Comparative study of Pap smear test and VIA test in cervical carcinoma screening among women aged over 20 years

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ABSTRACT

Objective

To compare the performance of VIA and Pap smear tests as screening tools in cervical carcinoma detection in women.

Methods

The prospective and retrospective study was conducted on 198 women. Cervical smears were collected with Ayres's spatula. Acetic acid was used and the results were categorized as VIA positive and VIA negative. The Pap smear was reported according to the Bethesda system 2001. Cervical biopsy was done for all the cases.

Results

VIA was positive in 47.47% of the cases and Pap smear was positive in 39.89% of the cases. Among 198 cases, 61 (30, 8%) cases had cervical carcinoma. When we compared VIA and Pap smear tests, 94 cases were positive to VIA, and 61cases were confirmed positive with Pap smear. The sensitivity and specificity for VIA were 88.5% and 84.68%, respectively. The sensitivity and specificity for Pap smear were 80.45% and 91.89%, respectively. The sensitivity of VIA was higher than that of Pap smear. However, the specificity of VIA was low as compared to Pap smear.

Conclusion

VIA is a cost effective test and could be alternatively used with Pap smear in screening of cervical carcinoma but the Papanicolaou test is the most effective test for early detection of cervical carcinoma.

Keywords: Pap smear test; VIA test; cervical carcinoma; women

INTRODUCTION

Cervical carcinoma is uncontrolled growth that starts in the uterine cervical epithelium cells caused by several factors include Human Papilloma Virus (HPV).[1] The normal cells of the cervix gradually develop pre-cancerous changes that turn into cancer. There are 2 main types of cervical carcinoma: squamous cell carcinoma and adenocarcinoma. The squamous cells cover the surface of the exocervix. The second type of cervical carcinoma is adenocarcinoma which develops from mucus-producing glands cells of endocervix.[1]

Cervical cancer rates have fallen in most of the developed countries, probably as a result of screening and treatment programs. In contrast, the rates in most developing countries have risen or remained unchanged. In 2008 there were 529,000 new cases of cervical carcinoma,

and more than 270,000 women die every year; 85% of them were from developing countries, especially in Africa where an estimated 53,000 women die of the cervical cancer every year. [2] Overall, 77% of new cases of cervical carcinoma and 88% of deaths occur in the developing world, where 95% of women have never been screened for this cancer.[3]
In sub-Saharan Africa, 34.8 new cases of cervical carcinoma are diagnosed per 100, 000 women annually, and 22.5 per 100,000 women die from the cervical carcinoma. These statistics were compared with 6.6 and 2.5 per 100,000 women, respectively, in North America. The drastic differences can be explained by lack of access to effective screening and services that facilitate early detection and treatment.[2]

Cervical carcinoma ranks as the second most frequent cancer among women in Rwanda. In 2008, Rwanda had 34.5 cases of cervical carcinoma and 25.4 deaths attributable to cervical cancer per 100,000 women.[4] Cervical carcinoma is rare in women under 30 years old and it is most common in women over 40 years, with the greatest number of deaths usually occurring in women aged between 50 and 60 years. Rwanda has a population of 3.90 million women over 15 years who are at risk of developing cervical carcinoma. Current estimates indicate that every year, 1304 women are diagnosed with cervical carcinoma and 921 die from the cervical cancer.[5] However, in Eastern Africa, about 33.6% of women in the general population are estimated to harbor cervical HPV infection at a given time,[6] and the HPV 16 or 18 types contribution to invasive cervical carcinoma ranged to 56.4% in 1994 and 91.5% in 2003.[7,8]

Cytology-based screening, however, has not proven to be as successful in low-resource settings of the developing world. Lack of trained pathologists and technicians and a deficiency of laboratories have contributed to that failure. Furthermore, Pap smears can miss cervical carcinoma, especially in low-quality laboratories; consequently they must be repeated every year to increase the chance of early detection.[9]

Epidemiological studies have consistently shown that the most important determinants of HPV infection in women are: the number of sexual partners, the age of initiation of sexual activity, and the sexual behavior of the male partner. Cervical carcinoma is preventable and curable if detected at early stage; but, in order to minimize cervical screening barriers in low-resource settings, strategies should be socially and culturally appropriate and health workers should be knowledgeable about correct procedures.[10] Although, the education about screening plays a vital role in cervical carcinoma prevention, most of Rwandese women are not aware about the symptoms and mode of transmission of cervical carcinoma.[3]

Papanicolaou (PAP) smear is a simple, safe, non-invasive and effective method for detection of pre-cancerous, cancerous and non-cancerous changes in the cervix and vagina. The use of acetic acid during visual examination of the cervix, termed visual inspection with acetic acid (VIA), has been advocated as an alternative screening method to PAP smears in developing countries.[11] In this regards, the aim of this study was to compare VIA test and Pap smear test in order of assess their role in cervical carcinoma screening.

METHODS

This study was prospective and retrospective, comparative study carried out at Butare University Teaching Hospital (BUTH/CHUB), in Rwanda, southern province, District of Huye, in the departments of Gynecology and Anatomical Pathology from April 2011 to August 2014. Women aged 20 years and above who attended the gynecology department at CHUB with complaints of vaginal discharge, pelvic pain, post-coital bleeding were enrolled in this study. Women who had undergone hysterectomy or treatment for cervical pre-cancer or cancer, women with visible growth of cancer on the cervix, who are in menstrual period and pregnant women were excluded from the study. A total number of 198 women diagnosed or screened for cervical cancer at CHUB were included in this study. In this study, prospective and retrospective methods have been used. In prospective method, 20 samples were collected. In retrospective method, 178 samples were collected using both files in Gynecology and Anatomical Pathology department.

Sample collection

During the data collection, the information on names, age, sex, the residential area, marital status and phone numbers, clinical pathological features of cervical carcinoma pelvic pain, vaginal bleeding, vagina discharge and grade of the tumor were obtained through a pre-designed structured data collection form.

The cervix was painted with 3–4% acetic acid and observed for aceto-white lesions (positive VIA) in gynecology department. Both negative and positive VIA results were collected by Ayres's spatula for Pap smear test. Samples were fixed in 95% ethyl alcohol and taken to the Pathology Department for interpretation. The Pap smear was reported according to the Bethesda system 2001. Patients with positive Pap smear results were again called back for biopsy. Biopsy served as the reference standard for cervical carcinoma diagnosis. Samples were analyzed using all steps of cytology and histopathology techniques. Cytology technique was Papanicolaou staining and histopathology technique was tissue processing. Samples were interpreted by a pathologist on light microscope (x400 magnification).

Data analysis

Data were registered on a paper data sheet and later analyzed using Microsoft Excel. Categorical variables were presented as frequency (n), percentage (%) in tables.

Ethical considerations

An authorization letter was given by INES administration. This study was carried out at CHUB after approval by the ethical committee of CHUB. The names of the patients were not recorded for ethical reason. All personal information was kept confidentially and only used for the study purposes.

RESULTS

In this study, the performance of VIA and Pap smear tests were analyzed and compared for a total of 198 women. The main symptoms as reason of testing were: the vaginal bleeding with 94 (47.47%) cases followed by pelvic pain with 65 (32.82%) cases and vaginal discharge with 39 (19.69%) cases.

Table 1. The distribution of patients screened for cervical carcinoma according to age.

Age range	Number of participants	Percentage
21-30 years	17	8.6
31-40 years	49	24.8
41-50 years	64	32.3
51-60 years	45	22.7
61-70 years	23	11.6
Total	198	100

In table 1, the age range 31-40 years and age range 41-50 years show a high number of women screened for cervical carcinoma.

Table 2. Distribution of VIA results according to age

Age group	Number of participants	Number of acetowhite positive	% of the total sample	Number of acetowhite negative	% of the total sample
21-30	17	4	2.02	13	6.56
31-40	49	11	5.55	38	19.19
41-50	64	29	14.64	35	17.67
51-60	45	38	19.19	7	3.53
61-70	23	12	6.06	11	5.55
Total	198	94	47.47	104	52.52

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In table 2, VIA positive tests were 47.47% overall. In the age range 51-60, 38(19.19%) acetowhite positives has been tested; VIA negative results were 52.52% overall.

Table 3. Distribution of positive Pap smear results according to age

Age range (years)	LSIL	% of the total sample	HSIL	% of the total sample	SCC	% of the total sample	Total Pap test positive	% of the total sample
21-30	2	1.01	0	0	0	0	2	1.01
31-40	5	2.52	1	0.5	4	2.02	10	5.05
41-50	3	1.51	1	0.5	7	3.53	11	5.55
51-60	6	3.03	2	1.01	30	15.15	38	19.19
61-70	4	2.02	2	1.01	12	6.06	18	9.09
Total	20	10.09	6	3.03	53	26.76	79	39.89

LSIL: Low Squamous Intraepithelial Lesions, HSIL: High Squamous Intraepithelial Lesions, SCC: Squamous Cell Carcinoma.

In table 3, Pap smear test was positive in 79 (39.89%) cases. Whereas a high level 53 (26.76%) of SCC were diagnosed.

Table 4. Distribution of negative Pap smear results according to age

Age range (years)	Normal	% of the total sample	ASCUS	% of the total sample	Benign cellular changes	% of the total sample	Total Pap test negative	% of the total sample
21-30	12	6.06	2	1.01	1	0.5	15	7.57
31-40	33	16.66	4	2.02	2	1.01	39	19.69
41-50	23	11.61	5	2.52	25	12.62	53	26.76
51-60	0	0	4	2.02	3	1.51	7	3.53
61-70	0	0	4	2.02	1	0.5	5	2.52
Total	68	34.34	19	9.59	32	16.16	119	60.1

Table 4 shows that 119 (60.1%) of women have been diagnosed as negative with Pap smear tests, Atypical Squamous Cells of Undifferentiated Significance (ASCUS) were 19 (9.59%) cases and 32 (16.16%) cases were benign cellular changes.

Table 5. Comparison of Pap smear test and VIA test

	Pap smear positive	Pap smear negative	Total
VIA positive	61	33	94
VIA negative	18	86	104
Total	79	119	198

In table 5, among 94 cases that were positive to VIA, 61 were confirmed positive with Pap smear, 18 of those that were negative to VIA were confirmed positive to Pap smear.

Table 6. Results of biopsy tests for cervical carcinoma screening.

Biopsy test result	Number of cases	% of the total sample
Chronic cervicitis	111	56.06
Mild dysplasia	20	10.1
Moderate dysplasia	2	1.01
Severe dysplasia	4	2.02
SCC	53	26.76
Adenocarcinoma	8	4.04
Total	198	100

Table 6 shows biopsy results as a confirmation test. Mild dysplasia, moderate dysplasia, severe dysplasia and SCC were considered as positive for neoplasia. Final diagnostic by histopathology was taken as gold standard.
Out of 198 cases, 111 (56.06%) were diagnosed as chronic cervicitis, 20 (10.1%) as mild dysplasia (CIN I), 2 (1.01%) as moderate dysplasia (CIN II), 4 (2.02%) as severe dysplasia, 53 (26.76%) as squamous cells carcinoma and 8 (4.04%) as adenocarcinoma. Hence, biopsy test showed 87 (43.9%) positive cases.

Table 7. Comparison of VIA and Pap smear tests to biopsy examination

Tests	Positive biopsy	Negative biopsy	Total
Positive VIA	77	17	94
Negative VIA	10	94	104
Positive Pap smear	70	9	79
Negative Pap smear	17	102	119

Table 7 compares VIA and Pap smear tests to biopsy test. It presents true positives and true negatives, false positives and false negatives. For VIA test, the true positives were 77 for the presence of cervical carcinoma; 10 cases were false negatives; true negatives were 94 cases and false positive were 17 cases. For Pap smear, 70 cases out of 198 cases were true positive for the presence of cervical carcinoma; 17 cases were false negatives; true negatives were 102 cases and false positive were 9 cases.

Table 8 presents sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of VIA and Pap smear tests

Table 8. Parameters of VIA and Pap smear tests

Parameters	VIA estimate	Pap smear estimate
Sensitivity = TP/TP+FN	77 /87 × 100 = 88.5%	70 /87 × 100 = 80.45%
Specificity = TN/TN+FP	94 / 111× 100 = 84.68%	102 /111 × 100 = 91.89%
Positive predictive value = TP/TP+FP	77/94× 100 = 81.91%	70 /79 × 100 = 88.6%
Negative predictive value = TN/TN+FN	94 / 104× 100 = 90.38%	102 /119 × 100 = 85.71%
Diagnostic accuracy = (TP+TN)/(P+N)	77+94/198 = 86.36%	70+102/198 = 86.86%

TP: True positive, FP: False positive, TN: True negative, FN: False negative

As shown in table 8, the sensitivity of VIA was 88.5% and that of Pap smear 80.45%. The specificity of VIA was 84.68%and that of Pap smear was 91.89%. The positive predictive value of VIA was 81.91% whereas that of Pap smear was 88.6%. The negative predictive value of VIA was 90.38% whereas that of Pap smear was 85.71%. The diagnostic accuracy of VIA was 86.36% whereas that of Pap smear was 86.86%.

DISCUSSION

The present study was conducted to compare the role of Acetic acid and Pap smear test as cervical carcinoma screening tools for women who attended CHUB. The age range of women involved in this study was 20-70 years. This age range is similar to that used by Khan S *et al* in 2007, where in their study, this screening method was studied in the age range of 25 to 65 years and also the age range of our study is related to that used by the American Cancer Society in 2013, which recommended all women to begin cervical carcinoma screening at age 21 to 65 years old.[1, 12] The age group ranging 51-60 years old was at high risk of developing the cervical carcinoma because this age group is the menopause period.

In this study, vaginal bleeding was the most common presenting complaint for cervical carcinoma with 63% of the cases. The second common complaint was pelvic pain in 23% and the last was vaginal discharge with 14% in case of cervical carcinoma. These complaints for cervical carcinoma are found in similar studies. In the study at Mysore Medical College and Research Institute by Suman K, in 2012, vaginal discharge was reported as the most common presenting complaint (77.14%) followed by pelvic pain (43%).[13] Also similar complaints were found in Sudan, where Dhabhadel et al, in 2008, reported pelvic pain as the most common complaint (56.8%) followed by vaginal discharge (27.43%).[14]

In present study, 10.1% cases of LSIL, and 3.03 % cases of HSIL were reported. In contrast, Lozowiski, *et al.*, in 1982, found that LSIL were 28.3% of cases and HSIL 70% of cases. In our study SCC cases (26.76%) are higher than SCC cases reported by Lozowiski et al. (1. 5%).[15] This large difference may be due to individual variations in the interpretation of Squamous Intra-epithelial Lesions.

In the present study, the proportion of women who were screened positive with VIA was 47.47% and with Pap smear it was 39.89%. Our findings were higher than those observed in other studies in India by Divya H *et al.*, in 2011, which showed 12% cases of VIA positive while positive Pap smear were 11.7% cases. Singh K *et al.*, in 2010 showed 16. 2% cases of positive VIA and 5.2% cases of positive Pap smear.[16, 17] The reason for higher positivity rates of VIA and Pap smear tests in the present study may be that the current study was conducted in a referral hospital. It was done on hospital based population in which high risk cases were screened.

In the present study, the sensitivity of VIA was higher (88.5%) than that of Pap smear (80.45%). This result is similar to that found in the study conducted by Vadehra K, et al., in 2006 where sensitivity of VIA was higher (96.4%) than that of Pap smear (71.4%).[18]

In our study, the specificity of VIA was lower at (84.68%) as compared to Pap smear (91.89%). Our results relate to the findings reported by Garg P. in 2011, where the specificity of VIA was 82% and that of Pap smear was 91.1%. [19]

In the present study, the positive predictive value of Pap smear was higher (88.6%) than that of VIA (81.91%). The present results are similar to that found in University of Zimbabwe/JHPIEGO cancer project (1999) where the positive predictive value of Pap smear was elevated (40.7%) than that of VIA (22.7%).[20]

The negative predictive value for VIA was high than that of Pap smear 90.38% and 85.71% respectively. Garg P, in 2011, has found the equivalent rate where negative predictive value for VIA was 99. 7% whereas Pap smears was 98.7%. [19]

In the current study, the diagnostic accuracy of VIA was (86.36%) whereas that of Pap smear was (86.86%). These results are similar to that found by Albert *et al.*, in 2012, where the diagnostic accuracy of VIA was 98.6% whereas for Pap smears it was 99.4%.[21]
The specificity of VIA for cervical carcinoma screening would guide to over-treatment of non-neoplastic lesions. VIA is of particular interest in CHUB because it only requires equipment locally obtainable, and can be competently performed by non-physicians with prior training. The Pap smear stills the best method for screening of cervical carcinoma because of its high specificity. In addition, the sensitivity of VIA is higher than that of Pap smear test. Thus, VIA and Pap smear test could be alternatively used in the screening of cervical carcinoma. Further study is needed to compare the new cervical cancer screening test

called HPV-DNA test with the tests used in the present study.

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