



COMPARISON OF DIAGNOSTIC ACCURACY OF PAPANICOLOU (PAP) SMEAR AND VISUAL INSPECTION USING ACETIC ACID (VIA) IN SCREENING OF CERVICAL CARCINOMA, TAKING BIOPSY AS GOLD STANDARD.

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ABSTRACT... Study Design: Cross-sectional descriptive study. **Setting:** Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur. **Period:** 05 August 2016 to 05 Feb 2017. **Material & Methods:** A total of 228 suspected patients of cervical carcinoma and age of 20-50 years were included. Patients with acute cervicitis, pregnant females, h/o abnormal cytology and obvious lesion on cervix were excluded. All the patients were underwent papanicolaou (PAP) smear and visual inspection using acetic acid. The results of papanicolaou (PAP) smear and visual inspection using acetic acid (VIA) were compared with cervical biopsy report. **Results:** In 110 papanicolaou (PAP) smear positive patients, 97 were True Positive and 13 were False Positive. Among, 118 papanicolaou (PAP) smear negative patients, 18 were False Negative whereas 100 were True Negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of papanicolaou (PAP) smear in screening of cervical carcinoma was 84.35%, 88.50%, 88.18%, 84.75% and 86.40% respectively. In 114 visual inspection using acetic acid (VIA) positive patients, 95 were True Positive and 19 were False Positive. Among, 114 visual inspection using acetic acid (VIA) negative patients, 20 were False Negative whereas 94 were True Negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of visual inspection using acetic acid (VIA) in screening of cervical carcinoma was 82.61%, 83.19%, 83.33% 82.46% and 82.89% respectively. **Conclusion:** This study concluded that papanicolaou (PAP) smear and visual inspection using acetic acid (VIA) in screening of cervical carcinoma are highly sensitive, accurate and having almost equal diagnostic accuracy.

Key words: Cervical Cancer, Histopathology, PAP Smear, Sensitivity, Visual Inspection.

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INTRODUCTION

Aberrant and unopposed growth of cells from any origin that have the ability to invade and spread to other body parts is called malignant neoplasia and when the origin is from cervix it is termed as Cervical malignancy.¹ Lower back ache, intermenstrual bleeding, pelvic pain, post coital pain and bleeding are the symptoms that point the diagnosis. Pain is attributed to nerve involvement.² Human papilloma virus (HPV) infection is the most common cause of cervical malignancy as much as 90% of the patients have Human papilloma virus infection however not all of the people who have Human papilloma virus infection develops cervical malignancy.³ Risk factors other than human papilloma virus infection

are immuno compromised state, smoking, multiple sexual partners, multiparty, use of COCPS and young age at first intercourse.⁴ Cervical malignancy has the edge over other malignancies in that is to some extent preventable where many other malignancies do not have this potential. This is due to the fact that cervical malignancy has a premalignant phase that takes 10 to 20 years to become malignant and this is the time period in which this pre invasive disease can be diagnosed and treated to prevent the progression to malignant disease. This diagnosis is relatively inexpensive and easily accessible.⁵ By strictly adhering to the cervical malignancy screening programme United States and most other developed countries have reduced the

incidence of cervical malignancy markedly. This screening programme is well organized, cost effective, accessible, acceptable and detects early premalignant stage of disease, this and avoiding other risk factors have been the reason of reducing the incidence of cervical malignancy and associated mortality.⁶

PAP smear cytology has been used as gold standard for a long period of time to screen for cervical cancer. It has reduced the incidence of cervical malignancy by 70 to 90% and mortality by 90%.⁷ Pap smear screening programme although very effective and suitable for the developed world but when applied to developing countries it has few shortcomings including need of expertise, financial burden due to need of histopathology, lack of trained cytopathologist and lack of follow up by the patients.⁸ To combat these problems another low cost and one step procedure has been adopted i.e visual inspection using acetic acid (VIA). VIA gives a on spot diagnosis and does not require histopathological cytological staff and expertise.⁹ Work has been going on to establish accuracy and ability of VIA to detect pre invasive cervical disease. Many comparative studies have been conducted for this purpose. Sensitivity was found to be comparable in one of the study i.e 71.4% and 78.6 and specificities were 97.8% and 92.6% for VIA and PAP smear respectively, Positive predictive values were 76.9% and 52.4% while negative predictive values were 97.1% and 97.7% respectively.¹⁰

In one study, VIA was 60% specific, 94.4% specific with positive predictive value of 50%, negative predictive value of 99.4%, and was found to be 98.6% accurate. PAP smear on the other hand was 60% sensitive, 100% specific positive predictive value of 100% and negative predictive value of 99.4% and accuracy of 99.4%.⁸

In past there was a controversy among the sensitivity and specificity of PAP smear and VIA to screen for cervical malignancy. The sample size was small in previous studies so there was need to conduct a study on large population to resolve the controversies. Local data was deficient so this study was conducted. The results of this study

would be applied to our general population to benefit from a safe, cheap and easily accessible screening programme without the need of cytologist and histopathologist in our limited resource population.

MATERIAL AND METHODS

It was a descriptive, Cross-sectional study done at Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur.

228 suspected cases of cervical carcinoma were evaluated with 95% confidence level, expecting cervical malignancy in 58%¹¹ having sensitivity of 78.6%¹⁰ with 7% margin of error and specificity 92.6%¹⁰ with 5% margin of error of visual inspection using acetic acid (VIA) in screening of cervical malignancy. Non-probability, consecutive sampling was done to select the cases. Patients included in study were 20-50 years of age, married females multipara of 1-5 having suspicion of cervical cancer while Pregnant females (assessed on ultrasonography), with Previous history of abnormal cytology or history of treatment for cervical intra-epithelial neoplasia (CIN) and patients with suspicion of acute cervicitis (assessed on history and per speculum examination) and Patients with gross lesion on cervix (assessed on examination) were excluded from study, Patients not willing to be included for this study were also excluded.

After taking informed consent and history of the patient, every patient was put in lithotomy position, per speculum examination for visualization of cervix and vagina was done. Squamocolumnar junction was visualized to rule out any obvious lesion. PAP smear was taken and sent for cytology, Then 5% acetic acid was applied with the help of a cotton swab on the cervix and cervix was visualized for a couple of minutes under good light and cervical lesions whether present or not noted. Punch biopsy was taken from cervix and sent for histopathology. Later results of papanicolaou (PAP) smear and visual inspection using acetic acid (VIA) were compared with biopsy report. All this data was recorded on a specially designed proforma. Collected data was analyzed through computer software SPSS version 20.0. Mean and

standard deviation was calculated for quantitative variable i.e. age. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of papanicoloau (PAP) smear and visual inspection using acetic acid (VIA), taking histopathology of cervical tissue as gold standard were calculated by the application of contingency table of 2x2.

Effect modifiers like age, duration of symptoms, parity and family h/o cervical carcinoma were controlled by stratification. Post-stratification 2x2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy.

RESULTS

Age range in this study was from 20-50 years with mean age of 38.06 ± 7.02 years. Majority of the patients 108 (47.37%) were between 31 to 40 years of age as shown in Table-I. All the patients were undergone papanicoloau (PAP) smear and visual inspection using acetic acid (VIA). papanicoloau (PAP) supported the diagnosis of cervical carcinoma in 110 (48.25%) patients. Biopsy confirmed cervical carcinoma in 115 (50.44%) cases where as 113 (49.56%) patients revealed no cervical carcinoma. In 110 papanicoloau (PAP) positive patients, 97 (True Positive) had cervical carcinoma and 13 (False Positive) had no cervical carcinoma on biopsy. Among, 118 PAP negative patients, 18 (False Negative) had cervical carcinoma on biopsy whereas 100 (True Negative) had no cervical carcinoma on biopsy as shown in Table-II. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of PAP smear in screening of cervical carcinoma was 84.35%, 88.50%, 88.18%, 84.75% and 86.40% respectively (Figure-2).

VIA supported the diagnosis of cervical carcinoma in 114 (50.0%) patients. Biopsy confirmed cervical carcinoma in 115 (58.06%) cases where as 113 (41.94%) patients had no cervical carcinoma. In 114 VIA positive patients, 95 (True Positive) had cervical carcinoma and 19 (False Positive) had no cervical carcinoma on biopsy. Among, 114 VIA negative patients, 20 (False Negative) had cervical

carcinoma on biopsy whereas 94 (True Negative) had no cervical carcinoma on biopsy as shown in Table-III. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of VIA smear in screening of cervical carcinoma was 82.61%, 83.19%, 83.33% 82.46% and 82.89% respectively (Figure-2).

Age (Years)	No. of Patients	%Age
20-30	29	12.72
31-40	108	47.37
41-50	91	39.91
Total	228	100.0

Table-I. Division of cases as per Age.
Mean ± SD = 38.06 ± 7.02 years

	Positive result on Biopsy	Negative result Biopsy	Total	P-Value
Positive on PAP Smear	97 (TP)*	13 (FP)***	110	0.640
Negative on PAP Smear	18 (FN)**	100 (TN)****	118	
Total	115	113		

Table-II. Comparison of PAP smear and biopsy report.

*-TP=True positive **-FP=False positive
-FN=False negative *-TN=True negative

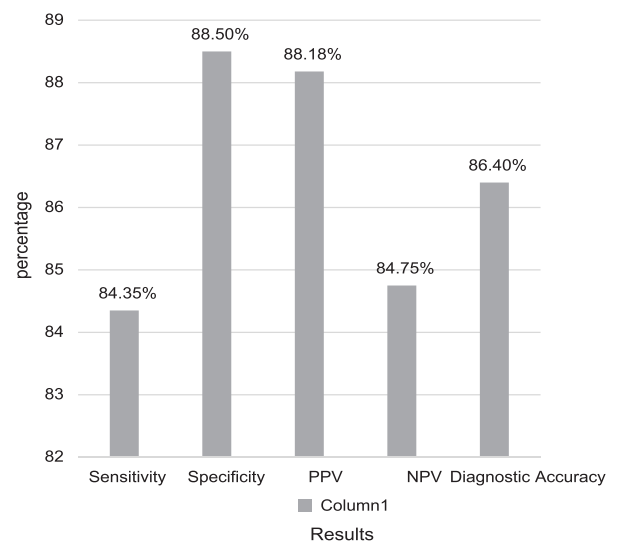


Figure-1. Diagnostic accuracy of PAP smear in screening of cervical carcinoma, taking biopsy as gold standard.

	Positive Result on Biopsy	Negative Result Biopsy	Total	P-Value
Positive on VIA	95 (TP)*	19 (FP)***	114	0.925
Negative on VIA	20 (FN)**	94 (TN)****	114	
Total	115	113		

Table-III. Comparison of visual inspection with acetic acid (VIA) and biopsy.

*-TP=True positive **-FP=False positive
 -FN=False negative *-TN=True negative.

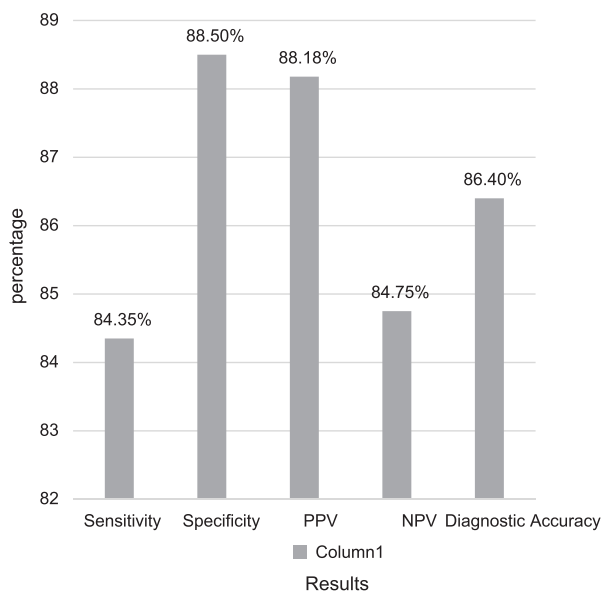


Figure-2. Diagnostic accuracy of VIA in screening of cervical carcinoma, taking biopsy as gold standard.

DISCUSSION

Although preventable Cervical malignancy is the second most common malignancy in females. Most common screening test used to screen and diagnose cervical malignancy is papanicoloau (PAP) smear but due to financial constraints and lack of experties developing countries do not opt for cytology-based screening. A low-cost screening test VIA i.e visual inspection using acetic acid rather used as it does not require expert professionals.¹¹ VIA is similar to colposcopy in some way as acetic acid is applied to cervix in both procedureds to look for any acetowhite lesion. Added benefit of VIA is that it does not require magnification. Our study was conducted for comparing the diagnostic accuracy of Pap smear and visual inspection with acetic acid (VIA)

for screening of cervical carcinoma comparing the results with the gold standard histopathology report of the biopsy taken.

A Study conducted by BanoA, Haq G, Sheikh A showed the sensitivity of w 71.4% and 78.6%, specificities were 97.8% and 92.6%, Positive predictive values were 76.9% and 52.4% and negative predictive values were 97.1% and 97.7% for VIA and of PAP smear respectively.¹⁰ An another study conducted by Albert SO, Oguntayo OA, Samerila had the sensitivity of 60% for both VIA and pap smear, specificity 94.4% and 100% positive predictive value 50% and 100%, negative predictive value 99.4% and 99.4%, accuracy of 98.6% and 99.4% for VIA and PAP smear respectively.⁸

Battacharyya AK, Nath JP, Deka H conducted a similar study to find out sensitivity of 89% for VIA and 52% for Pap smear. The specificity of VIA is 87% and 95% for PAP smear. VIA was 87% accurate as compared to Pap smear that was 93%.¹²

In a comparable research conducted by Omole-ohonsi A, Aiyedue TA, Umorus JU¹³ for the diagnosis of premalignant cervical lesion the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) estimates of VIA were 80.4%, 84.8%, 39.0%, and 97.3%, respectively, compared to 84.8%, 96.6%, 75.0%, and 98.1%, respectively for PAP smear.¹³

In his study Saleh HS et al¹⁴ while comparing PAP smear and VIA concluded that sensitivity was 50.1% and 90 %, specificity 93.1% and 37%, positive predictive value of 89.3% and 52 % and negative predictive value was 65.6% and 81 % for PAP smear and VIA respectively.¹⁴

Ngelangel¹⁵ performed cervical screening in four different ways i.e, magnified visualization with acetic acid (VIAM), visual inspection using acetic acid, PAP smear using spatula and cotton swab and PAP smear using cervical brush. Sensitivities were 34.1%, 37%, 14.3% and 19.1% for the methods respectively. The specificity rates were 90.7%, 90.7%, 97.5%, and 97.9%, respectively

for these methods. VIA was found to be the most specific out of all these methods in Philippines for cervical cancer screening. Ngelangel concluded that VIA should be opted for screening of precancerous cervical lesion in the Philippines.¹⁵

In another study VIA was compared to PAP smear in which VIA had sensitivity of 66.7%, specificity of 55.1%, positive predictive value of 19% and negative predictive value of around 90 %, for PAP smear test they were 75%, 82.1%, 39.1% and 95.5% respectively. This study was conducted by Keshavarzi F, Nankali A, Fakheri T, Rezaei M, Khoshay A, Eslamizao N.¹⁶ Accuracy of visual inspection using acetic acid was 58% and Pap smear accuracy was 81.1%.¹⁶

A study conducted in Africa where cervical and breast malignancies are responsible for half of the deaths in females. Doh¹⁷ recommended that an acceptable method for screening cervical cancer test in Cameroon Africa to be VIA. If any patient was screened positive after VIA or pap smear her colposcopic biopsy was taken, every tenth "negative" cervix was biopsied as for control group. Normal cervix does not show white changes. White changes near to the squamo-columnar junction was taken significant and labelled positive. Lesions with sharp borders were considered as high grade whereas faint border lesions were taken as low risk lesion. Sensitivity of 70.4% and 47.7% was noted for VIA and PAP respectively. Specificity was 77.6% and 94.2% for VIA and PAP respectively. PPV of VIA was 44% and NPV 91.3%. Doh concluded that PAP although having better testing qualities but VIA is an acceptable test and may be implemented as screening method in low resource countries.¹⁷

In a cross sectional observational study PAP smear was done in 160 patients of these 49 were having confirmed diagnosis of CIN or invasive disease. This confirmation was done by cervical biopsy and histopathology. Sensitivity, specificity, PPV and NPV for PAP smear were 61%, 97%, 91% and, 85% respectively. It was 86% accurate. These variables for Visual inspection using acetic acid were 74%, 48%, 64% and 60% respectively and accuracy was 63%. Sensitivity was enhanced

by 26% by combining the two procedures. Negative predictive value by 11% and diagnostic accuracy was increased by 2%.¹⁸

Singh et al¹⁹ found sensitivity of about 70.0% for PAP smear screening programme and 94 % for VIA, specificity of 97.2% for PAP smear and 87% for VIA. They reported PPV of 51.2% for PAP smear, 22.1% for VIA and NPV of 97.0% and 99.0% for the two procedures.

In India similar study was conducted by Goel. The study recruited 400 women of age between 30 and 35 years presenting to OPD in New Delhi India. All 400 woman underwent the three procedures i.e PAP smear, VIA and colposcopy. Concluded results had a sensitivity of 96.7%, almost double than PAP smear, which was found to be 50%. The specificity of VIA was around 36% which was much less than PAP smear, that was 97%. So Goel rejected VIA as better tool for endocervical lesions. 2 cases were not detected in the study because of low specificity of VIA. At the end although, VIA had higher false positive results. Goel concluded that VIA using acetic acid had higher sensitive for lesions on ectocervix. Its lower cost and easy use highlights its advantages in poor countries to be used as the primary screening tool for cervical cancer. However, due to its higher rate of false positive results VIA alone may lead to over treatment.²⁰

A study with larger number of cases were performed in Rural areas of Northeast Brazil, Bomfim²¹ where 1154 women underwent both PAP smear and VIA with colposcopy only when one or both tests resulted positive. Sensitivity of VIA and PAP smears was 100% and 18% and specificity was 78% and 100% for VIA and PAP smears respectively in detecting low grade squamous intra epithelial lesion and high grade squamous intra epithelial lesion. The positive predictive value (PPV) of VIA was around 16 % for low grade lesion and 3% for high grade squamous inta epithelial lesion. The negative predictive value (NPV) of VIA was 100% for both types of lesion. Negative predictive value of PAP smear was 97%. Bomfim concluded that VIA could be an excellent method and can be used for screening of cervical

malignant lesions moreover it does not always need expertise of cytopathologists and can be done by trained nurses and doctors.²¹

CONCLUSION

Papanicolaou (PAP) smear and visual inspection using acetic acid (VIA) are accurate tests with very good sensitive. Both are equally accurate. VIA has an added benefit of being cheap and easy so VIA can be used as screening test for cervical malignant lesions at its early stage. Using papanicolaou (PAP) smear and visual inspection with acetic acid have improved our ability of diagnosing cervical cancers and also improve patient care by accurate and in time diagnosis, helping to improve pre-operative management protocols for patients with cervical malignancy. Visual inspection with acetic acid (VIA) can replace papanicolaou (PAP) smear for screening of cervical malignant lesion in low resource settings where cytopathological services are not available at remote areas of developing countries to reduce morbidity and mortality as its having almost the same sensitivity and specificity as PAP smear cytology.


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REFERENCES

1. Karjane N, Chelmow D. **New cervical cancer screening guidelines, again.** *Obstet Gynecol Clin North Am.* 2013; 40(2):211–23.
2. Tarney CM, Han J. **Postcoital bleeding: A review on etiology, diagnosis, and management.** *Obstet Gynecol Intl.* 2014; 2014:192087.
3. Dunne EF, Park IU. **HPV and HPV-associated diseases.** *Infectious Dis Clin North Am.* 2013; 27(4):765–78.
4. Gadducci A, Barsotti C, Cosio S, Domenici L, Riccardo GA. **Smoking habit, immune suppression, oral contraceptive use, and hormone replacement therapy use and cervical carcinogenesis: A review of the literature.** *Gynecol Endocrinol.* 2013; 27(8):597–604.
5. Everett T, Bryant A, Griffin MF, Martin-Hirsch PP, Forbes CA, Jepson RG. **Interventions targeted at women to encourage the uptake of cervical screening.** *Cochrane Database Syst Rev.* 2011; (5):CD002834.
6. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al. **American cancer society, American society for colposcopy and cervical pathology, and American society for clinical pathology screening guidelines for the prevention and early detection of cervical cancer.** *CA Cancer J Clin.* 2012; 62(3):147-72.
7. Ahmed I, Arja R, Vibeke R. **Cervical cancer screening in primary health care setting in Sudan: A comparative study of VIA and Pap smear.** *Int J Women's Health.* 2012; 4:67-73.
8. Albert SO, Oguntayo OA, Samaila MOA. **Comparative study of visual inspection of the cervix using acetic acid (VIA) and papanicolaou (Pap) smears for cervical cancer screening.** *Ecanermedical Sci.* 2012; 6:262.
9. Gosh P, Gandhi G, Kochhar P, Zutshi V. **Visual inspection of cervix with Lugol's iodine for early detection of pre-malignant and malignant lesions of cervix.** *Indian J Med Res.* 2012; 136:265-71.
10. Bano A, Haq G, Sheikh A. **Pap smear versus visual inspection of cervix with acetic acid (VIA) for detection of cervical abnormalities.** *Pak J Surg.* 2013; 29(1):46-51.
11. Soler ME, Gaffikin L, Blumenthal PD. **Cervical cancer screening in developing countries.** *Prim Care Update Ob Gyns.* 2000; 7:118-123.
12. Bhattacharyya AK, Nath JP, Deka H. **Comparative study between Pap smear and visual inspection with acetic acid (via) in screening of CIN and early cervical cancer.** *J Midlife Health.* 2015; 6(2):53–8.
13. Omole-Ohonsi A, Aiyedun T A, Umoru J U. **Diagnostic accuracy of VIA compared to Pap smear cytology in detecting premalignant lesions of the cervix.** *Afr J Med Health Sci.* 2013; 12:25-30.
14. Saleh HS. **Can visual inspection with acetic acid be used as an alternative to Pap smear in screening cervical cancer.** *Middle East Fertility Society J.* 2014; 19:187–91.
15. Ngelangel CA. **Acetic-acid guided visual inspection vs cytology-based screening for cervical cancer in the Philippines.** *Int J Gynecol Obstet* 2003; 83.
16. Keshavarzi F, Nankali A, Fakheri T, Rezaei M, Khoshay A, Eslamizadeh N, et al. **Cervical visual inspection with acetic acid as an alternative screening test for cervical cancer detection.** *Int J Collaborative Res Int Med Public Health.* 2013; 5(1):60-6.

17. Doh AS. **Visual Inspection with acetic acid and cytology as screening methods for cervical lesions in Cameroon.** Int J Gynecol Obstet. 2005;89.
18. Sherpa P, Pant AD. **Correlation of visual inspection with cytological and histopathological findings in cervical neoplasia.** J Pathol Nepal 2017; 7:1070-73.
19. Singh KN, More S. **Visual inspection of cervix with acetic acid in early diagnosis of cervical intraepithelial neoplasia and early cancer cervix.** J Obstet Gynecol India. 2010; 60:55-60.
20. Goel A, Gandhi G, Batra S. **Visual Inspection of the cervix with acetic acid for cervical intraepithelial lesions.** Int J Gynecol Obstet. 2005; 88:25–30.
21. Bomfim S. **Visual inspection with acetic acid for cervical cancer detection.** Int J Gynecol Obstet. 2005:88.

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