Section: Pathology

Original Research Article

COMPARATIVE EVALUATION OF CONVENTIONAL SMEARS AND LIQUID-BASED CYTOLOGY USING SPLIT CYTOBRUSH SAMPLING IN CERVICAL CANCER SCREENING: A PROSPECTIVE STUDY

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ABSTRACT

Background: Liquid-Based Cytology (LBC) has increasingly been adopted in cervical cancer screening due to its improved sample adequacy and cleaner and more clear background compared to Conventional Smears (CS). **Objectives**: (1) To compare the adequacy of epithelial cell component in CS versus in LBC. (2) To evaluate the clarity of the background in CS versus LBC (3) To evaluate epithelial abnormalities detected on CS and LBC prepared from split cytobrush samples.
Materials and Methods: A prospective study was conducted over one year at a teaching hospital, analysing 102 cervical cytobrush samples split for CS and LBC preparation. Five blinded pathologists reported each smear. Categorical variables were compared using Chi-square test; $p < 0.05$ was considered statistically significant.
Results: Adequate cellularity was significantly higher in LBC (97%) than CS (85%) ($p = 0.003$). LBC produced significantly reduced inflammatory backgrounds ($p < 0.0001$), less haemorrhage, debris (scoring Likert scale). Percentage of cases with diagnostic architectural/morphological changes was found to be higher in LBC (96%) compared to CS (79%) ($p = 0.0003$). LBC yielded fewer unsatisfactory samples (2%) than CS (15%), and a higher proportion of NILM diagnoses ($p = 0.0023$).
Conclusion: LBC is significantly superior to CS in terms of adequacy, background clarity, and detection of diagnostic morphological changes. Adoption of LBC can reduce unsatisfactory rates and improve diagnostic accuracy by reducing misinterpretation of artefactual changes in cervical cancer screening and in turn reducing the need for a repeat smears.
Keywords: Liquid-based cytology, Conventional smear, Cervical cytology, Cytobrush, Diagnostic accuracy.

INTRODUCTION

Cervical cancer remains a major global health concern, ranking as the fourth most common cancer among women worldwide. Cancer survival has improved since the mid-1970s for all of the most common cancers except uterine cervix and uterine corpus.[1] The burden is disproportionately high in low- and middle-income countries, including India, where organized screening coverage remains suboptimal. The situation is more alarming in the rural areas where most women are illiterate and ignorant about the hazards of cervical cancer as well as healthcare resources are scarce.[2]

The introduction of the Papanicolaou (Pap) smear revolutionized screening and its implementation into health policy at a national level could reduce cancer burden in India; however, conventional smears (CS) suffer from limitations such as air-drying artifacts,

thick smears, obscuring inflammation, haemorrhage, and loss of diagnostic material.[2,3,4] Liquid-Based Cytology (LBC) was developed to address these shortcomings and offers advantages such as monolayered cell distribution, clearer background, and residual sample availability for ancillary testing (HPV testing, IHC, molecular assays).

Liquid based cytology (LBC) have reported higher, if not, on par efficacy to conventional Pap smears in improving adequacy in screening of premalignant/malignant conditions of cervix thereby effectively reducing unsatisfactory smears and also reducing unnecessary references to colposcopy.[5] Several studies have demonstrated superior or equivalent performance of LBC compared to CS in terms of adequacy, diagnostic accuracy, and reproducibility; however various studies differ on their results with regard to sensitivity, specificity, positive predictive value and negative predictive value in comparison to conventional smears.[6,7,8]

Given these variations in literature, the current study aims to compare the adequacy of epithelial cell component, to evaluate the clarity of the background and to evaluate epithelial abnormalities detected on CS and LBC prepared from split cytobrush samples in CS versus in LBC using split sampling from a single cytobrush, thereby eliminating sampling bias.

MATERIALS AND METHODS

A prospective analytical study was conducted for one year in the Department of Pathology at a tertiary care teaching hospital on a total of 102 cervical cytobrush samples collected using purposive sampling technique from gynaecology OPD patients and associated screening camps.

All routine cervical smears of individuals from the cervical cancer screening program and smears from symptomatic individuals visiting the OBG OPD, aged between 21 to 65 years were included for the study after obtaining informed written consent.

All cases with known history of cervical cancers and patients who underwent surgery for uterine/cervicovaginal lesions were excluded from the study.

Institutional Ethics Committee approval was obtained (Approval letter with reference no:SSIMS&RC/IEC/FAC/015-2023-24).

A cytobrush was used to collect cervical epithelial cells and the brush was first rolled on a glass slide for CS preparation. The same brush was then rinsed into LBC fixative for LBC processing. This ensured true split-sampling from a single instrument. CS were stained using rapid Pap stain. LBC samples were processed in a standardized automated system. Five blinded pathologists independently reported each sample according to The Bethesda System (TBS), 2014. A Likert scoring for different parameters were performed by the pathologists as follows:

Scoring Parameter	1	2	3	4	5
Inflammation	Obscuring	Dense dirty	Dense	Moderate	Mild
Haemorrhage & mucus	Obscuring	Dense	Moderate	Mild	Nil
Drying artefact	Global altering cytomorphology	Global not altering cytomorphology	Focal altering cytomorphology	Focal not altering cytomorphology	Nil
Diagnostic architectural/ morphological changes	Absent	Present but with obscuring factors	Present but with absence of transformation zone components	Present but inconclusive	Present and satisfactory

Scores 1 and 2 were categorised as unsatisfactory for evaluation and scores 3,4 and 5 were categorised as satisfactory for evaluation. Discordant cases were reviewed by a senior pathologist.

RESULTS

The 102 smears reported were assessed for various parameters. Chi square test was used to compare categorical variables. P value of <0.05 was considered as statistically significant.

Comparison of epithelial cell component

Liquid-based cytology had a higher number of adequate samples (97%) compared to conventional smears (85%). [Table 1, Figure 1a, 1b]

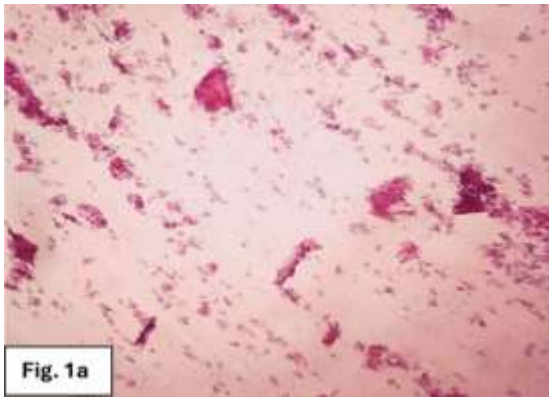

Fig 1a: Squamous cells overlapping - Conventional smear (Pap, 40x)

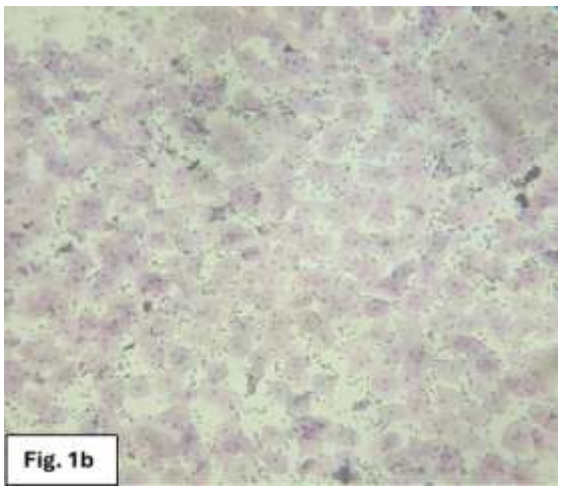

Fig 1b: Monolayered sheets of squamous cells in LBC (Pap, 100x)

Table 1: Comparison of epithelial cell component

Cellularity	CS	LBC
Adequate	87	99
Inadequate	15	3
$\chi^2 = 8.73$, $p = 0.003$		

Comparison of Inflammatory Background

Conventional smears showed a higher frequency of dense and dense dirty inflammation, as well as samples with haemorrhage, compared to liquid-based cytology. LBC samples showed significantly reduced background inflammation with fewer obscuring elements. [Table 2, Figure 2a, 2b]

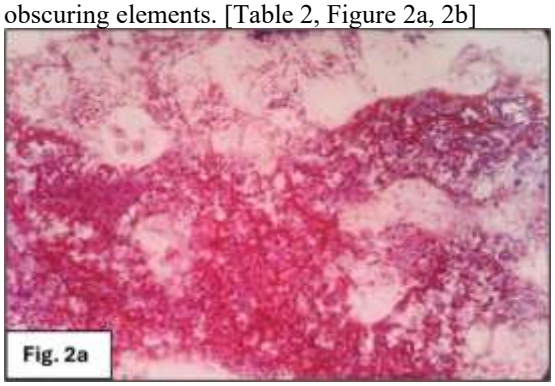

Fig 2a: Conventional smear showing hemorrhage obscuring cells - Diagnosed as Unsatisfactory (Pap, 40x)

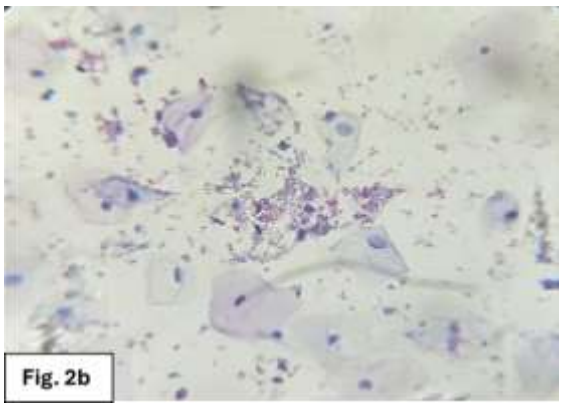

Fig 2b: Obscuring RBCs were cleared on LBC enabling a diagnosis of NILM (Pap, 100x)

Table 2: Comparison of inflammatory background

Inflammatory background	Conventional smear	Liquid based cytology
Mild	11	36
Moderate	18	28
Dense	30	12
Dense dirty	14	02
Haemorrhage	08	00
$\chi^2 = 40.14$, $p < 0.0001$		

Detection of Architectural/Morphological Changes

LBC showed architectural/morphological changes in 4 samples, in comparison to 21 of conventional smears. LBC was significantly superior in identifying diagnostic features. [Table 3, Figure 3a, 3b]

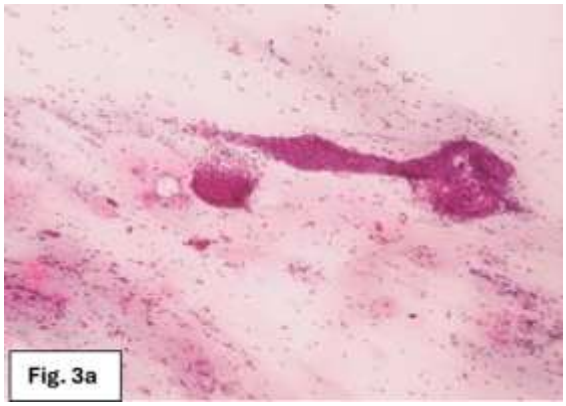

Fig 3a: Endocervical cell clusters- Conventional smears (Pap, 100x)

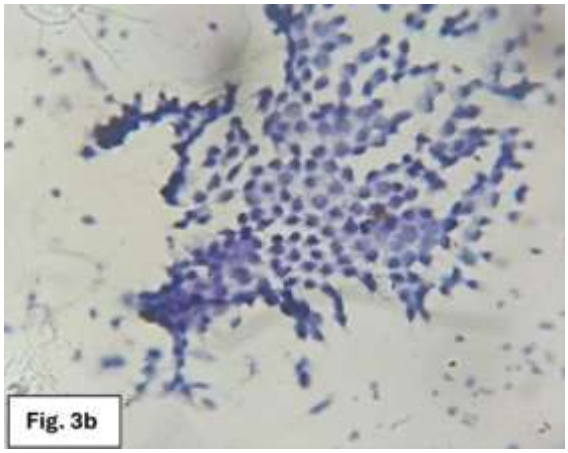

Fig 3b: Endocervical cell clusters - LBC (Pap, 400x)

Table 3: Comparison of architectural/morphological changes

Changes	CS	LBC
Present	21	4
Absent	81	98
$\chi^2 = 13.11$, $p = 0.0003$		

Cytological Diagnosis

Liquid-based cytology had significantly fewer unsatisfactory samples (2 out of 102, or 2%) compared to conventional smears (15 out of 102, or 15%). This suggests that liquid-based cytology is more likely to produce samples that are adequate for evaluation, thereby aiding accurate cytological diagnosis. [Table 4, Figure 4a, 4b]

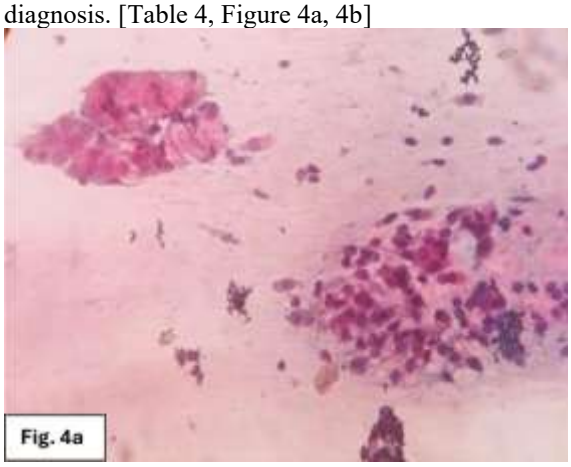

Fig 4a: Doubtful cells in conventional smear of a perimenopausal lady (Pap, 400x)

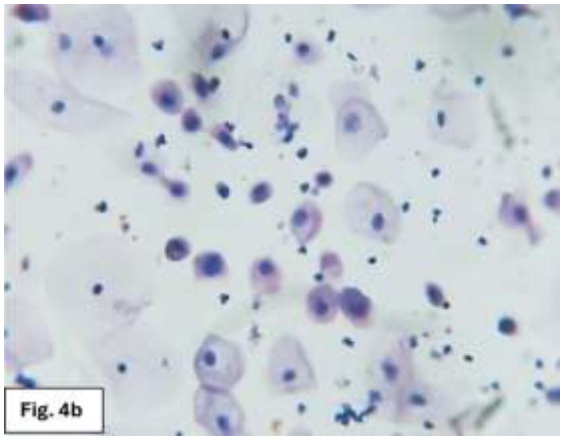

Fig 4b: Nuclear hyperchromasia and irregularity noted on LBC - ASC-H (Pap,100x)

Table 4: Comparison of cytological diagnosis

Diagnosis	CS	LBC
Unsatisfactory	15	2
NILM	84	99
Epithelial abnormalities	3	1
$\chi^2 = 12.17$, $p = 0.0023$		

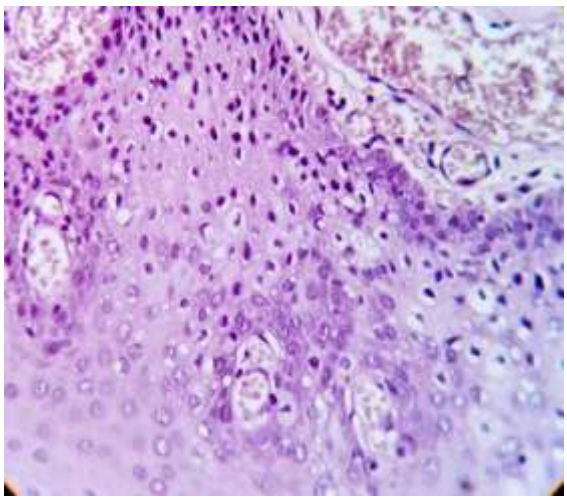

Fig 5: HPE diagnosis of squamous metaplasia with reactive cellular changes of case diagnosed as ASC-H on LBC (Pap,100x)

DISCUSSION

In this study, LBC significantly outperformed CS across multiple diagnostic parameters.

In the present study, Liquid-Based Cytology (LBC) demonstrated significantly higher adequacy (97%) compared to conventional smears (85%), consistent with the findings of Singh et al., who reported superior adequacy and lower unsatisfactory rates in LBC in their 1000-sample split-sample analysis.[7] Similar results were observed by Nayar & Wilbur, who described improved cellularity and preservation in LBC techniques as part of The Bethesda System updates.[11] The current study also showed that LBC produced significantly cleaner backgrounds with fewer obscuring elements such as haemorrhage and dense inflammation. This corresponds with Barrios et al., who demonstrated better visualization of premalignant lesions in patients with ASC-US due to the clearer background achieved in LBC preparations.[5] Biscotti et al,[10] similarly found that LBC markedly reduces background debris and enhances the interpretability of epithelial cells.

	Present study n= 102	Biscotti et al. (10) n=114	Karimi-Zarchi et al n=150	Nirali Patel et al n= 600	Sherwani et al n=160
Number of pathologists	5	2	-	2	-
Mean age (yrs)	40-49	38.4	42± 9.9	3rd decade	4th decade
Abnormal CS results %	2.9 n=03	-	20.0 n=30	9.7 n=58	15 n=24
Abnormal LBC results %	0.98 n=01	40.36 n=46	20.7 n=28	11 n=66	26.2 n=42
Abnormal Biopsy results %	0	51.75 n=59	-	-	-

Morphological and architectural abnormalities were more consistently detected in LBC (96%) compared to CS (79%). Comparable findings were reported by Bergeron et al,[9] where LBC identified diagnostic abnormalities more reliably than conventional cytology.

Additionally, Clavel et al,[12] and Monsonego et al,[13] reported that LBC improves detection rates of low-grade and high-grade squamous intraepithelial lesions by reducing sampling artifacts and enabling monolayer distribution of cells.[12,13,14]

The unsatisfactory smear rate in our study was significantly lower in LBC (2%) compared to CS (15%), mirroring the results of prior international and Indian studies. Davey et al. and Austin et al. both noted a substantial reduction in inadequate specimens using LBC, attributed to better specimen collection, reduced drying artifacts, and greater cellular preservation.[15]

Studies from India, including those by Srivastava et al. and Saha et al., have emphasized similar advantages, recommending integration of LBC into broader cervical screening initiatives.[4,16,17]

The higher proportion of NILM diagnoses in LBC in our study (97%) is also consistent with findings from large multicentre trials, including the ARTISTIC trial by Kitchener et al., which demonstrated improved screening accuracy and reduced misclassification using LBC.[18] Overcalling was also minimized in LBC—our study corrected several ASC-US and ASC-H cases to reactive changes—echoing findings by Barrios et al., who emphasized reduced false-positives with LBC.[5]

The present study encountered 2 cases of ASC-US and 1 case of ASC-H diagnosed on CS. Split sampling smears from LBC technique of the ASC-US cases turned out to be reactive cellular changes. The ASC-H case was diagnosed as ASC-US on LBC. The confirmatory diagnosis for the patient whose LBC diagnosis was ASC-H was later sent for biopsy and histopathological diagnosis of squamous metaplasia with reactive cellular changes was made (Figure 5).

Given India's cervical cancer burden and national guidelines emphasizing enhanced screening coverage, the superiority of LBC demonstrated in our study supports the wider adoption of LBC technologies, especially in tertiary centres or where HPV co-testing is feasible.[2]

Its ability to retain residual samples for molecular testing is an additional advantage highlighted by Ronco et al. and Schiffman et al., who demonstrated

the importance of integrating cytology and HPV testing for precision screening.[19,20]

Overall, the present study supports the growing body of evidence that LBC is superior to CS in adequacy, clarity, and diagnostic yield, reinforcing its role as the preferred screening modality in modern cervical cancer prevention programs.

CONCLUSION

Both CS and LBC are useful cervical cancer screening tools. However, LBC is significantly superior in terms of Adequacy, Clearer background, Detection of diagnostic morphological features and Lower unsatisfactory rates. Nevertheless, conventional smears with epithelial abnormalities are not to be neglected. It is advisable that LBC should be supplemented with CS or performed independently to come to an accurate diagnosis. However, histopathological diagnosis remains the gold standard in cases of discrepancy which in turn avoids unnecessary surgical intervention.

This study supports wider national adoption of LBC to enhance the accuracy and efficiency of cervical cytology screening in India.

Both conventional cytology (CS) and liquid-based cytology (LBC) serve as established modalities for cervical cancer screening. However, the findings of this study clearly indicate that LBC provides substantial advantages over CS. LBC demonstrates markedly improved sample adequacy, offers a cleaner and unobstructed microscopic background, and facilitates enhanced visualization of critical diagnostic morphological features. Furthermore, LBC is associated with significantly lower unsatisfactory smear rates, reducing the need for repeat test. Collectively, these strengths underscore the superior diagnostic performance of LBC and support its wider national implementation to enhance the quality, accuracy, and efficiency of cervical cytology screening in India.

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