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ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 4:50-57

A Prospective Study of comparison Pap's Smear, Vili's Test and Colposcopy In cervical cancer screening

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ABSTRACT

To determine the efficacy of pap`s smear and VILLI as screening tool in tertiary care centre. To screen sexually active women for detection of early neoplastic lesion of the cervix using VILI, Pap smear and Colposcopy if required.
1. To find out whether Pap smear and VILI is a simple, cost effective easy and reliable procedure to screen women for precancerous lesion and early cancer of cervix.
2. To determine the efficacy of VILI in picking up preinvasive and invasive cervical lesion.
It is a prospective study design in which each screening test was carried out independently (without knowledge of the results of the alternative test) in all selected women randomly without knowledge of the results. In this study, 1500 women were included. 10 women lost to follow up. All 1490 patients were studied in detail, pap smear, vili and colposcopy done. Then biopsy was taken in all patients and the non invasive methods were compared with biopsy results. Sensitivity, specificity of the tests was compared. Cytology has not been found to be a very effective screening programme. So there is a need to investigate alternative strategies which are more practical, feasible, effective, can be done by paramedical personnel and whose results are immediately. Pap`s smear is subjective test, slides can be mislabeled or lost. As compared to Pap smear, VILI is more sensitive. Specificity is high, this objective test with good evidence and of low cost.

INTRODUCTION

Carcinoma is the most common gynecological growth in the developing countries and the third most frequently diagnosed cancer in Indian women. Cancer of the cervix is preventable, yet approximately 493,100 new cases and more than 273,00 deaths each year among women worldwide.

While evidence of effective screening programs can be seen throughout the developed world's burden and impact of the disease remains high in the developing countries where 85% of disease related deaths occur. India, which accounts for one sixth of the world's population and bears one fifth of the world's burden of cervical cancer. There are approximately 130,000 new cases of cervical cancer in India per year and the disease is reported to be responsible for 20% of all female deaths. India's age standardized incidence rate (30.7 per100, 000) and age standardized mortality rate are the highest in south East Asia. Simultaneously, there is also evidence that India is on the verge of a large HIV epidemic. The Indian National AIDS Control organization estimates that the number of people living with HIV is approximately 5.1 million (38% of whom are women). This suggest cause for concern given the strong association between HIV and HPV to cervical neoplasia in HIV infected women.

Global evidence demonstrates that the key to reducing cervical cancer morbidity and mortality is early detection coupled with timely treatment of cervical precancerous lesions [1,7].

With early detection and timely treatment in mind, the World Health Organization recommends that poor source nations screen all women at least once in a lifetime with priority given to women at the age of 35-40 when high-grade likely-to-progress, but treatable dysplasia can be found1,8. There is some debate about whether this age limit is too high, 1,9 especially in countries with high HIV incidence. In India in 2003, 46.6% of HIV cases in women occurred in the 15-29 years age group1,5, as in many developing countries and resource-limited settings.

Carcinoma of cervix, due to its slow progression from pre-cancerous lesions to malignancy and easy accessibility to examination, gives us many opportunities for its early detection. It may be done through opportunistic examination of women attending outpatient clinics or through systematic Among all malignant tumors, cervical cancer is the one that can be most effectively controlled by screening. Cervical cytology often referred to as the Pap smear is perhaps the most well known of available screening methods. However, newer screening techniques such as visual inspection methods and HPV-DNA testing have also demonstrated potential for early detection in many settings. These technologies are currently being assessed by the Alliance for Cervical Cancer Prevention (ACCP) for their use in developing countries. As critical as detection is, the need for women with positive results to receive adequate and timely treatment for dysplasia, is paramount.

Detection of cytological abnormalities by microscopic examination of Pap smears and subsequent treatment of women with high-grade cytological abnormalities avoids development of cancer. Cytological screening at the population level every 3-5 years can reduce cervical cancer incidence up to 80%. Cytology based screening requires a laboratory infrastructure with high quality control system with microscopes and trained doctor/nurses, cyto-technicians and cytologists. Its benefits can only be achieved if quality is optimal at every step in the screening process, from information and invitation of the eligible target population to performance of the screening test and follow-up, and, if necessary, treatment of women with screen-detected abnormalities. In addition, it has a low sensitivity and low positive predictive value. Hence cytology based screening is beyond the capacity of the health services in many of the developing countries like ours. Although visual inspection with 5% acetic acid (VIA) is a test with good sensitivity, low specificity has been its limitation, which would result in excessive referrals and treatment of false-positive lesions subsequently increasing the referral load as well as the cost of unnecessary treatment on the health system. Thus, determining which women with positive VIA-based tests are at risk for significant cervical disease, performing appropriate diagnostic workups, and treating cancer precursors presents a major public health challenge.

Several studies have considered human papilloma virus (HPV) testing and repeat cytology as a triage method for women with atypical squamous.

Cells of unknown significance (ASCUS). However, these triage modalities are not feasible in a developing country such as India. Visual inspection of the cervix after application of lugol's iodine (VILI) is a simple, low-technology screening test, which is based on the colors taken up by cervical transformation zone. It requires low cost, minimal training of personnel’s has high sensitivity, low false negative rates, test results are immediately available, and women with positive test can be treated at the same visit. It is based on the ability of the trained health personnel to detect yellow, non-iodine uptake areas in the transformation zone of the cervix. It is currently being evaluated in experimental settings as alternative to cervical cytology.Visual inspection of the cervix after application of Lugol's iodine (VILI) -

* Squamous epithelium contains glycogen, whereas precancerous lesions and invasive cancer contain little or no glycogen. Iodine is glycophilic and is taken up by the squamous epithelium, staining it mahogany brown or black.
* Columnar epithelium does not change colour,
* Immature metaplasia and anti-inflammatory lesions are at most only partially glycogenated and, when stained, appear as scattered, ill-defined uptake areas.
* Precancerous lesions and invasive cancer do not take up iodine (as they lack glycogen) and appear as well-defined, thick, mustard or saffron yellow areas.This discussion reviews the role of direct visual inspection of cervix after application of lugol's iodine for the early detection of precancerous lesions of cervix at community level and at the tertiary level in low resource .

I have selected this topic for my study so that all women in the society can be screened for early cervical cancers and a curative treatment can be given to reduce the burden of invasive cancer from society.

MATERIALS AND METHODS

AIM:
To determine the efficacy of pap`s smear and VILLI as screening tool in tertiary care centre.

OBJECTIVE:
To screen sexually active women for detection of early neoplastic lesion of the cervix using VILI, Pap smear and Colposcopy if required.

SECONDARY OBJECTIVE
1. To find out whether Pap smear and VILI is a simple, cost effective easy and reliable procedure to screen women for precancerous lesion and early cancer of cervix.
2. To determine the efficacy of VILI in picking up preinvasive and invasive cervical lesion.
3. To compare the results of VILI with that of Pap smear and further confirmation with colposcopic guided biopsy in the abnormal Pap smear and VILI test result.

STUDY DESIGN:
It is a prospective study design in which each screening test was carried out independently (without knowledge of the results of the alternative test) in all selected women randomly without knowledge of the results. In this study, 1500 women were included. 10 women lost to follow up.

All selected cases were subjected to following procedure after taking informed consent in vernacular language:
1. Detailed history and examination
2. Specimen collection for cytology (Pap smear)
3. VILI
4. Colposcopic examination and colposcopic guided biopsy

INCLUSION CRITERIA
- All newly registered women attending obs, gynaec, family planning, infertility clinics.
- Apparently healthy
- All women after the at 21 or earlier if she is sexually active.
- With intact cervix.
- With no history of cervical neoplasia

EXCLUSION CRITERIA
- Active bleeding pv
- Profuse cervical and vaginal discharge
- Obvious cervical growth
- History of hysterectomy
- Surgical treatment of the cervix
- Iodine allergy
- Pregnant patient wanting continuation of pregnancy

Data Collection:
The details and purpose of the study were explained to the participants attending the OPD. A printed consent form was read out to the study participants and their signature or left thumb impression was obtained. Information on secio-demographic and reproductive variables was then collected during an interview using a questionnaire. Screening tests and diagnostic investigations were carried out.

RESULTS AND DISCUSSION

Table-1.1: Distribution of the cases according to Age

Age (In years)	No. of case (%)
<30	75(5%)
30-39	485(33%)
40-49	810(54%)
50-59	75(5%)
>60	45(3%)
Total	1490

Mean age was 44.5 yrs.(Standard deviation)
Commonest age group among patients was 40-49(53%) followed by the age group 30-39(31%)

Table 2: Distribution of cases according to Education

Age (In years)	No. of case (%)
Illiterate	15(1%)
Primary	60(40%)
High School	780(52%)
College	105(7%)
Total	1490

Table 3: Distribution of the cases according to age at 1st Coitus:

Age at 1st coitus (In years)	No. of case (%)
<=20	1104(74%)
>20	386(26%)
Total	1490

Mean age at 1st coitus was 17.36 yrs
Most of the patients in this study had Age at 1st coitus before or at 20 yrs of age(74%)

Table 4: Distribution of the cases according to Active married life:

Active Married Life (In years)	No. of cases (%)
<5	31(2%)
5 to 9	75 (5%)
10 to 14	342 (23%)
15 to 19	447 (30%)
20 to 24	283 (19%)
>24	312 (21%)
Total	1490

Mean AML was20-40 yrs

OBSERVATIONS ACCORDING TO SIGN & SYMPTOMS OF CASES

Table 5: Distribution according to Presenting Symptoms

Presenting symptoms	No. of case (%)
Pain in Abdomen	312(21%)
Excessive White Discharge	238(26%)
Post Coital Bleeding	15(1%)
Heavy Bleeding p/v	298(15%)
Post-Menopausal Bleeding	17(1.36%)
Intermestrual Bleeding	29(2%)
Scanty Menses	28(1.8%)
Others	402(27%)
Total	1490

Table 6: Distribution of women according to Pap Smear results

Pap Smear	No. of cases (%)
Normal	1341(90%)
ASCUS	25(1.7%)
LSIL	37(2.6%)
HSIL	59(3.8%)
AGUS	28(1.9%)
Total	1490

Table 6.2: Evaluation of Pap smear in reference to Biopsy

	BIOPSY POSITIVE	BIOPSY NEGATIVE	TOTAL
PAP POSITIVE	80(5.4%)	69(4.6%)	149(10%)
PAP NEGATIVE	54(3.6%)	1287(86.4)%)	1341(90%)
TOTAL	134(9%)	1356(91%)	1490

Table 6.3: Types of Pap test results:

Pap Smear Results	N(%)
TEST POSITIVE	149(10%)
TEST NEGATIVE	1341(90%)
TRUE POSITIVE (Pap +ve, Biopsy +ve)	80(5.4%)
FALSE POSITIVE (Pap +ve, Biopsy -ve)	69(4.6%)
TRUE NEGATIVE (Pap -ve, Biopsy -ve)	1287(86.4%)
FALSE NEGATIVE (Pap -ve, Biopsy +ve)	54(3.6%)

Table 7.1: Distribution of women according to VILI test results

VILI Test	No. of cases (%)
Positive	202(13.6%)
Negative	1288(86.4%)
Total	1490

Table 7.2: Evaluation of VILI with reference to Biopsy positive cases

VILI	TOTAL	BIOPSY			
		Negative	Positive		
			CIN-I	CIN-II	CIN-III
Negative	1288	1244	28	12	04
Positive	202	15	150	21	16
TOTAL	1490	1259	178	33	20

Table7.3: Types of VILI test results

VILI Smear Results	No of cases(%)
TEST POSITIVE	202(13.6%)
TEST NEGATIVE	1288(86.4%)
TRUE POSITIVE (VILI +ve, Biopsy +ve)	187(12.5%)
FALSE POSITIVE (VILI +ve, Biopsy -ve)	15(1.1%)
TRUE NEGATIVE (VILI -ve, Biopsy -ve)	1244(84.4%)
FALSE NEGATIVE (VILI -ve, Biopsy +ve)	44(2%)

Table 8: Comparison between Screening test Variables of Pap smear and VILI test in present study

Screening test	PAP	VILI	Differences statistically significant or not (Z –test)
SENSITIVITY (%)	59.70%	99.47%	0.01 significant
SPECIFICITY (%)	95.26%	92.53%	0.09 Not signficant
PPV (%)	55.26%	97.76%	0.01 significant
NPV (%)	95.97%	98.17%	0.06 not significant

Table 9: Colposcopic findings

Positive Colposcopic findings	No. of cases (n= 202)
Leukoplakia	30(14.85%)
Acetowhite epithelium	35(17.32%)
Punctuation	52(25.74%)
Mosaic pattern	77(38.11%)
Abnormal vessels	08(3.9%)

Table 10: Colposcopic results variable

	No.ofcases(%)
Colposcopy positive	202(13.6%)
Colposcopy negative	1288(86.4%)
True positive	190(12.8%)
True negative	1250(83.9%)
False positive	12(0.8%)
False negative	38(2.5%)

Table 11: Management of Biopsy Positive cases

PROCEDURE	CIN-I	CIN-II	CIN-III	TOTAL	ASSOC.CAUSE
ANTIBIOTICS	22	1	1	24	
CRYOTHERAPY	17	4	1	22	
MYOMECTOMY	3	1		4	
TAH	44	9	12	65	Fibroid-2 adenomyosis -3
TAH-BSO	34	7	5	46	Fibroid-2 ovarian cyst-4
VH	23	5	2	30	Prolapse 7
TL	1	1		2	
D&C WITH POLYPECTOMY	21	1		22	
LOST TO FOLLOW UP	13	2	1	16	
TOTAL	178	30	23	231	

SUMMARY AND CONCLUSION

- The present study was conducted in the Department of Obstetrics and Gynecology, Sir T. Hospital, Govt. Medical College, Bhavnagar, from 2011 to 2013. 1500 women attending Obstetrics and Gynecology OPDs were recruited, out of which 10 were excluded.

Cervical screening was done in rest 1490 women by taking Pap Smear and by visual inspection of cervix after application of lugol's iodine

- Pap smear was done in all 1490 women, Cytology results considered positive were ASCUS, LSIL, HSIL, or AGUS. Rests were considered negative. Thus1490 out of 149 were Pap positive and 1341 were Pap negative.
- Visual inspection of cervix with lugol's iodine was done in all 1490 women, to detect iodine non-uptake areas. Out of 1490 women, 202(13.6%) were VILI positive and 1288(86.4%) were VILI negative.
- On analysis of above two screening tests, Sensitivity and NPV of VILI were higher than Pap, which were statistically significant. While specificity and PPV of VILI were, lower than Pap, which were not statistically significant.
- The other advantages of VILI are its low cost, easy to do and can be done by paramedical workers an immediate results are obtained which can be treated at the same visit.
- Thus, VILI is reliable as a screening test for detecting pre invasive lesion for cervix.
- cytology has not been found to be a very effective screening programme. So there is a need to investigate alternative strategies which are more practical, feasible, effective, can be done by paramedical personnel and whose results are immediately. Pap`s smear is subjective test, slides can be mislabeled or lost. Trained cytoscreening and cytologists required. Reports are available after weeks and it is time taking. Proper system is required for communication between lab, doctor and patients. Therefore, this is not possible in developing countries.
- As compared to Pap smear, VILI is more sensitive. Specificity is high, this s objective test with good evIdence and of low cost.
- With high sensitivity, specificity, positive predictive value and negative predictive value VILI's test can be applied to large population for screening of cervical carcinoma.

Along with Colposcopy the sensitivity and specificity of VILLI increases. It is also of opd basis, instant findings and cost effective.

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