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Role of Visual Inspection After Acetic Acid (VIA), After Lugol's Iodine (VILI) Application and Colposcopy in Early Detection of Cervical Pre-Invasive Lesion in Unhealthy Cervix

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ABSTRACT

Objectives- *To determine the potential of VIA, VILLI and Colposcopy in cervical cancer screening and to compare their results with colposcopic guided biopsy which is the gold standard*

Methodology *Study was conducted on 200 Symptomatic patients with symptoms eg H/O cervical ulcer,vaginal discharge, postcoital bleeding and other gynaecological problems and asymptomatic patients with bad cervix .*

Results *Colposcopy in camparison with HPR for low grade lesion had sensitivity80%, specificity90%, PPN66.6%,NPV94.7%. For moderate dysplasia sensitivity 85.7%, specificity94.4%, PPV64.2%, NPV98.2.% and for severe dyspasia sensitivity 76.9%, specificity98.3%,PPV76.9%, NPV98.3%.VIA when compared with HPR has higher sensitivity (98.7%) & specificity (52.94%) & corresponding PPV (76%) & NPV (96.43%) VILI when compared with HPR sensitivity (97.4%), specificity (60.78%) ,PPV (78.95%),NPV (93.9%).*

Conclusion*. Combined use of VIA, VILI, colposcopy and colposcopic guided biopsy should be the standard protocol to evaluate all suspicious cervices .Hence "SINGLE VISIT" screen and treat strategy by doing VIA, VILI & colposcopy is cost-effective and more would be the compliance for treatment, which is crucial to bring down the incidence and mortality due to cervical cancer*

KEYWORDS : Colposcopy, cervical cancer, VIA, VILI.

INTRODUCTION

Cervical cancer is the second most common cancer in women world wide (schiffman et al,2001)[1].Though cancer cervix is preventable and inspite of advanced health care, it account for 7% of all female malignancy in developed countries & 24% in developing countries(Parkin et al,2001)[2].Developing countries harbour 80% of global estimates of cervical cancer and it remain leading cause of cancer related death and need rigourous preventive measures. (Murthy N S et al, 1990) [3]

World wide approximately 500,000 new cases (approximately one case per minute) of cervical cancer are diagnosed and 280, 000 death occur annually making it the second or third and cancer related cause of mortality(Parkin et al,2005)[4]

"Preventable but not prevented" remains the reality for women in developing countries. It is preventable and also curable, provided it is diagnosed early enough. Health education programmes coupled with early detection, appropriate management and availability of standard therapy have helped to reduce the morbidity and mortality upto 80% in many developed countries(Hakama M et al 1986).[5]

METHODOLOGY

The present study was conducted on 200 women with abnormal cervices in the Department of Obstetrics and Gynaecology, Shyam Shah Medical College and associated Gandhi Memorial Hospital (G.M.H.) Rewa (M.P.), from May 2009 to October 2010(18 month). Symptomatic patients with symptoms eg H/O cervical ulcer,vaginal discharge, postcoital bleeding and other gynaecological problems and asymptomatic patients with bad cervix on examination who attended outpatient department.

ExclusionCriteria:

1.Pregnant Women
2.Post hystectomy
3.Ovious cervical growth at the time of examination
4.Post radiaton
5.vaginits
6.Patient on intravaginal medicaton /menses

Inclusion Criteria:

Suspicious symptoms like leucorrhea, postcoital or intermenstrual bleeding and postmenopausal bleeding.

Suspicious cervix such as hypertrophied, unhealthy cervix after treating cervicitis, erosion which bleeds on touch.

Abnormal cytology report in apparently healthy cervix.

Colposcopic findings were documented and explained to the patient in post procedure counseling. VIA, VILI, colposcopy finding according to modified ried's scoring were compared with histopathological report and statistical significance was derived. Patients were asked to come for follow up and further treatment on the basis of HPR report. Patient was asked to attend hospital in case of complications e.g., bleeding, pain or foul swelling discharge etc.

OBSERVATION TABLES

Table 1 Association with various clinical complaints

Major Complaints	Total No. of cases (n=200)	Percentage (%)
Discharge per vaginum	160	80.0%
Pain Abdomen	37	18.5%
Itching in private parts	36	18.0%
Menstrual Irregularities	67	33.5%
Backache	6	3.0%
Burning micturation	9	4.4%
Others (Lump in abd / Prolapse uterus)	11	5.5%

Table 2 Correlation of Cytologic & Colposcopic finding

Colposcopic Diagnosis	Total No.	Cytology					
		Normal	Inflam.	ASCUS	LSIL	HSEL	Invasive Cancer
Normal	28 (14.00%)	3 (10.71%)	20 (71.43%)	1 (3.57%)	4 (14.29%)	0 (0.00%)	0 (0.00%)
Inflammation	79 (39.50%)	1 (1.27%)	65 (82.28%)	10(12.66%)	3 (3.80%)	0 (0.00%)	0 (0.00%)
CIN- I	48 (24.00%)	0 (0.00%)	26 (54.17%)	7 (14.58%)	15(31.25%)	0 (0.00%)	0 (0.00%)
CIN- II	28 (14.00%)	0 (0.00%)	8 (28.57%)	0 (0.00%)	4 (14.29%)	16(57.14%)	0 (0.00%)
CIN- III	13 (6.50%)	0 (0.00%)	1 (7.69%)	0 (0.00%)	4 (30.77%)	8 (61.54%)	0 (0.00%)
Inv. Ca	4 (2.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	3 (75.00%)
Total	200 (100.00)	4 (2.00)	120 (60.00)	18 (9.00)	30 (15.00)	25 (12.50)	3 (1.50)

Table 3 Correlation between VIA positive and colposcopic guided biopsy for
pre-invasive and invasive lesion.

VIA	Total No.	Colposcopic guided biopsy	
		Positive	Negative
VIA Positive	100 (50.00%)	76 (76.00%)	24 (24.00%)
VIA Negative	28 (14.00%)	1 (3.57%)	27 (96.43%)
Total	128	77 (60.16%)	51 (39.84%)

Sensitivity =98.70% Specificity = 52.94%

Positive Predictive Value = 76.0% Negative Predictive Value = 96.43%

χ^2=44.90, p<0.0001, Significant

Table 4 Correlation between VILI positive and colposcopic guided biopsy for
pre-invasive and invasive lesion.

VILI	Total No.	Colposcopic guided biopsy	
		Positive	Negative
VILI Positive	95 (47.50%)	75 (78.95%)	20 (21.05%)
VILI Negative	33 (16.50%)	2 (6.06%)	37 (112.12%)
Total	128	77 (60.16%)	57 (44.53%)

ensitivity =97.4% Specificity = 60.78%

Positive Predictive Value = 78.95% Negative Predictive Value = 93.9%

χ^2=51.28, p<0.0001, Significant

RESULT

The mean age of overall population in present study was 37.3±11.04 years. Maximum(35.5%) women belonged to 25-34 years of age group. Maximum number of dysplastic changes by colposcopy were seen in age group of 25-34 years and 35-44 years. High grade lesion was low in age <24 years and increase from 25 years onwards 15.4% in 25-34 yrs age group,25% in 35-44 yrs age group ,22.8% in 45-54 yrs age group & 33.3% in >55yrs age group. and 4 cases invasive carcinoma were detected between 45 yrs onwards out of the suspicious unhealthy cervixes.

Maximum number of high grade lesion(26.6%) and invasive cancer were found in lower socioeconomic status where as in middle socioeconomic status out of 68 cases (19%) high grade lesion were found in 13.2%. Illiteracy was significantly associated with maximum number of preinvasive and invasive lesion. out of 106 illiterate women,26 (24.5%)had high grade lesion and 4 cases had invasive lesion by cplposcopy and VIA positivity 59.4% and VILI positivity 53.7%. Maximum number of cervical lesion (71%) was seen in women married at or below 18 yrs of age. <18 yrs age of marriage showed more VIA positive (59.1%) & VILI positive (54.23%) could detect maximum cases of high grade lesion (25%) .

Colposcopy in camparison with HPR for low grade lesion had sensitivity80%, specificity90%, PPN66.6%,NPV94.7% . For moderate dysplasia sensitivity 85.7%, specificity94.4%, PPV64.2%, NPV98.2.% and for severe dyspasia sensitivity 76.9%, specificity98.3%,PPV76.9%, NPV98.3%.VIA when compared with HPR has higher sensitivity (98.7%) & specificity (52.94%) & corresponding PPV (76%) & NPV (96.43%) VILI when compared with HPR sensitivity (97.4%), specificity (60.78%) ,PPV (78.95%),NPV (93.9%).

STASTISTICAL ANALYSIS-.

Colposcopic findings were documented and explained to the patient in post procedure counseling. VIA, VILI, colposcopy finding according to modified ried's scoring were compared with histopathological report and statistical significance was derived. Variables like Sensitivity ,Specificity Positive Predictive Value ,Negative Predictive Value χ2 were calculated. p<0.0001 was taken as significant and conclutions were derived.

DISCUSSION

In present study, mean age of women was 37.3 _+(11.4)yrs (20yrs-74yrs).Maximum number of women belonged to age group from 25-34 yrs. In a study undertaken at JIPMER (Pondichery) ,the mean age of studied patients was 34.3 years (Raksha Arora 2000)[6]. In a study by **Bharati Bharani** (2004)[7] at Indore, the mean age of patients was 39.93 years. Cervical cancer is low in women under age of 24 yrs, but the incidence increases in women aged 35-40 and reached a maximum in 40's to 50's yrs of age.

In the present study 1 out of 16(6.2%) cases in the age group of 15 to 24 yrs was found to have moderate dyplasia. High grade lesions were increased from 25 yrs onwards, maximum no. of cases of high grade lesion (15) were found in 35-44 yrs age group. 4 cases of invasive cancer were detected between 45 yrs onwards out of the suspicious unhealty cervix.Maximum number of VIA positive cases were(56.6%-57%) between age group 35-54 yrs where as VILI positive were(55.5%-57.1%) between age group 45-74 yrs.

In present study,in all cervical lesions discharge per vaginum was the most common complaint 80%. Menstrual irregularities were found in 33.5% cases. There were 5case of post coital bleeding,out of them 2 had invasive cancer and 3 had high grade dysplasia . There were 7 cases of postmenopausal bleeding,out of them 2 had invasive cancer and 5 had high grade dysplasia .

In the study by **Swaminathan et al** (1994)[8] discharge per vagina was the most common complain, yet post menopausal bleeding was the harbinger of malignancy.

In present study comparing the results of cytology with colposcopy for low grade dysplasia: Cytology detected 30 cases of LSIL out of which only 15 (50%) were positive on colposcopy, shows 50% correlation. Whereas colposcopy alone detected 48 cases of CIN I of which 33 were negative on cytology. For high grade lesion- cytology detected 25 cases of HSIL of which 24 were positive on colposcopy, shows 96% correlation.

Talebian & **Shayan** (1977)[9] showed 100% correlation and **Seshadri et al** (1990)[10] showed 87.6% correlation between colposcopy and cytology. Correlation between cytology and colposcopy showed 97.1% concordance (**Guerra et al**)[11], with few false positive (2.5%) and false negatives (0.2%). Abnormal cytology and colposcopy had similar concordance but the risk of underestimation by cytology was significantly higher.

Comparison of sensitivity, specificity, positive predictive value and negative predictive value of Pap smear in various studies is tabulated :

Name of the study	Sensitivity (%)	Specificity (%)	Positive Predictive Value	Negative Predictive Value
Ritter et al[12]	70	98	85	95
South African Study[13]	53	95	47	95.7
Budapest Study (for cytology)[14]	47	77	-	-
Budapest study[14] (for combined cytology & colposcopy)	96	14	-	-
Present study LSIL HSIL	 31.2% 58.5%	 90.13% 99.3%	 50.0% 96.0%	 80.5% 90.2%

As a result, the combination of colposcopy parallel to cytology increases the sensitivity and accuracy of cervical cancer screening as observed in our study.In present study for low grade lesion colposcopy identified 38 cases of CIN I, of which 31 were positive by histopathology; whereas out of 40 cases of mild dysplasia confirmed by histopathology only 8 were negative on colposcopy.

For moderate dysplasia, colposcopy detected 28 cases of CIN II,of which 18 were positive on histology; where as out 21 cases were diagnosed by histopathology only 3 were negative on colposcopy.For severe dysplasia, colposcopically diagnosed 13 cases of CIN III were all positive on histology too. 4 cases of invasive carcinoma diagnosed by colposcopy out of which 3 were diagnosed by histology.

Comparison of sensitivity, specificity, positive predictive

value and negative predictive value of colposcopy in various studies is tabulated below:

Name of the study	Sensitivity (%)	Specificity (%)	Positive Predictive Value	Negative Predictive Value
Budapest Study[14]	87	15	-	-
Harare study[15] n=132 CIN Invasive cancer	 82 96	 99.6 99.2	 - -	 - -
KEM (Mumbai)[16] n=198	95	39.58	63.75	-
Present Study(n=200) CIN I CIN II CIN III	 66.6 64.2 76.9	 94.7 98.2 98.3	 80 85.7 76.9	 90 94.4 98.3

This clearly shows increased accuracy of colposcopy in cases of high grade lesions of cervix.A similar study by **Stufang Wu, et al** (2005)[17] showed correlation between colposcopy and histopathology had 55.56% sensitivity and 79.45% specificity.In present study sensitivity of VIA 98.7% and specificity 52.9% positive predictive value 76% and negative predictive value 96.43%. On applying result chai square test between VIA positive & colposcopy guided biopsy correlation was statistically significant.Several studies examining the accuracy of VIA have found the technique to be reasonably accurate but specificity is low.

Comparison of sensitivity, specificity, positive predictive value and negative predictive value of VIA:

Name of the study	Year	Sensitivity (%)	Specificity (%)	Positive Predictive Value	Negative Predictive Value
IARC[18]	2003	77 (58-94%)	86 (75-94%)	-	-
Shankar-narayan et al[19]	2004	79%	86%	-	-
Shastri et al[20]	2005	60%	88%	-	-
Sodhani et al[21]	2006	86.7%	90.7%	-	-
Present Study	2010	98.7%	52.9%	76.0%	96.4%

Our results are consistent with recent studies which have shown that VIA is more sensitive but usually less specific than colposcopy. The results of the current study and other reported study indicate that VIA is simple objective test. The result of this procedure is available immediately. It has been shown that follow-up can be performed immediately, which not only avoids recall but also increases compliance to diagnostic investigation and treatment. The test is not expensive and it is possible to train provides to detect acetowhite lesion with naked eye examination.

CONCLUSION:-

Visual inspection after acetic acid and after lugol's iodine application technique is a simple method to pick up high grade squamous intraepithelial lesion or early invasive cancer of cervix. VIA and VILI can be practised by clinician or paramedics on wide scale to screen cervices though pap smear has time tested.

Modern colposcopy is an intermediate link between cytology and histopathology.colposcopy is a highly sensitive tool in the early diagnosis of dysplasia and invasive cancer. Colposcopic guided biopsy is a **gold standard** for confirmation of diagnosis of CIN. Colposcopic diagnosis of high grade lesion is more spectacular, the only drawback lies in the possible over interpretation of low grade lesion, which regresses in due course of time with treatment/ observational follow up.

In our setup there is high non compliance rate, who need follow up for more than 24 months. An economic model suggests that immediate colposcopy was cheaper than cytological follow up.

Therefore, it is recommended, that Combined use of VIA, VILI, colposcopy and colposcopic guided biopsy should be the standard protocol to evaluate all suspicious cervices .Hence "SINGLE VISIT" screen and treat strategy by doing VIA, VILI & colposcopy which would eliminates the need for repeated visit, hence cost-effective and more would be the compliance for treatment, which is crucial to bring down the incidence and mortality due to cervical cancer.

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