, where cytology and HPV testing are not feasible, use a screening strategy with VIA method and offer treatment to the positive cases. All negative cases should be rescreened after 3-5 years. To improve compliance in low resource settings, treatment without histopathologic or colposcopy verification is considered as the most effective treatment. However, the main limitation of this test is its use in post-menopausal women because the transforma-

tion zone in these women is often inside the cervical canal.<sup>9</sup> So in Pakistan which is a resource poor country we should use VIA as screening method and treat if found positive

Our study was a hospital based study and sample size was small but VIA is a simple test that can be performed by health care provider after short training. It gives result immediately and we can offer treatment to patients at the same visit. So by this test we can improve our screening coverage to reduce morbidity and mortality associated with cervical cancer. We can exclude those who do not have disease and only those with positive results will refer for further workup. We recommend VIA at all levels including primary, secondary and tertiary care centers especially in remote areas of Pakistan. Hence, it can be accessible to every woman to cure cervical cancer at initial stages and avert its progression.

## Conclusion

In conclusion, VIA is highly sensitive screening method for cervical cancer. It is quite simple, affordable and better screening modality for detecting cervical cancer at an early stage. It can give better screening coverage for the disease in developing countries like Pakistan.

## Conflict of Interest

Authors have no conflict of interest and no grant/funding from any organization.

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