

# Evaluation of Visual Inspection of Cervix with Acetic Acid and Liquid Based in Cervical Cancer Screening with Cervical Biopsy

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## ABSTRACT

**Background:** Cervical cancer is the second most common cancer among women in developing countries. Cervical cancer generally develops slowly over a period of 10-15 years. Incidence and mortality related to cervical cancer both have declining in developed countries because of effective screening programs through Papanicolaou smear. Therefore, cervical cancer can be prevented through implementation of different methods of screening programs like visual inspection of cervix with application of acetic acid visual inspection with acetic acid, liquid based cytology and human papilloma virus deoxyribonucleic acid. The purpose of this study is to compare the efficacy of visual inspection with Acetic Acid with liquid based cytology in cervical cancer screening taking cervical biopsy as a gold standard.

**Methods:** The study was conducted at Paropakar Maternity and Women's Hospital, Kathmandu. One hundred forty four patients underwent visual inspection with acetic acid and liquid based cytology test followed by biopsy for confirmation of the lesion, when required. Data were obtained and statistically analyzed.

**Results:** Out of 144 screened patients, 62 (43.05%) were positive in visual inspection with acetic acid test. Eighteen (12.5%) cases were positive in liquid based cytology. Thirteen women were positive with both tests. Thirty-nine cases underwent histopathological examination including 13 cases who were positive in both tests. The sensitivity, specificity, positive predictive value and negative predictive value for visual inspection with acetic acid was 81.25%, 65.22%, 61.90% and 83.33%, whereas for liquid based cytology it was 100%, 91.30%, 88.89% and 94.87% respectively.

**Conclusions:** Liquid based cytology was more efficacious to diagnose atypical cells with higher sensitivity and specificity in comparison to that of visual inspection with Acetic Acid test.

**Keywords:** Cervical cancer; liquid based cytology; visual inspection with acetic acid

## INTRODUCTION

Cervical cancer is the fourth most common cancer worldwide with an estimated incidence of 5,28,000 cases and 2,66,000 deaths in 2012.<sup>1,2</sup> Whereas, it is the most or second most common cancer among women in developing countries.<sup>3</sup> Liquid based cytology (LBC) is the most common screening test for cervical cancer, as it is a non-invasive and effective method for detection of various changes in cervix and vagina. However, many developing countries do not have ample resources to implement cytology-based prevention programs which prompted the investigations of alternative low-cost screening technology such as visual inspection with acetic acid (VIA).<sup>4-6</sup> VIA has been advocated as an

alternative screening method to LBC in developing <sup>7,8</sup> VIA is a cost-effective screening method which is simple and can be performed by doctors and paramedics after a short course of training and gives instant results. The purpose of study was to compare the accuracy of VIA with LBC as a method of cancer screening, the gold standard being cervical biopsy in positive cases.

## METHODS

This comparative analysis was a cross-sectional study which was conducted in gynecology outpatient department of Paropakar Maternity and Women's Hospital for one year (August 2017- July 2018). Our study involved 144 women, who were screened for cervical

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cancer using LBC which was followed by VIA. Further, cervical biopsy was taken in those cases which showed intraepithelial lesion/Malignancy in LBCs or who were positive in VIA.

Women attending the outpatient department with gynecological problems like vaginal discharge, menorrhagia, intermenstrual bleeding, postcoital bleeding, postmenopausal bleeding and chronic pelvic pain and women who are sexually active or on oral contraceptives were included in this study. Pregnant women, women with active vaginal bleeding, frank growth in cervix, diagnosed case of cervical cancer or CIN and prior hysterectomy were excluded from this study.

The purpose, procedure, risks and benefits of VIA and LBC were explained to the woman beforehand and the verbal consent for the procedure was taken by the Gynecologist. Also, ethical approval was taken from the IRC of the hospital. The smears were timed so that they were not collected during the menstrual periods and the patients did not have intravaginal medications 48 hours before the test. Patients were placed in a lithotomy position, per speculum examination of cervix and vagina was done under direct light source. Cervix was exposed and examined for any gross abnormality. The squamocolumnar junction was visualized and the sample was taken by "cervex" brush, the tip of which was broken and placed into the alcohol based preservative fluid and was sent to the laboratory.

The slides were processed accordingly and a thin layer of cervical cells without debris was made on a glass slide. The smears were reviewed by Pathologists. LBC smears were reported as negative, reactive changes or atypical cells of undetermined significance (ASCUS) were considered to be negative screens. Smears classified as low grade squamous intraepithelial lesion (LSIL) or high grade squamous intraepithelial lesions (HSIL) and above were considered as positive screens.

After taking sample for cytology, a solution of 5% acetic acid was then applied to cervix using a cotton swab and positive or negative test was decided after one minute of application of acetic acid, during which time any area that became faintly white simply due to inflammation or physiological cell changes (metaplasia) will recede. When any of the findings like a well-defined thick opaque acetowhite lesion close to squamocolumnar junction or acetowhite area touching the transformation zone was observed, the result was reported as VIA-positive. On the other hand, if no persistent acetowhite lesion, faint and bluish white translucent acetowhite lesion or a

white-line indicative of squamocolumnar junction was observed, it was reported as VIA-negative.

If LBC was positive and VIA positive in the first setting, colposcopy directed biopsy was taken at a later visit and were reviewed by Pathologist. The histology of cervical biopsy was taken as a gold standard to compare the performance of VIA and cytology. Estimation of sensitivity, specificity and predictive values was performed on the women who had a final diagnosis of various grades of cervical dysplasia.

Data were entered and analyzed on SPSS software version 24. Mean and standard deviation were presented for age of the patients. Sensitivity, specificity, positive predictive value and negative predictive value of LBC and VIA were calculated separately using the standard statistical formulas.

## RESULTS

One hundred and forty four women were included in this study. Mean age of study population was  $38.93 \pm 9.28$  with a range from 17 to 70 years. One hundred and twenty three (85.4%) belonged to reproductive age and twenty one (14.6%) were post-menopausal.

The highest percentage of positive cases 7 (4.9%) in both VIA and LBC was in the age group of 36-45 years.

The most common presenting symptom was whitish discharge accounting 63(43.75%) of the total cases.

Of the 144 patients, 62 (43.05%) cases were screened positive in VIA test. In LBC, 18 (12.5%) cases were abnormal: out of which, 8 had HSIL, 10 had LSIL. 126 cases were negative in LBC, out of which 45 cases were normal, 6 cases had ASCUS and 75 showed reactive changes.

Thirteen women were positive in both tests, 5 cases were positive in LBC only and 49 cases were positive in VIA test only.

A total of 39 cases underwent histopathological examination. It included 13 women with both tests positive, out of which, two cases showed Cervical intraepithelial lesion- I (CIN-I), one case showed CIN-II, nine cases showed CIN-III and one case showed squamous cell carcinoma. Eight cases had VIA test positive but LBC was negative and histopathological examination showed cervicitis. Five cases were positive in LBC but VIA negative and histopathological examination showed CIN I in three cases and cervicitis in two cases. And 13 of the cases were all three tests negative.

On comparing the results of LBC with biopsy, it was found that LBC was positive in 18 cases and 16 were biopsy proven. Thirteen normal LBCs also showed normal in histopathological examination. LBC showed two abnormal cases which were normal in histopathological examination, thus showing a sensitivity of 100%, specificity of 91.30%, positive predictive value of 88.89%, negative predictive value of 100% for cytology (Figure 1, Table 2). And when the results of VIA was compared with biopsy, it was found that VIA was positive in 62 cases. Out of this, 13 were biopsy proven and 8 cases were normal/cervicitis in histopathological examination, whereas 3 VIA negative cases were positive in histopathological examination. 15 of the VIA negative cases were also normal in histopathological examination. Thus, VIA showed a sensitivity of 81.25%, specificity of 65.22%, positive predictive value of 61.90%, negative predictive value of 83.33% .

Table 1. Comparison of LBC with biopsy.

Surepath LBC (n=39)	Biopsy (n=39)					
	Normal/ Cervicitis	CIN I	CIN II	CIN III	CIS	SCC
Normal	4					
Reactive	9					
Atrophic	2					
ASCUS	6					
LSIL	2	5	1			
HSIL				9		1

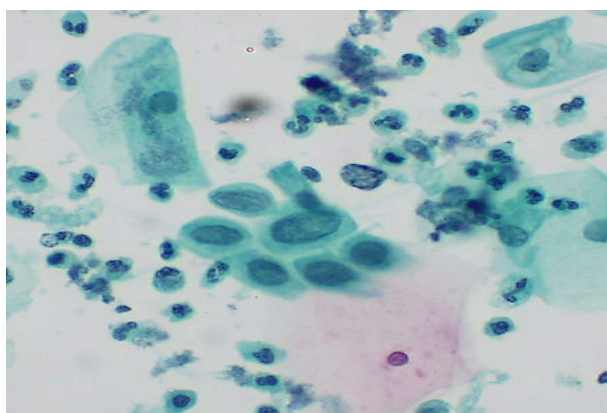


Figure 1. Surepath smear showing.

Table 2. Comparison of VIA with Biopsy.

VIA (n=39)	Biopsy (n=39)					
	Normal/ Cervicitis	CIN I	CIN II	CIN III	CIS	SCC
Positive	8	2	1	9		1
Negative	15	3				

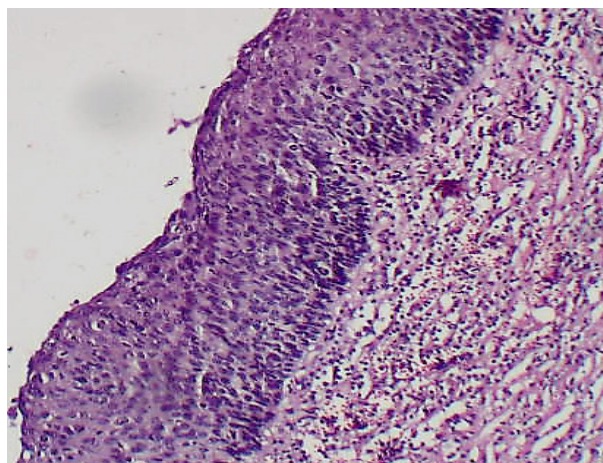


Figure 2. H&E section showing cervical high grade squamous intraepithelial intraepithelial lesion-III (CIN-III). lesion (HSIL).

## DISCUSSION

Cervical cancer is one of the most common malignancies among women worldwide. Routine-screening program has reduced mortality from squamous cell carcinoma, which comprises 80-90% of cervical cancers.<sup>1</sup>

The mean age group of our study was 38.93±9.28 which was similar to the study done by Naz et al<sup>1</sup> and Basu et al.<sup>9</sup> The most common presenting symptom was per vaginal whitish discharge which was similar to the report of Mahmud et al<sup>4</sup> as well as Rana et al.<sup>5</sup> But, in the study conducted by Khan et al<sup>10</sup>, the most common presenting symptom was lower abdominal pain which was followed by vaginal discharge. Whereas, in the study done by Hedge et al<sup>7</sup>, most common presenting symptom was menstrual irregularities.

Women with the age group of 35-46 years had the highest percentage of VIA positive and abnormal LBC (8.3%). Similar results were obtained in the study conducted by Hegde et al<sup>7</sup> and Dawood et al.<sup>11</sup> which showed 11.5% and 3.7%, respectively.

Our study compared VIA and LBC with histopathological examination which is considered as the gold standard. In this study, biopsy was done in all cases with positive LBC strongly, VIA positive cases and 13 (9.02%) cases negatives in both VIA and LBC but clinically suspicion cervix.

In our study, the sensitivity of VIA was 81.25%, specificity was 65.22%, positive predictive value was 61.90% and negative predictive value was 83.33%. The sensitivity, specificity, PPV and NPV of various studies are given in Table 4.

**Table 4. Comparison of efficacy of VIA in various studies.**

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present study	81.25	65.22	61.90	83.33
Mahmud et al <sup>4</sup>	78.5	99.3	84.6	98.6
Rana et al <sup>5</sup>	93	90	62.5	98
Hegde et al <sup>7</sup>	70.8	95	62.9	96.5
Rani et al <sup>12</sup>	94.55	63.64	86.67	82.35
Nakash et al <sup>13</sup>	82	68	77	75
Albert et al <sup>14</sup>	60	94.4	50	99.4

In our study, the sensitivity of LBC was 100%, specificity was 91.30%, positive predictive value was 88.89% and negative predictive value was 94.87%. The sensitivity, specificity, PPV and NPV of various studies are given in Table 5.

**Table 5. Comparison of efficacy of LBC/Conventional pap smear in various studies.**

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present study	100	91.30	88.89	94.87
Rani et al <sup>12</sup>	94.55	86.36	94.55	86.36
Singh et al <sup>15</sup>	100	97.29	83.33	100
Singh et al <sup>16</sup>	75.65	100	100	89.45
CC et al <sup>17</sup>	100	100	100	100
Sherwani et al <sup>18</sup>	97.6	50.0		
Hussein et al <sup>19</sup>	92	76	57	96
Batista et al <sup>20</sup>	66.67	100		

## CONCLUSIONS

Though VIA is a simple and feasible method for cervical cancer screening in developing countries, our study has concluded that LBC was more effective as it showed higher sensitivity, specificity, positive predictive value and negative predictive value in comparison to that of VIA.

## REFERENCES

- Naz U, Naseeb S, Shuja S. Concordance between visual inspection with acetic acid test and pap smear in detection of cervical Cancer. *J Surg Pak Int.* 2016;21 (1).[\[FullText\]](#)
- Saleh HS, Hameid AAAE, Mowafy HE, Sherif HE, Abdelsalam WA. Visual inspection of the cervix with (acetic acid or lugol's iodine) for cervical cancer screening. *Cerv Cancer Open Access.* 2016;1(1).[\[FullText\]](#)
- Sankaranarayanan R, Budukh AM, Rajkumar R. Effective screening programmes for cervical cancer in low-middle-income developing countries. *Bull World Health Organ.* 2001;79 (10).[\[FullText\]](#)
- Mahmud G, Tasnim N, Iqbal S. Comparison of visual inspection with acetic acid and pap smear in cervical cancer screening at a tertiary care hospital. *J Pak Med Assoc.* 2013;63.[\[FullText\]](#)
- Rana T, Zia A, Sher S, Tariq S, Asghar F. Comparative evaluation of PAP smear and visual inspection of acetic acid (VIA) in cervical cancer screening program in Lady Willingdon Hospital, Lahore. *Spec Ed Ann.* 2010;16. NO.1. <https://doi.org/10.21649/akemu.v16i1%20SI.171>
- Longatto-Filho A, Maeda MYS, Roteli-Martins C, Naud P, Derchain SFM, Hammes L, et al. Conventional Pap smear and liquid-based cytology as screening tools in low-resource settings in Latin America. *Acta Cytol.* 2005;49. [\[PubMed\]](#)
- Hegde D, Shetty H, Shetty PK, Rai S. Diagnostic value of acetic acid comparing with conventional Pap smear in the detection of colposcopic biopsy-proved CIN. *J Can Res Ther [serial online]* 2011 [cited 2020 June 13];7:454-8. Available from: <https://www.cancerjournal.net/text.asp?2011/7/4/454/92019>
- Onwuka CO, Ekanem I-OA. The utility of visual inspection with acetic acid in cervical cancer screening. *Edelweiss Cancer Open Access.* 2017;1(1):3-10.
- Basu PS, Sankaranarayanan R, Mandal R, Roy C, Das P, Choudhury D, et al. Visual inspection with acetic acid and cytology in the early detection of cervical enoplasia in Kolkata, India. *Int J Gynecol Cancer.* 2003;13:626-32. <http://dx.doi.org/10.1136/ijgc-00009577-200309000-00009>
- Khan S, Jha R, Pant PR. Accuracy of cytology, visual inspection with acetic acid or lugol's iodine in cervical cancer screening. *N J Obstet Gynaecol.* 2007;2(2):48-53. <https://doi.org/10.3126/njog.v2i2.1455>
- Dawood R, El-Tahmoudy M. Visual inspection techniques versus Pap smear in screening for premalignant and malignant lesions of the cervix in Menoufia governorate, Egypt. *Tanta Med J.* 2015;43(3):108-12. [\[FullText\]](#)
- Rani SA, Rama K. Comparative analysis of visual inspection with acetic acid and lugol's iodine and liquiprep TM in cervical cancer screening with cervical biopsy as gold standard. *IOSR J Dent Med Sci.* 2016;(7):54-62.
- Nakash A, Al-Assadi AF, Hussein AL-Safi ZA, Al-Diab JM. Naked eye visual inspection with acetic acid versus cervical

- smear as a screening test for cervical intraepithelial neoplasia. *Res Rep Gynaecol Obstet.* 2017;1(2):1-8.
14. Albert S, Oguntayo O, Samaila M. Comparative study of visual inspection of the cervix using acetic acid (VIA) and Papanicolaou (Pap) smears for cervical cancer screening. *E cancer Med Sci.* 2012 ;6:262. [\[PubMed\]](#)
  15. Singh U, Anjum, Qureshi S, Negi N, Singh N, Goel M, et al. Comparative study between liquid-based cytology and conventional Pap smear for cytological follow up of treated patients of cancer cervix. *Indian J Med Res.* 2018;147(3):263–7. [\[PubMed\]](#)
  16. Singh A, Joshi C, Kujur P, Chandrakar K, Shrivastava S. Liquid-based cytology versus conventional cytology for evaluation of cervical cytology in a tertiary care center of Chhattisgarh. *Int J Sci Study.* 2016;4(9):161-7.
  17. CC C, M A, OM M. A Comparative study on the use of liquid based cytology and conventional Pap smear in cervical screening. *J Med Med Res.* 2014;2(4):40–50.
  18. Sherwani RK, Khan T, Akhtar K, Zeba A, Siddiqui F, Rahman K, et al. Conventional Pap smear and liquid based cytology for cervical cancer screening- a comparative study. *J Cytol.* 2007 Sep 17;167–72. [\[FullText\]](#)
  19. Hussein T, Desai M, Tomlinson A, Kitchener HC. The comparative diagnostic accuracy of conventional and liquid-based cytology in a colposcopic setting. *Int J Obstet Gynaecol.* 2005;112:1542–6. <https://doi.org/10.1111/j.1471-0528.2005.00699.x>
  20. Batista Stabile SA, Ramos Evangelista DH, Talamonte VH, Lippi UG, Coelho Lopes RG. Comparative study of the results from conventional cervico-vaginal oncotoc cytology and liquid-based cytology. *Einstein (Sao Paulo).* 2012;10(4):466–72. <https://doi.org/10.1590/S1679-45082012000400013>