

Comparison of Visual Inspection with acetic acid and Pap smear in cervical cancer screening at a tertiary care hospital

Ghazala Mahmud, Nasira Tasnim, Saima Iqbal

Abstract

Objective: To determine the accuracy of visual inspection with acetic acid in comparison with Pap smear against colposcopic directed biopsy, for detection of pre-cancerous lesion.

Methods: The comparative cross-sectional study was conducted at the Maternal and Child Health Centre (MCHC), Pakistan Institute of Medical Sciences (PIMS), Islamabad, from January to December 2010. Every married women with age range 19 to 51 years underwent conventional cytology and visual inspection with 5% acetic acid. Distinct acetowhite areas were taken as positive, while cervical intra-epithelial neoplasia on cytology was labelled as Pap smear positive. Colposcopic directed biopsy was taken as the gold standard. SPSS 13 was used for statistical analysis.

Results: Of 519 subjects, 70(13.4%) were screened positive and 29(5.6%) were biopsy positive for cervical intra-epithelial neoplasia. Of these, 26(37.1 %) were positive on visual inspection; 14 (20 %) on cytology; and 30 (42.8%) on combined test. The sensitivity of visual inspection was 78.5% vs 61.1% for Pap smear ($p<0.001$). The specificity of visual inspection was 99.3% vs 99.4% for cytology ($p<0.1$). Significantly higher sensitivity and specificity was found for the combined test than either of the two alone; 93.1% and 99.1% respectively ($p<0.001$). The positive predictive value of visual inspection vs pap was 84.6% vs 78.5% ($p<0.001$) and negative predictive value was 98.6% vs 96.5% ($p<0.1$). Both values of combined test were significantly higher than either of the two tests alone ($p<0.01$).

Conclusion: Visual inspection with acetic acid has significantly higher sensitivity than Pap smear and may replace pap smear as a primary screening tool for universal screening. Combined test with higher predictive accuracy may be used for opportunistic screening.

Keywords: Visual inspection, Acetic acid, Pap smear. (JPMA 63: 1013; 2013)

Introduction

Cervical cancer remains one of the leading causes of cancer-related deaths among women. Worldwide about 500,000 new cases are reported every year. Of these, 300,000 end up in mortality. Almost 80% of these cases occur in low-resource countries.¹ Cervical cancer has been found to be the most prevalent malignant neoplasm among women in developing countries.² In Pakistan researched evidence puts 3.6% of total female cancers to be of cervical origin, affecting women mainly in fifth and sixth decades of life.³

Incidence and mortality related to cervical cancer are both declining in developed countries because of effective screening programmes through Papanicolaou (Pap) smear.^{4,5} The test is successful in detection of pre-cancerous lesion as well as early stage of cervical cancer and is widely used in developed countries.^{6,7} The pap smear screening is not replicable in developing countries because of its cost, scarcity of trained cytopathologist and multistage nature of the procedure. These potential

difficulties in cytology-based programme have prompted the investigations of alternative low-cost screening technology such as visual inspection with acetic acid (VIA). The result of VIA is immediately available and does not require lab support. Numerous studies have been conducted on its accuracy and its ability to detect pre-cancerous cervical lesions when compared with Pap smear. The outcome evaluation of these studies indicate that sensitivity of VIA ranges from 66% to 96%, and specificity between 64% and 98%.⁶⁻¹⁰ Authors comparing cytology with VIA have concluded that overall usefulness of VIA compares favourably with Pap test.¹⁰ Majority of these are conducted in primary healthcare facility and thus are not applicable to tertiary care hospitals.¹¹

VIA was introduced in the Maternal and Child Health Centre (MCHC) at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, in 2006 as a cervical screening tool.

However, the test is being used in conjunction with Pap smear and has not yet been able to replace the Pap test due to lack of controlled trials. This study was conducted to determine the potential of VIA to supplement or replace Pap smear at our tertiary care hospital where all modalities, including Pap smear and colposcopy, are available and yet majority of patients are lost to followup

.....
Maternal and Child Health Centre, Unit-I, Pakistan Institute of Medical Sciences, Islamabad.

Correspondence: Nasira Tasnim. Email: whcg82@hotmail.com

even before submission of their Pap smear samples.

Subjects and Methods

All married and sexually active women between 19 and 50 years of age presenting to the out-patient department at MCHC, PIMS, from January to December 2010 were recruited in the study after taking informed consent. Women who were pregnant, had history of abnormal cytology, post-menopausal patients, previous treatment for cervical intra-epithelial neoplasia (CIN) or obvious invasive cancer at the time of clinical evaluation or with severe cervicitis were excluded from the study.

The procedure was performed at the out-patient gynaecology clinic. For the purpose of the test, the patient was placed in lithotomy position and a lubricated speculum was inserted into the vagina under direct light source. Cervix was exposed and examined for any gross abnormality. Excess mucous and discharge was removed with swab. The squamocolumnar junction (SCJ) was visualised in entire extent and Pap smear was taken using conventional wooden Ayers spatula. A swab soaked in 5% acetic acid was applied to the cervix for one minute. It was then inspected for acetowhite area(s) adjacent to SCJ. The Pap smear samples were submitted by the patient to MCHC laboratory located at a distance of about 100 metres and lab number was reported by her to the cervical clinic for retrieval of reports if needed. Patients were asked to report back in the cervical clinic once the Pap smear report was available.

VIA test was labelled as positive when a well-defined opaque acetowhite lesion was found abutting or close to SCJ, while cytology was considered positive if reported as CIN or worse lesions. Colposcopy and directed biopsy was performed at the cervical clinic located under the same roof if either/both of the tests were positive or clinical suspicion of cervical lesion was found. A pre-designed proforma was filled by the evaluator which included general information about the subject, clinical findings at pelvic evaluation, results of VIA and results of colposcopy when indicated. Data was analysed using SPSS 13. Numeric and proportional distributions were calculated for sociodemographic variables. Sensitivity, specificity and predictive values of VIA and Pap smear were calculated separately and combined, using standard statistical formulas. Both the tests were than compared. Value of $p < 0.05$ was taken as significant.

Results

During the study period, 700 women were recruited. Of these, 519(74.2%) were analysed, while 181(25.8%) were excluded as they failed to submit Pap smear samples. The mean age was 32.2 ± 5.6 years and majority ($n=226$; 43.5%)

Table: Sociodemographic characteristics of study population.

Variables	Number	Percentage
Parity		
Nulliparous	8	1.50%
P1-4	226	43%
P5 and more	286	55.50%
Occupation		
House wife	384	73.80%
Teacher/Students	93	17.80%
Others	43	8.20%
SE status		
Middle class	231	44.40%
Poor	289	55.50%

SE= Socio Economic.

were multipara and housewives (Table-1). The major presenting complaint was vaginal discharge ($n=348$; 67%) followed by lower abdominal pain.

Of the 519 patients 70(13.4%) were screened positive; 29(41.4%) biopsy positive, and 41(58.5%) biopsy negative. Of the screened positive cases, 14(20%) were positive for Pap smear only; 26(37.1%) on VIA only; and 30 (42.8%) were positive on both the tests (Figure-1). The sensitivity

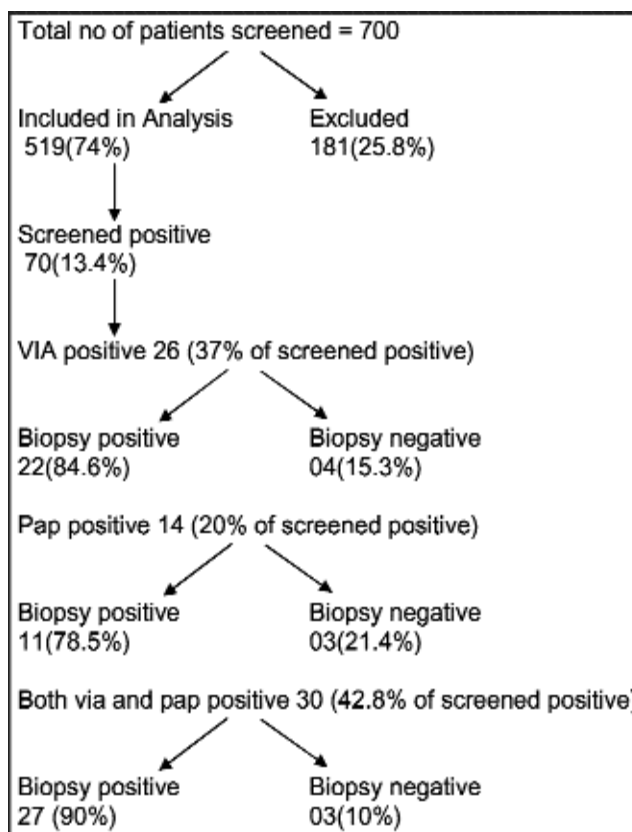


Figure-1: Distribution of screen positive and biopsy positive subjects.

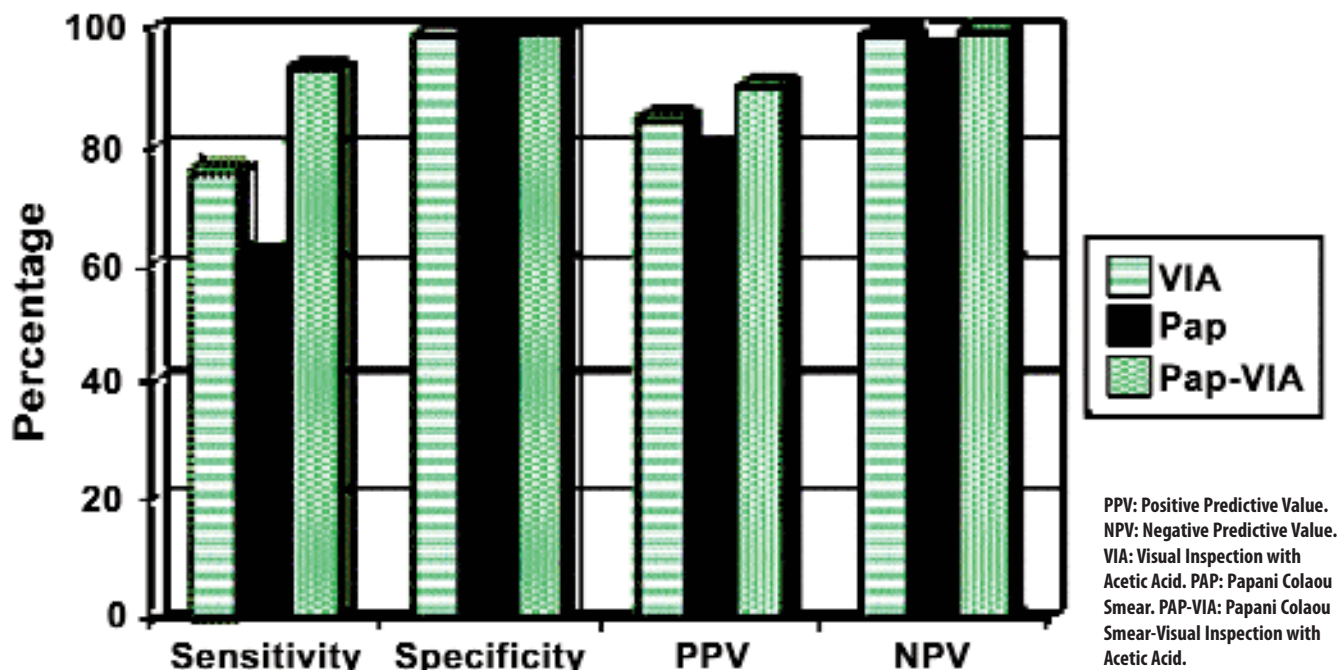


Figure-2: Accuracy of VIA versus Pap smear versus combined test.

of VIA versus Pap smear was (75.8% vs 61.1%; $p < 0.001$), (Figure-2). The specificity of VIA versus Pap smear was 99.3% vs 99.4% ($p < 0.1$). The sensitivity and specificity of combined test (Pap + VIA) was 93.1% and 99.3% respectively ($p < 0.01$). The positive predictive value (PPV) of VIA vs Pap test was 84.6% vs 78.5% ($p < 0.001$) and that of the combined test was 90% ($p < 0.0001$). Negative predictive value (NPV) of VIA vs Pap was 98.6% vs 96.5% ($p < 0.1$) while for the combined test it was 99.5% ($p < 0.01$).

Discussion

Because of its rapidity of performance and simplicity of the test, VIA has emerged as a promising alternative to Pap smear in the developing countries. Some previous reports have suggested that the test can achieve similar or better results than Pap smear in the detection of CIN. Our study revealed that VIA had significantly higher sensitivity than Pap smear 75.8% vs. 61.1% in biopsy positive cases. The sensitivity of VIA versus Pap smear in this regard has been variously reported as 31.6% vs 78.2%; 57.4% vs 79%; 59.7% vs 57.4%; and 93% vs 83% respectively.¹²⁻¹⁵ One of the reasons for such varied results is the experience and level of healthcare provider. High sensitivity of VIA reported in our study is attributed to experience of providers. The minimum level of VIA service provider was Third Year residents who were trained in the colposcopy clinic for three months before performing the test independently. This finding highlights the importance of training and experience for the

performance of visual evaluation. The issue is of utmost importance while developing screening protocols in remote areas where we must ensure adequate training and volume of evaluations to maintain the expertise of health worker before performing the test independently.

Specificity of VIA in our study was 99.1% vs. 99.4% for Pap smear. The findings are similar to other studies conducted locally and internationally. The reported specificities of both tests have been 87% vs 86%; 85% vs 93%; and 88.4% vs 98.6% respectively.¹³⁻¹⁷ The reason for false positive cases in our study was chronic inflammation of cervix. Similar reasons have been coated in other studies in addition to experience of VIA provider.¹⁸⁻²⁰

It is important to highlight that the sensitivity, specificity and predictive accuracy of combined test were significantly higher than either of the two tests alone. Thus in low-resource countries VIA can be utilised in two ways, for replacing the Pap smear for universal screening and complementary to Pap smear for opportunistic screening. In a tertiary care hospital where Pap smears is a norm, but its low sensitivity is the major issue, incorporation of VIA may improve detection rate of CIN and also provide quick results in case the patient is lost to follow-up as was seen in 26% of our cases. Similar recommendations have been made by other authors based on their results.²¹

One of the major concerns related to VIA screening

programme is a high false positive rate. Under the circumstances see-and-treat approach adopted at one-stop clinic cannot be implemented at our setup due to the potential hazard of over-treatment. The referral for colposcopy remains a better option before any surgical intervention. In places where colposcopy is not available under the same roof, combined test with better specificity is superior to single test. Other authors have suggested addition of visual inspection with lugols iodine (VILLI), visual inspection with acetic acid under magnification (VIAM) or human papilloma virus (HPV) testing as complementary test to improve specificity of VIA.²¹

The negative predictive value (NPV) of VIA in our study was 98.6%. Similar results were found in other local and international studies, conveying that if the test result is negative, women can be reassured and safely sent home.³

The study is limited by the fact that it was an opportunistic screening conducted in a population presenting with various symptoms. Such a high incidence of CIN (5.5%) may be an over-reflection of the disease in an otherwise low-risk population. Another local study conducted at a tertiary care hospital has shown an even higher incidence of CIN (16%) in hospital-based population probably due to similar reasons. Universal screening at a larger scale may depict a more accurate incidence of CIN in low-risk population. Incidence of CIN in this subset of population has been reported as 1.7% and 1.8% respectively.^{21,22}

Conclusion

Due to its rapidity of performance, VIA diminishes the probability of losing women before they are appropriately followed up and treated. Because of its low cost, better sensitivity and less complex nature of procedure, VIA can replace Pap smear as the primary screening tool for universal screening. However, for opportunistic screening, with high incidence of CIN, VIA may be used in combination with Pap smear due to high predictive accuracy of the combined test.

Acknowledgements

We are grateful to our postgraduate residents for ensuring optimum screening and meticulous record-keeping. We are also thankful to LHVs Ms Shahida Parveen and Ms Rubina who provided every possible support in the gynaecology and cervical clinics respectively, to Miss Ather Syed for helping in literature search, and Mr Mohammad Afzal and Mr Mohammed

Shafiq Arif for statistical assistance.

References

1. Sankaranarayanan R, Budukh AM, Rajkumar R. Effective screening programmes for cervical cancer in low- and middle-income developing countries. *Bull World Health Organ* 2001; 79: 954-62.
2. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001; (37 Suppl 8): S4-66.
3. Abbasi AN, Zahid S, Bhurgri Y, Ali N, Karsan F. Nasopharyngeal carcinoma - an update of treatment and acute radiation induced reactions from a tertiary-care hospital in Pakistan. *Asian Pac J Cancer Prev* 2011; 12: 735-8.
4. Haydaroglu A. Epidemiology in gynaecologic cancers. *Izmir, Turkey: Gynaecologic Oncology Symposium*; 2004.
5. Yuan CC, Ng HT, Wang PH. New strategies and advances in the management of cervical carcinoma. *Gan To Kagaku Ryoho* 2002; (29 Suppl 1): 143-9.
6. ACCP; EngenderHealth; IARC; JHPIEGO; PAHO; PATH. Pap smears: an important but imperfect screening method. Seattle, WA: PATH Publications; 2002.
7. Losell K, Dejmek A. Comparison of Papnet-assisted and manual screening of cervical smears. *Diagn Cytopathol* 1999; 21: 296-9.
8. Singh V, Sehgal A, Parashari A, Sodhani P, Satyanarayana L. Early detection of cervical cancer through acetic acid application - an aided visual inspection. *Singapore Med J* 2001; 42: 351-4.
9. Visual inspection with acetic acid for cervical-cancer screening: test qualities in a primary-care setting. University of Zimbabwe/JHPIEGO Cervical Cancer Project. *Lancet* 1999; 353: 869-73.
10. Tayyeb R, Khawaja NP, Malik N. Comparison of visual inspection of cervix and Pap smear for cervical cancer screening. *J Coll Physicians Surg Pak* 2003; 13: 201-3.
11. Gaffikin L, Lauterbach M, Blumenthal PD. Performance of visual inspection with acetic acid for cervical cancer screening: a qualitative summary of evidence to date. *Obstet Gynecol Surv* 2003; 58: 543-50.
12. 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. *Special Edition Annals of King Edward Medical University* 2010; 16: 104-7.
13. Arbyn M, Sankaranarayanan R, Muwonge R, Keita N, Dolo A, Mbalawa CG, et al. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. *Int J Cancer* 2008; 123: 153-60. doi: 10.1002/ijc.23489.
14. Gravitt PE, Paul P, Katki HA, Vendantham H, Ramakrishna G, Sudula M, et al. Effectiveness of VIA, Pap, and HPV DNA testing in a cervical cancer screening program in a peri-urban community in Andhra Pradesh, India. *PLoS One* 2010; 5:e13711. doi: 10.1371/journal.pone.0013711.
15. Shashtri SS, Dinshaw K, Amin G, Goswami S, Patil S, Chinoy R, et al. Concurrent evaluation of visual, cytological and HPV testing as a screening methods for the early detection of cervical neoplasia in Mumbai, India. *Bull World Health Organ* 2005; 83: 186-94.
16. Ardahan M, Temel AB. Visual inspection with acetic acid in cervical cancer screening. *Cancer Nurs* 2011; 34: 158-63.
17. Eftekhar Z, Rahimi-Moghaddam P, Yarandi F, Brojerdi R. Accuracy of visual inspection with acetic acid (VIA) for early detection of cervical dysplasia in Tehran, Iran. *Asian Pac J Cancer Prev* 2005; 6: 69-71.
18. Goel A, Gandhi G, Batra S, Bhambhani S, Zutshi V, Sachdeva P. Visual inspection of the cervix with acetic acid for cervical intraepithelial lesions. *Int J Gynaecol Obstet* 2005; 88: 25-30.