Original Article

Visual Inspection Using Acetic Acid (VIA) and Pap's Smear as Methods of Cervical Cancer Screening: An Experience of Dhaka Medical College Hospital, Dhaka, Bangladesh

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Abstract:

Background: National screening programme for cervical cancer has been running in Bangladesh since 2004 through visual inspection using acetic acid (VIA). However, Pap's smear is also used for the same, where it is available. ***Objectives:*** To see the effectiveness of VIA and Pap's Smear as cervical cancer screening methods. ***Methods:*** This prospective study was done on 600 women who attended the outpatient gynaecology clinic and cervical cancer screening programme underwent both VIA and Pap's smear cytology. Histopathology was taken as gold standard to compare the performance of VIA and cytology (Pap's smear). Hence, positive cases were further subjected to colposcopy directed biopsy. Then the sensitivity and specificity of VIA and Pap's smear were compared. The study was done in Dhaka Medical College Hospital, Dhaka, between July and December 2012. ***Results:*** On VIA, 46 had aceto-white lesions and on Pap's smear, 28 had atypical squamous cells of undetermined significance (ASCUS) or worse lesions out of 600 women screened. 22 were positive on both VIA and cytology; 24 were positive on VIA only; and 6 were positive on cytology only. Histological diagnosis of CIN/carcinoma cervix was found in 36 positive cases, who underwent biopsy (n=52). Among them, 20 were picked up from Pap's smear positive cases, whereas, 34 were VIA positive cases. VIA was found more sensitive (94.44%) than Pap's smear (55.55%), which was statistically significant ($p<0.001$). However, the specificity of VIA was slightly lower (97.87%) than that of cytology (98.58%). Positive predictive value (PPV) of VIA was 73.91% for VIA and 71.42% for Pap's smear, while Negative Predictive Value (NPV) were 9.63% and 97.2% respectively. ***Conclusion:*** VIA has got much more sensitivity and slightly lower specificity than that of Pap's smear in cervical cancer screening.

Keywords: Cervical cancer screening, visual inspection using acetic acid (VIA), Pap's smear, biopsy.

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Introduction:

Cancer of the cervix is the second most commonly diagnosed cancer and third leading cause of cancer death among females in less developed countries[1], as there were an estimated 527,600 new cervical cancer cases and 265,700 deaths worldwide in 2012[1]. In Bangladesh, a developing country of South Asia, every year an estimated 13,000 women are diagnosed withcervical cancer and 6,600 die from this disease[2].Unlike many cancers, cervical cancer can be prevented;cancer screening programs in the developed countries of Europe and North America have been followed by substantial reduction in disease burden[1-3]. Squamous cell cancer of the cervix and its precursor cervical dysplasia have been targeted successfully by screening because of the accessibility of the primary organ site (cervix), the acceptability of the current screening methods, the long preinvasive disease state in which it is feasible to detect disease and successfully intervene[4,5].The Papanicolaou (Pap) smear or Pap's test is an old and tested screening method for cervical lesions[4]. After several feasibility studies, bypassing cytology and going directly to colposcopy has been successfully implemented as a screening strategy for cervical dysplasia in low-resource settings[3,4]. Therefore, visual inspection using acetic acid

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(VIA) test is comparatively a new screening method,but being advocated by the World Health Organization (WHO) as cervical cancer screening test in a low-resource setting[3,5].In Bangladesh, cervical cancer screening programme has been running since 2004[2,3]. The Government of the People's Republic of Bangladesh (GOB) with the support of UNFPA has taken initiatives to develop cervical cancer screening programmebased on VIA throughout the country; hence, it becameone of the first countriesin the world to introduce VIA as the screening test for itsnational cervical cancer screening programme[2].However, Pap's smear is also used for the same, where it is available[3]. Several researches have been done in both developed anddeveloping countries in different regions of the world to see the effectiveness of different cervical cancer screening methods. However, there isno such report in the literature in our country. Therefore, present study aims to see the effectiveness of both VIA and Pap's smear cytology as cervical cancer screening methodsin Bangladeshi women.

Methods:

This prospective study was done on 600 women who attended the outpatient gynaecology clinic and cervical cancer screening programme in Dhaka Medical College Hospital, Dhaka, Bangladesh, which is one of the largest tertiary level treatment facility in the country. The study was conducted between July and December of 2012.

Exclusion criteria:

i) Those who refused to take part in any of the procedures of the study;

ii) Unmarried and pregnant women;

iii) Women who had history of abnormal cytology; and

iv) Women who previously treated for CIN/cancer.

After initial selection and obtaining written informed consent from each patient, the socio-demographic data were recorded in the study form. Then the patient underwent both VIA and Pap's smear cytology in the Department of Obstetrics &Gynaecology. Each recruited patient was placed in the lithotomy position. The procedure was carried out by the researcher who is also a pathologist, with the assistance of a trained physician, nurse or midwife, as per guideline of WHO[5]. ACusco's bivalve speculum was introduced under good lighting to visualize the cervix. The Ayre's spatula was used to scrape the transformation zone. This was then smeared on a clean slide and fixed with 95% ethyl alcohol for at least 15 minutes before transportation to the pathology laboratory for Papanicolaou staining. The Pap's smear cytology was reported in the followingcategories:i) negative for neoplastic cellular changes, ii) atypical squamous cells for undetermined significance, iii) low-grade intraepithelial lesion (LSIL) and high-grade intraepithelial lesion or worse (HSIL+)[6]. The cytology was interpreted in theDepartment of Pathology. Thereafter, 5% acetic acid solution was applied to cervix using a cotton swab and after 1 min, visual inspection of cervix was done for the development of any acetowhite area near squamocolumnar junction or close to the external os or presence of aceto-white growth. The VIA results were interpreted as positive when any of the following were observed:i) well-defined, opaque, acetowhite lesions touching the SCJ or the external os, if SCJ was not visible;ii) large circumferential acetowhite lesion surrounding the external os; iii) any pre-existing wart or leukoplakia turning intensely white after application of acetic acid; and iv) ulceroproliferative growth turning densely acetowhite after application of acetic acid[7]. As histopathology was taken as gold standard to compare the performance of VIA and cytology (Pap's smear), therefore,the positive cases were further subjected to colposcopy directed biopsy[5]. The histopathology was done in the Department of Pathology as well. The reports and photographs were collected from both of the departments. Sensitivity, specificity and predictive values and their 95% confidence intervals were calculated using 2 × 2 tables and standard formulae[8]. Then the sensitivity and specificity of VIA and Pap's smear were compared.The used statistical test was the Chi-square test and results were determined by using SPSS version 13.

Results:

Among the 600 participants of the study, 30-44 years group was the most (52.67%), 71.5% were married, 93.83% were in monogamous relationship and 65.67% had parity of 1-4(Table 1). After screening in the present study, on VIA test, 46 women had aceto-white lesions [Figure 1(a,b)], while on Pap's smear test, 28 women had atypical squamous cells of undetermined significance (ASCUS) or worse lesions [Figure 1(c)]. 22 were positive on both VIA and cytology; 24 were positive on VIA only; and 6 were positive on cytology only. Histological diagnosis of CIN/ carcinoma cervix was found in 36 positive cases, who underwent biopsy (n=52) [Figure 1(d,e)]. Among them, 20 were picked up from Pap's smear

positive cases, whereas, 34 were VIA positive cases. VIA was found more sensitive (94.44%) than Pap's smear (55.55%), which was statistically significant ($p<0.001$). However, the specificity of VIA was slightly lower (97.87%) than that of cytology (98.58%). Positive predictive value (PPV) of VIA was 73.91% and 71.42% for Pap's smear, while Negative Predictive Value (NPV) were 9.63% and 97.2% respectively(Table 2&3).

Table 1. Socio-demographic distribution of the study subjects (n=600).

Characteristics	Frequency	Percentage
Age		
15-29	178	29.67
30-44	316	52.67
45-59	106	17.66
Marital status		
Married	429	71.5
Divorcee	102	17
Widow	69	11.5
Sexual partner		
1	563	93.83
2 or more	37	6.17
Parity		
1-4	394	65.67
5 or more	206	34.33

Table 2. Sensitivity and Specificity of VIA test.

	Biopsy / histopathology Positive	Biopsy / histopathology Negative	Total
VIA Positive	34	12	46
VIA Negative	2	552	554
Total	36	564	600
Sensitivity: 34/36 ×100 = 94.4%; Specificity: 552/564× 100 = 97.87%; Positive Predictive Value: 34/46 × 100 = 73.91%, Negative Predictive Value: 552/554 × 100 = 99.63.%			

Table 3. Sensitivity and Specificity of Pap's smear test.

	Biopsy/ histopathology Positive	Biopsy/ histopathology Negative	Total
Pap's smear Positive	20	8	28
Pap's smear Negative	16	556	572
Total	36	564	600
Sensitivity:20/36×100=55.55%;Specificity:556/564×100=98.58%; Positive Predictive Value: 20/28 × 100 = 71.42%; Negative Predictive Value: 556/572 × 100 = 97.2%.			

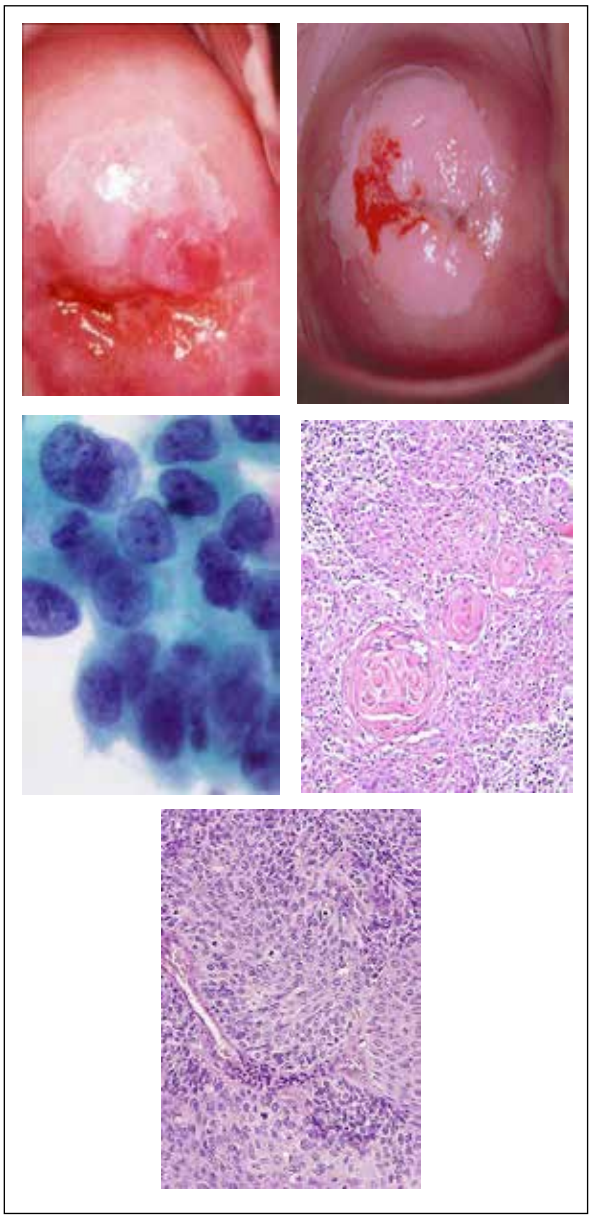

Figure 1: (From left) **a)** VIA shows transformation zone, where low-grade lesions visible as aceto-white epithelium attached to the squamocolumnar junction (SCJ) on the anterior ectocervix;**b)** VIA shows a high-grade lesion, positive diagnosis for cancerous cell activity; **c)** Pap's smear cytology shows high-grade cervical cell dysplasia; **d)** Histopathological slide shows well-differentiated cervical cancer as evidenced by keratin pearls and nests of neoplastic squamous cells invaded through stroma with chronic inflammation; **e)** Histopathological slide shows squamous cell carcinoma of the cervix, non-keratinizing type.

Discussion:

The large geographic variation in cervical cancer rates reflects differences in the availability of screening, which allows for the detection and removal of precancerous lesions, and human

papillomavirus (HPV) infection prevalence[1]. The present study was a comparative study of two screening methods for pre-invasive lesions of the cervix in women. VIA is comparatively a new screening method being advocated by the World Health Organization (WHO) as cervical cancer screening test in a low-resource settings[3,5], while Pap's test is an old and tested screening method for cervical lesions[4]. These two methods were compared in 600 patients who attended the outpatient gynaecology clinic and cervical cancer screening programme in Dhaka Medical College Hospital, Dhaka, Bangladesh. All the patients underwent both Pap's test and visual inspection of the cervix following acetic acid (VIA) wash. The present study has shown that VIA is more sensitive than Pap smear and also with comparable specificity and accuracy to Pap smear. Moreover, VIA is easy, cheap, and sometimes treatment can be administered at the same time[3,5].

The suitability of a screening test relates not only to its simplicity and safety but also to its accuracy, as measured by sensitivity and specificity[8]. The characteristics of VIA and Pap's smear cytology as cancer screening tests have been investigated in several cross-sectional studies in different countries. Doh et al.[6] did similar study in Cameroonand found that the sensitivity of VIA was much more (70.4% vs. 47.7%)than that of Pap's smear, while the specificity was diametrically opposite (77.6% vs. 94.2%); PPV was 44.0% vs. 67.2%. and NPV was 91.3% vs. 87.8%.Sankaranarayanan et al.[7] studied on VIA, involving 56,939 women aged 25-65 years, conducted in Burkina Faso, Congo, Guinea, India, Mali and Niger and found that the sensitivity, specificity, positive and negative predictive values for VIA were 76.8%, 85.5%, 9.4% and 99.5%. Akinola et al.[9]performeda study on 186 Nigerian women and found that the sensitivity of VIA was 100%, while that of Pap smear was 85.7%. The negative predictive value of VIA was 100%, while the positive predictive value was only 20%. Akiwuntan et al.[10] studied on205 consenting HIV-seropositive womenin Nigeria and found that the sensitivity of VIA was 76.0%, specificity 83.0% and positive predictive value 34.0%. In contrast, the sensitivity Pap's smear cytology was 57.0%, specificity of 95.0% and positive predictive value of 55.0%. Cronje et al.[11] studied on1286 women in South Africa and found that the sensitivity, specificity, and positive predictive values for cytologic examination were 53%, 95%, and 47%, respectively; for VIA were 79%, 49%, and 12%, respectively. Hegde et al.[12] experimented on 225 women of reproductive age in India and found that Pap's smear had a sensitivity of 83%, specificity of 98%, and positive predictive value of 80% and negative predictive value of 97.9%, while VIA had 70.8%, 95%, 62.9% and 96.5% respectively. Vadehra& Jha[13] analyzed the screening results of 500 women in Nepal and reported that VIA was more sensitive (96.4%) than Pap smear (71.4%), which was statistically significant. However, the specificity of VIA was lower (37.5 %) than that of cytology (56.3%). The PPV were 73% and 71.4 %, while NPV were 85.7 % and 52.9 % respectively. However, we were unable to find any comparable study done in Bangladesh. Our results varied from other studies conducted in the differentcountries and environment; however, in all those studies, VIA test was generally found more sensitive but less specific than that of Pap's smear cytology test which is in agreement with our study.

Prevalence of positive VIA test depends on the characteristic of the population studied e.g., asymptomatic women or symptomatic; co-incidental pathology of cervical dysplastic lesions and cervicitis or inflammation; cervical anatomy or area of transformation zone which is affected by age or menopausal status; or parity[7]. Besides, one of the major reasons for wide variation in results of VIA in many studies is the lack of standardized criteria for a positive result[14]. VIA is also provider dependent; hence, it is necessary that before it is used as part of a national screening programme, a uniform reproducible system for categorizing and reporting VIA findings should be put in place[2,3,14]. Standard training can then be provided to all health care providers for quality control[3,14].

A large-scale study comparing VIA and Pap smear reports to tissue biopsy reports and HPV typing may help to further evaluate the true state in this environment. This can be done by making use of single or double blinding of the cytopathologists or histopathologists so as to exclude bias[14].The results obtained from the present study could also be explained by the fact that the VIAs were performed by a single investigator and the Pap's smears were also reported by the same person. Thus, this excluded inter-observer variations from both methods.

Conclusion:

VIA has got much more sensitivity and slightly lower specificity than that of Pap's smear in cervical cancer screening.As we discussed earlier, VIA is

easy, cheap, and treatment can be administered at the same time. Hence, in a developing country like Bangladesh, for cervical cancer screening the preferable method is VIA. As Bangladesh Medical Research council is a policy making organization in national health care sector, it is recommended that cervical cancer screening in countrywide health facilities can be continued through visual inspection using acetic acid (VIA) method for any resource-poor setting e.g. union sub-centre or upazilla health complex. However, Pap's smear and histopathological examination should be done where facilities are available especially in district hospitals and medical college/university hospitals.

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