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A COMPARATIVE STUDY BETWEEN PAP SMEAR AND VISUAL INSPECTION WITH ACETIC ACID (VIA) IN SCREENING OF CIN AND EARLY CERVICAL CANCER

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ABSTRACT

Introduction: Present study was conducted to detect the specificity and sensitivity of each test for identifying cervical intraepithelial neoplasm (CIN) and cervical cancer by comparing with the histology from positively screened women.

Methodology: A prospective study was conducted in the department of obstetrics and Gynecology S.P. Medical College Bikaner on 500 gynecological cases. The PAP was evaluated by the Bethesda system and VIA was performed. All positive cases of VIA and pap's smear were scheduled for biopsy and histological evaluation. Statistically analysis was done.

Results: The sensitivity of VIA was higher (63.16%) than that of Pap smear (52.63%). The specificity of VIA was lower (97.62%) as compared to Pap smear (99.13%). The positive predictive value of Pap smear was 83.33% and that of VIA was 68.57%. The negative predictive value of Pap smear was 96.22% and that of VIA was 96.99%. The diagnostic accuracy of VIA was 95.0% which was comparable to that of Pap smear (95.6%).

Conclusion: VIA may be considered as an alternative to Pap smear in resource poor settings. However, in areas where cytology based screening is available, VIA may be useful as an adjunct to improve the sensitivity of cervical cytology.

KEYWORDS : Cervical intraepithelial neoplasia, Human Papillomavirus, Pap smear, Visual Inspection with Acetic Acid,

INTRODUCTION

Cervical cancer was the second most common cancer among women 15-44 years of age and in 2012 it was the fourth most frequent cancer and cause of cancer death among all women in the world[1].

The World Health Organization (WHO) has predicted that the percentage of new cervical cancer cases and deaths will increase by 40% and 46% from 2008 to 2025 in the developing world[2].

Primary prevention with safe and effective HPV vaccines are readily available, however, vaccine campaigns can be costly and complicated related to distribution requirements, like refrigeration and a three dose series[3]. Secondary prevention through screening with Pap smear cytology with or without Human Papillomavirus (HPV) contesting and treatment of precancerous lesions with ablative or excisional procedures can also be difficult to provide in low resource areas.

Pap smear cytology alone has worked to reduce cervical cancer incidence and mortality rates with serial testing[4]. However, cervical cytology and HPV testing is costly and resource intensive, requiring laboratory facilities, trained staff, and patient follow-up capabilities that may be difficult to implement in low resource areas.

Cervical cancer "see and treat" programs, endorsed by the WHO, Pan American Health Organization (PAHO), and Johns Hopkins Program for International Education in Gynecology and Obstetrics (JHPIEGO), offer a low cost and low resource alternative to Pap smear cytology and HPV testing. "See and treat" cervical cancer screening utilizes naked eye visual inspection of the cervix after the application of acetic acid (AA) or Lugol's iodine and, in the case of VIAM, visualization can be assisted by a low-level, handheld magnification device followed by immediate diagnosis and treatment of abnormal cervical lesions with cryotherapy or specialty referral for larger, more advanced lesions. VI techniques do not require laboratory facilities, can be performed outside the clinical setting, take minutes to complete, and are often performed by non-medical staff. Prior studies of VI have used licensed nurses[5], licensed physicians[6], and unlicensed community health workers (CHWs)[7].

VIA have been studied extensively in low resource environments, and their sensitivities and specificities found to be comparable to Pap smear cytology. VIA have shown higher sensitivity and lower specificity estimates than Pap smear cytology. Although Pap smear cytology testing seems to have a lower false positive rate than VIA, both Pap smear and VI techniques are viable and effective cervical cancer screening options[8].

Several recent studies tested various diagnostic tools for screening. However, the necessity of more research is clear to evaluate the performance of these new tools in different screening settings and with different cancer incidence. The aim of the present study was to evaluate the accuracy of the Pap smear and VIA to compare these screening tests for detection of cervical neoplasia.

MATERIAL AND METHOD

A prospective study was conducted in the department of obstetrics and Gynecology S.P. Medical College Bikaner on 500 gynecological cases.

Inclusion Criteria: Patients in the age group of 18-60 year which include in the study and priority were given to patients with the following risk factors Early marriage and pregnancy, Sexual activity at early age, Multiparity, Multiple sexual partners, Women with STI, leukorrhea and abnormal vaginal bleeding.

Exclusion Criteria: Unmarried patients below 18 years and above 60 years, Patient with bleeding P/V and active infection at the time of examination, Women with frank invasive cervical cancer.

Firstly, appropriate general, obstetrical and gynecological history was taken and full information about the process and reassurance were given to all participants. Examination of Vulva for any abnormalities then vagina and cervix were done after insertion of Cusco's bivalve speculum. Any discharge was removed by cotton swabs. Inspection of the cervix with the naked eye using a focus lamp were done then a PAP smear were taken by scrapping the squamocolumner junction gently by Ayre's spatula and cytobrush, immediately fixing the material in 95% alcohol on a glass slide to stain them by papanicolau stain. Visual inspection (VIA) after freshly prepared 4% acetic acid were applied with a cotton swab stick and observe for 1 minute for presence of a well-defined opaque acetowhite lesion next or close to the squamocolumnar junction (SCJ). The (VIA) testing's results were classified as: Negative or positive according to presence of a well-defined opaque acetowhite lesion next or close to the squamocolumnar junction (SCJ). The PAP was evaluated by the Bethesda system. A smear were considered as cytology-positive if the smear. Any slide with dysplasia (mild, moderate, severe), carcinoma in situ (CIS) or squamous cell carcinomawere considered positive histopathologically. All positive cases of VIA and pap's smear were scheduled for biopsy and histological evaluation. Statistically analysis was done.

OBSERVATIONS

The mean age of patients was 36.7±9.2 years with disease were more prevalent from age group 21-50 years. The mean parity was 2.88±0.94 with 45.4% had parity of 3, 24% had parity of 2. Here, 84.6% cases had

regular menstrual cycle followed by 8.8% had irregular menstrual cycle and 6.6% had achieved menopause. The women present with following complaints i.e. 42.2% cases had complaint of discharge, 39% cases had pelvic pain, 8.2% had UTI, 6.4% had inter-menstrual bleeding, and 4.2% had post-coital bleeding (Fig:1).

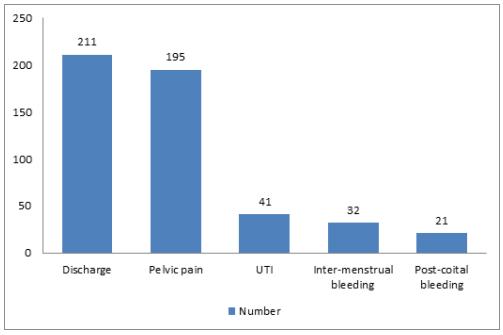

Fig: 1 Distribution of patients according to chief complaints.

On Per speculum findings we found that 64.8% cases had unhealthy cervix on per speculum finding, 35.2% had healthy cervix on per speculum findings (Fig: 2).

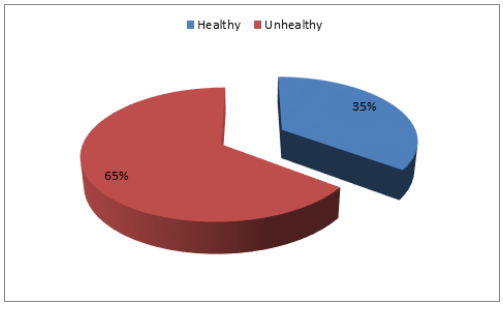

Fig: 2 Per speculum findings

On Pap smear test 89% cases were normal, 31 (6.2%) cases found to have ASCUS type of lesion, 20 (4%) cases had LSIL and 4 (0.8%) cases had HSIL type of lesion of pap smear test which shows that there were 24 cases were pap smear test positive. And, on VIA, 35 cases (7%) were VIA positive and rest 93% cases were VIA negative. Finally, we found that 71.8% cases were normal histopathology, 20.6% cases had chronic cervicitis, 2.2% had CIN-3, 4% had CIN-2 and 1.4% had CIN-2 on biopsy findings.

On comparing Pap smear and VIA with biopsy examination in diagnosis of cervical neoplasm we found that 38 out of 500 cases were positive for the presence of pre-malignant and malignant lesions in biopsy. Pap smear picked up 20 out of these 38 subjects. 18 subjects were missed on Pap smear and 4 cases were false positive and VIA picked up 24 out of these 38 subjects. 14 subjects were missed on VIA and 11 cases were false positive.

Thus, the sensitivity of VIA was higher (63.16%) than that of Pap smear (52.63%). The specificity of VIA was lower (97.62%) as compared to Pap smear (99.13%). The positive predictive value of Pap smear was 88.33% and that of VIA was 68.57%. The negative predictive value of Pap smear was 96.22% and that of VIA was 96.99%. The diagnostic accuracy of VIA was 95.0% which was comparable to that of Pap smear (95.6%) (Table: 1).

Table: 1 Comparison of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of VIA and Pap smear

Parameter	PAP Smear	VIA
Sensitivity	52.63%	63.16%
Specificity	99.13%	97.62 %
Positive Predictive Value	88.33%	68.57%
Negative Predictive Value	96.22%	96.99 %
Diagnostic Accuracy	95.60%	95.00%

DISCUSSION

Invasive cancer cervix is considered now as a preventable disease, PAP smear test is proved to be an effective screening method for early pre invasive change that precede invasive cancer especially when applied in an systematic organized regular set and has a wide coverage. Cost and effectiveness of various preventive strategies are therefore of great concern for health policy makers, other screening tools include human Papilloma virus (HPV) testing alone or with annual PAP smear and VIA test. HPV testing is not cost effective especially in developing countries. Many studies have been done to compare PAP to VIA smears for cervical cancer screening. Most of them were looking at sensitivities and specificities for both tests[9]. The present study was conducted to evaluate and compare the role of cytology and acetic acid test as cervical cancer screening tools.

The disease were more prevalent from age group 21-50 years. In concordance with this Dessari et al found that 305 cases (61%) were 21 to 40 years of age and 160 cases (32%) were 4-60 years of age; the mean age was 40.84 years. Most of the cases were observed in females within active reproductive age group[10]. Khodakarami et al found that the mean age of participating women was 36.0 years (SD, 7.9) and most of them (47%) were in the age category of 31–40 years[11].

Here, the most common complaint was discharge (42.2%), pelvic pain (39%). Saha R and Thapa M reported vaginal discharge as the most common presenting complaint in their study[12] Divya Hegde et al. also reported white discharge per vagina as the most common presenting complaint in cases of precancerous and malignant lesions[13].

In present study 31.2% had parity of 1-2, 64.4% had parity of 3-4. In concordance with this Nakash et al found that 48% had parity of >4 followed by 31.4% had a parity of 3-4, 6.4% had parity of 1-2[14]. Hinkula et al found that Multiparity seems thus to be an independent risk factor of cervicitis also in a country with effective national programmes for an early detection and treatment of CINs. Young age at first birth also plays a significant role in the aetiology of cervicitis and CIN3[15].

In our study majority 64.8% cases had unhealthy cervix on per speculum finding which includes erosion, ulceration, congested cervix, cervical growth and cervical polyp, 35.2% had healthy cervix on per speculum findings. In consistent with this study by Malathi et al found On per speculum examination (naked eye appearance) of these 200 women; 119 (59.5 %) cervices were found to be unhealthy (either having discharge, erosion, congestion, hypertrophy or polyp) while 81 (40.5 %) cervices were healthy[16].

Majority of cases (93%) were VIA negative and 35 cases (7%) were VIA positive. 20 (4%) cases had LSIL and 4 (0.8%) cases had HSIL type lesion in pap smear test which shows that there were total 24 cases were pap smear test positive. 31 (6.2%) cases found to have ASCUS and 89% cases were normal on pap smear test that we count as PAP smear negative. In consistent with this Surendra S Shastri et al.[17] found 508 (12.7%) cases were VIA positive and 101 (2.7%) cases were pap smear test positive. Similarly study by Wesley R et al.[18], Singh Kavita N et al.[19] and Ghaemmaghami F et al.[20] found that 1279 (45%), 122 (16.26%) and 191 (16.1%) cases were VIA positive and 217 (7.6%), 39 (5.2%) and 226 (19%) cases were pap smear test positive. The variation in the results of VIA positivity may also be attributed to the difference in the categories of the staff who screen the cases. Another factor that could affect the VIA test results is the lack of uniformity in the criteria used for VIA positivity in different studies.

On histopathology we found that 71.8% cases were normal, 20.6% cases had chronic cervicitis on biopsy findings. In concordance with this study conducted by Vadehra et al, Incidence of CIN/ cancer cervix in the study population was found to be 5.6 %[21].

In our study 38 out of 500 cases were positive for the presence of pre-malignant and malignant lesions in biopsy. Pap smear picked up 20 out of these 38 cases. 18 cases were missed on Pap smear. 4 case were false positive in this study. Thus, sensitivity of pap smear was 52.63%. specificity was 99.12%, positive predictive value was 83.3%, negative predictive value was 96.22% and diagnostic accuracy was 95.60%. The sensitivity and specificity for cytology in the Nakash et al[14] study were 46% and 88% respectively, by Cohn et al. and Gaffikin et al.[22,23], which were 44.3% and 90.6% respectively.

Similarly, VIA picked up 24 out of these 38 cases. 14 cases were missed on VIA. 11 cases were false positive in this study. Thus sensitivity of VIA was 63.16%, specificity was 97.62%, positive predictive value was 68.57%, negative predictive value was 96.99% and diagnostic accuracy was 95.00%. The sensitivity reported by

Nakash et al[14] study was 84.6% which significantly higher than that for pap smear (46%) a finding similar to that reported by Ghaemmaghami et al. [20], were the sensitivity of VIA and pap smear 74.3% and 37.1% respectively, and also by Cohn et al.[22] were the sensitivity of VIA was 76.7% which is higher than sensitivity of pap smear 4403%. Also by Rana et al.[24] were the sensitivity for VIA was 93% which was significantly higher than that for pap smear (83%).

The overall comparison is that in present study, the sensitivity of VIA was higher (63.16%) than that of Pap smear (52.63%). The specificity of VIA was lower (97.62%) as compared to Pap smear (99.13%). The positive predictive value of Pap smear was 83.33% and that of VIA was 68.57%. The negative predictive value of Pap smear was 96.22% and that of VIA was 96.99%. The diagnostic accuracy of VIA was 95.0% which was comparable to that of Pap smear (95.6%). In concordance with this the results in the present study are comparable to the study by Vadehra K et al. (100) in which sensitivity of VIA and Pap smear was 96.4% and 71.4% respectively. The specificity of VIA was 37.5% and that of cytology was 56.3%. The positive predictive value for VIA and Pap smear was 73% and 71.4% respectively. The negative predictive value for VIA and Pap smear was 85.7% and 52.9% respectively.

CONCLUSION

The sensitivity of acetic acid test is higher than that of cervical cytology. The high sensitivity of VIA is offset by its low specificity and high false positive rates as compared to Pap smear. The low specificity of VIA would lead to over-treatment of non-neoplastic lesions if 'see and treat' policy is used. Considering the low cost and immediate availability of results, VIA may be considered as an alternative to Pap smear in resource poor settings. However, in areas where cytology based screening is available, VIA may be useful as an adjunct to improve the sensitivity of cervical cytology.

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