Section: Obstetrics and Gynaecology

Research

COLPOSCOPY, VISUAL INSPECTION OF CERVIX WITH ACETIC ACID AND CYTOLOGICAL STUDY IN EARLY DETECTION OF CERVICAL INTRAEPITHELIAL LESION

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Abstract

Background: Cervical cancer is the commonest genital malignancy especially among low and middle socioeconomic class families. Hence early detection and identification of the cases can prevent the mortality related to the carcinoma. This study was carried out to compare the sensitivity and specificity of VIA, colposcopy, pap smear in the detection of premalignant lesions of the cervix in low resource settings. **Materials and Methods:** A prospective study was conducted among 300 women between 21 – 65 years of age. All women underwent per speculum examination and colposcopy and those who tested positive on screening underwent colposcopy guided biopsy. Visual inspection of cervix with acetic acid is considered positive if cervical epithelium becomes white and opaque with distinct margins within the transformation zone. Sensitivity, Specificity, Positive Predictive value, Negative predictive value was then calculated for Pap smear, VIA, Colposcopy. The statistical test used was chi square test and a p value of <0.05 was considered significant. **Result:** VIA positivity was seen among 47 patients (15.7%). Colposcopic examination revealed that 58 patients (19.3%) had abnormal findings. A total of 44 (14.6%) Pap smears were found to be abnormal. Among the abnormal reports 26 (8.6%) were LSIL, 10 (3.3%) were high grade squamous intraepithelial lesion (HSIL) and 8 (2.6%) were squamous cell carcinoma. It was found that colposcopy was sensitive (98%) in detecting moderate to severe dysplasia, but VIA was more specific (44.4%) in detecting moderate to severe dysplasia when compared to colposcopy. **Conclusion:** Colposcopy is the best test in early detection of cervical intraepithelial lesion (CIN). Combination of these three tests together will be able to detect majority of the CINs. Pap smear and VIA are cost effective tests, as these can be done in low resource setting.

INTRODUCTION

Cervical cancer is one of the most common cancers among Indian women. The data attained from Indian Cancer Registries indicate that cervical cancer contributes to approximately 6–29% of all cancer in females. The age-adjusted incidence rate of cancer cervix was found to vary widely among registries, highest being 23.07/100,000 in Mizoram State of India.[1] It is the commonest genital malignancy specially in low and middle socio-economic class of women. Contributing to the cervical cancer health burden in a country like India, is the lack of awareness among people and policy makers, that it is readily preventable when effective programs are implemented to detect and treat its precursor lesions.[2] The concept of cervical intraepithelial neoplasm (CIN) was introduced in 1968 when Richard suggested that dysplasias have the potential for progression. Most untreated CIN 1 and some CIN 2 lesions regress spontaneously, nevertheless, high grade CIN refers to a lesion that may progress to invasive carcinoma when left untreated.

PAP smear is a primary screening tool for CIN and colposcopy is a diagnostic test to evaluate patients with an abnormal cervical cytological smear or abnormal appearing cervix. Colposcopy is indicated when the immediate risk of CIN 2 or worse is 4% or greater, as determined by prior screening results or histology and current high-risk Human

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papillomavirus (HPV) and cytology results. Abnormal-appearing vaginal or cervical tissue should also be evaluated with colposcopy.[3] The performance and accuracy of colposcopy depends largely on the training experience and the skills of the colposcopist. Hence accuracy of colposcopy varies widely among studies in different part of the world.[4] Reids colposcopic index is a systematic, objective method of colposcopically grading the severity of premalignant lesions. The index considers four colposcopic signs: lesion margin, colour of acetowhitening, blood vessels and iodine staining. The use of the index helps to direct the clinician to perform a biopsy of the most significant abnormal cervical lesions and enhances the formulation of the colposcopic impression.

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. The attractive features of VIA include low cost, simple administration, its high sensitivity, immediate availability of results and accuracy comparable to good quality PAP smears.[5,6] This study was carried out to compare the sensitivity and specificity of VIA, colposcopy, pap smear in the detection of premalignant lesions of the cervix in low resource settings.

MATERIALS AND METHODS

This was a prospective study conducted among 300 women between the age group of 21 – 65 years attending the gynaecology department in a tertiary hospital. General physical examination and detailed systemic examination were done. Per speculum examination of cervix and vagina was done. The squamocolumnar junction was visualized, with the hooked end of Ayre's spatula, squamocolumnar junction was scraped gently throughout its circumference and material was transferred to the glass slides. Two such smears were fixed with 95% alcohol immediately and stained by Papanicolaou stain. A solution of 5% acetic acid was then applied to the cervix using a cotton swab. The cervix was then examined under 1-2 minutes under an adequate light source. The detection of any distinct acetowhite area was considered positive result. If no acetowhite areas were recorded, or if a whitish appearance is doubtful, the test result was considered negative.

All women then underwent colposcopy using the video colposcope COL PRO 222 DX [PRO MIS]. All patients who tested positive on screening underwent colposcopy guided biopsy. Biopsy was done using a punch biopsy forceps from abnormal areas detected by under colposcopic guidance. The excised tissue thus obtained was fixed in 10% formalin, processed and embedded in paraffin blocks; 5-6 micro thick sections were taken by a microtome and stained with haematoxylin and eosin. A test after visual inspection of cervix with acetic acid is considered positive if cervical epithelium becomes white and opaque with distinct margins within the transformation zone. For pap smear a finding of low grade squamous intraepithelial lesion (LSIL) and above is considered positive. If pap smear is positive and VIA/colposcopy is negative in the first setting, biopsy is taken at a later visit. All results were then compiled and analysed. Sensitivity, Specificity, Positive Predictive value, Negative predictive value was then calculated for Pap smear, VIA, Colposcopy. The statistical test used was chi square test and a p value of <0.05 was considered significant.

RESULTS

Out of the 300 patients studied, majority belonged to the age group of 41 – 50 years. The youngest subject was 23 years old while the oldest was 62 years. Around 64.7% subjects in the study belonged to the lower middle class income family. The main presenting complaint among the patients were white discharge per vagina (29.7%), followed by menstrual irregularity (27.0%) and abdominal pain (22.0).

Table 1: Distribution of cervical biopsy abnormalities in the study population

Histopathology report	Number of patients (%)
Normal	9 (15.0)
Cervicitis	11 (18.3)
Mild dysplasia	25 (41.7)
Moderate dysplasia	3 (5.0)
Severe dysplasia	8 (13.3)
Squamous cancer	4 (6.7)
Total	60 (100.0)

Table 2: Comparison between pap smear and colposcopy/colposcopy guided biopsy

PAP Smear	Colposopy/colposcopy guided biopsy	
	Abnormal (%)	Normal (%)
Abnormal 44 (14.6%)	43 (14.3)	257 (85.7)
Normal 256 (69.4%)	15 (5.8)	241 (94.1)

Chi square test, p value-<0.05

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Table 3 Comparison between VIA and colposcopy/colposcopy guided biopsy

VIA	Colposcopy		Total
	Abnormal	Normal	
VIA positive	23 (39.7)	24 (9.9)	47 (15.7)
VIA negative	35 (60.3)	218 (90.1)	253 (84.3)
Total	58 (100)	242 (100)	300 (100)

Chi-square test, p value = <0.05

Out of 47 VIA positive patients, 55.3% patients (26) had abnormal pap smear and 44.7% patients (21) had normal pap smear. Out of 253 VIA negative patients, 86.2% patients (218) had abnormal pap smear and 13.8% patients had normal pap smear.

Table 4: Comparison between pap smear and VIA

VIA	PAP smear		Total
	Abnormal (%)	Normal (%)	
VIA positive	26 (55.3)	21 (44.7)	47 (100)
VIA negative	218 (86.2)	35 (13.8)	253 (100)
Total	244 (100)	56 (100)	300 (100)

Chi-square test, p value<0.05

Table 5: Comparison of diagnostic values of VIA, pap smear and colposcopy

Screening Test	Sensitivity	Specificity	Negative Predictive Value	Positive Predictive Value
VIA	33.3%	44.4%	10.5%	77.3%
PAP smear	70.6%	11.1%	6.2%	81.8%
Colposcopy	98%	22.2%	66.7%	87.7%

It was found that colposcopy was sensitive in detecting moderate to severe dysplasia, but VIA was more specific in detecting moderate to severe dysplasia when compared to colposcopy.

VIA positivity was seen among 47 patients (15.7%). A total of 44 (14.6%) Pap smears were found to be abnormal. Among the abnormal reports 26 (8.6%) were LSIL, 10 (3.3%) were high grade squamous intraepithelial lesion (HSIL) and 8 (2.6%) were squamous cell carcinoma. Colposcopic examination revealed that 58 patients (19.3%) had abnormal findings. [Table 1] shows the cervical biopsy abnormalities reported among the 60 subjects who underwent biopsy.

DISCUSSION

Women in the age group 21 – 65 years were involved in our study with majority belonging to the age group of 41 – 50 years. While in the study conducted by Goel A et al., most of the study subjects belonged to the age group of 30 – 34 years.[7] In the study conducted by Khan S et al., the majority of the patients were in the age group of 20 – 29 years.[8] The mean parity in our study was 2.6. A mean parity of 3.2 was reported by Kavita et al.[9] Goel et al reported a mean parity of 2.77. In our study majority (65.0%) had 1 – 2 children.

Our study compared VIA with Pap smear with colposcopy or colposcopy guided biopsy being considered as gold standard. In our study colposcopy was done for all patients and biopsy was taken if positive findings were present on Pap smear, VIA, or colposcopy. Goel et al used similar methods, however they did LLETZ (large loop excision of transformation zone) instead of biopsy.[7] Jeronimo J et al and Megevand E et al used cytology and VIA to screen patients and if positive screening test or clinical suspicion invited women for colposcopy and did colposcopy guided biopsy if necessary.[10,11] In the study conducted by Khan S et al., VILI in addition to VIA and cytology and patients with positive findings were scheduled for colposcopy guided biopsies8.

VIA positive rate in our study was 15.6%. Goel et al had a similar rate of 12.5% of VIA7. Cecchini S et al and Shankarnarayanan et al reported positive VIA in 25.4% and 39.8% in their study.[12,13] Whereas Megevand E et al and Slawson et al reported an incidence of abnormal VIA of 3.13% and 4.2 % in their study.[11,14] The wide range is due to difference in interpretation since few studies used nurses or paramedical workers to do the test. It also depends on the study population since few studies were done on symptomatic hospital-based population and others as a mass screening test.

In our study 15.6% patients were VIA positive but 30.6% were Pap smear positive, but if VIA was done alone, the number of case detection would have been reduced by half. As per Pap smear 44 patients were abnormal (14.6%) but in colposcopy guided biopsy only 43(14.3%) were abnormal. Thus, in our study both Pap smear and colposcopy findings are comparable. But in case of 256 study subjects, where pap smear was found to be normal, 15 were colposcopically abnormal. Thus, colposcopy could detect 5.8% of new cases.

It was noted that 14.6% of the Pap smear in our study was abnormal considering LSIL and above as abnormal. Denny L reported an incidence of abnormal pap smear as 8.2%.[6] University of Zimbabwe /JHPIEGO Cervical Cancer Project found that 14.6% of the woman in their study had an abnormal pap smear.[5] Megevand E et al noted an

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abnormal pap smear in 13% of their study population.[11] However, Cecchini S et al., could detect abnormal pap smear only in 1% of their study population.[12] All these studies considered pap smear of LSIL and above as abnormal. A study done by Slawson et al considered pap smear of ASCUS and above as abnormal and found abnormal pap smear in 7.1% of the women in their study.[14]

The incidence of biopsy confirmed dysplasia in our study was 13.3%. Goel et al had a dysplasia rate confirmed on histopathology in 7.5% of their population.[7] Jeronimo J et al and Kavita et al had a dysplasia rate of 2.5% and 3.6% respectively.[9,10] Whereas Shankarnarayanan et al had an incidence of only 1.7% of dysplasia as confirmed by histopathology in their study.[13] Since these studies involved larger number of patients, their incidence of dysplasia was less in comparison to ours.

In our study VIA was positive only in 15.7% of patients. In 84.3% of the study subjects VIA was negative, but among these patients, an additional 13.83% (35 patients) had abnormal colposcopic finding. So, colposcopy helped in detecting 35 new cases which was VIA negative. In VIA positive patients 5 had normal biopsy report, 4 had chronic cervicitis, 6 had mild dysplasia,1 had moderate dysplasia, 4 had severe dysplasia, 2 had squamous carcinoma. In VIA negative patients 4 had normal biopsy report, 7 had chronic cervicitis, 19 had mild dysplasia, 2 had moderate dysplasia, 4 had severe dysplasia and 2 had squamous cell carcinoma. VIA missed 2 cases of squamous cell carcinoma.

In a study done by Kavita et al., out of 27 cases, 25 were detected by VIA and only 20 cases were detected by pap smear9. In a study done by Goel et al, out of 30 dysplasia cases, pap smear was positive in only 15 and VIA in 29 cases.[7] Jeronimo J et al found that pap smear detected 15 cases out of 35 CIN 1 and 5 cases out of 13 CIN 2-3, and VIA detected 20 cases out of 35 CIN 1 and 2 out of CIN 2-3.[10]

Shankaranarayan et al., in their study noted that cytology resulted in the detection of 79% (61 of 77) of mildly dysplastic lesions, VIA detected 70% (54 of 77) of these lesions; 6.5% of these had been missed by both tests.[13] In the same study by Shankarnarayanan et al., out of 51 women with moderate dysplasia or worse, 46 were detected by VIA; cytology detected 44 lesions and VIA detected 5 lesions (4 moderate dysplasia,1 carcinoma in situ) missed by cytology, whereas the latter detected 3 lesions (2 moderate dysplasia and 1 invasive carcinoma) missed by the former.[13]

In this study the most sensitive test was found to be colposcopy with 98% sensitivity, while the least sensitivity was seen in VIA. Considering specificity VIA was more specific in detecting moderate to severe dysplasia when compared to colposcopy. Similar results were shown by various authors with colposcopy being the most sensitive test.[15,16,17] While few studies have shown VIA to be the most sensitive test.[7,9,13] This difference may be due to the study setting and methods the studies have employed to reach the conclusion.

CONCLUSION

Pre-cancerous lesions were common in the age group 41-50 years and incidence of dysplasia increases with parity. Among the various tests such as VIA, colposcopy and pap smear, colposcopy is the best test in early detection of cervical intraepithelial lesion. Hence if we combine the above said tests, we will be able to pick up majority of the cases of cervical intraepithelial lesions at an early stage. Pap smear and VIA are cost effective tests, as these can be done in low resource setting.

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