

Comparison of Conventional Pap Smears versus Liquid Based Cytology for Clinicopathological Patterns of Cervical Lesions at a Tertiary Care Centre, Bangalore, India

CN ANUSHREE¹, SONAL PRIYANKER², NAGARAJ NARASAPPA HUGAR³, YA MANJUNATHA⁴

ABSTRACT

Introduction: Conventional Pap Smear (CPS) technique has been the mainstay for early detection of cervical cancer. However, its extensive use has not been possible due to the limitations, like presence of obscuring blood and inflammation, reducing its sensitivity markedly. False negativity of CPS is also very high, so Liquid Based Cytology (LBC) was introduced.

Aim: To compare cytomorphological patterns, diagnostic utility and adequacy of smears of cervical lesions on CPS and LBC.

Materials and Methods: This was a prospective descriptive study, conducted in the Department of Pathology of Dr. B R Ambedkar Medical College and Hospital, Bangalore for 19 months during November 2018 to May 2020 on 250 cases. The samples were taken with cervix-brush. First, a CPS was prepared and was immediately alcohol-fixed. After that the same brush head was rinsed in LBC vial containing methanol. Statistical analysis was done using the Statistical Package for the Social Sciences 22.0 (SPSS) and R environment 3.2.2 for data analysis.

Results: Most of the patients were in the fourth decade of life and 160 cases (64%) presented as white discharge per vaginum. Total 231 (92.4%) smears were satisfactory on CPS and 233 (93.2%) smears on LBC. The number of Low grade Squamous Intraepithelial Lesions (LSIL) increased from 4 cases (1.6%) in CPS to 6 cases (2.4%) in LBC in this study. Rate of detection of High grade Squamous Intraepithelial Lesion (HSIL) was more with LBC (11 cases, 4.4%) compared to that of CPS (7 cases, 2.8%). It was seen that in this study, sensitivity and specificity of LBC was higher than CPS in detecting LSIL and HSIL, except for the specificity of CPS, which was more than LBC in detecting LSIL. The present study showed overall sensitivity of 77.1% in CPS and 94.3% in LBC and specificity of 97.2% and 100% in CPS and LBC, respectively. The p-value calculated was <0.001, which was highly significant.

Conclusion: The LBC technique showed clear background, well preserved cytomorphological details, removal of extra mucus, blood and inflammatory cell infiltrate as compared to CPS technique. Atypical cells or abnormal cells were seen better and were detected more by LBC as compared to CPS.

Keywords: Conventional papanicolaou smear, High-grade squamous intraepithelial lesions, Low-grade squamous intraepithelial lesions, Squamous cell carcinoma

INTRODUCTION

Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women [1]. It is a major public health problem and in many developing countries with incidence and mortality over 75% [2]. Studies have shown that in India, 126,000 new cases of cervical cancer occur every year [3,4]. Before the development of invasive lesions, cervical cancer has well-defined premalignant lesions [5]. In their early stage of development as the cancer cells are localised, confined to the surface of the cervix and have not invaded into the adjacent tissues, it is completely and easily treatable. Once cancer metastasis to other parts of the body occurs, the disease becomes difficult to treat with increased morbidity and mortality. By increasing understanding of the pathogenesis of cervical cancer, it has helped us build best and effective screening methods for secondary prevention.

Papanicolaou GN introduced cervical cytology in 1940 [6]. This is being used globally as the standard screening test for premalignant lesions and cervical cancers [7]. Pap smear test is a very effective/affordable method of detecting, preventing and thus delaying the progression of cervical cancer. In low resource settings, a conventional Pap test is the main screening system, but in the developed countries, Liquid Based Cytology (LBC) is quite popular. In a developing country like India, accounting for quarter of the cervical cancer deaths, it is important to know the overall pattern of epithelial cell abnormality in the Pap smear [8].

Liquid Based Cytology was introduced later at around mid-1990s. Better sensitivity and increased detection of glandular abnormalities were noted in LBC preparations [9,10]. Because of radiotherapy, morphologic changes make it extremely difficult to interpret conventional Pap test results [11]. Liquid Based Cytology has advantages of less unsatisfactory smears, faster and more efficient method with accurate interpretation of less obscuring materials such as blood, mucous, inflammatory cells in smears and residual cell suspension can be used for testing human papillomavirus (HPV) Deoxyribonucleic Acid (DNA) and immunocytochemistry [12].

The aim of the study was to compare the diagnostic utility, adequacy of smears and cytomorphological features on both CPS and LBC methods in cervical lesions.

MATERIALS AND METHODS

The present prospective descriptive study was done on 250 cases of cervical cytology for a period of 19 months from November 2018-May 2020 in the Department of Obstetrics and Gynaecology in Cytopathology Laboratory of a tertiary care hospital, Karnataka, India. The cervical cytological smears were screened by conventional method and then compared with LBC (thin prep). The study was conducted with approval from Institutional Ethics Committee (IEC 504).

Inclusion criteria: Women above 20 years of age, who were referred from Obstetrics and Gynaecology Department for pap smears.

Exclusion criteria: Pap smears taken on post hysterectomy patients and already known cases of carcinoma were excluded from the study.

Sample size calculation: It was estimated using the following Daniel's sample size estimation formula.

$$n = \frac{Z^2 \times p(1-p)}{e^2}$$

Where, n = sample size

Z= Z score, with 95% confidence interval, Z is 1.96

p= proportion in the target population estimated to have particular characteristic.

In Cytopathology Laboratory, proportion of pap smear received was 8% (0.08).

e = margin of error, set as 5%, i.e. 0.05.

By substituting the values,

$$n = \frac{(1.96)^2 \times 0.08(1-0.08)}{(0.05)^2}$$

$$n = 112$$

Thus, sample size (n) obtained using the formula was 112. So, 250 cytological smears were studied.

The samples were collected with a cervix-brush. Firstly, CPS was prepared and immediately alcohol-fixed. Then, with the same brush head LBC sample was taken, rinsed in LBC vial containing methanol, which was transferred to the Cytopathology Laboratory for further processing using LBC Thin prep method. The revised 2014 Bethesda system was followed for specimen adequacy as well as reporting [13].

STATISTICAL ANALYSIS

The statistical software, namely, Statistical Package for the Social Sciences SPSS 22.0, and R environment version 3.2.2 were used for the analysis of the data and Microsoft Word and Excel were used to generate tables. Sensitivity, specificity and p-value were calculated using Chi-square/ Fisher Exact test.

RESULTS

Total 250 patients were included in the study. The youngest female examined was 21 years old and oldest was 70 years. Maximum number of females 90 (36%) were seen in age 40-49 years [Table/Fig-1].

Age (in years)	No. of patients	% of patients
20-29	50	20
30-39	76	30.4
40-49	90	36
50-59	23	9.2
≥60	11	4.4
Total	250	100

[Table/Fig-1]: Age-wise distribution of patients (N=250).

Most common clinical presentation noted was white discharge per vaginum (160 cases, 64%). About 32 (12.8%) females were asymptomatic and cervix appeared normal [Table/Fig-2].

Out of total 250 smears, 180 (72%) smears were inflammatory by CPS and 178 (71.2%) smears were inflammatory by LBC technique. Normal features were shown by 24 (9.6%) smears on CPS and 21 (8.4%) smears on LBC while 19 (7.6%) smears were unsatisfactory on CPS whereas 17 (6.8%) smears were unsatisfactory on LBC technique. Main reasons for unsatisfactory smears in CPS was due to reduced cellularity and dense inflammation with blood whereas, in LBC, it was due to reduced cell number and fewer slides showing degenerated cells. Epithelial abnormality was detected in 27 cases (10.8%) on CPS and 34 cases (13.6%) on LBC.

Clinical presentation of the patients	No. of patients	Percentage (%)
White discharge per vaginum	160	64
Friable cervix and bleeds on touch	12	4.8
Blood stained discharge	13	5.2
Congested cervix	13	5.2
Congested and hypertrophied cervix	7	2.8
Unhealthy and hypertrophied cervix	6	2.4
Unhealthy cervix with erosion	4	1.6
Irregular and pulled up cervix	3	1.2
Asymptomatic	32	12.8
Total	250	100

[Table/Fig-2]: Clinical presentation of patients (N=250).

Out of 180 (72%) inflammatory smears on CPS, 162 (64.8%) cases were of non specific inflammation and 18 (7.2%) cases were of specific inflammation. Out of 178 (71.2%) inflammatory smears on LBC, 160 (64%) cases were of non specific inflammation and 18 (7.2%) cases were of specific inflammation.

Candida was found to be the most common organism on inflammatory smear i.e. 8 (3.2%) cases on CPS 8 (3.2%) on both CPS and LBC while least common was Actinomyces i.e. 1 (0.4%) case in both CPS and LBC [Table/Fig-3].

Findings	No. of cases (CPS) n=250	No. of cases (LBC) n=250	p-value
Normal	24 (9.6%)	21 (8.4%)	0.639
Inflammation	180 (72%)	178 (71.2%)	0.843
a) Candida	8 (3.2%)	8 (3.2%)	1.000
b) Bacterial vaginosis	6 (2.4%)	7 (2.8%)	0.779
c) Actinomyces	1 (0.4%)	1 (0.4%)	1.000
d) Trichomonas vaginalis	3 (1.2%)	2 (0.8%)	0.653
e) Non specific inflammation	162 (64.8%)	160 (64%)	0.852
Epithelial abnormality	27 (10.8%)	34 (13.6%)	0.339
a) LSIL	4 (1.6%)	6 (2.4%)	0.523
b) HSIL	7 (2.8%)	11 (4.4%)	0.337
c) SCC	7 (2.8%)	7 (2.8%)	1.00
d) ASC-US	3 (1.2%)	3 (1.2%)	1.000
e) ASC-H	2 (0.8%)	5 (2%)	0.253
f) AGUS	4 (1.6%)	2 (0.8%)	0.411
Unsatisfactory	19 (7.6%)	17 (6.8%)	0.729
Total	250	250	

[Table/Fig-3]: Result of cytological findings by CPS and LBC (N=250).

Chi-square test/Fisher exact test; LSIL: low-grade squamous intraepithelial lesions; HSIL: high-grade squamous intraepithelial lesions; SCC: squamous cell carcinoma; ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells, cannot rule out HSIL; AGUS: atypical glandular cells of undetermined significance

Maximum number of epithelial abnormalities were noted in 40-49 years age group (total 90 patients), comprising 12 cases (4.8%) on CPS and 19 cases (7.6%) on LBC of total 250 patients. We compared cytomorphological features by both the techniques and with histopathology result (gold standard) in cases of epithelial abnormality. On CPS, minimum number of epithelial abnormalities were noted in 20-29 years age group (total 50 patients), comprising 2 cases (0.8%) of total 250 patients [Table/Fig-4].

On LBC, minimum number of epithelial abnormalities were noted in 20-29 years and ≥60 years age groups, both comprising of 2 cases (0.8%) out of total 250 patients [Table/Fig-5].

In CPS, overall sensitivity was 77.1% and specificity was 97.2%. Epithelial abnormalities in CPS vs histopathological findings are shown in [Table/Fig-6]. In case of LBC, overall sensitivity was 94.3% and specificity was 100%. Epithelial abnormalities in LBC vs histopathological findings are shown in [Table/Fig-7]. The histopathological features of the specific inflammation smears have been shown in [Table/Fig-8-11].

Age (years)	Total no. of patients	LSIL	HSIL	SCC	ASC-US	ASC-H	AGUS
20-29	50	0	0	1 (2%)	1 (2%)	0	0
30-39	76	2 (2.6%)	0	3 (3.9%)	1 (1.3%)	0	0
40-49	90	2 (2.2%)	4 (4.4%)	3 (3.3%)	0	1 (1.1%)	2 (2.2%)
50-59	23	0	2 (8.6%)	0	1 (4.3%)	0	1 (4.3%)
≥60	11	0	1 (9%)	0	0	1 (9%)	1 (9%)
Total	250	4 (1.6%)	7 (2.8%)	7 (2.8%)	3 (1.2%)	2 (0.8%)	4 (1.6%)
p-value	-	0.823	0.024*	1.000	0.254	0.094*	0.065*

[Table/Fig-4]: Age-wise distribution of epithelial abnormality in patients (n=27) (CPS). Chi-square test/Fisher exact test

Age (years)	Total no. of patients	LSIL	HSIL	SCC	ASC-US	ASC-H	AGUS
20-29	50	0	0	1 (2%)	1 (2%)	0	0
30-39	76	2 (2.6%)	0	3 (3.9%)	1 (1.3%)	1 (1.3%)	0
40-49	90	4 (4.4%)	7 (7.7%)	3 (3.3%)	1 (1.1%)	3 (3.3%)	1 (1.1%)
50-59	23	0	3 (13%)	0	0	0	1 (4.3%)
≥60	11	0	1 (9%)	0	0	1 (9%)	0
Total	250	6 (2.4%)	11 (4.4%)	7 (2.8%)	3 (1.2%)	5 (2%)	2 (0.8%)
p-value	-	0.621	0.003**	1.000	1.000	0.298	0.293

[Table/Fig-5]: Age-wise distribution of epithelial abnormality in patients (n=34) (LBC). Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups; Non-parametric setting for qualitative data analysis; Fisher exact test used when cell samples were small; p-value calculated was <0.001 which is highly significant

	TP	FP	FN	TN	Total	Se	Sp	PPV	NPV	Accuracy	p-value
NILM	0	6	2	25	33	0.0	80.7	0.0	92.6	75.8	0.491
LSIL	2	2	4	27	33	33.3	93.1	50.0	87.1	82.9	0.063*
HSIL	3	4	10	16	33	23.08	80.0	42.9	61.5	57.6	0.832
ASCUS	0	3	0	30	33	100.0	100.0	100.0	100.0	100.0	<0.001**
ASC-H	0	2	0	31	33	100.0	100.0	100.0	100.0	100.0	<0.001**
AGUS	0	4	0	29	33	100.0	100.0	100.0	100.0	100.0	<0.001**
SCC	2	5	9	17	33	18.2	77.3	28.6	65.4	57.6	0.763
Overall	27	6	8	209	250	77.1	97.2	81.8	96.3	94.4	<0.001**

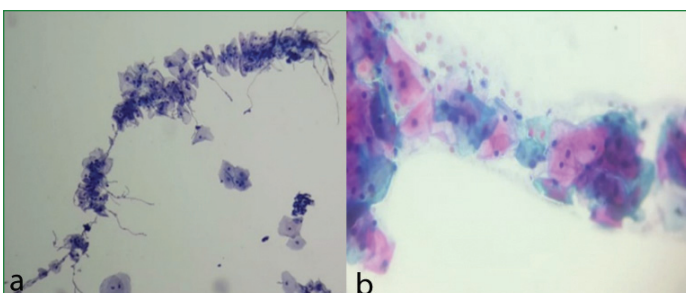
[Table/Fig-6]: CPS vs Histopathological findings.

LSIL: Low-grade squamous intraepithelial lesions; HSIL: High-grade squamous intraepithelial lesions; SCC: Squamous cell carcinoma; ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells, cannot rule out HSIL; AGUS: Atypical glandular cells of undetermined significance; *Suggestive significance (p-value: 0.05<p<0.10); **Moderately significant (p-value: 0.01<p<0.05); **Strongly significant (p-value: p<0.01); NILM: Negative for intraepithelial lesion or malignancy

	TP	FP	FN	TN	Total	Se	Sp	PPV	NPV	Accuracy	p-value
NILM	-	-	-	-	-	-	-	-	-	-	-
LSIL	3	3	2	26	34	60.0	89.3	50.0	92.9	85.3	0.007**
HSIL	8	3	5	18	34	61.5	85.0	72.7	78.3	76.5	0.004**
ASCUS	0	3	0	31	34	100.0	100.0	100.0	100.0	100.0	<0.001**
ASC-H	0	5	0	29	34	100.0	100.0	100.0	100.0	100.0	<0.001**
AGUS	0	2	0	32	34	100.0	100.0	100.0	100.0	100.0	<0.001**
SCC	4	3	9	18	34	30.8	85.0	57.1	66.7	64.7	0.248
Overall	33	0	2	215	250	94.3	100.0	100.0	99.1	99.20	<0.001**

[Table/Fig-7]: LBC vs Histopathological findings.

TP: True positive; FP: False positive; FN: False negative; TN: True negative; Se: Sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; NILM: Negative for intraepithelial lesion or malignancy



[Table/Fig-8]: Candidiasis: Papanicolaou's stain showing spore-like or shish kebab appearance of squamous cells with pseudo-hyphae of yeast forms. a) LBC (200X), b) CPS (200X).

DISCUSSION

Undoubtedly, Pap smear is an effective and affordable screening method for early detection of cervical precancerous lesions. Liquid Based Cytology is an alternate but better technique, as there is consistently reduced rates of unsatisfactory results, improved sample processing, clarity of microscopy, and small screening area. Furthermore, the potential for performing additional tests, like HPV testing on the residual sample, probably supports the acceptability of LBC among pathologists, gynaecologists and colposcopists. HPV testing is increasingly gaining importance as it is being used in screening programmes for triaging low-grade abnormalities, co-testing with cytology, and as a primary cervical cancer screening tool.

In the present study, females >20 years were included. Majority of women were in the 40-49 years age group, showing dysplasia, which is similar to studies done by Sherwani RK et al., [14], Shobana R and Saranya B [15] and Khamankar ST et al., [16]. However, the present study was in contrast to a study done by Garg V et al., which showed maximum cases in the second decade and Chinaka CC et al., in the fifth decade [17,18].

White discharge per vaginum (160 cases, 64%) was the most common complaint in the present study, which was similar to Sherwani RK et al., [14]. Shobana R and Saranya B [15] and Sharma P et al., [19]. This was followed by congested cervix and bloodstained discharge per vaginum (both 13 cases (5.2%)). However, postcoital bleeding was the most common complaint in a study conducted by Robert ME and Fu YS [20].

	TP	FP	FN	TN	Total	Se	Sp	PPV	NPV	Accuracy	p-value
NILM	0	6	2	25	33	0.0	80.7	0.0	92.6	75.8	0.491
LSIL	2	2	4	27	33	33.3	93.1	50.0	87.1	82.9	0.063*
HSIL	3	4	10	16	33	23.08	80.0	42.9	61.5	57.6	0.832
ASCUS	0	3	0	30	33	100.0	100.0	100.0	100.0	100.0	<0.001**
ASC-H	0	2	0	31	33	100.0	100.0	100.0	100.0	100.0	<0.001**
AGUS	0	4	0	29	33	100.0	100.0	100.0	100.0	100.0	<0.001**
SCC	2	5	9	17	33	18.2	77.3	28.6	65.4	57.6	0.763
Overall	27	6	8	209	250	77.1	97.2	81.8	96.3	94.4	<0.001**

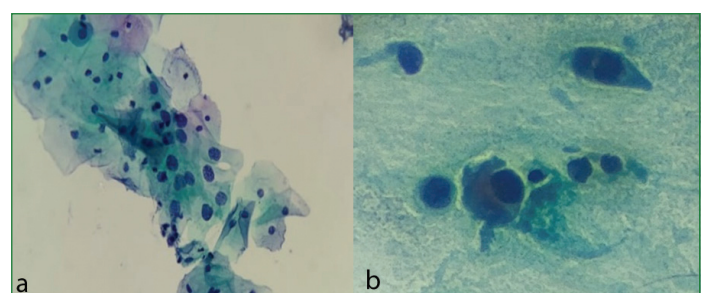
[Table/Fig-6]: CPS vs Histopathological findings.

LSIL: Low-grade squamous intraepithelial lesions; HSIL: High-grade squamous intraepithelial lesions; SCC: Squamous cell carcinoma; ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells, cannot rule out HSIL; AGUS: Atypical glandular cells of undetermined significance; *Suggestive significance (p-value: 0.05<p<0.10); **Moderately significant (p-value: 0.01<p<0.05); **Strongly significant (p-value: p<0.01); NILM: Negative for intraepithelial lesion or malignancy

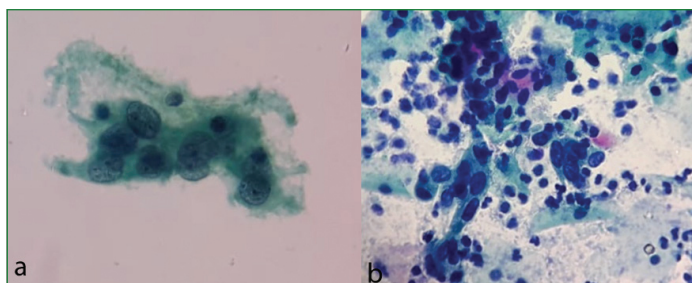
	TP	FP	FN	TN	Total	Se	Sp	PPV	NPV	Accuracy	p-value
NILM	-	-	-	-	-	-	-	-	-	-	-
LSIL	3	3	2	26	34	60.0	89.3	50.0	92.9	85.3	0.007**
HSIL	8	3	5	18	34	61.5	85.0	72.7	78.3	76.5	0.004**
ASCUS	0	3	0	31	34	100.0	100.0	100.0	100.0	100.0	<0.001**
ASC-H	0	5	0	29	34	100.0	100.0	100.0	100.0	100.0	<0.001**
AGUS	0	2	0	32	34	100.0	100.0	100.0	100.0	100.0	<0.001**
SCC	4	3	9	18	34	30.8	85.0	57.1	66.7	64.7	0.248
Overall	33	0	2	215	250	94.3	100.0	100.0	99.1	99.20	<0.001**

[Table/Fig-7]: LBC vs Histopathological findings.

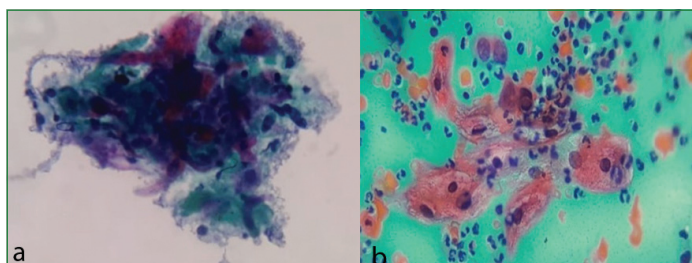
TP: True positive; FP: False positive; FN: False negative; TN: True negative; Se: Sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; NILM: Negative for intraepithelial lesion or malignancy



[Table/Fig-9]: ASC-H: Papanicolaou's stain showing cells with pleomorphism, variable N:C ratio and prominent nuclear irregularity. a) LBC (400X), (b) CPS (400X).



[Table/Fig-10]: HSIL: Papanicolaou's stain showing cells with enlarged hyperchromatic nuclei, highly irregular outlines and scant cytoplasm. a) LBC (400X), b) CPS (400X).



[Table/Fig-11]: SCC: Papanicolaou's stain showing cells exhibiting marked pleomorphism as well as some keratinized tadpole cells. Cytoplasm is deeply eosinophilic with irregular nuclear contour and pyknotic nucleoli. a) LBC (400X), b) CPS (400X).

We found that 92.4% (231 cases) smears were satisfactory in CPS compared to 93.2% (233 cases) in LBC. Most of the unsatisfactory smears in CPS were due to reduced cellularity, dense inflammation, and blood whereas, in LBC, reduced cell number was the cause and few slides showed degenerated cells [Table/Fig-12] [14,15,21,22].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	92.4	93.2
Sherwani RK et al., (2007), Aligarh [14]	97.3	98.9
Beerman H et al., (2009), Rotterdam [21]	99.1	99.87
Singh VB et al., (2015), Chandigarh [22]	95.7	98.3
Shobana R and Saranya B, (2019), Tamil Nadu [15]	92	96

[Table/Fig-12]: Studies showing satisfactory smears [14,15,21,22].

It was seen that LBC smears were more satisfactory than CPS. The number of LSIL increased from 4 cases (1.6%) in CPS to 6 cases (2.4%) in LBC in the present study. Other studies with similar results are shown in [Table/Fig-13] [14,15,23,24].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	1.6	2.4
Almonte M et al., (2007), Peru [24]	0.9	13.8
Sherwani RK et al., (2007), Aligarh [14]	10.6	18.1
Sykes PH et al., (2008), New Zealand [23]	21	24.4
Shobana R and Saranya B, (2019), Tamil Nadu [15]	8	12

[Table/Fig-13]: Studies showing LSIL cases [14,15,23,24].

It can be seen that LBC detected more HSIL cases than CPS. We found that the rate of detection of HSIL was more with LBC (11 cases, 4.4%) compared to that of CPS (7 cases, 2.8%). [Table/Fig-14] is showing similar results from various studies [14,15,18,21].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	2.8	4.4
Sherwani RK et al., (2007), Aligarh [14]	0.6	4.3
Beerman H et al., (2009), Rotterdam [21]	0.56	0.64
Chinaka CC et al., (2014), Nigeria [18]	8	10
Shobana R and Saranya B, (2019), Tamil Nadu [15]	2	6

[Table/Fig-14]: Studies showing HSIL cases [14,15,18,21].

The present study showed, 33.3% sensitivity in CPS and 60% in LBC for detecting LSIL. Sensitivity of other studies are shown in [Table/Fig-15] [15,25-27].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	33.3	60
Park IA et al., (2001), Korea [27]	89.6	82.8
Jeon YK et al., (2004), Korea [26]	73.7	78.9
Kim YR et al., (2005), Korea [25]	64	86
Shobana R and Saranya B, (2019), Tamil Nadu [15]	40	66

[Table/Fig-15]: Sensitivity of the screening tests in detecting LSIL [15,25-27].

Sensitivity of 23.08% in CPS and 61.5% in LBC for detecting HSIL was noted in the present study. In all the studies, it can be seen that LBC was a better test for detecting HSIL lesions.

The present study showed specificity of 93.1% for CPS and 89.3% for LBC in case of LSIL, which is similar to studies done by Lee JM et al., [28], Arbyn M et al., [29]. Specificity of other studies are shown in [Table/Fig-16]. But in contrast, studies done by Park IA et al., [27] and Shobana R and Saranya B [15], showed that LBC was more specific than to CPS [Table/Fig-16] [15,27-29].

For detecting HSIL, the present study showed 80% specificity for CPS and 85% for LBC. Specificity for other studies is shown in [Table/Fig-17] [15,28,29].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	93.1	89.3
Park IA et al., (2001), Korea [27]	69.8	83
Lee JM et al., (2006), Orlando [28]	96.1	75.9
Arbyn M et al., (2008), Netherlands [29]	81.2	78.8
Shobana R and Saranya B, (2019), Tamil Nadu [15]	93	94

[Table/Fig-16]: Specificity of the screening tests in detecting LSIL [15,27-29].

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	80	85
Lee JM et al., (2006), Orlando [28]	96.5	98.3
Arbyn M et al., (2008), Netherlands [29]	96.7	97
Shobana R and Saranya B, (2019), Tamil Nadu [15]	100	96

[Table/Fig-17]: Specificity of the screening tests in detecting HSIL [15,28,29].

The present study showed that specificity of LBC is better than CPS in detecting HSIL. (Studies done by Lee JM et al., [28] and Arbyn M et al., [29] also showed similar results. The study done by Shobana R and Saranya B [15] showed that CPS was better in detecting HSIL than LBC.

The present study showed overall sensitivity of 77.1% in CPS and 94.3% in LBC and specificity of 97.2% and 100% in CPS and LBC, respectively. Comparison of sensitivity and specificity with other studies is shown in [Table/Fig-18,19] [14,15,18,23,30,31]. In all these studies, it can be seen that LBC has a better overall sensitivity than CPS. In the present study, LBC had higher specificity, which was similar to Sykes PH et al., [23], Sherwani RK et al., [14], Shobana R and Saranya B [15], Chinaka CC et al., [18] and Karimi-Zarchi M et al., [30]. However, Hussein T et al., [31] showed higher specificity for CPS.

Study	CPS (%)	LBC (%)
Present study, (2022), Bangalore	77.1	94.3
Sherwani RK et al., (2007), Aligarh [14]	53.7	97.6
Sykes PH et al., (2008), New Zealand [23]	73.7	79.1
Chinaka CC et al., (2014), Nigeria [18]	86	100
Shobana R and Saranya B, (2019), Tamil Nadu [15]	55.5	83

[Table/Fig-18]: Overall sensitivity [14,15,18,23].

Study	CPS (%)	LBC (%)
Present study, Bangalore (2022)	97.2	100
Hussein T et al., (2005), UK [31]	82	76
Sherwani RK et al., (2006), Aligarh [14]	50	50
Sykes et al (2008), New Zealand [23]	69	69
Karimi-Zarchi M et al., (2013), Iran [30]	66	77.7
Chinaka CC et al., (2014), Nigeria [18]	97	100
Shobana R and Saranya B, (2019), Tamil Nadu [15]	83.7	86.5

[Table/Fig-19]: Overall specificity [14,15,18,23,30,31].

Limitation(s)

Since from the same patient, the sample was taken twice for both techniques, in some cases the sample collected was inadequate or less. Sometimes, the patients were non cooperative during sample collection for the second time.

CONCLUSION(S)

From this study, it was concluded that smears prepared by LBC technique had clear background, well preserved cytomorphological details, less mucous, blood and inflammatory cell infiltrate as compared to CPS technique. Atypical cells or abnormal cells were better seen by LBC as compared to CPS. In LBC, the residual specimens can be used for immunocytochemistry and HPV DNA by the Polymerase Chain Reaction (PCR). Screening programmes using CPS have successfully reduced cervical cancer, but newer tests like LBC for HPV testing might enhance screening. In future, LBC technique can be used with desired modification to overcome the limitations of studies.

REFERENCES

- Nandini NM, Manoli NS. Cervical cytology screening methods for cervical lesions update. *Issues Dev Med Med Res.* 2022;11:90-110.
- Castellsagué X. Natural history and epidemiology of HPV infection and cervical cancer. *Gynecol Oncol.* 2008;110(3):S4-7.
- Sankaranarayanan R, Nene BM, Dinshaw K, Rajkumar R, Shastri S, Wesley R, et al. Early detection of cervical cancer with visual inspection methods: A summary of completed and on-going studies in India. *Salud Pública de México.* 2003;45(S3):309-07.
- Sreedevi A, Javed R, Dinesh A. Epidemiology of cervical cancer with special focus on India. *Int J Womens Health.* 2015;7:405.
- Valdespino VM, Valdespino VE. Cervical cancer screening: State of the art. *Curr Opin Obstet Gynecol.* 2006;18(1):35-40.
- Papanicolaou GN. Introduction of Pap smear in early detection of cervical malignancies. *Am J Clin Path.* 1940;19:301-08.
- Vaghela BK, Vaghela VK, Santwani PM. Analysis of abnormal cervical cytology in papanicolaou smears at tertiary care center-A retrospective study. *Int J Biomed Adv Res.* 2014;5:47-49.
- Stewart BW, Wild CP. International agency for research on cancer. *World Cancer Rep.* 2014;2014.
- Utagawa ML, Pereira SMM, Makabe S, Maeda MYS, Marques JA, Santoro CLF, et al. Pap test in a high-risk population comparison of conventional and liquid-based cytology. *Diagn Cytopathol.* 2004;31(3):169-72.
- Burnley C, Dudding N, Parker M, Parsons P, Whitaker CJ, Young W. Glandular neoplasia and borderline endocervical reporting rates before and after conversion to the SurePath™ liquid-based cytology (LBC) system. *Diagn Cytopathol.* 2011;39(12):869-74.
- Zannoni GF, Vellone VG. Accuracy of Papanicolaou smears in cervical cancer patients treated with radiochemotherapy followed by radical surgery. *Am J Clin Pathol.* 2008;130(5):787-94.
- Kavatkar AN, Nagwanshi CA, Dabak SM. Study of a manual method of liquid-based cervical cytology. *Indian J Pathol Microbiol.* 2008;51(2):190.
- Nayar R, Wilbur DC. The Bethesda system for reporting cervical cytology: A historical perspective. *Acta Cytologica.* 2017;61:359-72.
- Sherwani RK, Khan T, Akhtar K, Zeba A, Siddiqui FA, Rahman K, et al. Conventional Pap smear and liquid based cytology for cervical cancer screening-A comparative study. *J Cytol.* 2007;24(4):167.
- Shobana R, Saranya B. Comparison of conventional Papanicolaou smear and liquid-based cytology for cervical cancer screening. *Int J Sci Study.* 2019;6(12):64-73.
- Khamankar ST, Belekar V, Bhagat VM, Baviskar SR. Cervical cancer screening: Risk factors for cervical neoplasia among rural women of Nanded, Maharashtra. *Innovative J Med Health Sci.* 2014;4:312-16.
- Garg V, Thakral RK, Sharma VK, Agarwal AK, Gupta K, Vedi A. Conventional Pap (Papanicolaou) smear cytology in primary screening of cervical lesions and its comparison with manual liquid based cytology. *Indian J Pathol Oncol.* 2016;3(3):485-90.
- Chinaka CC, Abudullahi M, Mohammed OM. A comparative study on the use of liquid based cytology and conventional Pap smear in cervical screening. *J Med Res.* 2014;2(4):40-50.
- Sharma P, Rahi M, Lal P. A community-based cervical cancer screening program among women of Delhi using camp approach. *Indian J Community Med.* 2010;35(1):86.
- Robert ME, Fu YS. Squamous cell carcinoma of the uterine cervix- A review with emphasis on prognostic factors and unusual variants. *Semin Diagn Pathol.* 1990;7(3):173-89.
- Beerman H, Van Dorst EB, Kuenen-Boumeester V, Hogendoorn PC. Superior performance of liquid-based versus conventional cytology in a population-based cervical cancer screening program. *Gynecol Oncol.* 2009;112(3):572-76.
- Singh VB, Gupta N, Nijhawan R, Srinivasan R, Suri V, Rajwanshi A. Liquid-based cytology versus conventional cytology for evaluation of cervical Pap smears: Experience from the first 1000 split samples. *Indian J Pathol Microbiol.* 2015;58(1):17.
- Sykes PH, Harker DY, Miller A, Whitehead M, Neal H, Wells JE, et al. A randomised comparison of SurePath liquid-based cytology and conventional smear cytology in a colposcopy clinic setting. *Br J Obstet Gynaecol.* 2008;115(11):1375-81.
- Almonte M, Ferreccio C, Winkler JL, Cuzick J, Tsu V, Robles S, et al. Cervical screening by visual inspection, HPV testing, liquid-based and conventional cytology in Amazonian Peru. *Int J Cancer.* 2007;121(4):796-02.
- Kim YR, Kim YT, Kim SH, Kim JH, Kim JW, Park YW. Comparative analysis of conventional Papanicolaou smear, fluid-based thin-layer method and cervicography. *Korean J Obstet Gynecol* 2005;2932-40.
- Jeon YK, Kim OR, Park KW, Kang SB, Park IA. Liquid-based cytology using MonoPrep2 [TM] system in cervicovaginal cytology: Comparative study with conventional Pap smear and histology. *Korean J Cytopathol.* 2004;15(1):33-39.
- Park IA, Lee SN, Chae SW, Park KH, Kim JW, Lee HP. Comparing the accuracy of ThinPrep Pap tests and conventional Papanicolaou smears on the basis of the histologic diagnosis: A clinical study of women with cervical abnormalities. *Acta Cytol.* 2001;45(4):525-31.
- Lee JM, Kelly D, Gravitt PE, Fansler Z, Maksem JA, Clark DP. Validation of a low-cost, liquid-based screening method for cervical intraepithelial neoplasia. *Am J Obstet Gynecol.* 2006;195(4):965-70.
- Arbyn M, Bergeron C, Klinkhamer P, Martin-Hirsch P, Siebers AG, Bulten J. Liquid compared with conventional cervical cytology: A systematic review and meta-analysis. *Obstet Gynecol.* 2008;111(1):167-77.
- Karimi-Zarchi M, Peighambari F, Karimi N, Rohi M, Chiti Z. A comparison of 3 ways of conventional pap smear, liquid-based cytology and colposcopy vs cervical biopsy for early diagnosis of premalignant lesions or cervical cancer in women with abnormal conventional pap test. *Int J Biomed Sci.* 2013;9(4):205.
- Hussein T, Desai M, Tomlinson A, Kitchener HC. The comparative diagnostic accuracy of conventional and liquid-based cytology in a colposcopic setting. *Br J Obstet Gynaecol.* 2005;112(11):1542-46.

PARTICULARS OF CONTRIBUTORS:

- Associate Professor, Department of Pathology, Dr. B R Ambedkar Medical College, Bangalore, Karnataka, India.
- Postgraduate Student, Department of Pathology, Dr. B R Ambedkar Medical College, Bangalore, Karnataka, India.
- Postgraduate Student, Department of Pathology, Dr. B R Ambedkar Medical College, Bangalore, Karnataka, India.
- Professor and Head, Department of Pathology, Dr. B R Ambedkar Medical College, Bangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sonal Priyanker,
C/o Dr. Ajeet Kumar, Near Pushpanjali Vihar Apt., Saristabad Road, Gardanibagh
Patna-800001, Bihar, India.
E-mail: drsonalpriyanker05@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Apr 14, 2022
- Manual Googling: Jun 18, 2022
- iThenticate Software: Jun 21, 2022 (18%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 26, 2022**

Date of Peer Review: **May 14, 2022**

Date of Acceptance: **Jun 18, 2022**

Date of Publishing: **Jul 01, 2022**