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Original Research Article

Comparing the effectiveness of liquid based cytology with conventional PAP smear and colposcopy in screening for cervical cancer and it's correlation with histopathological examination: a prospective study

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ABSTRACT

Background: Cervical cancer remains worldwide the second most common cancer among women and is unique among human cancers, entirely attributable to infection. Although routine cytological screening has resulted in large reduction in the cervical cancer burden in our country, still the incidence rates continue to be unabated for want of effective screening programs.

Methods: This is a prospective study which was conducted in the Department of Obstetrics and Gynecology. The study included 200 women who were randomly selected attending gynecology OPD and who fulfilled the inclusion criteria. All the selected patients were subjected to pap smear, LBC and colposcopy and histopathology done for suspected cases.

Results: The differences of sensitivity and specificity between LBC, PAP smear and colposcopy in detection of premalignant lesions were analyzed using the chi square test. The sensitivity of LBC (89.5%) was significantly higher than sensitivity of PAP smear (47.37%). $P < 0.001$. The specificity of PAP smear (95.06%) was higher than LBC (77.16%). The statistical analysis between LBC and PAP smear; LBC and colposcopy were significant ($P=0.000 < 0.05$).

Conclusions: Liquid based cytology increases the sensitivity of cervical cancer detection and its ability to do molecular testing using the same sample. LBC also improves sample quality by reducing the number of unsatisfactory smears, reduces the number of false negative smears, causes reduction in interobserver bias and less time consuming.

Keywords: Cervical cancer, Colposcopy, LBC, Molecular testing, PAP Smear, Unsatisfactory smears

INTRODUCTION

Cervical cancer remains worldwide the second most common cancer among women and is unique among human cancers, entirely attributable to infection.

It is the fact that most cervical carcinomas occur in women who have never been screened or who have not been screened adequately. The Indian Council of Medical

Research (ICMR) says the incidence of cervical carcinoma in India varies from 20 to 35 / 100,000 women between age group 35 to 64 years in comparison with developed countries, it is as low as 1 to 8 / 100,000 women.¹ Although routine cytological screening has resulted in large reduction in the cervical cancer burden in our country, still the incidence rates continue to be unabated for want of effective screening programs. We have passed a long way since 1928 when Dr.

Papanicolaou first proposed cancer cells on a vaginal smear. This PAP smear now evolved to liquid based Cytology. HPV DNA testing methodology was approved by FDA in 2000 and the first cervical cancer vaccine i.e. the human papillomavirus vaccine hit the market in 2006. But still the high or increasing incidence and mortality from cancer cervix highlight the need for continued screening. The only gynecological cancer that satisfies the WHO criteria for Implementation of screening program is the cervical cancer.²

A defined Precancerous lesion remains the target of screening and preventive treatment programs and represents a genuine surrogate for cancer risk. In the conventional PAP tests, the false-negative rate for invasive carcinoma range from 16-82%. The false negative rate for preinvasive lesions is difficult to establish, as in case of invasive carcinomas, cases can be obtained from tumour registries, whereas many of the studies of preinvasive lesions suffer from 'verification bias' (i.e. cases are referred for biopsy only on the basis of an abnormal smear, and women with negative PAP smears do not undergo biopsy).

Colposcopic impression more often overestimated (40%) than underestimated (23%) the severity of disease. Colposcopy is subject to interobserver variability. In 1996, one of the important landmarks occurred in the history of Pap test when the Food and Drug Administration (FDA) approved ThinPrep as an alternative to the conventional cervicovaginal smear, which was followed 3 years later by approval of the Aucocyte Prep (now known as SurePath). The newest is the MonoPrep, approved in 2006.

Objectives of present study were to screen women attending gynecology outpatient department with cytology and colposcopy and correlating with histopathology, to do histopathological examination of all colposcopy directed biopsies and to compare and evaluate the sensitivity and specificity of PAP, smear, liquid based cytology and colposcopy in detection of premalignant and malignant lesions of cervix.

METHODS

This is a prospective study which was conducted in the Department of Obstetrics and Gynecology. The study included 200 women who were randomly selected attending gynecology OPD and who fulfilled the inclusion criteria. Patient was counseled regarding the procedure.

Informed consent obtained. Social, medical, obstetric and gynaecological history obtained. General examination was performed With the patient in lithotomy position and under good illumination, un-lubricated Cusco's self retaining speculum was introduced into vagina and the cervix was visualized.

Inclusion criteria

Women in the age group 21 to 70 years.

Exclusion criteria

- Menstruation
- Pregnancy
- Post partum period
- Age <21 yrs and >70 yrs
- Diagnosed or already treated as carcinoma
- Women with post hysterectomy.

Samples were collected from cervix using a broom sampling device. Collected sample was transferred into a labeled container of fixative solution. The vial container was then shaken and then transported. Cytological smear processed and analysed using manual method.

Using Ayre's spatula Pap smear was taken and fixed on a slide with 95% ethanol.

The colposcope with magnification from 5X to 25 X with inbuilt green filters was used. cervix cleansed with saline and inspected followed by visualization under green filter for abnormal vasculature. 3% acetic acid applied to cervix & findings in each quadrant of the transformation of cervix was examined and the findings were marked. Then Lugol's iodine was applied and findings noted. If the Colposcopy is abnormal, biopsy was taken and sent for histopathological examination. In case of unsatisfactory colposcopy, endocervical sampling was done. If the colposcopy is normal, biopsy is taken from the transformation zone.

RESULTS

The mean age of the study group was 41.6 with range of 23 to 70 years. The mean age at marriage was 20.66+2.838 years. The average duration of married life was 20.99+9.39 years. The mean parity was 3.03+0.948 with a range of 0-7.

112 women had inflammatory smear of which 1.78% had SIL / carcinoma. Of women with ASCUS, LSIL, HSIL in LBC smear 22.2%, 32.43% and 77.27% were found to have SIL/CA respectively.

Most of the women had inflammatory smear of which 7.69% had SIL invasive Cancer. Of the women with ASCUS, LSL, HSIL in PAP smear 60%, 60%, 77.7% were found to have SIL / Carcinoma respectively.

112 women had inflammatory smear of which 1.78% had SIL /carcinoma. Of women with ASCUS, LSIL, HSIL in LBC smear 22.2%,32.43% and 77.27% were found to have SIL/CA respectively.

Table 1: Correlation of pap smear with histopathology.

PAP Smear	SIL and CA										
	Normal			LSIL		HSIL		Carcinoma		Total	
	No	No	%	No	%	No.	%	No	%		
Normal	6	6	20.69	2	6.9	-	-	8	27.5		
Inflammatory	7	7	5.38	3	2.31	-	-	10	7.69		
ASCUS	1	1	20	1	20	1	20	3	60		
LSIL	5	5	50	1	10	-	-	6	60		
HSIL	1	1	11.11	5	55.55	1	11.11	7	77.7		
Carcinoma	-	-	-	-	-	2	100	2	100		
Unsatisfactory	1	1	6.67	1	6.67	-	-	2	13.33		
Total		21		13		4		38			

Table 2: Correlation of liquid based cytology with histopathology.

LBC	No.	SIL and CA									
		Normal		LSIL		HSIL		CA		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%
Normal	11	10	90.91	1	9.09	-	-	-	-	1	9.09
Inflammatory	112	110	98.21	1	0.89	1	0.89	-	-	2	1.78
ASCUS	9	7	77.78	2	22.22	-	-	-	-	2	22.22
LSIL	37	25	67.57	9	24.32	3	8.11	1	-	12	32.43
HSIL	22	5	22.72	7	31.82	9	40.91	3	4.54	17	77.27
Carcinoma	3	-	-	-	-	-	-	-	100	3	100
Unsatisfactory	6	5	83.33	1	16.67	-	-	4	-	1	16.67
Total	200	162	-	21	-	13	-	-	-	38	-

Table 3: Correlation of colposcopy with histopathology.

Colposcopy	No.	SIL and CA									
		Normal		LSIL		HSIL		Carcinoma		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%
Normal	113	112	99.12	1	0.88	-	-	-	-	1	0.88
Erosion	23	21	91.3	1	4.35	1	4.35	-	-	2	8.7
A W area	42	18	42.86	16	38.1	7	16.67	1	2.38	24	57.14
Punctation	6	1	16.67	2	33.33	2	33.33	1	16.67	5	83.33
Mosaic	6	-	-	1	16.67	3	50	2	33.33	6	100
Polyp	4	4	100	-	-	-	-	-	-	-	-
Unsatisfactory	6	6	100	-	-	-	-	-	-	-	-
Total	300	162		21		13		4		38	

Table 4: comparison of LBC with PAP smear and colposcopy.

	LBC	PAP	Colposcopy
Sensitivity	89.5%	43.37%	92.1%
Specificity	77.16%	95.06%	88.27%

Of 113 women with normal colposcopic appearance, 2.44% had SIL / carcinoma. Among the 23 women with erosion, 15.62% had SIL/Carcinoma. Of the 54 women with abnormal colposcopic finding 35 had SIL / CA.

The differences of sensitivity and specificity between LBC, PAP smear and colposcopy in detection of premalignant lesions were analyzed using the chi square

test. The sensitivity of LBC (89.5%) was significantly higher than sensitivity of PAP smear (47.37%). P <0.001. The specificity of PAP smear (95.06%) was higher than LBC (77.16%).

The statistical analysis between LBC and PAP smear; LBC and colposcopy were significant (P=0.000<0.05).

DISCUSSION

PAP Smear

The papanicolaou smear test is the only screening test that has been universally accepted and has stood the test of time for the early detection of cervical cancer. Even

screening women once in their lifetime at the age of 35 could reduce the cervical cancer mortality by 26% as suggested by South African data.³

In present study Pap smear was taken in 200 randomly selected women attending gynecology OPD, of whom 26(13%) had squamous cell abnormalities, 15(7.5%) samples were unsatisfactory. False negative rates were 10% in whom the disease was undiagnosed. False positive rates were 4% in whom disease was over diagnosed.

In current study, Sensitivity of Pap smear was 47.37%, Specificity of Pap smear was 95.06%, Positive predictive value was 69.23%, Negative predictive value was 88.51%.

The pap smear despite being credited with a 70% reduction in mortality for cervical cancer, its false negative rate amounting to 10% is still a cause for cancer attributing to sampling errors. Liquid based cytology has been developed to address the sampling errors of conventional pap smear.

Table 5: Comparison between present PAP study and similar studies are shown in the following table.

Study	Sensitivity	Specificity
Shastri SS et al ⁴	57.4%	98.6%
Khanna A et al ⁵	50%	78%
Present study	47.37%	95.06%

Liquid based cytology

In my study liquid based cytology was performed in 200 random women attending Gynecology OPD of whom 71(35.5%) had squamous cell abnormalities 6 (3%) were unsatisfactory samples False negative rates were 2% False positive rates were 18.5%.

Table 6: Comparison between present LBC study and similar studies.

Study	Sensitivity	Specificity
Sherwani RK et al ⁶	97.6%	50%
Ferris et al ⁷	53%	99.5%
Present study	89.5%	77.16%

Table 7: Comparison of unsatisfactory smears between present study and other studies among PAP smear and LBC.

Study	PAP smear	LBC
Bergeron et al ⁸	11.6%	0.8%
Ferris et al ⁷	3.8%	1.2%
Present study	7.5%	3%

In present study, sensitivity of liquid based cytology was 89.5%, specificity of LBC was 77.16%, positive

productive value was 47.89%, negative predictive value was 96.9%.

Colposcopy

All the 200 randomly selected women in one study underwent colposcopy. Of the 200 women screened 146 had normal colposcopic findings. 54 had abnormal colposcopic findings.

Among 54 abnormal colposcopic findings,

- 19 (35.19%) had LSIL
- 12 (22.22%) had HSIL
- 4 (7.41%) had invasive carcinoma

On application of acetic acid 54 women who showed acetowhite areas and other abnormal colposcopic findings.

- 31 (57.41%) had pre invasive lesions of cervix,
- 4 (7.41%) had invasive carcinoma of cervix.

Of 6 women who showed acetowhite area with mosaic pattern, all the

- 6 women had SIL and CA
- 5 out of 6 who showed punctuation had SIL/CA.

The accuracy and performance of colposcopy largely depends on training experience and the skills of the colposcopists.

Table 8: Comparison between present colposcopic study and other similar studies.

Study	Sensitivity	Specificity
Surabi K et al ⁹	100%	96.4%
Khanna A et al ⁵	93%	92.6%
Present Study	92.1%	88.27%

CONCLUSION

Liquid based cytology and PAP smear

- The sensitivity of LBC was higher.
- The specificity of LBC was lower than PAP smear.
- There is reduction in the rate of unsatisfactory smears in LBC compared to PAP Smear
- There is reduction in the number of false negative rates in LBC compared to PAP smear.

Table 9: Comparison between LBC AND PAP smear.

	LBC	PAP
Sensitivity	89.5	47.37
Specificity	77.16	95.06
Unsatisfactory smears	3%	7.5%
False negative Rates	2%	10%

Liquid based cytology and colposcopy

The sensitivity and specificity of colposcopy were higher compared to LBC in present study. But Colposcopy being time consuming can be performed as secondary level of screening in detecting cervical lesions earlier.

Liquid Based cytology techniques reduce the average lifetime number of smear tests for a woman primarily from the reduction of inadequate slide production and consequential reduction in rescreening. The average number of Colposcopies is expected to increase as the number of borderline and screening test results increases.

The differences in sensitivity and specificity between LBC, PAP smear and colposcopy in detection of premalignant lesions were analyzed using the chi square test. The sensitivity of LBC (89.5%) was significantly higher than sensitivity of PAP smear (47.37%). $P < 0.001$. The specificity of PAP smear (95.06%) was higher than LBC (77.16%). The statistical analysis between LBC and PAP smear; LBC and colposcopy were significant ($P=0.000 < 0.05$)

All the 200 women studied were screened with LBC, PAP smear and colposcopy.

Liquid based cytology increases the sensitivity of cervical cancer detection and its ability to do molecular testing using the same sample. LBC also improves sample quality by reducing the number of unsatisfactory smears, reduces the number of false negative smears, causes reduction in interobserver bias and less time consuming.

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