COMPARISON OF METHODS OF VISUAL INSPECTION OF CERVIX WITH CERVICAL CYTOLOGY IN DETECTION OF PRE-INVASIVE LESIONS OF CERVICAL CANCER

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ABSTRACT

BACKGROUND

Due to increasing incidence of Cervical cancer, a screen-and-treat programs based on visual screening can be cost-effective approach for even the low resource settings.

The aim of this study was to determine the sensitivity, specificity, positive predictive value and accuracy of Visual Inspection with Acetic Acid and Lugol's iodine as a screening method for pre-malignant and malignant lesions of cervix.

MATERIALS AND METHODS

A prospective study carried out in Department of Obstetrics and Gynaecology in Bharati Medical College and Hospital, Sangli. Women of age 35-65 years with particular Gynaecological complaints attending OBGY OPD from Jan. 2014 – Dec. 2014 included in study after taking the informed consent. Analysis was done.

RESULTS

Good Sensitivity and Specificity of VIA i.e. 76.9% and 77.9% and VILI i.e. 76.9% and 75.4% make them better methods to detect precancerous and cancerous lesions of cervix. On comparing VIA and VILI and Pap smear, a significant correlation was found amongst them.

CONCLUSION

In low resource settings, screening by Pap smear has not been successful in reducing incidence of cervical cancer. VIA and VILI are cheaper and easily available and can be used by medical and paramedical personnel on a large scale basis.

KEYWORDS

Cervical cancer, VIA, VILI, Pap smear.

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INTRODUCTION/BACKGROUND

According to the World Health Organisation, cervical cancer is the second most common type of cancer among females and was responsible for over 250,000 deaths in 2005. Approximately, 80% of these deaths occurred in developing countries. It constitutes 9.5% of all cancers, 25% of all cancers in women, 68.5% of Gynaecologic cancers. The lowest incidence 2.6/100000 is noted in Israel. India with an incidence of 47.2/100000 women stands third highest in world incidence. The lifetime risk of carcinoma cervix is 2.4% in India. Approximately 1,00,000 new cases of advanced stages (Stage III and IV) occur per year, which account for nearly (75.7%) of all new cases detected. Whereas in developed countries, 90% of cases are diagnosed in early stages (Stage I and II) and only 10% cases in stage III and IV. This discrepancy is due to lack of mass and regular screening by available methods in our country, which in turn reflects the poor prognosis.

Prompted by the need for optimal strategies for cervical cancer screening in low resource settings, the role of visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI) has been widely studied in several recent studies, which suggest that VIA and VILI closely match the Pap smear in its performance in detecting cervical cancer precursor.¹ Cancer cervix has been considered preventable, because it has a long pre-invasive state. Cancer cervix has been considered preventable, because it has a long pre-invasive state. Invasive carcinoma develops from precancerous lesions; i.e.

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It is observed that mild dysplasia takes 5 years to change to CIS, moderate dysplasia takes 3 years to change to CIS and severe dysplasia takes 1 year to change to CIS. Then there is a latent period of almost 10 years or more for carcinoma in situ to become invasive cervical cancer. Hence, this period can be made useful for early detection.

The most effective method of screening employed in the developed world has been cytology based using Pap smears which has contributed considerably to reducing incidence of and mortality from cervical cancer.

However, this method of screening requires excessive resources in terms of laboratories, equipment, trained personnel and transport of specimens.² This has led to a search for alternative screening methods that can be more cost-effective for application in low-resources settings. Visual inspection-based screening tests, such as naked eye visual inspection or 'down staging,' visual inspection with 3-5% acetic acid (VIA), VIA with magnification (VIAM) and Visual inspection post application of Lugol's iodine (VILI) are a set of alternative screening mechanisms, which have been studied for their effectiveness in low and middle income countries including India.³

AIMS AND OBJECTIVES

To evaluate the sensitivity, specificity, positive predictive value and accuracy of Visual Inspection with Acetic Acid and Lugol's iodine as a screening method for pre-malignant and malignant lesions of cervix.

METHODS AND MATERIALS

The present study was done on Gynaecological patients attending outpatient Department of Obstetrics and Gynaecology in Bharati Vidyapeeth Medical College and Hospital, Sangli. After taking a detailed history and consent for the screening, the data was collected. Total 131 patients were included in the study and were screened with Cervical cytology, VIA and VILI as screening methods for pre-cancerous and cancerous lesions of cervix. Patients positive for cervical cytology or VIA or VILI were subjected to colposcopy and colpo-guided biopsy if colpo positive.

Inclusion Criteria

Women of the age of 35 to 65 yrs. with gynaecological complaints.

Exclusion Criteria

1. Females with active bleeding per vaginum; 2. Patients with frank growth on cervix; 3. Post hysterectomy patients; 4. Females who have never been sexually active.

RESULTS

We screened 131 patients with gynaecological complaints and the data was analysed. Out of 131 patients, maximum patients i.e. 74 patients (56.4%) were in age group 35-44 years. So women in reproductive age group should be offered screening for carcinoma of cervix; 60 patients (45.8%) were second paras followed by multiparous patients. The most common complaint is p/v discharge, i.e. 113 (58%) patients. Almost equal number of patients, i.e. 37 (28.5%) and 36 (28.2%) had normal looking cervix and Erosions on cervix respectively. On Pap smear examination of 131 patients, 78 patients (59.6%) were normal and 39 (29.8%) had inflammatory smear. VIA was

done for 131 patients; 34 patients (25.9%) were positive for VIA; 2 patients (1.6%) were positive for carcinoma. VILI was done in all 131 patients. Only mustard yellow/canary yellow areas were considered positive and area of partial uptake were considered negative; 37 patients (28.2%) positive for VILI, 2 patients (1.6%) were positive for carcinoma. Colposcopy was done for 56 patients and 24 patients (42.9%) were diagnosed with chronic cervicitis followed by 16 patients (28.6%) who had LSIL. Biopsy of only 8 patients was taken and out of which 2 patients (25%) were positive for adenocarcinoma and a similar number were positive for invasive carcinoma and 3 (37.5%) showed CIN1. Good Sensitivity and Specificity of VIA, i.e. 76.9% and 77.9% and VILI i.e. 76.9% and 75.4% make them better methods to detect precancerous and cancerous lesions of cervix.

Fig. 1: Distribution of Patients According to Presenting Complaints

Fig. 2: Distribution of Patients According to Clinical Impression of Cervix on Per Speculum

Fig. 3: Distribution of Patients According to Inference on VIA

Fig. 4: Distribution of Patients According to VILI

Fig. 5: Distribution of Patients According to Type of Smear (PAP) - BETHESDA METHOD

Fig. 6: Distribution According to Colposcopy

Fig. 7: Distribution of Patients According to Biopsy Findings

Relation between Age and VIA and VILI

Age Group	VIA Positive (n=36)	VILI Positive (n=39)
35-44	28 (78%)	26 (67%)
45-54	6 (16.6%)	12 (30.5%)
55-64	2 (5.4%)	1 (2.5%)
Total	36	39

Patients in the age group of 35 to 44 years of age group were maximum VIA positive, that is 28 (78%) and VILI positive i.e. 26 (67%).

Comparison of VIA and VILI

VIA	VILI		Total		
	Diseased	Non Diseased			
Positive	30	6	36	Sensitivity = (true positive) =	76.92%
	83.30%	16.70%	100.00%	Specificity = (true negative) =	93.48%
Negative	9	86	95	Predictive value of a positive test =	83.33%
	9.50%	90.50%	100.00%	Predictive value of a negative test =	90.53%
Total	39	92	131	Percentage of false negative =	23.08%
	29.80%	70.20%	100.00%	Percentage of false positives =	6.52%

Chi square=68.118, p <0.001. This is highly Significant.

Comparison of PAP with VIA

VIA	Clinical Cytology		Total		
	Positive	Negative			
Positive	10	26	36	Sensitivity = (true positive) =	76.92%
	27.80%	72.20%	100.00%	Specificity = (true negative) =	77.97%
Negative	3	92	95		
	3.20%	96.80%	100.00%		
Total	13	118	131		
	9.90%	90.10%	100.00%		

Chi square =17.703, p=0.00. Highly significant.

Relation between Parity and VIA and VILI

Parity	VIA Positive (n=36)	VILI Positive (n=39)
Primipara	6 (16.6%)	9 (23.0%)
Second para	12 (33.4%)	15 (38.5%)
Multipara	18 (50%)	15 (38.5%)
Total	36	39

Maximum patients who were VIA and VILI positive were para two or more.

Relation between Presenting Complains with VIA and VILI

Presenting Complaints	VIA Positive (n=36)	VILI Positive (n=39)
No complains	3 (8.3%)	2 (5.1%)
Discharge per vaginum	14 (39%)	16 (41%)
Intermenstrual bleeding	1 (2.7%)	2 (5.1%)
Postcoital bleed	1 (2.7%)	0 (0%)
Pain in lower abdomen	10 (28%)	9 (23%)
Pruritus Vulvae	6 (16.6%)	8 (20.7%)
Postmenopausal Bleed	1 (2.7%)	2 (5.1%)
Total	36 (100%)	39 (100%)

The most common complaint in VIA and VILI positive cases was discharge per vaginum i.e. 14 (39%) and 16 (41%) respectively followed by pain in abdomen i.e. 10 (28%) and 9 (23%) for VIA and VILI positive.

Relation between Clinical Findings and Visual Screening Methods

Clinical Findings	VIA (n=36)	VILI (n=39)
Normal	15 (41.7%)	19 (48.7%)
Erosion	6 (16.7%)	13 (33.4%)
Chronic cervicitis	13 (36.2%)	5 (12.9%)
Atrophic	1 (2.7%)	0 (0%)
Hypertrophic	1 (2.7%)	2 (5.0%)
Total	36 (100%)	39 (100%)

Maximum patients who were VIA positive i.e. 15 (41.7%) and VILI positive i.e. 19 (48.7%) had clinically normal cervix

Comparison of VILI and Cervical Cytology

	Clinical Cytology				
VILI	Positive	Negative	Total	Sensitivity = (true positive)=	76.92%
Positive	10	29	39		
	25.60%	74.40%	100.00%	Specificity = (true negative)=	75.42%
Negative	3	89	92		
	3.30%	96.70%	100.00%		

Comparison Between VIA and Biopsy

VIA	Cervical Biopsy		Total		
	Diseased	Non Diseased		Sensitivity = (true positive)=	76.92%
Positive	10	26	36	Specificity= (true negative)=	77.97%
	27.80%	72.20%	100.00%	Predictive value of a positive test =	27.78%
Negative	3	92	95	Predictive value of a negative test =	96.84%
	3.20%	96.80%	100.00%	Percentage of false negative =	23.08%
Total	13	118	131	Percentage of false positives =	22.03%
	9.90%	90.10%	100.00%		

Chi square is 17.703; p= 0.000. Highly significant.

Comparison of VILI and Biopsy

VILI	Cervical Biopsy		Total		
	Diseased	Non Diseased		Sensitivity = (true positive)=	76.92%
Positive	10	29	39	Specificity= (true negative)=	75.42%
	25.60%	74.40%	100.00%	Predictive value of a positive test =	25.64%
Negative	3	89	92	Predictive value of a negative test =	96.74%
	3.30%	96.70%	100.00%	Percentage of false negative =	23.08%
Total	13	118	131	Percentage of false positives =	24.58%
	9.90%	90.10%	100.00%		

Chi square = 15.347; P=0.00. Highly significant.

DISCUSSION

Cervical cancer is one of the leading causes of cancer deaths in women worldwide with an estimated 4,70,600 new cases and 2,33,400 deaths per year.⁴ A quarter of burden is experienced in India, where 1,26,000 new cases and 71,000 deaths attributable to cervical cancer annually. Cervical cancer is a potentially preventable cancer. It is preceded by premalignant lesions, which take as many as 5-15 years to progress to invasive cancer. The main screening method has been Pap smear, which is available to a small percentage of population. Cytology based screening programs are difficult to organise in India owing to limited infrastructure, trained personnel and funds.⁵ Thus in developing countries like ours, there is need for alternative screening strategies which are available on large scale, cost-effective, easy and can be done by a paramedical worker.

Visual screening tests are inherently subjective and provider dependent. This leads to high false positive and low specificity. At best they have moderate sensitivity, but one which is higher than cytology in many low resource settings.

The subjective nature of visual testing is much reflected by wide range in test performance characteristics in various settings and limited reproducibility.⁶

Visual methods of screening are being investigated in few years as screening methods for detection of carcinoma cervix. Some workers attempted to do Unaided Visual Inspection of Cervix to identify cases suspicious for Precancer and Cancer. This method was to have low positive predictive value ranging from 2-6%.⁷ Then attempts made to visualise cervix for precancerous lesion after application of 3-5% acetic acid and Lugol's iodine. VIA is more sensitive than conventional Cytology in detecting intraepithelial lesions.⁸ And the colour

changes with VILI are easier to appreciate.^{9,10,11} The advantage of these methods is that the results are immediately available and one can apply "See and Treat" policy in suitable cases.

CONCLUSION

1. On comparing VIA and VILI and Pap smear, a significant correlation was found amongst them.
2. In low resource settings, screening by Pap smear has not been successful in reducing incidence of cervical cancer. The disadvantage are that it is not feasible on large scale basis.
3. VIA and VILI are cheaper and easily available and can be used by medical and paramedical personnel on a large scale basis.
4. Biopsy can be taken from VIA and VILI positive areas in the field, even in situations when a colposcope is not available.
5. Aim at reducing the incidence of cervical cancer by identifying the causes and risk factors is indeed an uphill task. Cancer screening is the main weapon for early detection of cervical cancer at a premalignant stage.
6. Screening by Pap smear is not feasible due to several limitations like inadequate coverage of large population, lack of infrastructure and resource required for cytological screening.
7. By VIA and VILI, mass screening can be done at a very low, affordable price even at a low resource setting by trained medical and paramedical staff and treatment modalities can be offered. Hence, by these screening tools a large number of population that go undetected can be screened and treated.
8. Still larger studies are required to apply it universally.

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