



A Comparative Study Between Pap Smear And Liquid Based Cytology As A Screening Modality For Cervical Cancer And Its Further Management

KEYWORDS

Cervical cancer, Pap Smear, liquid based cytology test

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ABSTRACT

As a screening test the liquid based cytology is superior than conventional pap smear. This is a comparative cross sectional study. 100 patients were studied after taking consent. It was observed that findings on histopathology showed 59% normal, LSIL 19%, HSIL 10%, carcinoma 6%, while pap smear showed normal finding 54%, LSIL 16%, HSIL 12%, carcinoma 7%, and liquid based cytology had normal finding 58%, LSIL 19%, HSIL 10% and carcinoma 6%. Histopathology was used as a gold standard method. Sensitivity and specificity of pap smear in detection of cervical cancer was 90.2% and 80.7% respectively, while positive predictive value and negative predictive value was 80.4% and 92.6% respectively, while sensitivity and specificity of liquid based cytology in detection of cervical cancer was 97.6% and 96.6% respectively and positive predictive value and negative predictive value is 95.2% and 98.3% respectively. Liquid based cytology has added advantage over conventional Pap smear since its sensitivity and specificity is higher.

Introduction:

Cervical cancer remains the fourth most common cancer in women and seventh most common overall worldwide¹. There is widespread acceptance that regular screening is the single most important public health strategy to reduce cervical cancer incidence and subsequent mortality. Screening tests such as conventional cytology (commonly referred to as the Pap smear) are used to identify pre-cancers, which can be treated to prevent the occurrence of invasive cancer or allow the disease to be identified at an earlier stage, permitting more effective treatment².

The Papanicolaou (Pap) smear has been the cornerstone of screening for cervical neoplasm for over 50 years⁴.

The liquid-based Thin Prep Pap Test was developed as a replacement to the conventional method of preparing the cervical cytological specimen and was approved for clinical use in the United States in May 1996. The sampling device(s) containing the cervical cell sample from the patient is rinsed directly into a vial containing a buffered preservative fluid; the vial is then sent to the cytopathology laboratory for automated slide preparation using the ThinPrep20Q0 processor³.

Hence we planned the study to compare Pap smear and liquid based cytology test for screening of cervical cancer.

Aim & Objectives:

1. To compare the efficacy of conventional PAP smear and liquid based cytology for the detection of cervical cancer.
2. To study the Sensitivity and Specificity of conventional PAP smear and liquid based cytology.

Material and Methods:

A cross sectional study was conducted in Obstetrics and Gynecology Department, Government Medical College, Akola during period of May 2013 to October 2015 year.

Women in the sexually active age group coming to the OPD with any of the following complaints namely per vaginal discharge, bleeding per vagina, post coital bleeding, irregular menses and recurrent genital infection were included under the study. Women who were

pregnant, younger than 18 years of age, older than 18 years but sexually inactive, attending OPD during menses, with obvious mass per vagina, treated/undergoing treatment for carcinoma cervix were excluded from the study.

Permission from the head of the institute as well as Ethical Committee Clearance was taken before starting the study. Informed consent was taken from the patients prior to examination and taking samples for the study. Confidentiality of the data was maintained.

Data was analyzed using SPSS software version 17. Suitable descriptive and inferential statistics was applied to narrate the situation and compare the results.

Results:

It was observed that most of the study population (59%) on histopathology had normal findings, while 19%, 10% and 6% study participants had Low Grade Squamous Intra Epithelial Lesions (LSIL), High Grade Squamous Epithelial Lesions (HSIL) and carcinoma respectively.

On PAP smear 54% women had normal findings while 16%, 12% and 7% had LSIL, HSIL and carcinoma respectively.

Similarly for 58% of the study participants, normal findings were recorded on liquid based cytology. LSIL was recorded for 19%, HSIL for 10% and carcinoma for 6% of the patients.

With histopathology as gold standard, sensitivity and specificity of PAP smear for the detection of cervical cancer was found 90.2% and 84.7% respectively and that for liquid based cytology was 97.6% and 96.6% respectively.

Table 3 shows the comparison of LBC results with the gold standard-Histopathology findings. From the table, 57 normal results were in agreement for the two tests with 1 result reported as Normal on LBC being reported as LSIL on histopathology. About 5 results reported as ASCUS agreed for both tests with 1 each result reported as ASCUS on LBC being reported as LSIL and HSIL on histopathology. About 6 results reported as carcinoma agreed for both tests. 7 results reported as HSIL agreed for both tests with 1 and 2 results reported as HSIL on LBC being reported as LSIL and Normal on histopathology.

16 results reported as LSIL agreed for both tests with 2 results reported as LSIL on LBC being reported as HSIL on histopathology. There was a statistically significant difference Cytologic diagnosis of LBC compared with Histopathology Results amongst study Population, (p value - 0.05)

Table 4 shows the comparison of PAP smear results with the gold standard- Histopathology findings. From the table, 54 normal results were in agreement for the two tests. About 6 results reported as ASCUS agreed for both tests with 4 and 1 results reported as ASCUS on PAP smear being reported as LSIL and HSIL on histopathology. About 6 results reported as carcinoma agreed for both tests with 1 results reported as carcinoma on PAP smear being reported as HSIL on histopathology. About 7 results reported as HSIL agreed for both tests with 5 results reported as HSIL on PAP smear being reported as Normal on histopathology. About 15 results reported as LSIL agreed for both tests with 1 results reported as LSIL on PAP smear being reported as HSIL on histopathology There was a statistically significant difference cytological diagnosis of PAP smear compared with Histopathology results amongst study Population. (P value - 0.05)

The false positives of PAP smear results consisted of 5 ASCUS (5/6; 83%), 1 LSIL (1/15; 6.6%), 5 HSIL (5/7; 71%), 1 Carcinoma (1/6; 16%) and zero normal (0/54; 0%) with the total being 12 (12/90; 13.33%).

The false positives of LBC results consisted of 2 ASCUS (2/5; 40%), 3 LSIL (3/16; 18%), 3 HSIL (3/7; 42%), 0 Carcinoma (0/6; 0%) and 1 normal (1/57; 0%) with the total being 9 (9/91; 9.8%).

Discussion:

The conventional Pap smear (CPS) has been the mainstay of screening for cervical cancer and its precursor lesions for approximately 50 years without major changes in the techniques related to preparation and interpretation. Despite its success as a preventive screening tool for cervical cancer, CPS has its limitations. To overcome these problems, a new slide preparation method namely the Liquid Based Cytology (LBC) was introduced. In the manual liquid based method, cells are uniformly dispersed by a membrane, from a suspension of cells in a polymer solution. As with most screening tests, the CPS suffers from imperfect sensitivity and specificity. Although a clinician may have excellent collection and sampling technique, only approximately 20% of the cells collected are smeared on the glass slide in CPS. In our study the LBC method was found to be comparable to the conventional PAP smear on some parameters and superior on few others. Liquid based cytology has recently become an alternative to CPS in the detection of intraepithelial lesions as well as in invasive carcinoma of the uterine cervix. The present work was done to compare the efficacy of conventional PAP smear and liquid based cytology for the detection of cervical cancer.

Liquid based cytology showed better performance as a screening test for cervical cancer than conventional Pap smear. Liquid based cytology had a higher sensitivity (92%) and specificity of (96.6%) as compared with PAP smears with sensitivity (90.2%) and specificity of (84.7%) respectively. Also the PPV and NPV was higher (95.2% and 98.3% respectively) of Liquid based cytology as compared with PAP smears (80.4% and 92.6% respectively). The higher negative predictive value of both the tests suggested the low prevalence of the disease as to what the reports by ICO suggested the prevalence of HPV infection being about 5%.⁴

When comparison of reports was made between Pap smear and Histopathology and Liquid Based cytology to Histopathology a total of 88 reports matched between Pap smear and Histopathology as compared 91 reports between Liquid based cytology to Histopathology. As histopathology has been considered as the gold standard test a relatively more agreement by Liquid based cytology makes the test a better test in terms of accuracy as compared to Pap

smears. Pap smears showed a higher number of False positive tests at every stage of the disease as compared to Liquid based cytology thus indicating Pap smear as an inferior screening test. When reports compared within the two screening tests itself, suggested 90 reports out of 100 on mutually agreement to the same diagnosis seen.

There were total of 6 carcinoma detected by histopathology which correlated exactly to 6 by liquid based cytology but 7 by Pap smear which is to be considered erroneous as the specific extra slide of carcinoma on pap smear had a normal tissue on histopathology and further more as LSIL on Liquid based cytology. With 2 ASCUS reported on Rap smear and only 1 on liquid based cytology as CIN1 and CIN 2 on histopathology indicating he relative risk of underdiagnosed on behalf of the screening is higher for Pap smear as compared to Liquid based cytology but can be strengthened for liquid based cytology with the help of reflex HPV testing.

These findings confer superiority to LBC as a screening test over CPS for detecting those patients with actual disease and those without it. Baker JJ et al., 2002 showed that LBC was significantly better than CPS in detecting biopsy-proven disease and in screening of benign abnormalities.⁵

False positives and false negatives comprise the area of overlap. In the present study the total false positive Pap and LBC were 9 and 2 respectively indicating a lower sensitivity of Pap smear as a screening test and false negatives were 4 and 1 respectively when compared to Histopathology which increases burden upon the diagnostic facility and thus bringing discredit to the screening test.

In the present study, LBC resulted in a decrease in the false-positive detection over the PAP smear, which was ASCUS (40% vs. 83%), HSIL (42% vs. 71%) and carcinoma (0% vs. 16%) and the total false-positive rate (9.8% vs. 13.33%). In the detection of LSIL, PAP smear resulted in a decrease in the false positive detection over LBC (6.6% vs. 18%).

This study clearly indicated that in spite of the different methodologies, the LBC systems adequately preserved cellular structure for morphologic evaluation and yields high-quality slides.

Conclusion:

Liquid based cytology has added advantage over conventional Pap smear since its sensitivity and specificity is higher. Thus is should be used a screening tool for cervical cancer.

Table 1: Comparison of Pap Smear Vs Histopathology

Pap Smear	Histopathology		Total
	Positive	Negative	
Positive	37	9	46
Negative	4	50	54
Total	41	59	100
Sensitivity			90.20%
Specificity			84.70%
Positive Predictive Value			80.40%
Negative Predictive Value			92.60%
Efficacy			87.00%

Table 2: Comparison of Liquid Based Cytology Vs Histopathology

Liquid Based Cytology	Histopathology		Total
	Positive	Negative	
Positive	40	2	42
Negative	1	57	58
Total	41	59	100
Sensitivity			97.60%
Specificity			96.60%
Positive Predictive Value			95.20%
Negative Predictive Value			98.30%
Efficacy			97.00%

Table 3: Results Liquid Based Cytology compared with Histopathology

			Histopathology Results					Total
			ASCUS	Carcinoma	HSIL	LSIL	Normal	
Liquid Based Cytology	ASCUS	Count	5	0	1	1	0	7
		% within Histopath Results	83.3%	0.0%	10.0%	5.3%	0.0%	7.0%
	Carcinoma	Count	0	6	0	0	0	6
		% within Histopath Results	0.0%	100.0%	0.0%	0.0%	0.0%	6.0%
	HSIL	Count	0	0	7	1	2	10
		% within Histopath Results	0.0%	0.0%	70.0%	5.3%	3.4%	10.0%
	LSIL	Count	1	0	2	16	0	19
		% within Histopath Results	16.7%	0.0%	20.0%	84.2%	0.0%	19.0%
	Normal	Count	0	0	0	1	57	58
		% within Histopath Results	0.0%	0.0%	0.0%	5.3%	96.6%	58.0%
	Total	Count	6	6	10	19	59	100
		% within Histopath Results	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Table 4: Results Pap Smear compared with Histopathology

			Histopathology Results					Total
			ASCUS	Carcinoma	HSIL	LSIL	Normal	
Pap Smear	ASCUS	Count	6	0	1	4	0	11
		% within Histopath Results	100%	0.0%	10.0%	21.1%	0.0%	11.0%
	Carcinoma	Count	0	6	1	0	0	7
		% within Histopath Results	0.0%	100.0%	10.0%	0.0%	0.0%	7.0%
	HSIL	Count	0	0	7	0	5	12
		% within Histopath Results	0.0%	0.0%	70.0%	8.5%	3.4%	12.0%
	LSIL	Count	0	0	1	15	0	16
		% within Histopath Results	0.0%	0.0%	10.0%	78.9%	0.0%	16.0%
	Normal	Count	0	0	0	0	54	54
		% within Histopath Results	0.0%	0.0%	0.0%	0.0%	91.5%	54.0%
	Total	Count	6	6	10	19	59	100
		% within Histopath Results	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

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