Original Article

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Visual Inspection of Cervix wiih Acetic Acid as A Method of Cervical Cancer Screening in Tertiary Hospital

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ABSTRACT

Background: *Cervical cancer belongs to a glorious natural history which favors well implemented secondary prevention. Considering the various constraints in our country, our study aimed to evaluate Visual Inspection of Cervix with Acetic Acid (VIA) as an alternative or adjunct to cervical cytology (Pap smear) in early detection of cervical cancer and also to assess its effectiveness as a screening method in a tertiary center outside of low resource settings.*

Materials and methods: *This cross-sectional descriptive study was carried out at Gynae OPD of Chittagong Medical College Hospital (CMCH) from January to December 2012. A total of 1600 sexually active women with 21 to 60 years old were enrolled in this study by purposive sampling technique. The women underwent a complete clinical evaluation, including Pap smear and VIA. Any positive test was referred to colposcopy and directed biopsy. Finally, data were analyzed with the help of SPSS 16 software.*

Results: *Out of 1600, VIA was positive in 135(8.4%) and cytology was positive in 74(4.6%) cases of the true positive 48 cases. The sensitivity of VIA (75%) was much higher than that of Pap smear (48%). The sensitivity ratio 1.54 (p<0.001). The positive predictive value for detection of CIN2 and above was 17% for VIA and 16% for pap (p=0.5). Moreover, patients of lost to follow-up before colposcopy and biopsy were only 4.44% with VIA positive cases while 28.38% with positive Pap smear (p<0.0001).*

Conclusions: *The high sensitivity of VIA indicates that it may be a feasible alternative test for detection of precancerous lesions of the cervix not only in limited-resource settings but also in a well-equipped tertiary hospital.*

Key words: Cervical cancer screening; CIN; Pap smear; VIA.

Introduction

Cervical cancer is a major public health problem for developing countries. It is the second most common cancer among women worldwide, with an estimated 5,00,000 new cases each year[1]. It is evidenced that, approximately 83% of the world's new cases and 85% of all cervical cancer deaths reported are from developing countries[2]. It is the leading cause of death from cancer among women in developing countries, where it causes about 190,000 deaths each year[3]. About 22 - 29% of the women are affected by cervical cancer in different areas of Bangladesh[4]. Incidence and the mortality rate of cervical cancer has markedly decreased in developed countries since cytologic cervical cancer screening was introduced more than 50 years ago. But in our country, 80% of diseases are detected at the last stage when it is not curable. However, it is 100% curable if detected in an earlier stage only by screening.

Invasive cervical cancer is preceded by a long premalignant phase known as Cervical Intraepithelial Neoplasia (CIN)[5]. In progression of invasiveness, it takes about 10 years, a long gap in which detection and treatment is easily possible. The goal of cervical cancer screening is the detection and treatment of precancer before cancer develops[6-8]. In developed countries, Papanicolaou (Pap) smear is highly effective having widespread screening programs. But, in developing countries, it is not feasible as there is a lack of trained cytotechnologists and cytology labs. Often a long interval (1-3 months) between the Pap screenings and test result is available. Additionally, only a small percentage of women with positive Pap smears have diagnostic evaluation and treatment, because facilities are insufficient for health centers that are able to treat preinvasive lesions. On the other hand VIA has demonstrated high sensitivity for detecting CIN and cervical cancer, but it is limited by low specificity.

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VIA has the advantage of requiring only low technology equipment. And the result is available within a couple of minutes, which make VIA a realistic alternative for low resource settings. Besides, in our country, Pap smear is available in only some selected private and public health centers of urban areas. Also there are several barriers regarding patient's compliance with follow-up. The test is not free even in government hospitals. Patients have to pay a fee about 150 to 200 taka which in some cases is equivalent to a family's income for a day. In addition, there is no nationwide quality control system to assure accurate screening. Thus alternative strategies are being investigated including Visual Inspection of Cervix with Acetic Acid (VIA). VIA is based on aceto-whitening of the Cervical Intraepithelial Lesions (CIN) turning white when exposed to 5% acetic acid. Our study aimed to evaluate weather VIA has a role as a screening test not only in first level health centers in low resource areas but also in tertiary hospital where Pap testing has been the norm .The institute differs from low resource settings in that it has the latest generation equipment,well trained personnel and cytology lab for the evaluation and diagnosis of cervical cytology.

Materials and methods

It was a cross-sectional descriptive study carried out at Gynae OPD of CMCH from January to December 2012. Total 1600 sexually active women with 21 to 60 years old visited OPD were included in the study after fulfilling the criteria and giving informed consent. Pregnant, H/O abnormal cytology, previous treatment for CIN or cancer, chronic cervicitis until properly treated and obvious cancer at the time of clinical evaluation were excluded .Study subjects had a complete physical examination and pelvic evaluation done. The Pap smears sampling and VIA were performed by the same evaluator.

A speculum examination was done with a direct visual examination of the cervix to identify cervicitis, leucorrhoea, polyps, ulcers etc. A Pap smear sample was then taken using a conventional wooden Ayres spatula.The smear was fixed with ethanol for 30 minutes.Then VIA was done with gentle application of 5% acetic acid using a small piece of cotton for one minute. The cervix was carefully inspected for any aceto-white lesions, particularly in the Transformation Zone (TZ) to constitute as positive. VIA positive cases were informed immediately and a colposcopy was done on the same day.Women with a negative VIA were given an appointment on the next week to receive their Pap results and to have colposcopy if the Pap was positive. A directed biopsy was then taken and fixed in 20% buffered formalin only if an aceto-white lesion was found during colposcopy of any positive VIA or PAP tests. Women without aceto-white lesions during the colposcopic evaluation were considered as normal and did not have a biopsy. The results of the Pap smear were reported according to revised 2001 Bathesda system. Pap was positive in any cytology diagnosis that included Atypical Squamous Cells of Undetermined Significance (ASCUS) Low Grade Intraepithelial Lesion (LSIL) High Grade Intraepithelial Lesion (HSIL) or invasive cancer. Pap smears were screened and reviewed by pathologists. Biopsies were evaluated by pathologists blinded to the VIA results. Women with a final histology of CIN-2 or above were considered as cases for the statistical analysis. Any abnormal cytology or VIA but without colposcopy and biopsy was considered as lost to follow-up and excluded from the statistical analysis as their final status was unknown on biopsy. The evaluator filled out a form with general examination on each women, clinical findings at pelvic evaluation,results of the VIA, colposcopy and biopsy when indicated. Then, data were analyzed using SPSS 16 software.

Results

We evaluated a total of 1600 sexually active women between 21 and 60 years old who fulfilled the eligibility criteria and provided informed consent (Although WHO recommends VIA screening for women in the age group between 30 and 49).

Regarding socio-demographic profile, the maximum women (41.8%) were between 31 to 40 years of age group followed by 31.4% were in the 41 to 50 years age group. About 63.6% respondents were from urban area and 36.4% were from rural area. About 83% were housewives and 5% were service holders. An important finding is that 12% women were garments worker. It was found that about 31.2% only had completed primary level and only 13.1% had completed secondary level or above. The income was up to 10,000/ month in 63.5% cases (Table I).

Table I Socio-demographic variables

Characteristics	Frequency (n=1600)	Percentage (%)
Age (In Years)		
21 to 30	196	12.3
31 to 40	669	41.8
41 to 50	503	31.4
51 to 60	232	14.5
Residence		
Urban	1018	63.6
Rural	582	36.4
Occupation of the respondents		
Housewife	1328	83
Service holder	80	5

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Garment worker	192	12
Education level		
Illiterate	320	20.12
Literate	576	36.42
Primary	496	31.20
Secondary	208	13.10
Monthly family income (In taka)		
<5000	312	19.5
5001-10000	704	44
10001-15000	345	21.5
15001-20000	126	7.9
>20000	113	7.1

In findings regarding risk factors, 47.1% respondents were married at age 16-20 years, 33.1% were married at age 21-25 years. In terms of parity,most of the women were multiparous, only 8.1% of women were nulliparous. Use of contraception were predominant among 71.1%. Among the contraceptive user, most of them (66%) used hormonal method (Table II).

Table II Findings regarding risk factors

Characteristics	Frequency (n=1600)	Percentage (%)
Married at age		
<16 years	188	11.8
16-20 years	754	47.1
21-25 years	529	33.1
26-30 years	116	7.2
>30 years	13	0.8
Parity		
Nulliparous	130	8.1
2	656	41
3	507	31.7
4	162	10.1
>4	145	9.1
Use of Contraception		
Yes	1138	71.1
No	462	28.9
Types of contraception		
Hormonal	1056	66
Non hormonal	544	34

Among 1600 women, 135 of them (8.4%) were found VIA positive and 74 (4.6%) had positive Pap smear of the true positive (48 cases) 11 women (0.68%) had a positive result on both tests. The sensitivity of VIA (75%) was more than Pap smear (47.91%). The sensitivity ratio was 1.54 (p<0.001). The specificity of VIA (93.67%) was comparable to Pap smear (96.77%). However, the positive predictive value (PPV) of VIA vs Papsmear was 26.67% vs 31.08% (Table III).

Table III Statistical comparison of VIA and Pap

Validity	VIA	Pap
Sensitivity	75%	47.91%
Specificity	93.67%	96.77%
Positive predictive value	26.67%	31.08%

Sensitivity ratio 1.54, p<0.001.

Table IV depicts the data of screening for cervical cancer done with Visual Inspection with Acetic Acid (VIA) and with conventional Pap smears. During the study, total 152 cases of biopsy was done. Among them CIN-1 was 20 cases, CIN-2 was 25 cases and CIN-3 was 3 cases, invasive cervical cancer was 01 case, the rest 104 cases were chronic cervicitis or metaplasia. It was found that the women with positive tests CIN 1 found in 20 respondents where 13 were VIA positive, 11 were Pap positive and 4 were both positive. CIN 2-3 found in 28 cases where 23 (82.14%) were VIA positive, 12 (42.86%) were Pap positive and 9 (32.14%) were both positive. Out of 48 cases VIA could detect 36 (75%) positive by histopathology, 23 (47.91%) were Pap positive and 13 (27.08%) were both positive.

Table IV Detection of different categories of cervical intraepithelial lesions by screening (VIA and Pap smear)

Total 1600	VIA positive		PAP smear		p value positive	VIA & PAP positive	
	No.	%	No.	%		No.	%
	135	8.4	74	4.6	0.0001	11	0.68
CIN 1 (n=20)	13	65	11	55	0.4	4	20
CIN 2-3 (n=28)	23	82.14	12	42.86	0.06	9	32.14
CIN 1-3 (n=48)	36	75	23	47.91	0.09	13	27.08

p value is for McNemar's chi-squared test.

The Positive Predictive Value (PPV) for detection of CIN 2 or worse was 16.21% for the Pap smear and 17.04% for the VIA (p = 0.5). One of the important finding of the study was among the 135 women who had a positive VIA, 6 of them (4.44%) did not return for colposcopy and biopsy. In contrast, of the 74 women with a positive Pap smear, 21 of them (28.38%) did not return for colposcopy and biopsy (p<0.0001). These patients were lost despite repeated efforts to contact them with phone calls (Table V).

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Table V Comparison of PPV and lost in follow up between VIA and pap smear

	VIA positive		PAP smear positive		p value
	No.	%	No.	%	
Total 1600	135	8.4	74	4.6	
Predictive value of positive test (For CIN2-3)	23	17.04	12	16.21	0.5
No. of patients lost in follow up	6	4.44	21	28.38	<0.0001

Discussion

Developing country like Bangladesh has limited resource but disease burden is high. In developed country, mostly screening tests are Pap smear based. In recent decade Human Papilloma Virus (HPV) DNA testing has been shown very high sensitivity and is being recommended in high resource countries[9]. However, its current price and technology requirements make these options unrealistic for poor areas. This study was done to determine the potential of VIA to supplement or replace the Pap smear in screening in a tertiary care center.

In our study,the prevalence of VIA or positivity of VIA was 8.4% which is consistence with other research studies in Asia and Africa where positivity range from 6.6% to 27.4%[10-13]. Various studies on the prevalence of cervical epithelial cell abnormality in the Pap smear revealed 4.3% in a tertiary hospital in Kuwait, 5% in a large referral hospital in Saudi Arabia which is consistent with our study 4.8%[14-15].

Regarding the sensitivity and specificity, our result was less than that reported by Sankaranarayana et al[10]. But the University of Zimbabwe/JHPIEGO found VIA vs pap smear as 77% vs 44% had similarity with our study[16]. VIA is a simple and affordable screening test with acceptable sensitivity and specificity in the range 50-88.6% and 66.7-89.7% respectively[16]. This wide range is due to variation in age of the women, type of provider, and their training[17]. Here we should emphasize that in our study the evaluators were trained even with experience in colposcopy,while in other studies the evaluators are health workers with less training. It highlights the importance of training and refresher training to increase the expertization for the performance of visual evaluations. This issue should be kept in mind during the development of protocols in remote areas also to maintain the quality of the health workers. Other fact that the patients did not visit the tertiary hospital for cancer screening purpose, but rather with specific gynecological complaints. It is notable that they had come to visit the hospital when the dyskaryotic changes in the cervical epithelium had already occurred. All these patients were married and most of them were multiparous.

In the context of our country like Bangladesh where premarital sex is forbidden, age at marriage can be taken as the age at the first sexual intercourse. Our study demonstrated that the average age at marriage was around 16 when they were in their teens. These patients had increased risk of HPV as there was a biological predisposition of the immature cervix of the adolescent to persistent HPV infection,which augmented the risk of cancer development. Therefore, family planning, sexual education and HPV vaccination should be targeted toward this early age group. However, information provided in this study will in addition encourage further utilization of VIA as a screening method for cervical cancer in tertiary hospital.

Majority of the cervical abnormalities in our study were detected in women <40 years, indicating VIA is effective in premenopausal age. Regrettably, so far, another important finding concerned the percentages of women with positive tests who were lost to follow up before colposcopy and treatment. The percentage was significantly lower in VIA positive women (4.44%) than in women with a positive Pap smear (28.38%) p<0.0001. This happened because the VIA-positive women knew their abnormal result immediately during the first visit and they immediately received special counseling about the finding and the importance of returning colposcopy and biopsy. So, this ensures good compliance for screen positive women. On the contrary, to know about the result of Pap smear (Either positive or negative), women had to return one week later for a second visit, which many of them did not do and so never received special counseling about the significance of any positive result. This percentage of participants with abnormal cytology lost before colposcopy might be considered as a source of bias at the time of statistical analysis and comparison with VIA. However, this result does reflect the real problems faced with screening based on the Pap test in developing countries[18].

However, the PPV was calculated considering as cases only women with CIN 2-3 on histology, which is about 17.04% that is consistent with Shankarnarayana et al[11]. This result outline the potential benefits of using VIA at all levels of health care systems in developing countries[11].

The results of the current study and other reported studies indicate that VIA is a simple objective test. The immediate result of this test, allowing an algorithm of further investigation to be carried out to detect cervical lesions. In our study, the high specificity (High false positive rate) indicated that many subjects were recalled for colposcopy, in which the objectivity of the test can further be improved possibly by magnification. Treatment of preinvasive lesions can be performed immediately

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which not only avoids recall but also increases compliance to diagnostic investigation and treatment. Lack of awareness, illiteracy and poverty make the Pap test more difficult. So, VIA can be used as a screening method in developing countries not only in rural areas and small health centers but also in tertiary hospitals with better resources. It is not expensive and it is a real time test, biopsy and treatment can be done in the same sitting, thus decreasing the probability of losing the patient. The "Screen and Treat" method was followed in our country since 2008. The RCT in Dindigul district in south INDIA found there was a reduction in cervical cancer incidence and mortality by 25% and 35% respectably,with a single visit VIA followed by treatment done by mid-level providers[11].

Conclusion

Our study outline the potential benefit of VIA to detect precancerous lesions of cervix and the availability of immediate results overcome the problem of "lost to follow-up" that's occur in Pap smear. So, in developing country like Bangladesh, to achieve earlier diagnosis, follow-up and treatment VIA is a suitable primary screening alternative for a large population not only in low resource settings but also in well- equipped tertiary hospital.

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Disclosure

All the authors declared no competing interest.

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