Agreement Between Visual Inspection with Acetic Acid and Papanicolaou's Smear as Screening Methods for Cervical Cancer

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ABSTRACT

Objective: To determine degree of agreement between visual inspection with acetic acid (VIA) and Papanicolaou's (Pap) smear as screening methods for cervical cancer.

Study Design: A cross-sectional study.

Place and Duration of Study: Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore, from July to December 2012.

Methodology: Two hundred and fifty women in reproductive age group presenting with various gynaecological complaints were included in the study. A Papanicolaou's smear was taken and visual inspection with 5% acetic acid was done. VIA was reported as positive or negative according to acetowhite changes and cytology result was graded as CIN 1, 2, 3 and squamous carcinoma. Those women who showed positive result with either VIA or Pap smear or both were further subjected to colposcopic directed biopsy which was taken as gold standard. Results were computed using Statistical Package for Social Sciences (SPSS) version 16 and statistical test used was kappa.

Results: Out of 250 women, VIA was positive in 55 (22%) patients and Pap smear was abnormal in 27 (10.8%). Histological diagnosis of CIN/cancer was made in 36 out of a total 62 patients who underwent biopsy.

Conclusion: There was a fair agreement between VIA and Pap smear, with VIA detecting more abnormalities than cytology. In the absence of Pap smear availability, VIA may be a reasonable cervical cancer screening method, especially in low resource settings.

Key Words: Cervical cancer screening.   Pap smear.   Visual inspection with acetic acid.   Agreement.

INTRODUCTION

Cervical cancer accounts for about 3.6% of all cancers in Pakistani women.[1] The annual worldwide burden of cervical cancer is more than 530,000 new cases and 275,000 deaths with the majority occurring in low and middle income countries, where cervical cancer screening and early treatment are uncommon.[2,3] Although the incidence of cervical cancer has decreased in developed countries as a result of screening by cytology, it is still the single largest cause of lives lost to cancer in developing countries as cytology based screening programmes are almost non-existent and ineffective.[4] It has been estimated that only about 5% of women in developing countries have been screened for cervical dysplasia in the past 5 years, compared with about 85% in developed countries.[5] Most women present themselves for diagnosis and treatment when it is too late.[1] Incidence of cervical cancer in Pakistan is 13.6/100,000 population and currently cervical cancer screening coverage is only 1.9%.[1]

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Conventional cervical cytology is the most widely used cervical cancer screening test in the world.[3,6] Papanicolaou's (Pap) smear is a simple, safe, non-invasive and effective method for detection of pre-cancerous, cancerous and non-cancerous changes in the cervix. One study showed that Pap smear had sensitivity of 83.3% and specificity of 97%.[7] However, this method of screening is difficult to implement in low resource countries due to lack of laboratory infrastructure and trained professionals.[8]

There has been a strong need for a screening test that is simpler and can be interpreted immediately and combined with treatment, if necessary, at the initial visit. The use of acetic acid during visual inspection of cervix termed as visual inspection with acetic acid (VIA) has been advocated as an alternative screening method to Pap smear in developing countries. The attractive features of VIA include low cost, simple administration, real time screening of results, treatment, if needed, can be provided at the same time and accuracy compared to good quality Pap smears.[9,10] Studies show that it has sensitivity of 93% and specificity of 90%.[7] The benefit of establishment of agreement between these two methods would be to implement VIA as a standard screening test instead of Pap smear.

This study was done to assess local evidence in Pakistan regarding agreement between Pap smear and

VIA, as screening method for cervical cancer screening in low resource-setting.

METHODOLOGY

This cross-sectional study was conducted in Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore, from July to December 2012. Women of child bearing age presenting with various gynaecological complaints were included in the study after informed consent was taken. Unmarried, pregnant or postmenopausal women, women with acute cervicitis or obvious lesion on cervix were excluded as women with hysterectomy or cervical pre-cancer or cancer. A complete history regarding any white discharge per vagina, postcoital bleeding and previous Pap smears was obtained. Clinical data was noted on a structured proforma.

After putting woman in modified lithotomy position, per speculum examination of cervix and vagina was done. After visualizing the squamocolumnar junction, it was gently scraped throughout its circumference and Pap smear taken. The cytological results of Pap smear were reported as CIN 1, 2, 3 or squamous carcinoma. A solution of 5% acetic acid was then applied to cervix using a cotton swab and cervix examined for 1 or 2 minutes under adequate light source. To avoid artefacts due to trauma by Pap smear, standardized interpretation guides were used to interpret results of VIA. Any sharp, distinct, well-defined, dense acetowhite areas with or without raised margins were considered as VIA positive result and negative if no acetowhitening.

Women with positive result with VIA, Pap smear or both were called for a second visit for colposcopic directed biopsy which was taken as a gold standard. Results were computed using Statistical Package for Social Sciences (SPSS) version 16. The kappa statistic was used to measure agreement between Pap smear and VIA.

RESULTS

Of the 250 women screened for cervical carcinoma, 167 (66.8%) belonged to the 39 - 45 years age group (Figure 1).

The major presenting complaint was menstrual irregularities (46.2%), 28 women complained of white discharge per vaginum (11.2%), 1.6% (4) of women had previous history of Pap smear.

Of the 250 women examined using VIA, 55 (22%) were positive. Twenty seven (10.8%) patients were positive with Pap smear. Out of these 27, 11 had CIN 1, 6 had CIN 2, 7 had CIN 3 and 3 had squamous carcinoma. Twenty patients were positive on both VIA and cytology. So 62 patients had cervical biopsies performed on them. Histopathology showed CIN/ carcinoma in 36 patients who underwent biopsy (14.4%).

On comparison of Pap smear and histopathology, Pap smear picked 22 out of 36 biopsy proven cases. Out of these, 9 had mild dysplasia, 6 had moderate dysplasia and 5 cases had severe dysplasia. Two cases showed squamous carcinoma (Table I).

When comparing VIA and histopathology, VIA picked 33 out of 36 biopsy proven cases, 11 cases showing mild dysplasia, 10 moderate, 9 severe dysplasia and 3 squamous carcinoma (Table II).

Comparison of VIA and Pap smear results showed that of the 55 women who screened positive on VIA, 20 also had positive Pap smear whereas 35 had a negative Pap smear. Of the 195 examinations normal by VIA, 7 showed abnormalities by Pap smear. On the basis of these values, kappa statistic was found to be 0.401, which showed fair agreement between the two. The biopsy detection rate of Pap smear was 8% and that of VIA, 13%. So, VIA performed better in the detection of dysplasia.

DISCUSSION

Cervical cancer is a potentially preventable cancer. It is preceded by pre-malignant lesions which may take 5 - 15
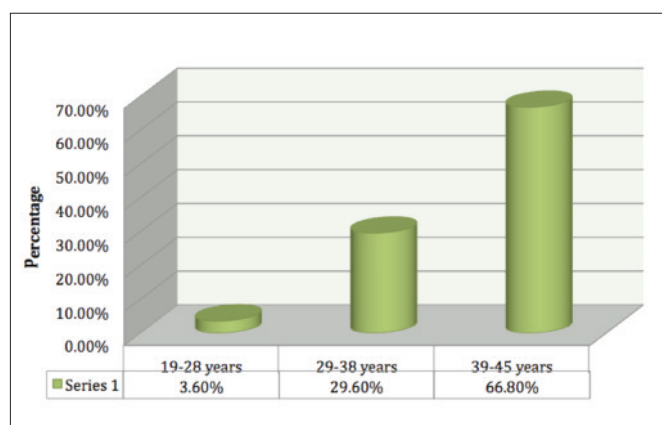

Figure 1: Age distribution of patients.

Table I: Comparison of Pap smear with histopathology.

Histopathology	CIN 1	CIN 2	CIN 3	Sq CA	Total
Normal	3	1	1	0	5
Mild dysplasia	4	2	3	0	9
Moderate dysplasia	3	2	1	0	6
Severe dysplasia	1	1	2	1	5
Sq carcinoma	0	0	0	2	2
Total	11	6	7	3	27

Table II: Comparison of VIA and histopathology.

Histopathology	VIA positive	VIA negative	Total
Normal	22	4	26
Mild dysplasia	11	2	13
Moderate dysplasia	10	1	11
Severe dysplasia	9	0	9
Sq carcinoma	3	0	3
Total	55	7	62

years to progress to invasive cancer. If detected and treated timely, pre-invasive disease has nearly 100% cure rate with simple surgical procedure, while advanced cancers have less than 35% survival rates.[11]

Khan *et al*. and Gravitt *et al*. studied the age range of 25 - 65 years.[14,15] Kruy conducted similar study in HIV infected Cambodian women.[16] In this study, majority of women belonged to age group 39 - 45 years (66.8%). This is similar to the study conducted by Hegde.[12] This is a reflection of the age composition of women attending various gynaecological clinics. Age of the target population is an important determinant of the performance of different cervical cancer screening tests.[17]

This study compared VIA with Pap smear and colposcopic biopsy taken on second visit if positive findings were present on Pap smear or VIA or both. Hegde performed colposcopy on all patients.[12] Khan *et al*. used visual inspection with Lugol's iodine in addition to VIA and cytology and patients with positive findings were scheduled for colposcopic guided biopsies later on.[14]

VIA positive rate was 22% in this study. There is wide range in VIA positive rate that has been reported so far. Mbamara *et al*. reported positive VIA in 8.3% of women in their study,[18] and Kruy reported VIA positive in 19% women.[16] The wide range is due to difference in interpretation since few studies used nurses or paramedical workers to do the test. It also depends on the study population since few studies were done on symptomatic hospital based population and others as a mass screening test.

Ten desimal eight percent patients were positive on Pap smear in this study considering CIN1 and above as abnormal. Kruy showed 8.5% of abnormal Pap smears in their study.[16]

This study showed biopsy confirmed dysplasia in 14.4% of patients, similar to 11.5%, showed by Hegde.[12] This high rate of dysplasia may be due to the fact that these studies were hospital based with small sample size. Another study showed dysplasia rate of 3.6% since it involved larger number of patients.[23]

Cytology based screening program which was introduced over 5 decades ago has been very difficult to establish and implement on large scale in developing countries due to its high cost and expertise. This study showed fair agreement between results of Pap smear and VIA in detection of abnormal cervical lesion.[21] Another study also showed fair agreement between the two.[8] Most of the abnormal smears detected by the Pap test were among the women who had suspicious cervical appearance on visual inspection. As collaborated in other studies, no special skill or extensive training is required before the widespread commencement of visual inspection of cervix.[19,20] VIA

confers a very high NPV, which means that when a test is negative, the women can go home re-assured that she is not likely to have a neoplastic cervical lesion; eliminating the need for follow-up visits.[7] VIA can be done in primary health care centres where there may be no doctors and which are very close to the rural women and women with suspicious appearance can be referred for further evaluation and management. This will ultimately improve the utilization of cervical cancer prevention services. The 2009 ACCP fact sheet recommends that until HPV testing becomes feasible and affordable, programs should consider introducing or expanding VIA plus cryotherapy (one stop treatment) as a cervical prevention strategy.[22]

There were several limitations to this study. First, cervical biopsy and histology, the gold standard for diagnosis of cervical neoplasia, was not performed on all women. Therefore, we were not able to determine the test characteristics of VIA and Pap smear (sensitivity, specificity, positive and negative predictive values) and thus limited in the conclusions that we could have made the accuracy of VIA compared to Pap smear. Secondly, this was a hospital based study and study sample was small. Furthermore, VIA results are operator dependent and may result in a large number of referrals. This means that initial training and ongoing quality control are of paramount importance. In addition, patients were called for second visit for colposcopy which lead to varied logistic problems.

CONCLUSION

This study shows VIA to be a reasonable and effective alternative to Pap smear, as there is fair agreement between the two methods. However, the low PPV of VIA does present the problem of many false positives, a see-and-treat method were implemented in a high-risk population with a high incidence of cervical cancer, the qualities of the VIA test may improve.

REFERENCES

1. WHO/ICO HPV Information centre. Human papilloma virus and related cancers [Internet]. 2010. Available from: http:www.who.int/ hpvcentre/publications/en

2. Ferlay J, Shin HR, Bray F, Forman D. GLOBOCAN 2008, cancer incidence and mortality worldwide: IARC cancer base no. 10. France: *International Agency for Research on Cancer;* 2010.

3. Sahasrabuddha W, Parham GP, Mwanahamuntu MH. Cervical cancer prevention on low and middle income countries; feasible, affordable, essential. *Cancer Prev Res (Phila)* 2012; **5**:11-7 .

4. 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.

5. 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. *Ecancermedicalscience* 2012; **6**:262.

6. Duraisamy K, Jaganathan KS, Bose JC. Methods of detecting cervical cancer. *Adv Bio Res* 2011; **5**:226-32.

7. Bhatla N, Mulchopadhyay A, Kriplani A, Pandey RM. Evaluation of adjunctive tests for cervical cancer screening in low resource settings. *Indian J Cancer* 2007; **44**:51-5.

8. Rana T, Zia A, Sher S. Comparative evaluation of Pap-smear and VIA in cervical cancer screening programme in LWH, Lahore. *Special Edition Ann* 2010; **16**:104-7.

9. Nelson R. HPV testing most successful in cervical cancer developing countries. *N Engl J Med* 2009; **360**:1385-94.

10. 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 .

11. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD. Cost effective-ness of cervical cancer screening in five developing countries. *N Engl J Med* 2005; **353**:2158-68.

12. Hegde D, Shetty H, Shetty K, Rai S. Diagnostic value of VIA comparing with conventional Pap-smear in the detection. Pap-smear in the detection of colposcopic proven CIN. *NJOG* 2011; **6**:7-12.

13. Dinshaw KA, Shastri SS. Screening for cervical cancer in India. *Natl Med J India* 2001; **14**:1-3.

14. 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 Gynecol* 2007; **2**:48-53.

15. Gravitt PE, Paul P, Katki HA, Vendantham H, Ramakrishna G, Sudula M, *et al*. Effectiveness of VIA, Pap smear and HPV DNA testing in a cervical cancer screening programme in a peri urban community in India. *PLoS One* 2010; **5**:e13711.

16. Kruy L, Autumn D, Joseph H. Comparing VIA to cytology in detection of pre-cancerous lesions of cervix in HIV infected Cambodian women. *J Int Assoc Physicians AIDS Care (JIAPAC)* 2011; **1**:1-4.

17. Syrjanen K, Derchain S, Roteli MC. Value of conventional Pap smear, liquid based cytology, visual inspection and HPV testing as optional screening tools among Latin American women < 35 or = >35 years of age. *Accta Cytol* 2008; **52**:641-53.

18. Mbamara SU, Ulcah CO, Ikpeze O. Correlation between visual inspection of cervix and Pap-smear test for cervical carcinoma screening. *J Cancer Res Exp Oncol* 2011; **3**:8-13.

19. Ahmed T, Ashrafunnessa, Rehman J. Development of a visual inspection programme for cervical cancer prevention in Bangladesh. *Reprod Health Matters* 2008; **19**:78-85.

20. Gaffikin L, Lauterbach M, Blumenthal PP. Performance of VIA for cervical cancer screening: a qualitative summary of evidence to-date. *Obstet Gynecol Surv* 2003; **58**:543-50.

21. Anthony J, Joanne M. Understanding inter-observer agree-ment: the kappa statistic. *Fam Med* 2005; **37**:360-3.

22. ACCP. Cervical cancer prevention fact sheet. Lenexa: *ACCP;* 2009.

23. Singh KN, More S. Visual inspection of cervix with acetic acid in early diagnosis of CIN and early cancer cervix. *J Obstet Gynecol India* 2010; **60**:55-60.

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