



Comparison of conventional Papanicolaou smear and liquid-based cytology: A study of cervical cancer screening at a tertiary care centre in Bengaluru.

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ABSTRACT:

Introduction: Cervical cancer is the fourth commonest cancer affecting women worldwide and the second most common cancer in women aged 15-44 years. The Papanicolaou (Pap) smear has been the cornerstone of screening for cervical neoplasm for the last 50 years. Liquid-based cytology (LBC) was introduced in mid-1990s as an alternative technique to process cervical samples has many benefits over PAP. A new second generation technique, Liqueprep, was introduced after a decade has the advantage of a much lower cost. However, the information available on second generation liquid based cytology is limited.

Objectives: to look for the efficacy of Liquid based cytology and to compare it to that of conventional cytology.

Methodology: This hospital based comparative study was undertaken 100 women who attended Gynaec OPD during 2017 at a tertiary care hospital in Bengaluru. Two cervical smears are simultaneously prepared from each subject, one for PAP smear and another for LBC followed by colposcopy & biopsy.

Results: Among the study subjects, 89% of PAP smear analysis and 100% of smears in LBC showed satisfactory smear. Cytological abnormality was detected in 11% & 21% in PAP & LBC respectively. The present study showed higher sensitivity and specificity of 100% and 75% by LBC when compared to Pap smear (55% and 100% respectively).

Conclusion: The present study showed that liquid based cytology is better in detecting cervical lesions when compared to conventional smear.

Keywords: Papanicolaou smear, liquid-based cytology, cervical cancer, screening, tertiary care centre.

I. INTRODUCTION:

Cervical cancer is the fourth commonest cancer affecting women worldwide and has also the seventh position of all malignancies. It is the second most common cancer in women between 15 and 44 years of age.¹ Almost 70% of the global burden of cervical cancer falls in areas with lower levels of development, and more than one-fifth of

all new cases are diagnosed in India. For women in India, cervical cancer is the second most common cancer. It is the second most common cause of cancer deaths when both genders are combined.²

Frequently performed cytology screening programs have led to a decline in cervical cancer incidence and mortality in developed countries. In contrast, cervical cancer remains largely uncontrolled in high-risk developing countries because of ineffective or no screening program.³

The Papanicolaou (Pap) smear has been the cornerstone of screening for cervical neoplasm for the last 50 years.⁴ But the accuracy of this important screening tool remains controversial. Several recent meta-analyses have reported quite low Pap smear sensitivities – in the range of 50% but as low as 20%.⁵

Liquid-based cytology (LBC) was introduced in mid-1990s as an alternative technique to

process cervical samples. LBC is proposed to have many benefits over CPS such as less number of unsatisfactory (U/S) smears.⁶ More representative transfer of cells from collecting device, evenly distributed cellular material, the choice of using residual cellular material for human papillomavirus (HPV) testing, reduced screening time and possibly higher rate of high grade squamous intraepithelial lesion (HSIL) detection.

Reviews of published studies indicate that liquid based cytology is probably more sensitive than PAP smear in detecting cervical neoplasia and it improves sample adequacy.⁷ However, this first generation liquid based cytology technology requires an automated instrument which leads to increased costs.

A new second generation technique, Liqueprep, was introduced after a decade of the advent of liquid based cytology, this had the advantage of a much lower cost. However, the information available on second generation liquid based cytology is limited.

Hence this study intends to look for the efficacy of Liquid based cytology and to compare it to that of conventional cytology.

Objectives of the study:



1. To describe the sociodemographic characteristics of study subjects
2. To compare the adequacy of the smear of conventional PAP smear and liquid based cytology
3. To compare the efficacy of conventional PAP smear and liquid based cytology for the detection of cervical cancer.
4. To compare the sensitivity, specificity and predictive values of conventional Pap smear cytology and liquid-based cytology with cervix biopsy.

II. MATERIALS AND METHODS:

This hospital based cross-sectional study was conducted at the Department of Obstetrics & Gynaecology, at a tertiary care hospital in Bengaluru.

The study was conducted on 100 women who attended Gynaec OPD with symptoms and signs highly suspicious for cervical malignancy.

Inclusion Criteria:

1. Women with symptom like:
 - a. abnormal vaginal discharge
 - b. post-coital bleeding
 - c. post-menopausal bleeding
 - d. intermenstrual bleeding
2. Women in whom cervix appeared unhealthy on speculum examination like:
 - a. hypertrophy
 - b. redness or congestion
 - c. irregular surface
 - d. erosions

Exclusion criteria:

1. Pregnant women
2. Frank growth over the cervix and/or who had never been sexually active
3. Women with active vaginal bleeding
4. Hysterectomized women,
5. had undergone prior treatment for CIN or cancer cervix

Methodology: After obtaining clearance from the Institutional ethical committee, the study subjects who fulfilled the inclusion & exclusion criteria were recruited for the study. After obtaining proper consent, all the study participants were evaluated by detailed clinical history and physical examination. Pap smear specimen was collected by an Ayers spatula and smeared on a slide and fixed with 95% of ethanol (conventional Pap smear cytology (CPAP)). Liquid-based cytology (LBC) was done using Cytobrush specimen and was collected in a vial containing preservative for liquid-based preparation.

All the patients who have abnormal findings in exfoliative cytology are subjected for colposcopy.

Cervix was cleared off the mucous discharge using a swab soaked in normal saline initially. Later cervix was gently wiped with 3% acetic acid and the examination repeated and is looked for abnormal aceto-white areas. Then Lugol's iodine is applied all over the cervix and looked for abnormal iodine negative areas. Any abnormal or suspicious lesions like aceto-white areas or iodine negative areas or abnormal vessels are noted and cervical biopsy is taken from these areas and the sample is sent for histopathological examination. If colposcopy did not show any suspicious lesions, it is considered normal and biopsy is deferred in these cases.

III. RESULTS:

a. Sociodemographic profile of study subjects

Among the study subjects, majority were in the age group of 30-40 years, were illiterates and from urban area. Majority of subjects were premenopausal, with 1-2 parity. 11-20 years were the age at marriage, and majority were using OCPs for family planning. Majority were having normal BMI (table 1).

b. Presenting complaints and comorbidities among the study subjects:

Abnormal vaginal discharge was the most common presenting complaint seen in 59% of study subjects. Post-menopausal bleeding was the most common menstrual abnormality. Unhealthy cervix was seen in 76% of study subjects (table 2).

c. Adequacy of smear

Among the study subjects, 89% of pap smear analysis showed satisfactory smear and 100% of smears in liquid based cytology were satisfactory (table 3).

d. Comparison of PAP smear & Liquid based cytology results

In PAP smear, inconclusive smears were seen in 10% cases. NILM i.e. Negative for intraepithelial lesion or malignancy was seen in 79% of the cases. Cytological abnormality was detected in 11% of the cases. None of the smears by liquid based cytology were inconclusive. NILM i.e. Negative for intraepithelial lesion or malignancy was seen in 79% of the cases. Cytological abnormality was detected in 21% of the cases (table 4).

e. Correlation of findings of PAP smear and LBC in relation to Biopsy findings

Table 5 compares sensitivity, specificity, positive predictive value and negative predictive value of Pap smear and liquid based cytology.



Liquid based cytology is consistently better compared to Pap smear in all the above parameters.

IV. DISCUSSION:

The Pap smear has been utilized for cervical cancer screening for more than 50 years. Despite being credited with a 70% reduction in mortality for cervical cancer, the false negative rate is still a cause for concern. Liquid based cytology has been developed to address the sampling problems of conventional Pap smear.

In this study the efficacy of Liquid based cytology was compared with Pap smear in detecting abnormal cervical smears and both the techniques were compared with colposcopy findings or with biopsy when indicated.

Majority (79%) of the patients included in our study belonged to 4th and 5th decades of life. Similar results were seen in other studies conducted by Shobana⁸ et al., Abhinaya⁹ et al., Sangeeta¹⁰ et al., Uma¹¹ et al., Shanmugapriya¹² et al., also showed similar results with age of 40years.

Satisfactory parameters like air drying artefact and obscuring blood were absent with liquid based cytology when compared to Pap smear (9% and 18% respectively). This may be because of immersion of cells into the liquid fixative. Only conventional smears were unsatisfactory due to thick smear, which was not a problem with liquid based cytology due to even distribution of cells. (Table 6)

Almost all the studies comparing liquid based cytology with Pap smear showed similar results. The lower number of unsatisfactory specimens reflects the superiority of the liquid based cytology over the conventional method.

Our study showed higher sensitivity and specificity of 100% and 75% by liquid based cytology when compared to Pap smear (55% and 100% respectively) which was concordant to many studies comparing the efficacies of both the techniques. Lower sensitivity of Pap smear which can be explained by the fact that the malignant cells are missed in the smears due to high obscuration of the slides by blood, mucous and air drying artefacts. (Table 7)

Positive predictive value and Negative predictive value of Pap smear were 100% and 30.8% respectively and the same by liquid based cytology were 95.24% and 100% in our study. Since all the accuracy parameters are better by liquid based cytology it can be concluded that liquid based cytology is a superior to conventional Pap smear in screening of cervical cancer.

Conclusion: The present study showed that liquid based cytology is better in detecting cervical lesions when compared to conventional smear. Hence liquid based cytology can be incorporated in clinical practice for routine screening of cervical cancer. It increases the number of satisfactory smears. In addition it has an advantage of collecting material for HPV-DNA test when deemed necessary.

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Table 1: Socio-demographic profile of study subjects

Characteristics	Number (Percentage)	
Age	30-40	56 (56.0)
	41-50	23 (23.0)
	51-60	16 (16.0)
	61-70	4 (4.0)
	>70	1 (1.0)
Education	Illiterate	43 (43.0)
	1-7	13 (13.0)
	8-10	13 (13.0)
	11-12	10 (10.0)
	Degree +	21 (21.0)
Domicile	Rural	36 (36.0)
	Urban	64 (64.0)



Menopausal status	Pre-menopausal	72 (72.0)
	Menopausal	28 (28.0)
Parity	0	3 (3.0)
	1-2	53 (53.0)
	3-5	41 (41.0)
	6-10	3 (3.0)
	No	94 (94.0)
Age at marriage	11-20	63 (63.0)
	20-30	37 (37.0)
Family planning method	OCP use	7 (7.0)
	Barrier method	3 (3.0)
	IUCD	5 (5.0)
BMI	<18.5	13 (13.0)
	18.5-25	56 (56.0)
	25-30	30 (30.0)
	>30	1 (1.0)

Table 2: Presenting complaints and comorbidities among the study subjects

Characteristics		Number (Percentage)*
Abnormal vaginal discharge		59 (59.0)
Pain abdomen		32 (32.0)
Post-coital bleeding		14 (14.0)
Menstrual abnormalities	Post-menopausal bleeding	16 (16.0)
	Menstrual disturbances	12 (12.0)
	Inter menstrual bleeding	15 (15.0)
Loss of weight & appetite	Loss of weight	3 (3.0)
	Loss of appetite	10 (10.0)
Comorbidities	Diabetes	3 (3.0)
	HIV	5 (5.0)
	HTN	1 (1.0)
STD/genital warts		6 (6.0)
Unhealthy cervix		76 (76.0)

*Multiple responses

Table 3: Distribution of study subjects based on adequacy of smear

Test	Characteristics	Number (Percentage)
PAP smear	Pap smear satisfactory	89 (89.0)
	Pap smear air artifact	9 (9.0)
	Pap smear bloody smear	18 (18.0)
Liquid based cytology	Liquid based cytology satisfactory	100 (100.0)
	Liquid based cytology air artifact	0
	Liquid based cytology bloody smear	0

Table 4: Distribution of study subjects based on cytological results

Cytological report	PAP smear	Liquid based cytology
Inconclusive	10 (10.0)	0
NILM	79 (79.0)	79 (79.0)
ASCUS	0	9 (9.0)
LSIL	10 (10.0)	0
HSIL	0	11 (11.0)
Squamous cell carcinoma	1 (1.0)	1 (1.0)



Table 5: Correlation of findings of Papsmear and LBC in relation to Biopsy findings

	PAP smear vs biopsy	LBC vs biopsy
Observation		
True positive	11	20
False positive	0	1
False negative	9	0
True negative	4	3
Correlation		
Sensitivity	55.0	100.0
Specificity	100.0	75.0
Positive predictive value	100.0	95.2
Negative predictive value	30.8	100.0
Accuracy	62.5	95.8
p-value	0.04	<0.001

Table 6: Studies comparing satisfactory smears by Pap smear and LBC

Author	Conventional cytology Sample size (%)	Liquid based cytology Sample size (%)
Shobana ⁸ et al	100 (92.0)	100 (96.0)
Sangeeta ¹⁰ et al	310 (92.1)	310 (98.39)
Uma ¹¹ et al	94 (78.72)	78 (92.55)
Chinmayee ¹³ et al	97 (86.66)	97 (88.7)
Bolick ¹⁴ et al	39,408(81.14)	10,694(88.16)
Papillo ¹⁵ et al	1,8613(86.17)	8,574(93.46)
Carpenter ¹⁶ et al	5,000(80.00)	2,727(89.22)
Diaz-Rosario ¹⁷ et al	74,573(77.82)	56,095(80.59)
Weintraub ¹⁸ et al	1,30,381(72.02)	39,864(91.73)
Hutchinson ¹⁹ et al	446(73.54)	446(79.60)
Lee ²⁰ et al	7,223(70.62)	7,223(78.31)
Wang ²¹ et al	972(70.88)	972(79.55)
Present study	100(89)	100(100)

Table 7: Studies comparing sensitivity and specificity of both the techniques

Author	Sensitivity		Specificity	
	Pap smear Sample size (%)	LBC Sample size (%)	Pap smear Sample size (%)	LBC Sample size (%)
Abinaya ⁹ et al	120 (39.10)	120 (100.0)	120 (100.0)	120 (100.0)
Shobana ⁸ et al	100 (55.5)	100 (83.0)	100 (83.7)	100 (86.5)
Uma ¹¹ et al	94 (37.3)	94 (100.0)	94 (84.3)	94 (97.29)
Shanmugapriya ¹² et al	200 (43.37)	200(89.5)	200(95.06)	200(77.16)
Sherwani ²² et al	160 (46.3)	160 (2.4)	160 (50)	160 (50)
Nadereh ²³ et al	506(66)	506(83)	506(86)	506(98)
Kavatkar ²⁴ et al	105(68)	105(76)	105(79)	105(86)
Present study	24(55)	24(100)	24(100)	24(75)