RESEARCH ARTICLE

Comparison between Visual Inspection of Cervix and Cytology Based Screening Procedures in Bangladesh

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Abstract

Background: Cervical cancer continues to be a major problem in Bangladesh with approximately 18,000 new cases annually of which over 10,000 women die from it. Visual inspection of the cervix after 3-5% acetic acid (VIA) application is a simple and easy to learn method for cervical cancer screening, although cytology-based screening is more often applied in developed countries where it has successfully reduced the prevalence of cervical cancer. Objective: To compare the efficacy of VIA and cytology-based primary methods for cervical cancer screening in Bangladesh. Materials and Methods: This hospital based comparative study was conducted at the VIA centre and Colposcopy Clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) from October 2008 to October 2010. Results: Among 650 women, 74 (11.4%) were VIA+ve and 8 (1.2%) had abnormalities in their Pap smear reports. During colposcopy, 38 (7.7%) women had different grades of CIN and 4 (0.6%) had cervical cancer. The gold standard histology findings proved 20 women had CIN I, 14 had CIN II/II and 4 had cervical cancer. Among the 38 histology diagnosed abnormalities, VIA test could identify 30 abnormalities including two cervical cancers. However, Pap smear could detect only 8 cases of histological abnormalities (2 low grade and 6 had high grade lesion) and it missed all the cervical cancer cases. The sensitivity and specificity of VIA were 88.9% and 52.1%. The positive predictive value (PPV) and negative predictive value (NPV) were 41.0%, and 92.6% respectively. Moreover, the sensitivity, specificity, PPV and NPV of Pap smear were 33.3%, 95.8%, 75.0% and 79.3%, respectively. Conclusions: VIA test should be used as the primary screening tool even with its low sensitivity and specificity in low resource countries like Bangladesh. False positive results may be greater, but overtreatment can be minimized by colposcopy evaluation of the VIA positive women.

Keywords: Comparison - VIA - Pap smear - Bangladesh

Asian Pac J Cancer Prev, **14 (12)**, 7607-7611

Introduction

Cervical cancer continues to be a major problem in Bangladesh and it constitutes 17,686 new cases annually and each year 10,364 women die from it (Ferlay et al., 2008). According to hospital records in Bangladesh, it constitutes about 22-29% of all female cancers (Akhter et al., 1998).

Visual inspection of the cervix after 3-5% acetic acid (VIA) application is a simple and easy to learn method of cervical cancer screening. On exposure to this solution, abnormal cells of the cervical epithelium temporarily turn white and reveal aceto-white epithelium of the abnormal transformation zone. Several studies showed the advantages of VIA, including its simplicity, high sensitivity and instant results (Singh et al., 2001; Ghaemmaghami et al., 2003; Geol et al., 2005). Little infrastructure is required and the cost of launching a VIA-based programme is low. Therefore the Government of Bangladesh (GOB) initiated the implementation of the VIA-based screening programme in collaboration with UNFPA (United Nations Population Fund) and Bangabandhu Sheikh Mujib Medical University (BSMMU) in the year 2004. VIA is continuing at Maternal and Child Welfare Centres (MCWCs), District Hospitals (DHs), Medical College Hospitals (MCHs) and BSMMU. Trained Family Welfare Visitors (FWVs), Senior Staff Nurses (SSNs) and Doctors offer VIA to all married women 30 years and above to detect the pre-cancer and early cervical cancer among women visiting VIA centres of different districts in Bangladesh (Ahmed et al., 2008; Nessa et al., 2010). Screen positive women are referred to BSMMU and various government MCHs for colposcopy evaluation and management. Cervical cancer screening programme is an ongoing programme and colposcopy becomes an important part of this prevention programme. Women with pre-cancers are managed by loop electrosurgical excision procedure (LEEP) at the colposcopy clinic of BSMMU and different MCHs (Ahmed et al., 2008; Nessa et al., 2010).

Cytology-based screening has become the ideal

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screening method and it has successfully reduced the prevalence of cervical cancer in many developed countries (Sankaranarayanan et al., 2001). Therefore it was necessary to compare the efficacy of VIA and cytology-based method among the population in our health infrastructure settings before implementing this method throughout the country. In the present study comparison was made between VIA and cytology-based screening as primary method of cervical cancer screening at the VIA centre of BSMMU. Also the awareness status of women on the methods of cervical screening was assessed.

Materials and Methods

This hospital based comparative study between VIA and cytology-based screening procedures was conducted on 650 women at the VIA centre and colposcopy clinic of BSMMU from October 2008 to October 2010. Women more than 30 years of age attending the gynaecological outpatient department (GOPD) of BSMMU are routinely referred to the VIA centre. Moreover women are referred to the VIA centre of BSMMU by general practitioners and other service providers of the surrounding areas. The Institution Review Board of BSMMU gave permission to complete the study. During the study period every 5th woman of 30-45 years attending the VIA centre were invited and counseled to join the study. If the 5th women did not match the age range or did not agree to join the study, consecutive women were considered for recruitment. Women with pregnancy, vaginal bleeding, history of hysterectomy or treatment for cervical pre-cancer or cancer were not included. After counseling, motivating and recruiting the study population at the VIA centre, the women were sent to the colposcopy clinic of BSMMU for data collection and examination. After informed consent and taking their relevant history, the study subject had a complete physical and pelvic examination. A speculum examination was performed for each woman and Pap smear was collected with wooden spatula and cytobrush by trained medical officers and sent to the histopathology department of BSMMU after fixation with ethanol for 30 minutes. An acetic acid (5%) soaked cotton ball was applied for 1-2 minutes on the cervix before naked eye evaluation of cervix under 100-watt illumination. The test results were divided in two categories as VIA negative and VIA positive. When any of the findings like a well defined dense opaque acetowhite lesion close to the squamo-columnar junction or acetowhite area touching the transformation zone was observed the result was reported as VIA positive. On the other hand if no acetowhite lesion, faint or a white line indicative of squamo-columnar junction was observed, the result was reported as VIA negative. Immediately after VIA, the same woman had colposcopy by one of the six colposcopists involved in the study following the method described by the IARC manual on colposcopy (Sellors et al., 2003). Women with normal colposcopy findings did not have colposcopy guided biopsy, only women with abnormal colposcopy findings had it.

The results of VIA, Pap smear and colposcopy examination were compared with histological diagnosis. The histology finding was considered as gold standard against which the sensitivity and specificity of VIA, Pap smear and colposcopy were calculated using standard statistical methods.

Results

More than half (56.9%) of the recruited woman (N=650) attended from Dhaka, and the remaining attended from other 37 districts of Bangladesh. About half of them (52.0%) were in the 30-35 years age group. A good number had primary (38.2%) and secondary education or more (48.9%). Majority (84.5%) were housewives, and about two third of the families belonged to the middle class income group. More than half (56.2%) of the women had been married before 18 years of age and about one third had their first delivery before 18 years (Table 1).

Two-third (69.2%) of the women referred for cervical cancer screening were aware about cervical cancer and half of the women (47.4%) knew about prevention of the disease. About one third of them had knowledge on VIA only, 6.2% knew about Pap smear only and 14.0% knew about both the tests. Majority (69.5%) came to know about the tests from doctors (Table 2).

Among 650 women, 74 (11.4%) were VIA+ve and 8 (1.2%) had abnormality in the Pap smear report. During colposcopy, 38 (7.7%) women had different grades of CIN

Table 1. Socio-Demographic and Reproductive Characteristics (n=650)

Characteristics		No. (%)
Home district:	Dhaka	370 (56.9)
	Narayanganj	32 (4.9)
	Comilla	30 (4.6)
	Gazipur	28 (4.3)
	Others (34 Districts)	190 (29.2)
Age (years)	30-35 years	338 (52.0)
	36-40 years	202 (31.1)
	41-45 years	110 (16.9)
Religion:	Muslim	616 (94.8)
	Hindu	32 (4.9)
	Christian	2 (0.3)
Education of women	No Education	84 (12.9)
	Primary	248 (38.2)
	Secondary	151 (23.2)
	Higher Secondary	68 (10.5)
	Graduate & above	99 (15.2)
Occupation of women	House wife	549 (84.5)
	Day labor	10 (1.5)
	Service holders	81 (12.5)
	Business	10 (1.5)
Monthly family income		
Poor (up to Tk. 5000)		126 (19.4)
Lower middle class (Tk. 5001 to 10000)		202 (31.1)
Middle class (Tk. 10001 to 30000)		241 (37.1)
Higher middle class and upper class (> Tk. 30000)		81 (12.5)
Age of marriage of women	≤ 17 years	365 (56.2)
	18-20 years	172 (26.4)
	21 years and above	113 (17.4)
Age of first delivery	≤ 17 years	197 (30.3)
	18-20 years	203 (31.2)
	21-25 years	169 (26.0)
	26 years and above	56 (8.6)
	Nulipara	25 (3.9)
Parity	No Children	25 (3.9)
	1-2 Children	506 (77.8)
	3-5 Children and more	169 (18.3)

Table 2. Knowledge of Women on Cervical Cancer Screening (n=650)

Characteristics	No. (%)
Knowledge about Test available for Cervical Cancer Prevention :	
VIA	177 (27.2)
Pap smear	40 (6.2)
Both	91 (14.0)
Not known	342 (52.6)
Source of information on VIA (n=308)	
Doctor (GOPD, Private, NGO, others)	214 (69.5)
Nurse/FWV	48 (15.6)
TV	20 (6.5)
Poster/Brochure	16 (5.2)
Relatives	10 (3.2)

Table 3. Results of the Tests (n=650)

Tests		No. (%)
Result of VIA:	VIA+ve	74 (11.4)
	VIA-ve	542 (83.4)
	Unsatisfactory	34 (5.2)
Result of Pap smear:	Normal	638 (98.2)
	ASCUS	4 (0.6)
	Low grade lesion	2 (0.3)
	High grade lesion	2 (0.3)
	Unsatisfactory	4 (0.6)
Colposcopy Results:	Normal	584 (89.8)
	CIN-I	42 (6.5)
	CIN-II/III	8 (1.2)
	Cervical Cancer	4 (0.6)
	Unsatisfactory	12 (1.9)
Histology Result:	Not Necessary	584 (89.8)
	Normal	24 (3.7)
	CIN-I	22 (3.4)
	CIN-II/III	14 (2.2)
	Cervical Cancer	4 (0.3)
	Unsatisfactory	4 (0.6)

and 4 (0.6%) had cervical cancer. Women with normal colposcopy did not have cervical biopsy, 66 women with abnormal colposcopy findings had colposcopy guided biopsy (Table 3).

The gold standard histology findings proved 20 women had CIN-I, 14 had CIN-II/II and 4 had cervical cancer (Table 4). Among the 38 histology diagnosed abnormalities, VIA test could identify 30 abnormalities including two cervical cancers. However, Pap smear could detect only 8 cases of histological abnormalities (2 low grade and 6 had high grade lesion) and it missed all the cervical cancer cases. Colposcopy could identify all 30 cases of cervical abnormalities, however 16 colposcopy diagnosed low grade CIN revealed normal and 8 colposcopy diagnosed low grade CIN revealed high grade CIN on histology.

The histology finding was considered as gold standard against which the sensitivity and specificity of VIA, Pap smear and colposcopy were calculated using standard statistical methods. Pap-smear had been considered positive when cytology report showed Atypical Squamous Cells of Undetermined Significance (ASCUS) lesions or more. In case of colposcopy or histology findings, CIN-II/III and cancer cases were considered as positive and normal and CIN I findings were considered as negative. During calculation sensitivity and specificity, unsatisfactory findings of VIA, Pap smear, colposcopy or histology were considered as normal or negative.

The sensitivity and specificity of VIA were 88.9%

Table 4. Histology Findings in Relation to VIA, Pap Smear and Colposcopy

Results		Histology findings					Total
		Normal	CIN-I	CIN-II/III	Cancer	Unsatisfactory	
VIA Test	VIA+ve	8	14	14	2	1	39
	VIA-ve	8	6	0	0	0	14
	Unsatisfactory	0	0	0	2	11	13
Pap Smear	Normal	14	16	8	4	12	54
	ASCUS	0	0	4	0	0	4
	Low grade lesion	0	2	0	0	0	2
	High grade lesion	0	0	2	0	0	2
	Unsatisfactory	2	2	0	0	0	4
Colposcopy finding							
	CIN-I	16	18	8	0	0	42
	CIN-II/III	0	2	6	0	0	8
	Cancer	0	0	0	4	0	4
	Unsatisfactory	0	0	0	0	12	12
Total		16	20	14	4	12	66

Table 5. Sensitivity and Specificity of VIA*, Pap Smear, and Colposcopy*****

Test		Histology positive	Histology negative	Total
VIA	Positive	16	23	39
	Negative	2	25	27
	Total	18	48	66
Pap smear	Positive	6	2	8
	Negative	12	46	58
	Total	18	48	66
Colposcopy	Positive	10	2	12
	Negative	8	46	54
	Total	18	48	66

*Sensitivity: 16/18×100=88.9%, Specificity: 25/48×100=52.1%, Positive predictive value (PPV): 16/39×100=41.0%, Negative predictive value (NPV): 25/27×100=92.6%; **Sensitivity: 6/18×100=33.3%, Specificity: 46/48×100=95.8%, Positive predictive value (PPV): 6/8×100=75.0%, Negative predictive value (NPV): 46/58×100=79.3%; ***Sensitivity: 10/18×100=55.6%, Specificity: 46/48×100=95.8%, Positive predictive value (PPV): 10/12×100=83.3%, Negative predictive value (NPV): 46/54×100=85.2%

and 52.1%. The positive predictive value (PPV) and Negative predictive value (NPV) were 41.0%, and 92.6% respectively (Table 5).

Table 5 shows the sensitivity, specificity, PPV and NPV of Pap smear were 33.3%, 95.8%, 75.0% and 79.3% correspondingly. The sensitivity and specificity of colposcopy were 55.6% and 95.8% (Table 5).

Discussion

In this study comparison was made between VIA test with Pap smear to detect cervical pre-cancer and early malignancies at an urban health set up. Among 650 recruited women, about two fifth (41.2%) knew about VIA test, and one fifth (20.2%) knew about Pap smear. More knowledge on VIA is probably due to introduction of this service at government health infrastructures free of cost. Majority of the women (69.5%) came to know about the VIA test from doctors as doctors are taking the opportunity of referring women to these easily available services. However, this hospital based data provides information from women referred mainly by doctors in an urban setting. On the other hand, population based data from rural areas of Bangladesh revealed that about one tenth of rural women knew about 'VIA' where facility

of VIA was available, and only about 1% knew about VIA where facility of VIA was unavailable (Nessa et al., 2013). This indicates that availability of screening services influences awareness level about screening among the people. Another study in the Bangladeshi rural community also showed that limited availability of the services was related to less knowledge on prevention and screening tests (Ansink et al., 2008). The Government has a strong heath infrastructure and it is already adopting cervical cancer screening programme in Bangladesh. Scale up of the screening services towards majority of the existing health facilities of the upazila and union level will improve awareness and acceptance of the services. It was interesting to note that 20.2% of the recruited women of this study knew about Pap smear which is probably related to availability of Pap smear services for a long time in large hospitals and some of the private set up in Dhaka.

In the present study, among 650 women, 74 (11.4%) were VIA+ve and 8 (1.2%) had abnormality in the Pap smear report. This VIA positivity is higher than the VIA positivity of the general population of Bangladesh which is about 4.8% (Nessa et al., 2010). This difference in the result may be related to attendance of more high risk cases at VIA centres of BSMMU. A wide range of VIA positivity has been observed among different population. One study in Nepal showed that only 2.9% of women had VIA positive result (Dhaubhadel et al., 2008). In Peru 6.9% of the women had VIA positive report (Jeronimo et al., 2005). Other studies in India and Philipines showed VIA positivity similar to this study (around 10%) (Ngelangel et al., 2003; Sankaranarayana et al., 1998; Sankaranarayana et al., 2007).

In this study, 74 (11.4%) women were VIA positive and it could identify 38 (57.6 %) histology proven cervical abnormalities and the sensitivity, specificity and PPV of VIA to detect CIN II/ III lesions were 88.9% , 52.1% and 41.0%. Almost similar sensitivity and specificity of VIA with a lower PPV were observed by another study at BSMMU (Nessa et al., 2010). On the other hand only 8 (1.2%) women had abnormal Pap smear (ASCUS or more) and it could identify 6 histology diagnosed cervical abnormalities and the sensitivity, specificity and PPV of Pap smear were 33.33%, 95.8% and 75.0% respectively. Another study comparing VIA and Pap smear in Bangladesh reported much lower sensitivity (2%) and slightly higher specificity (98%) for cytology-based as opposed to almost similar sensitivity (79%) and specificity (57%) for VIA-based screening to detect high grade disease (Rahman et al., 2009). The better sensitivity of Pap smear in the present study may be related to collection of the specimen with spatula and cytobrush by physicians in an institutional set up, instead of collection with spatula only by paramedics at primary health care set up in the study by Rahman et al., 2009. Both of these studies in Bangladesh showed that Pap smear is unable to detect many cases of cervical pre-cancer and cancer. Other factors related to the ineffectiveness of Pap smear may be inadequate preparation, presence of debris in the material, improper concentration of locally available fixation material, less trained staff etc and all these factors discourage to promote Pap smear for primary screening in low resource countries. Large scale national and regional cytology screening programme in several countries in Latin America and the Caribbean have been largely ineffective in reducing cervical cancer burden compared with high income developed countries (Sankaranarayana et al., 2008).

Several studies have explored direct visualization as an alternative to cytology-based cervical cancer screening in low resource settings. One study in India comparing VIA and Pap smear showed a higher sensitivity of VIA (96.7%) and Pap smear (50%) than our study. However the specificity of VIA (36.4%) was lower than that of Pap smear (97%), resulting in high false-positive rates for VIA (Goel et al., 2005). The present study showed higher specificity (52.1%) of VIA with lower false positive rate. Even though the high false positive rate is an important limitation of VIA-based screening. A study in Nigeria showed higher sensitivity of VIA (100%) and Pap smears (85.7%) with a positive predictive value of 20% (Akinola et al., 2007). Another study of Nigeria showed low sensitivity of VIA (60%) and Pap smear (60%), with high specificity of VIA (94.4%) and Pap smear (100%) (Albert et al., 2012). The sensitivity of VIA-based screening to detect CIN II/ III lesions and invasive cervical cancer varies from 31-95% and the specificity varies from 49-97% in different cross sectional studies. The PPV ranged from 5-20% and the NPV ranged from 92-99% (Sankaranarayana et al., 2005). Therefore the sensitivity, specificity, PPV and NPV of VIA test in the present study is comparable to other studies and is reasonable to implement for a screening programme. In the present study, colposcopy showed low sensitivity (55.6%) and this was because of consideration of only CIN-II/III and cancer cases as positive and CIN I cases as negative during the statistical calculation.

This study compared VIA and Pap smear in diagnosing pre-cancer and early cervical cancer in the actual heath set up in Bangladesh. Based on results of this study, we can conclude that VIA test is an appropriate screening test to diagnose cervical pre-cancer and cancer in the present socioeconomic condition of Bangladesh with reasonable sensitivity, PPV and NPV. However low specificity (52.1%) found in this study is obviously related to high false positive rate. This important limitation of VIA is also related to risk of overtreatment. Moreover VIA test is a subjective test, depends on experience of provider and interpretation of the result is difficult among postmenopausal women. However, overtreatment related to VIA can be minimized by colposcopy as government has encouraged development of colposcopy clinic in referral centres all over the country. It was also observed that compliance of VIA positive women to colposcopy clinic in Bangladesh is high (Basu et al., 2010). The recently adopted "see and treat" policy at the colposcopy clinics of Bangladesh (Nessa et al., 2013) should improve treatment acceptance and lead to effective screening outcome. In spite of all the limitations of VIA, implementing VIA in low-resource countries may provide realistic approach to building up human resources and infrastructure that may make possible the highly anticipated low-cost HPV testing in the near future (Sankaranarayana et al., 2011). Apart

from low sensitivity of Pap smear (33.3%) in this study, it requires materials for collection of specimens, trained providers, appropriate cytological laboratory services and these are less organized in Bangladesh. Moreover Pap smear requires multiple visits and all these make Pap smear an expensive and difficult method of cervical cancer screening for Bangladesh. However, a cost effective, simple, sustainable method is required for nationwide scale up of this screening method in Bangladesh. Therefore VIA-based screening seems an appropriate method for cervical cancer screening at the current situation. The government can spread VIA method to a wider geographical area with reasonable resources. This will improve awareness among population on screening, and availability of screening services. Moreover, expansion of VIA-based screening programme will improve awareness on cervical cancer prevention and will be helpful for introduction of 'HPV vaccination programme' by the Government in near future.

In conclusion, VIA test should be used as the primary screening tool even with its low sensitivity and specificity in low resource countries like Bangladesh. False positive results may be greater, but overtreatment can be minimized by colposcopy evaluation of the VIA positive women. Political commitment to spread out the programme throughout the country, increase of enough trained manpower for efficient management of pre-cancer of women are necessary for eventual decrease of cancer of the population.

Acknowledgements

We are grateful to the Ministry of Health and Family Welfare, the Directorate General of Health Services, the Directorate General of Family Planning, UNFPA, Bangladesh, for their valuable financial and technical support and active cooperation in developing the "Cervical and Breast Cancer Screening Programme' and IARC for supporting the colposcopy training programme. We show our gratitude to our patients and doctors of BSMMU related to the cervical cancer prevention programme for their priceless support.

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