# Cervical visual inspection with acetic acid as an alternative screening test for cervical cancer detection

Farahnaz Keshavarzi <sup>1</sup>, Anisodowleh Nankali <sup>1\*</sup>, Taravat Fakheri <sup>2</sup>, Mansour Rezaei <sup>3</sup>, Ahmad Khoshay <sup>4</sup>, Nasrin Eslamizadeh <sup>5</sup>, Shirin Naseeri Bookani <sup>5</sup>

<sup>1</sup> MD; Assistant Professor of Obstetrics & Gynecology, Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran <sup>2</sup>MD; Associate Professor of Obstetrics & Gynecology, Maternity Research Center, Imam Reza Hospital, Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran <sup>3</sup>PhD; Assistant Professor of Bio Statistics, Faculty of Health, Social Development and Health Promotion Research Center, Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran <sup>4</sup> MSc, Master of Science in Nursing Education, Faculty of Nursing and Midwifery, Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran <sup>5</sup> MD; Gynecologist, Department of Gynecology, Imam Reza Hospital, Kermanshah University of Medical Sciences(KUMS), Kermanshah, Iran

\* Corresponding author: Dr. Anisodowleh Nankali Clinical Research Development Center, Imam Reza Hospital Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran Tel: 0098 831 4276309 | Fax: 0098 831 7248839 | Email: anis nankali@yahoo.com

## **Abstract**

**Background:** Cervical cancer is one of the major causes of women death worldwide. Our goal was to compare the visual inspection of cervix with acetic acid (VIA) and Pap smear, for screening of pre-cancer and cancer of cervix.

Methods: VIA and Pap smear tests were performed on 468 women. All positive results were referred for colposcopy and cervical biopsy. 44 patients with negative VIA were also referred for colposcopy and cervical biopsy.

**Results:** 43 patients had positive VIA and 23 patients had positive Pap smear results. Sensitivity, specificity, positive predictive value and negative predictive value of VIA were 66.7%, 55.1%, 18.6% and 91.5%, respectively and for Pap smear test they were 75%. 82.1%, 39.1% and 95.5%, respectively. Test accuracy for VIA and Pap smear were 56.7 and 81.1, respectively.

**Conclusion:** VIA has high sensitivity but low positive predictive value. By considering the low price of this test and its availability, it can be proposed as a screening method in cervical cancer.

**Key words:** Cervical cancer, Pap smear, visual inspection with acetic acid, Screening

#### Introduction

Cervical cancer is the second most common cancer in women worldwide.<sup>1</sup> About 470,000 women are reported with cervical cancer annually with 80% of these occurring in developing countries.<sup>2</sup> According to world health organization's reports, about 260,000 women have died of cancer in 2005 nearly 95% of them in developing countries.<sup>3</sup> Cervical cancer has a prolonged incubation period so in case of early diagnosis with screening methods it can be prevented.<sup>4</sup> Pap smear is a screening method which has been used for so long.<sup>5</sup> The high incidence of cervical cancer in developing countries, represent that Pap smear screening test in the developing world was not effective.<sup>6</sup> Proper Pap smear test includes many steps which are not available in many countries.<sup>7</sup> Cervical cancer screening in Iran is based on Pap smear test but it is more available in urban areas. False negative results of Pap smear are reported over 30% in recent studies<sup>8</sup>, so suitable methods for screening is required.<sup>7,9</sup> Visual inspection with acetic acid (VIA) has been proposed as a screening method for cervical cancer.<sup>10,11</sup> The application of acetic acid coagulates the protein of the nucleus and cytoplasm and makes the proteins opaque and white. The dysplastic cells have large nuclei and acetic acid usage causes dysplastic lesions to turn white.<sup>12</sup>

Some studies propose VIA as a screening method but some other studies have not confirmed VIA as a substitute in screening methods.<sup>7, 13-15</sup> Our goal was to evaluate sensitivity, specificity; positive predictive value and negative predictive value of VIA as a screening method in cervical cancer and compare it with Pap smear test.

#### **Materials & Methods**

This cross-sectional study was performed on women who were referred to Kermanshah Motazadi gynecology clinic for vaginal discharge, abnormal uterine bleeding or cervical cancer screening.

This study was performed on 481 patients in which 5 patients were excluded because of unsatisfactory Pap smear results and 8 patients left the study. Sample size of 468 patients was selected with 95% confidence. Exclusion criteria were pregnancy, active vaginal bleeding, and previous history of cervical cancer, hysterectomy or cervical conization.

All patients underwent Speculum examination, then cervical smear was taken using a wooden spatula and cotton swab after written consent was obtained. Meanwhile acetic acid 5% was applied on cervix with a thick cotton swab and after 1 minute, direct visual inspection was performed with a white 100 Watt halogen lamp. Any white lesions were considered as positive result. This examination was performed by two trained senior obstetrics and gynecology assistants.

In case of abnormal Pap smear test results (ASCUS, CIN or invasive cancer) or positive VIA, patients were referred for colposcopy. 44 women with polyp or lesion of cervix but with negative test result were referred to colposcopy. Standard colposcopy procedure was performed by a gynecologist blinded to the results of VIA test. A cervical biopsy from any abnormal area was taken. In addition, random biopsy were obtained from the four cervical quadrants where did not

appear to be any abnormality. Endocervical curettage was performed if colposcopy results were unsatisfactory.

As colposcopy was not performed on all patients, the accurate sensitivity and specificity of these two tests could not be calculated but approximate values were achieved by using Chi square test and Kappa coefficient.

### Results

Of 468 participants, 41 patients (8.7%) were menopause. Mean age was 36.2 years and mean parity number was 3.2 (range: 0-8). (Table 1).

23 Pap smear results were positive in which 11 cases had ASCUS, 7 cases had low SIL, one case had high SIL and 4 cases had squamous cell carcinoma. All positive results were referred for colposcopy and cervical biopsy. Positive VIA was detected in 43 patients and all positive results were referred for colposcopy and cervical biopsy in which 7 patients had low SIL, one patient had high SIL, 3 cases had cervical cancer and 32 cases had benign lesions. Patients with benign lesions included 12 cases of metaplasia, 15 cases of chronic cervicitis and 5 cases were normal. In cases that underwent colposcopy and biopsy, 20 patients had positive VAI and positive Pap smear results and 3 cases had negative VAI and positive Pap smear and 44 cases had both negative VAI and Pap smear. Colposcopy was unsatisfactory in 18 cases and for these patients Endocervical curettage were done. (Table 2)

In one case who had negative VIA and positive Pap smear colposcopy and cervical biopsy reported cervical cancer. Sensitivity, specificity, positive predictive value and negative predictive value of VIA were 66.7%, 55.1%, 18.6% and 91.5%, respectively and for Pap smear test they were 75%. 82.1%, 39.1% and 95.5%, respectively (table 3). Test accuracy of VIA and Pap smear were 56.7 and 81.1, respectively. The agreement rate of both Pap smear and VIA according to Kappa was 40.9 %. (Table 3)

#### Conclusion

VIA has been proposed as a cervical cancer screening method in recent decades. In our study, VIA sensitivity and specificity were 66.7 and 55.1, respectively. In previous studies, VIA sensitivity was reported between 37- 96 and also specificity range of 36-91 had been mentioned. Positive predictive value (PPV) of VIA was 18.6% in our study. VIA PPV has been reported 3.8-90% in previous studies. 9, 15, 20-22

The reason of these wide ranges are differences in gynecological symptoms, source of light, differences in training and skills, infection, inflammation, cervical metaplasia, changes in cervical anatomy, lack of a standardized test definition and absence of blinding. <sup>23-25</sup>

The reason of low PPV and specificity of VIA in our study was positive consideration of all white lesions. Existence of cervical polyp, inflammation and metaplasia cause false positive

VIA.<sup>26</sup> In Cagle's study 95.7% of positive VIA cases had inflammation in histopathology report.<sup>27</sup> In our study about 46.87% of false positive VIA had inflammation and 37.5% had metaplasia. A study in El Salvador village showed that inflammation makes false positive VIA results to become twice.<sup>28</sup> False positive VIA had no relationship with specific genital infections except for HPV.<sup>10</sup>

VIA can be performed with short time education, it has low price; it's available and needs little facilities. <sup>7, 29, 30</sup> VIA is a subjective test which cannot be interpreted as good as objective tests. High level of false positive results can lead to excessive colposcopy and overtreatment but its diagnostic value can be increased by repeating the test. <sup>9</sup>

Our study showed that we can use VIA as a screening method for cervical cancer detection. In areas with low facilities VIA is a helpful method in cervical cancer screening. When colposcopy is not available it is recommended to use VIA accompanying with Pap smear.

**Acknowledgments:** The authors are grateful to Kermanshah University of Medical Sciences for their support.

**Funding:** This work was performed in partial fulfillment of the requirements for the degree of M.D. of Nasrin Islamizadeh and Shirin Naseeri Bookani's project thesis at Kermanshah University of Medical Sciences.

**Conflict of Interest:** There was no conflict of interest.

#### References

- 1. Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: *GLOBOCAN*, 2008. Int J Cancer 2010; 127(12):2893-917.
- 2. Shastri SS, Dinshaw K, Amin G, et al. Concurrent evaluation of visual, cytological and HPV testing as screening methods for the early detection of cervical neoplasia in Mumbai, India. *Bulletin of the World Health Organization* 2005; 83(3):186–194.
- 3.Kathy S, Emma O, Patricia C, et al. Comprehensive cervical cancer control: a guide to essential practice. *World Health Organization*, 2006.
- 4. Sherigar B, Dalal A, Durdi G, et al. Cervical Cancer Screening by Visual Inspection with Acetic Acid- Interobserver Variability between Nurse and Physician, *Asian Pacific Journal of Cancer Prevention*, 2010, 11(3): 619-22

- 5. Gaffikin L, McGrath JA, Arbyn M, Blumenthal PD. Visual inspection with acetic acid as a cervical cancer test: accuracy validated using latent class analysis. *BMC Med Res Methodol*. 2007; 7: 36.
- 6. Denny L, Quinn M, Sankaranarayanan R. Screening for cervical cancer in developing countries. *Vaccine* 2006; 24 Suppl 3: S3/71–77.
- 7. Vedantham H, Silver MI, Kalpana B, et al. Determinants of VIA (Visual Inspection of the Cervix After Acetic Acid Application) Positivity in Cervical Cancer Screening of Women in a Peri-Urban Area in Andhra Pradesh, India, *Cancer Epidemiol Biomarkers Prev* 2010; 19(5): 1373–80.
- 8. Eftekhar Z, Yarandi F, Moosavi A, et al. Accuracy of acetic acid 5% in early detection of cervical dysplasia. *The Iranian Journal of Obstetrics, Gynecology & Infertility* 2000; 1(4): 9-13.
- 9. Ghaemmaghami F, Behtash N, Modares Gilani M, et al. Visual inspection with acetic acid as a feasible screening test for cervical neoplasia in Iran, *Int J Gynecol Cancer* 2004; 14(3):465-9.
- 10.Denny L, Kuhn L, Pollack A, Wright TC JR. Direct visual inspection for cervical cancer screening: an analysis of factors influencing test performance. *Cancer* 2002; 94(6): 1699–707.
- 11. Murillo R, Luna J, Gamboa O, et al. Cervical cancer screening with naked-eye visual inspection in Colombia. *Int J Gynaecol Obstet* 2010; 109(3):230-4.
- 12. Hatch KD. *Handbook of colposcopy: diagnosis and treatment of lower genital tract neoplasia and HPV infections*, Boston: MA: Little Brown; 1989.
- 13. Kumar Y, Mishra G, Gupta S, Shastri S. Cancer screening for women living in urban slums acceptance and satisfaction, *Asian Pac J Cancer Prev* 2011; 12(7):1681-5.
- 14. Luciani S, Munoz S, Gonzales M, et al. Effectiveness of cervical cancer screening using visual inspection with acetic acid in Peru. *Int J Gynaecol Obstet* 2011; 115(1):53-6.
- 15.Hasanzadeh M, Esmaeili H, Tabaee S, Samadi F. Evaluation of visual inspection with acetic acid as a feasible screening test for cervical neoplasia, *J Obstet Gynaecol Res* 2011; 37(12): 1802-6
- 16. Ngelangel CA, Limson GM, Cordero AD, et al. Acetic-acid guided visual inspection vs. cytology-based screening for cervical cancer in the Philippines. *Int J Gynecol Obstet* 2003; 83(2):141–150
- 17. Doh AS, Nkele NN, Achu P, et al. Visual inspection with acetic acid and cytology as screening methods for cervical lesions in Cameroon. *Int J Gynaecol Obstet* 2005; 89(2):167–73
- 18. Cronjé HS, Parham GP, Cooreman BF, et al. A comparison of four screening methods for cervical neoplasia in a developing country. *Am J Obstet Gynecol* 2003; 188(2):395–400

- 19. Sankaranarayanan R, Basu P, Wesley RS, et al. Accuracy of visual screening for cervical neoplasia: results from an IARC multicentric study in India and Africa, *Int J Cancer* 2004; 110(6):907-13.
- 20. Sarian LO, Derchain SF, Naud P, et al. Evaluation of visual inspection with acetic acid (VIA), Lugol's iodine (VILI), cervical cytology and HPV testing as cervical screening tools in Latin America. *J Med Screen* 2005; 12(3):142–9.
- 21. Almonte M, Ferreccio C, Winkler JL, et al. Cervical screening by visual inspection, HPV testing, liquid-based and conventional cytology in Amazonian Peru. *Int J Cancer* 2007; 121(4):796–802.
- 22. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *N Engl J Med* 2009; 360(14):1385–94.
- 23. Sauvaget C, Fayette JM, Muwonge R, et al. Accuracy of visual inspection with acetic acid for cervical cancer screening. *Int J Gynaecol Obstet* 2011; 113(1):14-24.
- 24. Aggarwal P, Batra S, Gandhi G, Zutshi V. Can visual inspection with acetic acid under magnification substitute colposcopy in detecting cervical intraepithelial neoplasia in low-resource settings? *Arch Gynecol Obstet* 2011; 284(2):397–403
- 25. Mahé C, Gaffikin L. Screening test accuracy studies: how valid are our conclusions? Application to visual inspection methods for cervical screening. *Cancer Causes Control* 2005;16(6):657–66
- 26. Pothisuwan M, Pataradool K, Tangjitgamol S, et al. Visual inspection with acetic acid for detection of high grade lesion in atypical squamous cells and low grade squamous intraepithelial lesions from cervical Pap smear, *J Gynecol Oncol* 2011; 22(3): 145-51
- 27. Cagle AJ, Hu SY, Sellors JW, et al. Use of an expanded gold standard to estimate the accuracy of colposcopy and visual inspection with acetic acid. *Int J Cancer* 2010; 126(1):156-61.
- 28. Davis-Dao CA, Cremer M, Felix J, Cortessis VK. Effect of cervicitis on visual inspection with acetic acid. *J Low Genit Tract Dis* 2008; 12(4):282-6.
- 29.Pimple SA, Amin G, Goswami S, Shastri SS. Evaluation of colposcopy vs cytology as secondary test to triage women found positive on visual inspection test. *Indian J Cancer* 2010; 47(3):308-13
- 30. Zhang YZ, Ma JF, Zhao FH, et al. Three-year follow-up results of visual inspection with acetic acid/Lugol's iodine (VIA/VILI) used as an alternative screening method for cervical cancer in rural areas. *Chin J Cancer* 2010; 29(1):4-8.

**Table 1:** Characteristics of patients in two screening tests of visual inspection with acetic acid (VIA) and Pap smear in cervical cancer detection

characteristics	mean ± SD
Mean age (years)	36.2 <u>+</u> 8.6
The average age at menarche (years)	11.3 <u>+</u> 2.1
The average age of marriage (years)	17.2 <u>+</u> 4.2
The average number of parity	3.2 <u>+</u> 1.2

**Table 2:** Distribution of histopathologic findings in two screening tests of visual inspection with acetic acid (VIA) and Pap smear in cervical cancer detection

VIA	Pap smear	number	Low SIL	High SIL	carcinoma	benign lesions
+	+	20	7	1	3	9
+	-	23	0	0	0	23
-	+	3	0	0	1	2
-	-	44	3	0	0	41

**Table 3:** The validity of two screening tests of visual inspection with acetic acid (VIA) and Pap smear in cervical cancer detection

Test	Sensitivity%	Specificity%	positive predictive value%	negative predictive value%
VIA	66.7	55.1	18.6	91.5
Pap Smear	75	82.1	39.1	95.5