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Research Article

Correlation of Pap smear and visual inspection with acetic acid for screening of premalignant and malignant lesion of cervix

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ABSTRACT

Background: Cervical cancer still remains a leading cause of morbidity and mortality among women worldwide. Despite attempts to increase screening over the past several decades, incidence and mortality rates of cancer cervix have not shown substantial reduction. The conventional method of screening by cervical cytology/pap smear has failed to reduce the disease burden due to lack of patient compliance for repeated testing and a relatively sophisticated infrastructure. Therefore, alternative methods such as visual inspection after application of acetic acid (VIA), visual inspection with Lugol's Iodine (VILI) and human papillomavirus (HPV) DNA testing have been developed. The aim of present study was to compare Pap smear and VIA and evaluate their usefulness as tools for screening of premalignant and malignant lesions of cervix.
Methods: This was a crossectional study over 5 months from 1 Jan 2015 to 31 may 2015 in which 212 patients attending the obstetrics and gynecology department, BHU were enrolled. Pap smear was taken followed by VIA. Pap smears were sent to pathology department, BHU where they were reported as per Bethesda System, 2001. Cervical biopsies were done in positive cases. Data obtained and statistically analyzed.
Results: The present study was conducted over a period of 6 months among 212 patients age of 18-60 years screened. Positive results obtained from cytology were 26, VIA was positive in 28 women. Cervical biopsy was done in 34 women who had positive results by either test. Histology in 31 cases was suggestive of cervical intraepithelial carcinoma (CIN).
Conclusions: VIA, though less specific has comparable sensitivity to Pap smear and may be used as a primary screening tool for cervical cancer. In combination both the tests have a higher predictive accuracy.

Keywords: Ca cervix, Pap smear, VIA, Screening

INTRODUCTION

Cervical cancer is the second most common cancer among women globally. In 2010, an estimated 550,700 new cases and 286,823 deaths due to cervical cancer have been reported. Cervical cancer accounts for the highest number of deaths from cancer among women in India. Importance of cervical screening is repeatedly emphasized because invasive cervical cancer is preceded by a long phase of precancerous lesion which is easily detectable by routine screening and can be treated effectively by simple methods. This makes cervical cancer easily preventable if routinely screened.[1,2] Pap smear is well known to be effective in reducing the population wide incidence of invasive cervical carcinoma when at least 70% population is screened with good quality pap smears on a regular basis. However this 70% population coverage is difficult to achieve in developing countries. Despite the importance of public health, there are no effective prevention programs in India. An effective cervical screening program needs a consistent access to supplies, trained providers, reliable

transportation of specimen, a high quality well equipped laboratory, trained cytopathologists and a quality control system which are often not met on a regular basis. Even poor technique of cervical smear collection and poor preservation leads to program failure.[3,4]

Alternative simple and low-cost technique screening test like VIA, VILI which can be done in peripheral areas and do not demand high technical skills are being evaluated. HPV DNA testing is quite expensive. VIA based on the ability of the trained health worker to detect acetowhite in the cervical transformation zone, is currently being evaluated as a potential alternative or an adjunct to cervical cytology. Studies show that VIA has similar sensitivity but somewhat lower specificity when compared to pap smear. The aim of present study is to compare pap smear and VIA and evaluate their usefulness as tools for screening of premalignant and malignant lesions of cervix so that VIA can be used in peripheral areas where cytology is not available.

METHODS

This was a crossectional study conducted over a period of 5 months from I Jan 2015 to 31 may 2015 in which 212 patients (18-60 years) attending the obstetrics and gynecology department, BHU were enrolled. Patients with the risk factors like: early age at marriage/pregnancy/sexual activity, multiparity multiple sexual partners.

Unmarried patients, pregnant women, women with active bleeding per vaginum, frank growth on cervix, post-hysterectomy patients, and women who had never been sexually active or had undergone prior treatment for cervical intraepithelial neoplasia (CIN) or cancer cervix were excluded from the study.

Patients who fulfilled the selection criteria were explained the procedure and informed consent taken with relevant history. Firstly, a Pap smear was taken with Ayre's spatula and cytobrush close to transformation zone and slides fixed in 95% ethanol. Then, cervix was washed with normal saline, visualized followed by application of 3% acetic acid. Results of VIA were recorded after1 minute as negative, and positive. Positive cases were scheduled for biopsies and histological evaluation. Pap smears were sent to Department of pathology, BHU where they were reported as per Bethesda System, 2001. Cervical Biopsy and histopathological studies were done in positive cases. Data was obtained and statistically analyzed.

RESULTS

Positive results obtained from cytology were 26, VIA was positive in 28 women. Cervical biopsy was done in 34 women who had positive results by either test. Histology in 31 cases was suggestive of cervical intraepithelial carcinoma (CIN) [Table 1].

Table 1: Presenting complains of patients.

Presenting complains	No. of patients	(Percentage)
Vaginal discharge	161	75.94
Pain lower abdomen	30	14.15
Post coital bleeding	9	4.24
Pruritis vulva	5	2.36
Intermenstrual bleeding	4	1.89
Post-menopausal Bleeding	3	1.42
Total	212	

The commonest presenting complaint was vaginal discharge in 161 patients (75.94%) followed by lower abdominal pain in 30 patients (14.15%). Other presenting complaints were postictal, intermenstrual or postmenopausal bleeding and pruritis vulvae [Table 2].

Table 2: Finding on per speculum examination.

Finding on per speculum examination	No of patients	(Percentage)
Normal looking cervix	92	43.39
Unhealthy cervix	105	49.53
Suspicious looking cervix	15	7.08
Total	212	

On per speculum examination a normal looking cervix was seen in 92 patients (43.39%) and 105 patients (49.53%) showed an unhealthy cervix. The abnormalities of in unhealthy cervix were erosion, and ectopy.15 patients (7.08 %) had a suspicious looking cervix [Table 3].

Table 3: Pap smear reporting (Bethesda system).

NILM	**186(87.8%)**
	Normal -137(73.6%) Inflammatory smear - 49(26.4%)
ECA	26 (12.2%)
	ASCUS and ASCUS-H - 9(34.6%) LSIL (HPV and CIN1) - 12(46.1%) HSIL (CIN 2 and CIN 3) - 5(19.3%) SQUAMOUS CELL CARCINOMA - 0
Total	**212**

Pap smear was positive in 26 cases which included 9 cases of ASCUS/ASCUS-H, 12 cases of LSIL and 5 of HSIL. It was reported negative for intraepithelial lesion or malignancy in 186 patients (87.8%).Out of these 49 (26.4%) were inflammatory smears [Table 4].

Cervical biopsy was taken in 34 cases, positive by Pap smear or VIA. 5 positive cases were missed with Pap smear screening. One case which was positive on Pap smear was normal on histopathology [Table 5].

Table 4: Comparison of Pap with histopathological findings.

Pap smear	Histopathological findings		
	Positive	Negative	Total
Positive	26	1	27
Negative	5	2	7
Total	31	3	34

Table 5: Comparison of VIA with histopathological findings.

VIA	Histopathological findings		
	Positive	Negative	Total
Positive	28	2	30
Negative	3	1	1
Total	31	3	34

On comparison with histopathology 3 cases were found to be missed by VIA. Two cases which were positive on VIA showed no dysplasia on histopathology, however dense inflammation was seen [Table 6].

Table 6: Comparison of Pap smear+VIA with histopathological findings.

Pap + VIA	Histopathological findings		
	Positive	Negative	Total
Positive	30	1	31
Negative	1	2	3
Total	31	3	34

Taken together pap smear and VIA detected 30 positive cases. Out of 31 positive cases showing dysplasia, only one case was missed [Table 7].

Table 7: Analysis of Pap smear and VIA.

Test	Sensitivity	Specificity	PPV	NPV
Pap Smear	83.9	66.7	96.3	28.6
VIA	90.3%	33.3	93.3	25
PapSmear + VIA	96.8	66.7	96.7	66.7

The sensitivity of VIA was found to be greater (90.3%) than Pap smear (83.9%). However Pap smear was more specific in determining the epithelial cell abnormalities. Combining together greater sensitivity with good specificity can be achieved.

DISCUSSION

Premalignant lesions of cervix take about 5-15 years to progress to invasive cancer. If timely detected, pre-invasive disease has nearly 100% cure rate with simple surgical procedure, while advanced cancer has less than 35 per cent survival rates. In most developing countries like India, universal screening has not yet been possible. Pap smear despite being a good cervical screening test is available mainly in urban areas which leads a large proportion of population to remain unscreened and leave cervical abnormalities undetected for long. Cytology based screening programmes prove unsuccessful due to limited infrastructure and lack of trained cytopathologists. In the present study, women from all the age groups were included because 299risk for cervical cancer increases from onset of sexual activity to elderly.[3,5] A study done by Luthra et al showed mean ages for mild, moderate and severe dysplasia to be 33.8, 35.2 and 40.2 years.[6] All women should be screened at least once by the age of 30-35 yr. and then followed 3 yearly. In present study the sensitivity of VIA was found to be higher (90.3%) compared to that of Pap smear, (83.9%). Pap smear showed specificity of 66.7% while VIA had a specificity of only 33.3%.This shows that though VIA has good sensitivity and can be used as a screening tool in detection of precancerous cervical lesion it should be followed by other tests which are more specific before definitive treatment is given. A study by Shuchi et al showed, sensitivity of VIA was 84.20%, which was similar to that in present study.[7] However specificity was higher, 55.2%. In a metaanyalsis done by Fahey et al.[8] involving 62 studies conducted over 8 years the mean sensitivity and specificity of cytology was 58% (range 11–99%) and 68% (range 14–97%), respectively. In a more recent metaanalysis by Nanda et al. the sensitivity of cytology to the detection of CIN 2 or worse lesions ranged from 18% to 98% and the specificity ranged from 17% to 99%.[9] In the IARC multicenter study done in India and Africa by Sankaranarayanan et al. in 2004, which included 11 cross-sectional studies, the sensitivity of VIA ranged from 56.10% to 93.90% and the specificity ranged between 74.20% and 93.80%.[10,11] Thus, the present studies show comparable results to previous studies. Various reasons attributed for lower specificity of VIA in this study could be due to higher percentage patients having infection and inflammation that can take up acetowhite stain, faint acetowhite areas misinterpreted as positive. The sensitivity of Pap smear has been found to be lower in developing countries, probably due to the large percentage of inflammatory smears which may mask mild dysplasia. In other study the sensitivity of VIA versus Pap smear in this regard has been variously reported as 31.6% vs. 78.2%; 57.4% vs. 79%; 59.7% vs. 57.4%; and 93% vs. 83% respectively.[12]

Although the value of repeated Pap smears in screening for this disease and its precursors has long been established in the West, it is clear that logistic requirements cannot be met in developing countries in the foreseeable future. Alternative methods for low resource settings such as VIA by trained paramedical workers offer hope for universal screening. Testing schemes for which results are not immediately available, especially in less developed countries, result in unacceptably high rates

of loss to follow up among the tested population VIA offers this advantage. Together VIA and Pap smear can detect most possible abnormalities with a good specificity and sensitivity. In present study combined sensitivity for Pap smear was 96.8 %and combined specificity was 66.7. % Adjunctive testing is one way of improving specificity of the test without compromising sensitivity.[13,14]

CONCLUSION

Although population-based programs with Pap smear have reduced cervical cancer incidence and mortality in high-income countries, such programs fail to reduce cervical cancer burden in low resource setting due to poor organization, lack of coverage, and lack of quality assurance. In such settings, screening of carcinoma cervix by Pap smear can be replaced by cheaper and easily available visual methods like VIA. Our study showed that VIA had sensitivity comparable to Pap smear and can therefore be a suitable potential alternative/adjunctive screening test, not even when screening with Pap smear is available, it should be combined with visual screening methods like VIA, as many cases of CIN missed by Pap smear were picked up by the visual tests, and combined testing reduced the number of biopsies taken based on either test alone.

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REFERENCES

1. Bhattacharyya AK, Nath JD, and Deka H Comparative study between Pap smear and visual inspection with acetic acid in screening of CIN and early cervical cancer J Midlife Health. 2015;6(2):53–8.
2. Bhatia N, Mukhopadhyay A, Kriplani A, Pandey RM, Gravitt PE, Shah KV, Iyer VK, Verma K. Evaluation of adjunctive tests for cervical cancer screening in low resource settings. Indian J Cancer. 2007;44:51-5.
3. Sale HS Can visual inspection with acetic acid is used as an alternative to Pap smear in screening cervical cancer? Middle East Fertility Society Journal. 2014;19(3):187–91.
4. Perkins RB, Langrish SM, Stern LJ, Figueroa J, Simon CJ. Comparison of visual inspection and Papanicolau (PAP) smears for cervical cancer screening in Honduras: should PAP smears be abandoned? Trop Med Int Health. 2007;12(9):1018-25.
5. Ghosh P, Gandhi G, Kochhar PK, Zutshi V, and Batra S. Visual inspection of cervix with Lugol's iodine for early detection of premalignant & malignant lesions of cervix Indian J Med Res. 2012;136(2):265–71.
6. Luthra UK, Prabhakar AK, Seth P, Agarwal SS, Murthy NS, Bhatnagar P, et al. Natural history of precancerous and early cancerous lesions of the uterine cervix. Acta Cytol. 1987;31:226–34.
7. Consul S, Agrawal A, Sharma H, Bansal A, Gutch M, Jain N. Comparative study of effectiveness of Pap smear versus visual inspection with acetic acid and visual inspection with Lugol's iodine for mass screening of premalignant and malignant lesion of cervix Indian J Med Paediatric Oncol. 2012;33(3):161–5.
8. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. Am J Epidemiol. 1995;141:680–9.
9. Nanda K, McCrory DC, Myers ER, Bastian LA, Hasselblad V, Hickey JD, et al. Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytological abnormalities: a systematic review. Ann Intern Med. 2000;132:810–9.
10. Sankaranarayanan R, Thara S, Sharma A, Roy C, Shastri S, Mahe C, et al. Accuracy of conventional cytology: Results from a multicentre screening study in India. J Med Screen. 2004;11:77–84.
11. IARC handbooks of cancer prevention: Cervix cancer screening. Lyon, France: IARC Press;2005.
12. Mahmud G, Tasnim N, Iqbal S. Comparison of Visual Inspection with acetic acid and Pap smear in cervical cancer screening at a tertiary care hospital. J Pak Med Assoc. 2013;63(8):1013-6.
13. Satyanarayana L, Asthana S, Bhambani S, Sodhani P, Gupta S. A comparative study of cervical cancer screening methods in a rural community setting of North India. Indian J Cancer. 2014;51:124-8.
14. Ferris DG, Wright TC, Litaker MS, Richart RM, Lorincz AT, Sun XW, et al. Triage of women with ASCUS and LSIL on Pap smear reports management by repeat Pap smear, HPV DNA testing or colposcopy. J Fam Pract. 1998;46:125-34.

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