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Original Research

Is visual inspection with acetic acid (VIA) a useful method of finding pre-invasive cervical cancer?

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Purpose of investigation: The prospects for effective cytological screening in the majority of developing countries are limited. This study evaluated visual inspection with acetic acid (VIA) for the diagnosis of CIN 2-3 in case findings. *Materials and Methods*: In this prospective study, 1437 asymptomatic women were screened using VIA followed by colposcopy-biopsy of all cases. The predictive efficacy of VIA was determined based on pathological confirmation of CIN 2-3 on colposcopy-directed biopsy. *Results*: In 388 (27%) out of 1437 cases, the VIA was positive. In 31 (2.1%) cases, CIN 2-3 was confirmed on cervical biopsy. The sensitivity, specificity and negative predictive value (NPV) of the VIA were 41.9%, 73.3%, and 98.2%, respectively. *Conclusion*: The present study confirmed the value of VIA for screening, with sensitivity of 41.9% and NPV of 98.2%. Future studies should determine the best place for VIA testing alongside other types of testing in screening algorithms.

Keywords

Screening; Cervical cancer; Cervical dysplasia; Colposcopy; Visual inspection with acetic acid; Iran

1. Introduction

Over 80% of new cervical cancer cases globally are diagnosed in developing countries. In some countries, cervical cancer is the leading cause of cancer death in women and the second most frequent malignancy after breast cancer. Systematic screening guidelines in developed countries have changed the epidemiology of cervical cancer. In many underdeveloped regions, lack of these organized screening programs has led to the late diagnosis of this malignancy in it' s advanced stages [1–3]. Development of new screening methods through appropriate use of cytological screening has been encouraging in developing countries [4–11].

The World Health Organization has approved visual inspection of the cervix using acetic acid (VIA) as a screening method for cervical cancer. Studies have shown comparable efficiency of VIA and cytology, with the former being simpler and easier to perform by paramedical nurses in developing countries [1, 3, 12]. VIA is reported to be highly sensitive and specific (80% and 92%, respectively) in detection of high grade CIN [13–15]. In a study in India, VIA revealed sensitivity of 67.9% for CIN 3 detection [16]. In a meta-analysis, sensitivity of 73.2% was observed for detection of CIN 2 and more lesions by VIA [17]. The goal of this study was to evaluate the accuracy of VIA for diagnosis of CIN 2-3 in case findings.

2. Material and methods

This prospective cross-sectional study assessed sexual active women in all age groups, referred by a charity center to a third-level medical center located in Tehran for cervical screening from 2011 to 2014. Socio-economic situation of participants in the study was in a wide range from low to moderate level. The subjects were enrolled into study and demographic information was collected after informed consent was obtained. Pregnant, hysterectomized women and patients with known invasive or pre-invasive cervical lesions were excluded from the study. All of 1437 cases underwent screening by visual inspection with acetic acid (VIA).

A trained nurse carried out the VIA. Acetic acid (3%) was applied to the cervix for about one minute and cervix observed without magnification in white light. After observing the posture of the Squamocolumnar junction (SCJ) as to satisfactory or unsatisfactory, the VIA results were reported as negative, positive (fine or dense) or strongly positive (very opaque). In a two-month training course before taking part in the study, the nurse checked her VIA test reports with an expert Gyneco-oncologist who was involved in the research.

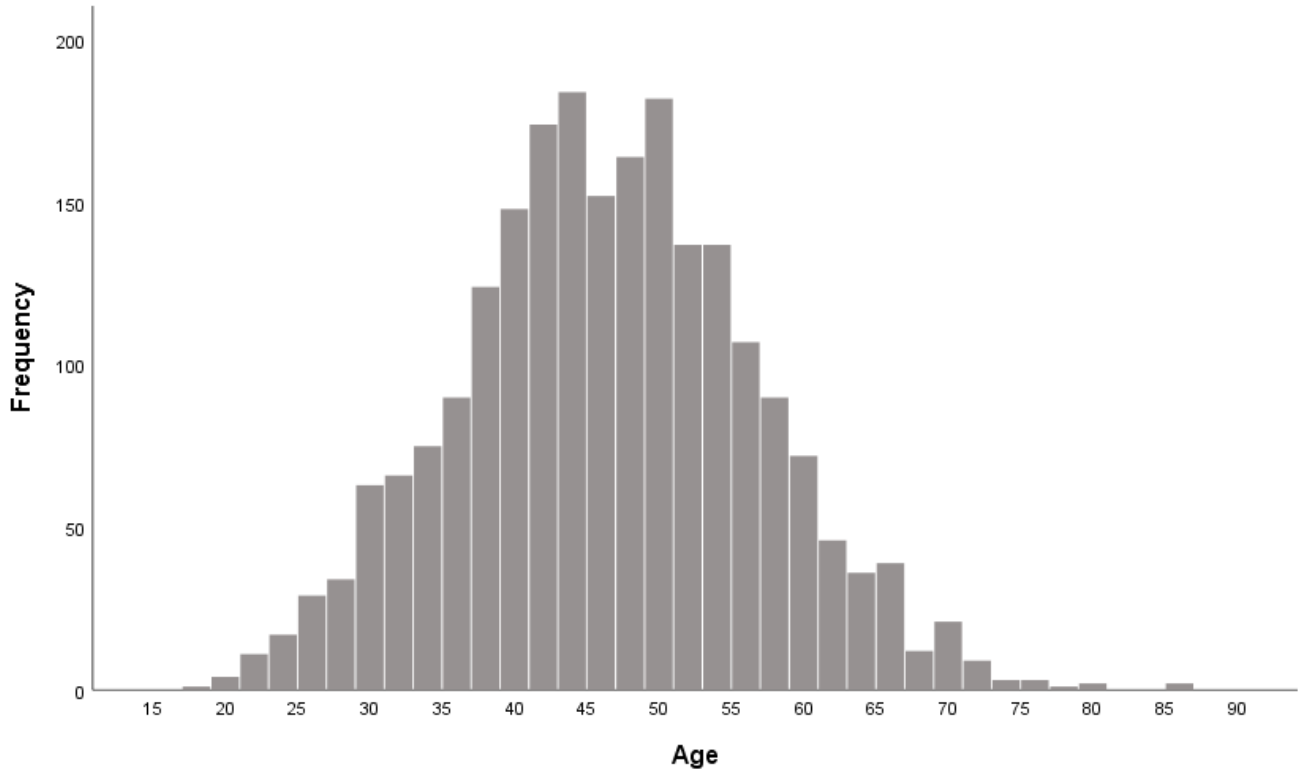

Fig. 1. Hidtogram of age distribution of study subjects.

Table 1. Sensitivity, specificity, positive and negative predictive value of VIA test in CIN2 or more case finding.

Test	Accuracy rate	Sensitivity (95% CI)	Specificity (95% CI)	PPV[1] (95% CI)	NPV[2] (95% CI)
Strong positive VIA	89.77 (88.06-91.27)	16.13 (5.45-33.73)	91.39 (89.8-92.81)	3.97 (1.29-9.04)	98.02 (97.11-98.7)
Positive VIA	72.65 (70.25-74.93)	41.94 (24.55-60.92)	73.33 (70.93-75.63)	3.35 (1.8-5.66)	98.28 (97.3-98.98)

[1]Positive predictive value. [2]Negative Predictive value.

In all cases, colposcopy-biopsy was carried out for purpose of comparison and the results were recorded.

In Colposcopic report sheet, findings were categorized as satisfactory examination, leukoplakia and acetowhite lesion. The location of lesions as well as presence of punctuations, mosaicism or abnormal vessels were recorded. High score colposcopy was described in the presence of a dense acetowhite, lesions in more than one quadrant, pilling, punctuation, mosaicism or abnormal vessels. Biopsy samples were preserved in formalin and delivered to a pathology laboratory located in an academic medical center. Samples were reported by one of three highly experienced pathologists, with more than 15-year work experience. The pathology report positive for CIN 2-3 on the Colposcopic biopsy was regarded as the gold standard.

Descriptive statistics were used to represent the data. The mean and standard deviation were used for continuous data, frequency, and proportion for categorical data. Predictive values such as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. R-Package version 3.0.1 was used for data analysis [18]. Subgroup analyses of strongly VIA positive and VIA positive cases were also carried out.

3. Results

Of the 1437 asymptomatic subjects screened (VIA followed by colposcopy). The mean age of the cases was 45.41 $\pm$ 10.84 with a range of 18 to 86 years. Age distribution of study subjects is presented in Fig. 1. Of these, 388 (27%) were VIA positive and 126 (8.8%) were strongly VIA positive. In 145 out of 388 (37.4%) VIA positive cases, SCJ was observed and in 243, (62.6%) it was not observed. In 64 out of 126 (50.8%) strongly positive VIA cases, SCJ was observed and in 62 (49.2%), it was not observed (SCJ is not usually seen in postmenopausal women due to lack of hormones). Table 1 shows the predictive values for the VIA for CIN 2-3.

The VIA positive test diagnosed 13 out of 31 CIN2-3 cases. The strongly positive VIA diagnosed that 5 out of 31 CIN 2-3 cases.

4. Discussion

The present study revealed that strongly positive and positive VIA detected CIN 2-3 case with a sensitivity of 16.13% and 41.94%, respectively. In both groups, the negative pre-

Table 2. Comparison of results of different studies regarding VIA test screening in CIN2 or more case finding.

Study	No.	Positive VIA N (%)	Positive CIN_2N (%)	Sensitivity	Specificity	PPV[1]	NPV[2]
Arab *et al.* (Strong VIA) Present Study	1437	126 (8.8)	31 (2.1)	16.13	91.39	3.97	98.02
Arab *et al.* VIA Present Study	1437	388 (27)	31 (2.1)	41.94	73.23	3.35	98.28
Zong *et al.* [22]	3763	698 (18.5)	22 (0.59)	77.3	81.2	24.4	99.8
Fokom-domgue *et al.* [23]	47782	8314 (17.4)	1577 (3.3)	82.4	87.4		
Apollinair *et al.* [4]	640	38 (5.9)	8 (1.2)	72.9	95.2		
Poomtavorn *et al.* [14]	200	59 (29.5)	32 (16)	59.4	76.2	32.2	90.8
Gaffikin *et al.* [24]				66-96	64-98		
Basu *et al.* [25]				55.7	82.1		

[1]Positive predictive value. [2]Negative Predictive value.

dictive value was 98%. The accuracy of both was considerable at 89.7% for strongly positive VIA and 72.6% for positive VIA results (Table 1).

The design of this article was cross-sectional and treatment was performed, however, the treatment information was not included in the design. In this project, women who have started their sexual activity, regardless of their age, are included in the study group. since the women in the study came from acharity organization, and had no previous screening history, no age related limit was set and all women were tested.

Comparison of results of this study with other studies that included VIA as screening and colposcopy-biopsy as the gold standard for CIN 2-3 case findings are shown in Table 2.

In the present study, the influence of subjectivity in VIA test was strong. For the strongly positive VIA 8.8% positive tests and for overall positive VIA 27% positive tests were reported.

If objectivity of testing is implemented, such as in a study in Thailand [14] the efficacy could improve. The criteria for a positive VIA were to find the lesions to be near an SCJ, well defined and opaque. VIA was considered to be negative in the presence of lesions which were faint or translucent, positive acetowhite over a polyp or Nabothian cyst, the narrow acetowhite rim around SCJ or lesions distant from SCJ.

One limitation of the present study was the lack of awareness of the exact location relative to the SCJ and the size of the lesion. This could make the VIA more subjective. Another important clinical aspect is the level of experience of the paramedical nurse who reported the VIA. A longer training session and a period of supervised performance could improve the quality of the test. Other helpful methods such as VIA with magnification (VIAM) would upgrade the efficiency of the test. Another important clinical aspect is pretest probability in the study population.

The high negative predictive value of the present study for the strongly positive VIA and overall positive VIA was 98%. This is comparable to the negative predictive values of VIA reported by Li-Ju Zong *et al.* (99.8%) and by Poomtavor *et al.* (90.8%) [14, 15].

VIA could be valuable in conjunction with other screening tests for diagnosis of CIN 2-3 in case findings. VIA and HPV testing have been suggested in combination instead of the PAP smear and HPV testing in developing countries. VIA is easy and could be performed during Gynecologic visits without extra-charge and without high technology requirement requirement but the HPV test was not available for these people due to cost related issues. It is shown to reduce women's mortality from cervical cancer in developing countries [19, 20]. VIA in combination with HPV testing could be an indicator of the need for colposcopy. VIA and pelvic exams should be repeated annually [21].

5. Conclusions

VIA is a simple procedure that can be carried out by a paramedical nurse. It is not expensive and worked well for screening in the present study (sensitivity of 41.9% and NPV of 98.2%). An accuracy of 89.7% and specificity of 91.3% for strongly positive VIA results and less accuracy and specificity of positive VIA results were reported (Table 1). These tests could be included in the screening algorithms in combination with cytology or HPV testing. A future study could determine the best place for VIA in screening programs and algorithms alongside other types of tests.

Limitation: In the present study, a trained nurse was under very careful teaching by an expert Gyneco-oncologist, which is not offered in normal teaching courses. Therefore, such excellent results of VIA might be due to this supervision.

Author contributions

Study concept and design: M.A*, A.M; Acquisition of data: M.A*, A.M, GH.F; Analysis and interpretation of data: M.A , A.M, GH.F, R.GH; Drafting of the manuscript: M.A*, A.M, GH.F, M.M; Critical revision of the manuscript for important intellectual content M.A*, A.M, M.M, S.S, M.S; Statistical analysis: M.A*, R.GH; Administrative, technical, and material support: M.A*, A.M, S.S; Study supervision: M.A*, A.M; Editing and submit articles: M.A*, GH.F.

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Conflict of interest

The author declares that she has no conflicting interest.

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