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Original Research Article

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

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ABSTRACT

Background: 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, Liquiprep 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. The objective was to look for the efficacy of LBC and to compare it to that of conventional cytology.
Methods: This hospital based comparative study was undertaken 100 women who attended gynaecology OPD during 2017 at a tertiary care hospital in Bengaluru. Two cervical smears were simultaneously prepared from each subject, one for Pap smear and another for LBC followed by colposcopy and 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% and 21% in pap and 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).
Conclusions: 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

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]

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 LBC technology requires an automated instrument which leads to increased costs.

A new second generation technique, Liquiprep 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 LBC is limited.

Hence this study intended to look for the efficacy of LBC and to compare it to that of conventional cytology.

Objectives

The objectives of this study were to describe the sociodemographic characteristics of study subjects, to compare the adequacy of the smear of conventional Pap smear and LBC, to compare the efficacy of conventional Pap smear and LBC for the detection of cervical cancer and to compare the sensitivity, specificity and predictive values of conventional Pap smear cytology and LBC with cervix biopsy.

METHODS

This hospital based cross-sectional study was conducted at the department of obstetrics and gynaecology, at a tertiary care hospital in Bengaluru.

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

Inclusion criteria

Women with symptoms like abnormal vaginal discharge, post-coital bleeding, post-menopausal bleeding, intermenstrual bleeding were included in the study. Women in whom cervix appeared unhealthy on speculum examination like hypertrophy, redness or congestion, irregular surface and erosions were also included in the study.

Exclusion criteria

Pregnant women, women with frank growth over the cervix and/or who had never been sexually active, women with active vaginal bleeding, hysterectomized women and those who had undergone prior treatment for CIN or cancer cervix were excluded from the study.

Methodology

After obtaining clearance from the institutional ethical committee, the study subjects who fulfilled the inclusion and 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). 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 were noted and cervical biopsy was taken from these areas and the sample is sent for histopathological examination. If colposcopy did not show any suspicious lesions, it was considered normal and biopsy was deferred in these cases.

RESULTS

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 pre-menopausal, 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).

Presenting complaints and co-morbidities 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).

Table 1: Socio-demographic profile of study subjects.

Characteristics		Number (percentage)
Age (in years)	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 (in years)	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 (kg/m^2)	<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 co-morbidities 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 and appetite	Loss of weight	3 (3.0)
	Loss of appetite	10 (10.0)
Co-morbidities	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.

Tests	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)

Continued.

Tests	Characteristics	Number (percentage)
LBC	LBC satisfactory	100 (100.0)
	LBC air artifact	0
	LBC bloody smear	0

Table 4: Distribution of study subjects based on cytological results.

Cytological report	Pap smear	LBC
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 Pap smear and LBC in relation to biopsy findings.

Findings	PAP smear versus biopsy	LBC versus 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.

Authors	Conventional cytology sample size (%)	LBC sample size (%)
Shobana et al[9]	100 (92.0)	100 (96.0)
Sangeeta et al[11]	310 (92.1)	310 (98.39)
Singh et al[12]	94 (78.72)	78 (92.55)
Dhananjaya et al[14]	97 (86.66)	97 (88.7)
Bolick et al[15]	39,408 (81.14)	10,694 (88.16)
Papillo et al[16]	1,8613 (86.17)	8,574 (93.46)
Carpenter et al[17]	5,000 (80.00)	2,727 (89.22)
Diaz-Rosario et al[18]	74,573 (77.82)	56,095 (80.59)
Weintraub et al[19]	1,30,381 (72.02)	39,864 (91.73)
Hutchinson et al[20]	446 (73.54)	446 (79.60)
Lee et al[21]	7,223 (70.62)	7,223 (78.31)
Wang et al[22]	972 (70.88)	972 (79.55)
Present study	100 (89)	100 (100)

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

Authors	Sensitivity		Specificity	
	Pap smear sample size (%)	LBC sample size (%)	Pap smear sample size (%)	LBC sample size (%)
Abinaya et al[10]	120 (39.10)	120 (100.0)	120 (100.0)	120 (100.0)
Shobana et al[9]	100 (55.5)	100 (83.0)	100 (83.7)	100 (86.5)

Continued.

Authors	Sensitivity		Specificity	
	Pap smear sample size (%)	LBC sample size (%)	Pap smear sample size (%)	LBC sample size (%)
Singh et al[12]	94 (37.3)	94 (100.0)	94 (84.3)	94 (97.29)
Shanmugapriya et al[13]	200 (43.37)	200 (89.5)	200 (95.06)	200 (77.16)
Sherwani et al[23]	160 (46.3)	160 (2.4)	160 (50)	160 (50)
Behtash et al[24]	506 (66)	506 (83)	506 (86)	506 (98)
Kavatkar et al[25]	105 (68)	105 (76)	105 (79)	105 (86)
Present study	24 (55)	24 (100)	24 (100)	24 (75)

Adequacy of smear

Among the study subjects, 89% of Pap smear analysis showed satisfactory smear and 100% of smears in LBC were satisfactory (Table 3).

Comparison of Pap smear and LBC results

In Pap smear, inconclusive smears were seen in 10% cases. NILM (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 LBC were inconclusive. NILM was seen in 79% of the cases. Cytological abnormality was detected in 21% of the cases (Table 4).

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 LBC. LBC is consistently better compared to Pap smear in all the above parameters.

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. LBC has been developed to address the sampling problems of conventional Pap smear.

In this study the efficacy of LBC 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 Shobana et al, Abhinaya et al, Sangeeta et al, Uma et al and Shanmugapriya et al also showed similar results with age of 40 years.[8-12]

Satisfactory parameters like air drying artefact and obscuring blood were absent with LBC 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 LBC with Pap smear showed similar results. The lower number of unsatisfactory specimens reflects the superiority of the LBC over the conventional method.

Our study showed higher sensitivity and specificity of 100% and 75% by LBC 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 LBC were 95.24% and 100% in our study. Since all the accuracy parameters are better by LBC it can be concluded that LBC is a superior to conventional Pap smear in screening of cervical cancer.

CONCLUSION

The present study showed that LBC is better in detecting cervical lesions when compared to conventional smear. Hence LBC 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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Conflict of interest: None declared
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