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The Utility of Visual Inspection with Acetic Acid in Cervical Cancer Screening

Chidi Okorie Onwuka[1]*, Ima-Obong A. Ekanem[2]

Abstract

Objective: Cervical cancer is potentially preventable but still remains a leading cause of cancer mortality in in developing countries like Nigeria. Cytology-based screening programmes are difficult to maintain in these countries. Developing a cheap and reliable alternative is an important public health measure in these regions. This study was carried out to compare the utility of VIA and Pap smear as Cervical cancer screening methods in HIV-infected and non HIV-infected women.

Methodology: Between March, 2013 and March, 2014, 461 consenting women, comprising 231 HIV positive women (HPW) and 230 HIV negative women (HNW) were recruited and screened for cervical cancer using conventional Pap smear and VIA simultaneously in University of Uyo Teaching Hospital. The Pap smear findings were classified using the 2001 Bethesda system. Patients with a positive Pap smear or abnormal VIA findings were recalled for biopsy. The results of the two tests were compared using biopsy as the gold standard.

Results: The overall sensitivity, specificity, positive predictive value and negative predictive value for VIA were 100%,80%,76.9%, and 100%, respectively compared to 80%, 100%, 100%, and 88.2% for conventional Pap smear. Visual inspection of the cervix with acetic acid for cervical cancer screening is not specific but has a high negative predictive value.

Conclusion: This study does not support a "see-and-treat" approach in cervical cancer management using VIA only. In resource-challenged areas, VIA can be applied on a large scale basis in primary screening for cervical cancer so as to triage, women who will benefit from further evaluation before applying the appropriate treatment.

Keywords: Cervical cancer; Pap smear; VIA; Cytology

Introduction

Cervical cancer is the commonest malignant tumour of the female genital tract and one of the leading causes of cancer mortality in women worldwide with a global annual incidence of over 500,000 [1,2]. Greater than 85% of these new cases and about 88% of these cancer related deaths occur in resource-poor countries [2]. It is the second most common cause of cancer related deaths in regions of the world where women do not have access to regular gynaecological care and screening [3].

Most cases of cervical cancer are Human papilloma virus (HPV) associated [4-6]. Early onset of sexual activity, early age at first pregnancy, high parity and multiple sexual partners are associated with the risk of HPV infection [7]. Other risk factors include presence of other sexually transmitted diseases, low socioeconomic class, cigarette smoking and immunosuppression from any cause, vitamin deficiency, and long term oral contraceptive use [7].

Unlike most cancers, invasive cervical cancer is potentially preventable because it is preceded by long precancerous stages which are most often detected by cervical smear. In developed countries, routine and organized cytology-based screening programmes with adequate treatment of precancerous lesions have dramatically reduced the incidence and mortality of cervical cancer. These require a reliable health care infrastructure, political support, adequate number of trained personnel, and multiple clinic visits. All of these factors make the implementation of such programmes difficult in low-resource countries where other health needs are competing for the available resources. This makes

Affiliation:
[1]*Department of Pathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria*
[2]*Department of Pathology, University of Calabar Teaching Hospital, Calabar, Nigeria*

***Corresponding author:**
Chidi Okorie Onwuka,
Department of Pathology, University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria, Tel: +234 (0) 8035473424,
E-mail: dronwuka@yahoo.com

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the development of alternative methods for cervical cancer screening necessary in such resource-poor settings. Visual inspection of the cervix with acetic acid (VIA) is one of such alternatives and requires the application of 3% to 5% acetic acid to the cervix which is then examined after one minute for the characteristic acetowhite lesions suggestive of cervical neoplasia.

Visual inspection with acetic acid requires minimal equipment, does not require any laboratory, can be performed by non-physicians with adequate training, is inexpensive and yields immediate results. The WHO has endorsed VIA for cervical cancer screening in less developed countries with non-existent or poorly executed cervical cancer prevention programmes since about 80% of all cervical cancer cases occur in these countries [8]. Visual inspection with acetic acid is not without its draw backs. Acetowhite lesions are not unique to cervical precancerous lesions. This generates false positive cases that can lead to overtreatment which can in turn overwhelm the treatment centres [8]. Also, it is subjective since it depends on the clinician's interpretation of what is seen, and is not an appropriate screening method for postmenopausal women due to fibrosis and leucoplakia of the cervix [8].

This study was carried out to compare the sensitivity, specificity, positive predictive value, and negative predictive value of visual inspection with acetic acid and Pap smear of the cervix as cervical cancer screening methods among HIV-negative and HIV-positive women in this region of Nigeria with high HIV prevalence.

Materials and Methods

This comparative cross-sectional study was carried out in the cytology clinic of University of Uyo Teaching Hospital, Uyo after approval of the study protocol by the Ethical committee of the hospital.

A total of 461 ever-married or sexually active consenting women were recruited for this study by word of mouth. Patients bleeding per vaginum, patients with previous abnormal Pap smear result and pregnant women were excluded.

The study participants were educated about cervical cancer, the screening methods, objective of the study, and the possibility of an abnormal result. Those who were willing to take part in the study signed a written informed consent.

A questionnaire was administered to obtain information on each participant's socio-demographic factors and relevant risk factors. Participants' confidentiality was ensured. The procedure was explained to each of the participants. The Pap smear was taken while observing standard protocol and promptly immersed in 95% ethyl alcohol fixative contained in a coplin jar. With the vaginal speculum still in place after collecting the sample for Pap smear, a cotton swab soaked in 5% freshly prepared acetic acid was applied to the cervix. The cervix was examined after one minute for the characteristic aceto-white appearance typical of cervical neoplasia by unaided naked eye examination. Photographs of the cervix were taken before and one minute after applying the acetic acid using a Canon Power shot A80 5X optical zoom 16.0 mega pixels camera. Findings on VIA were recorded immediately and classified based on the criteria from International Agency for Research in Cancer into Negative or Positive. Lesions that were positive or suspicious on VIA were biopsied in women who gave consent for the procedure.

The alcohol-fixed smeared slides were then stained with Pap stain using standard protocol at the histopathology laboratory of the hospital. The 2001 Bethesda System (TBS) of reporting cervical and vaginal cytology was used as the basis for cytology classification.

Women who had an abnormal cytology with a normal VIA finding were recalled for biopsy. The biopsy materials were processed by the formalin fixed paraffin embedded method using standard protocols. The cervical biopsies were classified according to the WHO classification of cervical tumors.

The results of the two screening tests for each patient were compared using the biopsy result as the reference standard. For this, all Pap smears with the diagnosis of ASCUS or worse lesion were considered positive while all abnormal VIA findings were considered positive. The threshold of positive biopsy is CIN-1 and worse lesions

The data collated were analyzed using statistical package for social sciences version 20 (SPSS 20) and the results presented as tables. The level of significance was set at P less or equal to 0.05. The findings of this study were compared with those of previous studies.

Results

The results of 449 participants (97.4%), comprising 226 HPW and 223 HNW were suitable for statistical analysis. Women who did not come back for a cervical biopsy after an abnormal Pap result or a positive VIA were excluded in the calculation for sensitivity and specificity.

Table 1 shows the socio-demographic characteristics of the study participants who were aged between 18-60 years with a mean age of 35.24±9.26 years and 35.63±8.44 years in the control- and case- participants respectively. More than half of the HNW were married (64.1%) and had a secondary or tertiary level of education (75.6%). Only about one-third of the HPW were married (36.7%) but most of them also had secondary or tertiary level of education (76.1%).

Most of the women in this study attained menarche at or below 14 years of age (72.6% of the HNW and 67.3% of the HPW) and also had their sexual debut at or below 18 years (55.2% of the HNW and 68.1% of the HPW) but most of the HPW (57.1%) had four and above lifetime number of sexual partners unlike the HNW (39.2%). The study shows that majority of the participants have a parity between 0 and 2 (57.8% of controls and 69.5% of cases). Only one-tenth of the

study participants in both groups had ever used combined oral contraceptive pills while about one-third of them occasionally take alcohol. Most of the study participants are non-smokers (99.6% of HNW and 99.1% of HPW).

Table 2 shows the positivity rates of VIA and Pap test. Twenty six out of the 226 case-participants (11.5%) and 23 of the 223 control-participants (10.3%) were positive by VIA, while 10.6% of the case-participants (24 out of 226) and 4.9% of the control-participants (11 out of 223) were detected positive by Pap test. A positive Pap test was considered ASCUS or worse lesions. The difference in positivity rate between the two study groups is significant for Pap test ($P<0.05$) but not significant for VIA ($P>0.05$).

Further analysis shows the distribution of the Pap test results in the study population (Table 3). Out of the 231 HPW, 22 (9.7%) had an inflammatory smear and the rest sub-classified as NILM (180 cases, 79.6%), ASCUS (6 cases, 2.7%), LGSIL (13cases, 5.6 %), HGSIL (5 cases, 2.2%). Five of the HPW (2.2%) had inadequate smears due to scant cellularity and excessive mucus obscuring the squamous epithelial cells. There was no case of cervical cancer in the case-participants. Twelve of the HNW (5.4%) had an inflammatory smear while the results of the rest were classified as NILM (200 cases, 89.7%), ASCUS (4 cases, 1.8%), LGSIL (3 cases, 1.3%), HGSIL (3 cases, 1.3%), and Squamous cell carcinoma (1 case, 0.4%).

These results make the prevalence of cervical epithelial cell abnormality in this study to be 4.8% in the control-participants and 10.7% in the case-participants and show that there is a significant relationship between HIV status and abnormal Pap test result ($p <0.05$).

Table 4 shows the distribution of VIA results in relation to Pap test results. In the control group, VIA was positive in 16.7% of the inflammatory smears and 8.5% of the NILM. Fifty per cent of the ASCUS, 100% of the LGSIL and 66.7% of HGSIL were detected negative by VIA. The SQCC was positive by VIA. Among the HPW, 22.7% of the inflammatory smear and 6.7% of NILM were positive on VIA while 83.3% of ASCUS, 53.8% of LGSIL and 80% of the HGSIL were negative on VIA. This shows that VIA and Pap tests are more likely to agree on a negative result.

All the cases that were negative on both VIA and Pap tests were confirmed truly negative by biopsy (normal cervices, inflammatory, squamous papilloma, endocervical polyp). All the cases that were positive on both VIA and Pap tests were confirmed truly positive on biopsy (CIN-1, CIN-2, CIN-3, and SCC). Two out of the 5 cases that were VIA positive but Pap negative were confirmed positive by biopsy (1 CIN-1 and 1 CIN-2) while 3 were reported negative (2 normal, 1 Nabothian cyst).

When the HIV status and only positive screening tests were considered, 7 out of the 9 VIA positive subjects biopsied in the control group (77.8%) and 3 out of the 4 VIA positive patients

Characteristics	HIV negative (n=223)	HIV positive (n=226)
Age	Number (%)	Number (%)
18 - 24	15 (6.7)	14 (6.2)
25-30	61 (27.4)	61 (27.0)
31-36	64 (28.7)	62 (27.4)
37-44	49 (22.0)	53 (23.5)
above 45	34 (15.2)	36 (15.9)
Marital status		
single	60 (26.9)	89 (39.4)
married	143 (64.1)	83 (36.7)
divorced	5 (2.2)	12 (5.3)
widowed	15 (6.7)	42 (18.6)
Educational Level		
none	2 (0.9)	4 (1.8)
primary	30 (13.5)	50 (22.1)
secondary	56 (25.1)	82 (36.3)
tertiary	135 (50.5)	90 (39.8)
Age at Menarche		
≤ 14	162 (72.6)	152 (67.3)
≥ 15	61(27.4)	74 (32.7)
Age at first intercourse		
≤ 18	123 (55.2)	154 (68.1)
≥ 19	100 (44.8)	72 (31.9)
N0. of past sexual partners		
1 _ 3	157 (70.4)	121 (53.5)
≥ 4	66 (29.6)	105 (46.5)
Life time No. of sexual partners		
1_3	136 (61.0)	97 (42.9)
≥ 4	87 (39.0)	129 (57.1)
Parity		
0-2	129 (57.8)	157 (69.5)
3_5	73 (32.7)	51 (22.6)
≥ 6	21 (9.4)	18 (8.0)
Oral contraceptive use		
yes	29 (13.0)	24 (10.6)
No	194 (87.0)	202 (89.4)
Alcohol use		
Yes	96 (43.0)	74 (32.7)
No	127 (57.0)	152 (67.3)
Smoking		
Yes	1 (0.4)	2 (0.9)
No	222 (99.6)	224 (99.1)

Table 1: Socio-demographic and Clinical characteristics.

Screening Test	Result	HNW No.(%)	HPW No.(%)	P value
VIA	Negative	200 (89.7)	200(88.5)	0.75
	Positive	23 (10.3)	26(11.5)	
	Total	223(100)	226(100)	
PAP	Negative	212 (95.1)	202 (86.3)	0.03
	Positive	11 (4.9)	24 (10.6)	
	Total	223 (100)	226 (100)	

The difference in positivity rates between the two study groups is significant for Pap test ($P<0.05$) but not significant for VIA ($P>0.05$).

Table 2: Positivity rate of VIA and Pap test in the study-participants.

biopsied in the case-participants (75%) were confirmed positive. All the positive Pap smears biopsied in the two groups (6 control- and 2 case-participants) were confirmed positive by biopsy. This shows that Pap test is more specific than VIA in both groups of study participants.

Discussion

Due to the unique association between HIV and HPV in the pathogenesis of cervical cancer, regions with high HIV prevalence also have high rates of cervical cancer since women comprise about 50% of adults living with HIV/AIDS [9,10]. Many studies have been done to compare the performance of VIA and Pap smear as cervical cancer screening tools with a wide range of results. To the best of our knowledge, no published data exist for such a study in this region of Nigeria with a high prevalence of HIV infection (Figure 1).

The socio-demographic characteristics of the study participants in this study are similar to those noted in related studies [11-13].

This study showed that VIA was positive in 26 (11.3%) of the HPW and 23 (10.3%) of HNW while Pap smear cytology showed epithelial cell abnormality in 24 (10.7%) of the HPW and 11(4.8%) of the HNW. There was no statistically significant relationship between HIV status and VIA positivity (p=0.75) but HPW were 2.5 times more likely to be Pap positive than HNW (p< 0.01). These discrepancies in the positivity of VIA and Pap test when used on the same group of patients have also been observed in several studies [14-18]. VIA tends to be more sensitive but less specific and labels more women positive than Pap test. Reports from South African and Zambian studies have noted a higher VIA positivity in HPW ranging from 32.6% [14] to 43.7% [15], respectively. A study in Botswana by Ramogola-Masire et al. among 2,175 HPW showed 15.2% VIA positivity that were histologically confirmed CIN [16]. Similar VIA studies in Mali and Tanzania conducted on women regardless of their HIV status have also reported varying positivity ranging from 2.6% [17] to 7.1% [18] respectively. The discrepancies noted with these VIA studies may be attributable to a lack of reproducibility of this screening method, differences in exclusion criteria and age differences. Also regional variation in HIV prevalence, HPV and cervical neoplasia burden may account for the regional discrepancies observed in VIA studies. The rate of VIA positivity observed in this present study is however supported by studies that recorded similar frequencies [19,20]. The low

	HIV Status			
PAP Result	**HNW No. (%)**	**HPW No. (%)**	**chi-square**	**p value**
INFLA	12 (5.4)	22 (9.7)	12.12	0.03
NILM	200 (89.7)	180 (79.6)		
ASCUS	4 (1.8)	6 (2.7)		
LGSIL	3 (1.3)	13 (5.8)		
HGSIL	3 (1.3)	5 (2.2)		
SQCC	1 (0.4)	0 (0)		
TOTAL	**223(100)**	**226 (100)**		

infla(inflammatory),nilm (negative for squamous intraepithelial lesion/ malignancy), ascus(atypical squamous cells of uncertain significance), lgsil(low grade suamous intraepithelial lesion), hgsil(high grade squamous intraepithelial lesion), sqcc(squamous cell carcinoma). Hpw (hiv positive women), hnw (hiv negative women). Five smears of hpw were inadequate. These results make the prevalence of cervical epithelial cell abnormality in this study to be 4.8% in the control-participants and 10.7% in the case-participants and show that there is a significant relationship between HIV status and abnormal Pap test result (p <0.05).

Table 3: Distribution of Pap results according to HIV status.

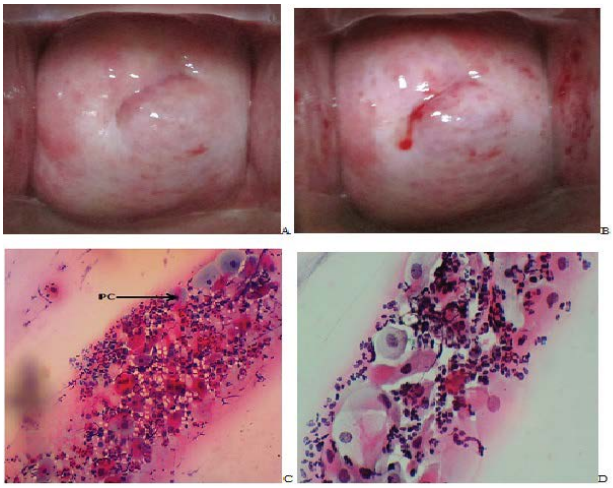

Figure 1: Gross photographs from the cervix of a 56 year old postmenopausal HNW with cervicitis before (a) and one minute after applying 5% acetic acid (b). There was diffuse whitening which was enhanced on VIA. Easy bruising was also seen. The Pap smear shows cervicitis with reactive epithelial cells, some displaying polychromasia (PC). Pap stain x10 (C) and Pap stain x 40 (D).

		PAP Smear Result in No (%)					
	VIA	**INFLAM**	**NILM**	**ASCUS**	**LGSIL**	**HGSIL**	**SQCC**
HNW	**Negative**	10 (83.3)	183 (91.5)	2 (50.0)	3 (100)	2(66.7)	0 (0)
	Positive	2(16.7)	17(8.5)	2 (50.0)	0 (0)	1 (33.3)	1 (100)
	Total	**12 (100)**	**200(100)**	**4 (100)**	**3 (100)**	**3(100)**	**1 (100)**
HPW	**Negative**	17 (77.3)	168 (93.3)	5 (83.8)	7(53.8)	4(80.0)	0 (0)
	Positive	5 (22.7)	12 (6.7)	1 (16.7)	6 (46.2)	1 (20)	0 (0)
	Total	**22 (100)**	**180 (100)**	**6 (100)**	**13 (100)**	**5 (100)**	**0(0)**

This shows that VIA and Pap tests are more likely to agree on a negative result.

Table 4: Distribution of VIA results in relation to Pap test results and HIV status

positivity of VIA noted in this study might be because of the low prevalence of abnormal cervical cytology in both the cases and control groups used in this study, recording only distinct acetowhite areas as positive and not including cervix with postmenopausal leukoplakia nor faint and suspicious whitish appearance. The problem of inter-observer variability is also relevant [21].

Using biopsy positive cases as gold standard, this study showed that VIA is more sensitive but less specific than Pap test. A threshold of CIN-1 or worse lesion was considered a positive biopsy. The sensitivity of VIA in the total study population regardless of HIV status was 100% while that for Pap test was 80%. Combining VIA and Pap test gave a sensitivity of 100%. When the HIV status was considered, the sensitivity of VIA and VIA+PAP was 100% in both groups of women while that for Pap test was 85.7% in the HNW and 66.7% in the HPW. This higher sensitivity of VIA noted in this study is supported by findings in several studies that have yielded a wide range of results. The values for the sensitivity of VIA reported in literature range from 60 to over 90% while that for cytology span from 23% to 99% [22,23]. Rana et al reported sensitivities of 31.6% vs 78.2% for VIA and Pap smear respectively while Gravitt et al found 59.7% vs 57.4% in a similar study [24,25]. The sensitivity pattern seen in this study is similar to that observed by Akinola et al in Lagos, Nigeria [12]. Various reasons account for the varied result in most studies comparing the sensitivity of VIA and Pap smear in biopsy positive cases. One such factor is the threshold of positive histopathology (Figure 2). This study used a threshold of CIN 1 or worse while other studies used CIN 2 or worse lesions. Also, the problems with conventional Pap smear may contribute to the lower sensitivity of Pap test observed in this and other studies. Conventional Pap test has a lesser sensitivity in detecting precancerous lesions of the cervix due to potential limitations which include inadequate transfer of cells to slide, inhomogeneous distribution of abnormal cells and obscuring factors such as inflammatory cells and blood [26]. Because of this limitation, a potentially dysplastic lesion can be wrongfully considered an inflammatory smear thereby causing a lower sensitivity in comparison studies. This shows the advantage of liquid-based cytology in Pap test. Another important factor is inter-observer differences in reporting a positive VIA. This study reported only cervixes or lesions on the cervix that show distinct whitening after one minute of acetic acid application as positive. This may account for the positivity rate of VIA obtained in this study. This buttresses the importance of adequate training and experience in performing a VIA. Training protocol needs to be developed in remote areas for adequate training and evaluations to maintain the expertise of health workers involved in administering VIA.

The specificities of VIA, Pap test, and VIA+Pap test in the total study population were 80%, 100% and 100%, respectively. According to HIV status, these values were 81.8%, 100%, and 100% in the HNW and 75%, 100, and 100% in the HPW respectively. These findings show that Pap test is more specific than VIA and are supported by reports from other Nigerian [11-13] and international studies [25-27]. The commonly reported specificity for VIA ranges from 60 to over 90% while that for conventional Pap smear spans from 7% to 97% for specificity [22,23]. The reasons for the false positive cases noted in this study included postmenopausal state, postmenopausal cervicitis, chronic cervicitis, nabothian cysts, and squamous papilloma. These reasons have been noted by the IARC and other studies [28,29] (Figure 3).

In this present study, it was observed that combining VIA and Pap smear increased the sensitivity of Pap test and the specificity of VIA. This is similar to the finding by Mahmud et al in Pakistan in a study done to compare VIA and Pap smear in cervical cancer screening [30] (Figure 4). This finding is important and points to the fact that VIA can be utilised in two ways in resource-limited and developing countries. First, due to its higher sensitivity, it can be utilized in mass screening exercise to triage women who would benefit from further evaluation by other more specific methods of cervical cancer screening. Secondly, due to the improved sensitivity and specificity of the combined tests, VIA can be used to complement conventional Pap smear in opportunistic screening of women with no assurance of follow up contact and in tertiary institutions with limited cytopathologist and absent liquid-based Pap smear preparations.

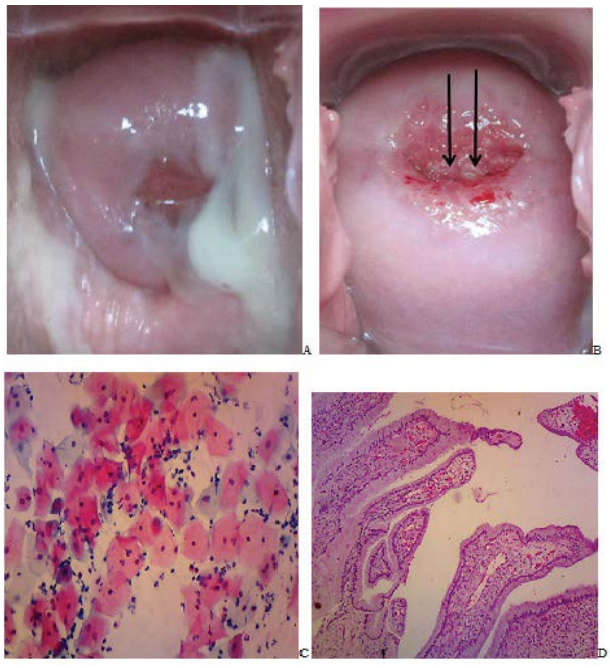

Figure 2: Gross photographs from the cervix of a 40 year old premenopausal HNW showing copious discharge before VIA (A). On applying 5% acetic acid, the discharge was removed to show a suspicious acetowhite lesion around the external os (Arrows in B). The Pap smear shows NSIL: benign superficial and intermediate cells with an inflammatory background (C). A biopsy confirmed the lesion to be an Endocervical polyp.

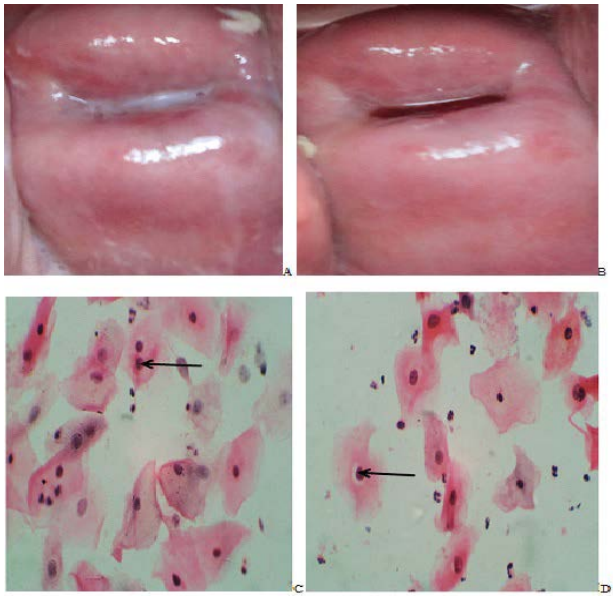

Figure 3: Gross photographs of the cervix of a 36 year old HPW showing whitish discharge (A).VIA removed the discharge and shows a negative result (B). The Pap smear shows LSIL: superficial and intermediate cells with nuclear enlargement but normal nucleocytoplasmic ratio, mild hyperchromasia and finely granular chromatin. Some cells show nuclear membrane folding (arrow in C) and perinuclear halo (arrow in D). C and D, Pap stain x 40.

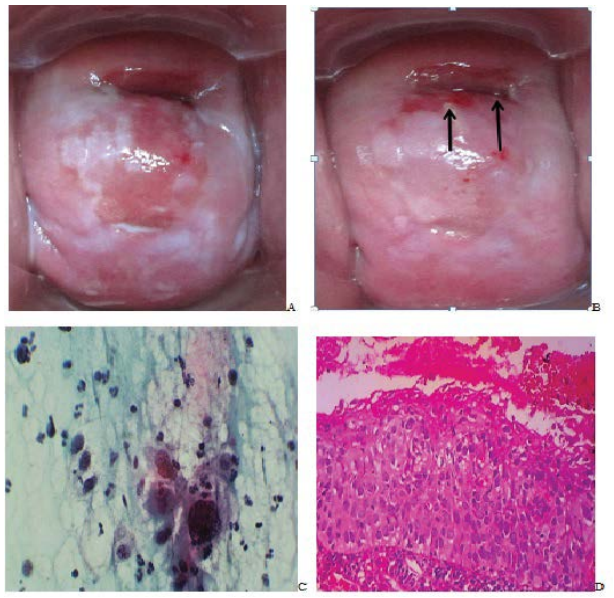

Figure 4: Gross photographs from the cervix of a 40 year old HPW showing. Before VIA there were whitish discharges (A). On VIA, a distinct acetowhite lesion is seen towards the external os (B). Pap smear shows HSIL: intermediate cells with severe nuclear abnormality including irregular contours, hyperchromasia, clumped chromatin and pleomorphism. These cells are disposed singly and in clusters (C, Pap stain x40). Biopsy shows CIN-3 with full thickness dysplasia, superficial ulceration and haemorrhage (D, H/E x 10).

One major problem with VIA is its lack of specificity. VIA is more sensitive but less specific than Pap smear in detecting precancerous lesions of the cervix and if used as an alternative to Pap smear may result in increased referral for colposcopy and biopsy which could be burdensome in some developing countries. Also, in settings where the 'see-and-treat approach is adopted without confirmation using other screening modalities, VIA would lead to over treatment. However, in resource-poor settings, due to the increased risk of HPV infection in HIV- infected women, and the accelerated progression from cervical neoplasia to invasive cancer in HPW, the benefits of overtreatment, increased referral for colposcopy and biopsy far outweigh the danger of failure to diagnose a potentially dysplastic lesion. More so, to prevent an overtreatment, VIA can be used in a large scale programme to triage women who would benefit from further evaluation including VILI (visual inspection with Lugol's Iodine), VIAM (visual inspection with acetic acid under magnification), Pap smear, colonoscopy and directed biopsy, and HPV DNA testing.

This study also showed that VIA has a higher negative predictive value (NPV) than Pap test. The NPV of VIA, Pap test, VIA+Pap in the total study population in this study were 100%, 88.2%, and 100%, respectively. These values were 100%, 91.7%, and 100 in the control group, and 100%, 80%, and 100% in the case-participants, respectively. Other studies have reported a NPV for VIA to be close to or more than 90% which support the finding in this study [22-25]. Also, the negative percentage agreement between VIA and Pap test was higher than the positive percentage agreement in this study (93.1% vs 65.4%). This further supports that VIA has a high NPV. This high NPV of VIA is of benefit in resource-limited areas as a woman who tests negative by VIA can be reassured and sent home without further evaluation with more costly protocol. This is important because the vulnerable groups for cervical cancer are the poor, rural dwellers, and HPW [31].

The positive predictive value (PPV) for VIA, Pap test, and VIA+Pap in the total study population in this study were 76.9%, 100%, and 100%, respectively. Considering the HIV status, these values are 77.8%, 100%, and 100% in the HNW and 75%, 100%, and 100% in the HPW, respectively. The reported value for PPV of VIA in previous studies ranges from 3.8% to 90% [32]. This finding of comparable PPV of VIA and Pap test in this study differs from that seen in most of the work cited. This might be because in this study, only distinct acetowhite lesions where reported as positive thereby limiting sources of false positive cases seen in most studies. Conditions that have been reported to cause a false positive VIA include cervical polyp, inflammation, postmenopausal leukoplakia, and metaplasia [33, 34]. In this study, 5 out of the 22 inflammatory smears in HPW and 2 out of 10 inflammatory smears in the HNW were reported positive by VIA but none of the positive VIA was diagnosed inflammatory by biopsy. In

comparing VIA and biopsy, no false positive case was due to cervicitis in this study.

The results of this present study and that of other reported studies show that VIA is comparable to cytology as a cervical cancer screening tool and can be used in resource poor settings in both HPW and HNW for cervical screening. Because of its affordability, simplicity and rapidity of performance, VIA has emerged as one of the promising alternatives to Pap smear in low-resource settings for cervical cancer screening. VIA is cheap, easy to perform by a trained nurse and the result is available immediately allowing the triaging of women who may require further investigation to identify and treat cervical lesions. Triaging would help reduce the workload on the limited number of cytotechnologists and cytopathologists in resource-poor settings if a large scale cervical cancer screening program is to be carried out. Furthermore, in places where cytology services are available, VIA can be used as an adjunct to improve on the sensitivity of conventional cervical cytology in detecting cervical neoplasia since conventional Pap smear is noted to be associated with a high rate of false negativity from sampling and interpretative errors [35]. The major concern about VIA is its low specificity [high rate of false positivity] which may lead to over referral and overtreatment but the danger of missing a potentially dysplastic lesion far outweighs the cost of an overtreatment. Moreover overtreatment can be prevented by confirming positive cases by other methods before commencement of treatment.

This study shows that cervicitis has no significant effect on the result of VIA. Only 22.7% of the inflammatory smears in the HPW and 16.7% of the inflammatory smears in the HNW were detected positive by VIA. Using biopsy as gold standard, none of the positive VIA was detected as inflammatory. This finding is supported by studies that have shown no association between a false positive VIA to specific genital tract infections other than HPV [34].

Factors noted to be associated with VIA positivity in this study includes age and Pap smear positivity. It was also noted that postmenopausal women are more likely to present with a false positive VIA. In the age distribution of VIA result, older women are more likely to present with a positive VIA ($p<0.05$). This finding is similar to that seen in IARC studies [28]. The IARC recommends that VIA should not be used in postmenopausal women for cervical cancer screening [28].

Conclusion

VIA is more sensitive but less specific than conventional Pap test. This finding is similar to that reported in the literature. VIA could be used as an alternative to cytology in resource poor settings in both HPW and HNW for primary cervical screening. Due to its sensitivity, affordability, simplicity, and rapidity of performance, VIA can be used for mass cervical cancer screening. This would help triage women for further evaluation before applying the appropriate treatment. This study therefore does not support the 'see-and treat' approach in cervical cancer management because VIA is not specific. Also, the 'see-and-treat' approach will prevent generation of data to know what is being treated and the depth of the lesion that is being treated may not be reached, giving a false sense of safety.

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