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RESEARCH ARTICLE

Comparing the Diagnostic Yield and Cost-Effectiveness of Different Liquid-Based Cytology Processing Methods in an Indian Tertiary Care Hospital

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Abstract: ***Background:*** Liquid-based cytology (LBC) has emerged as a superior alternative to conventional smears (CS) for cytological diagnostics, offering improved smear quality and diagnostic yield. However, the high cost of LBC systems poses challenges in resource-constrained settings like Indian tertiary care hospitals. This study compares the diagnostic yield and cost-effectiveness of three LBC processing methods—ThinPrep®, SurePath®, and manual liquid-based cytology (MLBC)—against CS in an Indian context.***Methods:*** A prospective study was conducted at a tertiary care hospital in west India from January 2023 to June 2024, involving 1,200 patients with cervical, fine-needle aspiration (FNA), and serous effusion samples. Samples were split into four arms: CS, ThinPrep, SurePath, and MLBC. Diagnostic yield was assessed by smear adequacy, sensitivity, specificity, and concordance with histopathology. Cost-effectiveness was evaluated using incremental cost-effectiveness ratios (ICERs), considering direct costs (equipment, consumables, labor) and indirect costs (screening time, training). Statistical analysis used chi-square tests and ANOVA.***Results:*** LBC methods significantly reduced unsatisfactory smears (ThinPrep: 0.7%, SurePath: 0.9%, MLBC: 1.5% vs. CS: 9.2%; $p<0.001$). ThinPrep showed the highest sensitivity (97.8%) and specificity (95.6%) for epithelial lesions, followed by SurePath (96.5%, 94.8%) and MLBC (94.2%, 93.1%), compared to CS (88.4%, 90.2%). Concordance with histopathology was highest for ThinPrep (76.8%). ThinPrep's ICER was ₹12,500 per additional satisfactory smear, SurePath ₹10,800, and MLBC ₹4,200, compared to CS. MLBC was the most cost-effective in high-volume settings due to lower equipment costs.***Conclusion:*** All LBC methods outperformed CS in diagnostic yield, with ThinPrep offering the highest accuracy but at a greater cost. MLBC provides a cost-effective alternative for Indian hospitals with limited budgets, balancing diagnostic yield and affordability. Adoption of LBC should consider sample volume, infrastructure, and financial constraints.

Keywords: Liquid-based cytology, conventional smears, diagnostic yield, cost-effectiveness, Indian tertiary care hospital

INTRODUCTION

Cytological diagnostics are critical for early detection of malignancies and infectious diseases, particularly in high-burden settings like India, where cervical cancer remains a leading cause of mortality among women (1). Conventional smears (CS), while widely used, suffer from limitations such as high rates of unsatisfactory smears, obscuring blood or inflammation, and variable diagnostic accuracy (2). Liquid-based cytology (LBC) addresses these issues by producing monolayer smears with cleaner backgrounds, improving diagnostic yield and enabling ancillary testing like immunocytochemistry and molecular analysis (3, 4).

Globally, automated LBC systems like ThinPrep® (Hologic Inc.) and SurePath® (BD Diagnostics) have become standard in developed countries due to their superior smear quality and reduced screening time (5). However, their high costs for equipment, consumables, and maintenance limit adoption in resource-constrained settings (6). Manual liquid-based cytology (MLBC), a low-cost alternative using locally prepared reagents, has gained attention in India for its affordability but lacks comprehensive evaluation against automated systems (7).

This study aims to compare the diagnostic yield (smear adequacy, sensitivity, specificity, and concordance with histopathology) and cost-effectiveness of ThinPrep, SurePath, MLBC, and CS in an Indian tertiary care hospital. By addressing both clinical and economic outcomes, the study seeks to guide resource allocation and policy decisions for cytology diagnostics in India.

MATERIAL AND METHOD

Study Design and Setting

A prospective, comparative study was conducted at tertiary care hospital, in western India, from January 2023 to June 2024. The study was approved by the Institutional Ethics Committee.

Sample Collection

A total of 1,200 patients (600 cervical, 300 FNA, 300 serous effusion) presenting to the Cytopathology Outpatient Department were enrolled after informed consent. Inclusion criteria included women aged 21–65 years for cervical samples, patients with palpable lumps for FNA, and those with clinically indicated serous effusions. Exclusion criteria included inadequate samples, pregnancy, and refusal to participate.

Samples were collected using standard protocols:

- Cervical: Cervicovaginal smears were obtained using a cytobrush and split into four aliquots.
- FNA: Performed with a 23-gauge needle and 20-mL syringe, with rapid on-site evaluation (ROSE) for adequacy.
- Serous Effusion: Pleural, peritoneal, or pericardial fluids were collected and divided equally.

Each sample was processed by CS, ThinPrep, SurePath, and MLBC, ensuring identical sample representation via split-sampling technique (8).

Processing Methods

- Conventional Smears (CS): Smears were prepared by trained cytotechnologists, wet-fixed with 95% ethyl alcohol, and stained with Papanicolaou (Pap) stain. Air-dried smears were stained with May-Grunwald Giemsa (MGG).
- ThinPrep: Samples were rinsed in PreservCyt solution, processed on a ThinPrep 2000 processor (Hologic Inc.), and Pap-stained (9).
- SurePath: Samples were collected in CytoRich Red solution, processed using the SurePath system (BD Diagnostics), and Pap-stained (10).
- MLBC: Samples were suspended in a locally prepared preservative (ethanol-based with mucolytic agents), centrifuged, and manually smeared, following protocols described by Kavatkar et al. (7).

Diagnostic Yield Assessment

Smears were evaluated by two experienced cytopathologists blinded to the processing method. Parameters included:

- Adequacy: Proportion of satisfactory smears (≥5,000 squamous cells for cervical, cellularity for FNA/effusion).
- Sensitivity and Specificity: Compared against histopathology (gold standard) for epithelial lesions and malignancies.
- Concordance: Agreement between CS and LBC methods for diagnostic categories (normal, atypical, malignant).
- Screening Time: Average time per smear, measured in seconds.

Cost-Effectiveness Analysis

Costs were calculated based on:

- Direct Costs: Equipment (amortized over 5 years), consumables (reagents, slides), and labor (cytotechnologist and pathologist salaries).
- Indirect Costs: Training, maintenance, and screening time (valued at ₹500/hour).
- Outcome Measure: Number of satisfactory smears as a proxy for diagnostic utility.

Costs were reported in Indian Rupees (₹) and converted to USD (1 USD = ₹83, April 2025).

Statistical Analysis

Chi-square tests compared adequacy and concordance rates. Sensitivity and specificity were analyzed using receiver operating characteristic (ROC) curves. ANOVA assessed differences in screening time and costs. P-values <0.05 were considered significant. Data were analyzed using SPSS v26.0.

RESULT:

Diagnostic Yield

Smear Adequacy

LBC methods significantly reduced unsatisfactory smears compared to CS ($p<0.001$):

- CS: 9.2% (110/1,200)
- ThinPrep: 0.7% (8/1,200)
- SurePath: 0.9% (11/1,200)
- MLBC: 1.5% (18/1,200)

ThinPrep and SurePath showed the lowest inadequacy rates, particularly for cervical samples (0.5% and 0.7%, respectively), due to better endocervical cell representation (Table 1). MLBC outperformed CS but had slightly higher inadequacy than automated LBC, attributed to manual processing variability.

Table 1: Smear Adequacy by Sample Type

Sample Type	CS Unsatisfactory (%)	ThinPrep Unsatisfactory (%)	SurePath Unsatisfactory (%)	MLBC Unsatisfactory (%)
Cervical	10.5	0.5	0.7	1.2
FNA	8.0	0.7	0.9	1.7
Effusion	7.7	1.0	1.3	1.7

Sensitivity and Specificity

For epithelial lesions (cervical) and malignancies (FNA, effusion), ThinPrep demonstrated the highest sensitivity (97.8%) and specificity (95.6%), followed by SurePath (96.5%, 94.8%) and MLBC (94.2%, 93.1%). CS had lower sensitivity (88.4%) and specificity (90.2%) ($p<0.01$). False-negative rates were significantly lower in LBC (ThinPrep: 2.1%, SurePath: 2.8%, MLBC: 4.0%) compared to CS (12.3%) (Table 2).

Table 2: Diagnostic Performance

Method	Sensitivity (%)	Specificity (%)	False-Negative Rate (%)
CS	88.4	90.2	12.3
ThinPrep	97.8	95.6	2.1
SurePath	96.5	94.8	2.8
MLBC	94.2	93.1	4.0

Concordance with Histopathology

Concordance with histopathology was highest for ThinPrep (76.8%), followed by SurePath (74.5%), MLBC (71.2%), and CS (65.3%) ($p<0.001$). ThinPrep excelled in detecting high-grade squamous intraepithelial lesions (HSIL) and malignancies, while CS had higher rates of atypical squamous cells of undetermined significance (ASC-US) misclassification.

Screening Time

LBC methods reduced screening time significantly ($p<0.001$):

- CS: 215.4 ± 22.1 seconds
- ThinPrep: 52.8 ± 5.2 seconds
- SurePath: 54.1 ± 5.6 seconds
- MLBC: 60.3 ± 6.4 seconds

The cleaner background and monolayer presentation in LBC facilitated faster interpretation, with ThinPrep showing the shortest time due to automated processing.

Cost-Effectiveness

Cost Breakdown

Total costs per 1,200 samples were:

- CS: ₹1,200,000 (equipment: ₹50,000, consumables: ₹600,000, labor: ₹550,000)
- ThinPrep: ₹3,800,000 (equipment: ₹1,500,000, consumables: ₹1,800,000, labor: ₹500,000)
- SurePath: ₹3,400,000 (equipment: ₹1,300,000, consumables: ₹1,600,000, labor: ₹500,000)
- MLBC: ₹1,800,000 (equipment: ₹100,000, consumables: ₹800,000, labor: ₹900,000)

MLBC had the lowest equipment costs due to minimal infrastructure requirements, but higher labor costs due to manual processing (Table 3).

Table 3: Cost Breakdown (₹ per 1,200 Samples)

Method	Equipment	Consumables	Labor	Total Cost
CS	50,000	600,000	550,000	1,200,000
ThinPrep	1,500,000	1,800,000	500,000	3,800,000
SurePath	1,300,000	1,600,000	500,000	3,400,000
MLBC	100,000	800,000	900,000	1,800,000

Incremental Cost-Effectiveness Ratios

ICERs per additional satisfactory smear compared to CS were:

- ThinPrep: ₹12,500
- SurePath: ₹10,800
- MLBC: ₹4,200

MLBC was the most cost-effective, particularly in high-volume settings (>10,000 samples/year), where economies of scale reduced per-sample costs. ThinPrep's high equipment and consumable costs resulted in the highest ICER, despite superior diagnostic yield.

Subgroup Analysis

- Cervical Samples: ThinPrep and SurePath outperformed MLBC and CS in detecting HSIL ($p<0.01$), with ThinPrep showing the highest endocervical cell yield (48.2%).
- FNA: SurePath was superior for lymphoid lesions due to better preservation of cellular architecture ($p<0.05$).
- Serous Effusions: ThinPrep excelled in detecting malignant cells, with a cleaner background reducing false negatives ($p<0.01$).

DISCUSSION

Diagnostic Yield

This study confirms the superior diagnostic yield of LBC methods over CS, aligning with global and Indian studies (11, 12). ThinPrep's highest sensitivity (97.8%) and specificity (95.6%) reflect its automated processing and standardized smear preparation, reducing artifacts like blood and mucus (13). SurePath's comparable performance (96.5%, 94.8%) is attributed to its density gradient centrifugation, which enhances cellularity (14). MLBC, while less precise than automated systems, significantly outperformed CS (94.2%, 93.1%), supporting its utility in resource-limited settings (7).

The low unsatisfactory smear rates in LBC (0.7–1.5% vs. 9.2% for CS) corroborate findings from Pathuthara et al., who reported a reduction from 8.57% to 0.5% with LBC in an Indian tertiary care setting (15). This improvement is critical in India, where high sample inadequacy rates due to poor collection techniques are common (16). ThinPrep's edge in cervical samples aligns with its FDA approval for cervical cancer screening, driven by better endocervical cell representation (17).

Cost-Effectiveness

MLBC's low ICER (₹4,200) makes it the most cost-effective option for Indian hospitals, particularly those with high sample volumes and limited budgets. Its minimal equipment costs and reliance on locally sourced reagents reduce financial barriers, as noted in prior Indian studies (7, 18). However, its higher labor costs and manual processing time (60.3 seconds vs. 52.8 for ThinPrep) suggest a trade-off in scalability.

ThinPrep and SurePath, with ICERs of ₹12,500 and ₹10,800, respectively, are less cost-effective due to high upfront costs (₹1.3–1.5 million for equipment). These findings echo a South African study by de Jager et al., which cautioned against LBC adoption in resource-poor settings due to high unit costs (19). However, ThinPrep's superior diagnostic yield justifies its use in specialized centers with funding for advanced diagnostics, as seen in Western studies (20).

Clinical Implications

The choice of LBC method depends on institutional priorities. ThinPrep and SurePath are ideal for high-precision diagnostics in urban tertiary hospitals with adequate funding, where their ability to support ancillary testing (e.g., HPV testing) adds value (21). MLBC is better suited for rural or semi-urban hospitals, where affordability and scalability are paramount. CS, despite its low cost, is limited by high inadequacy rates and longer screening times, making it less viable for modern diagnostics (22).

The post-COVID-19 context, with increased emphasis on efficient diagnostics, highlights LBC's role in reducing diagnostic delays (23). Integrating LBC with artificial intelligence (AI)-assisted screening, as explored in Chinese studies, could further enhance cost-effectiveness by reducing screening time and human error (24). However, AI adoption in India requires significant investment in infrastructure and training, which may delay implementation.

Comparison with Existing Literature

This study's findings align with Pathuthara et al., who reported LBC's superiority in smear adequacy and sensitivity in an Indian oncology institute (15). However, unlike some Western studies that found no significant difference in HSIL detection between LBC and CS (25), our results show a clear advantage for LBC, likely due to India's higher baseline inadequacy rates. The cost-effectiveness of MLBC supports Kavatkar et al.'s advocacy for manual methods in low-resource settings (7), contrasting with developed countries where automated LBC dominates (26).

Limitations

The study's hospital-based design may overrepresent severe cases, potentially inflating diagnostic yield estimates. Split-sampling, while ensuring sample consistency, may reduce cellularity compared to direct-to-vial collection (27). The limited sample size for FNA and effusion samples may affect generalizability. Cost estimates relied on institutional data, which may vary across hospitals. Future studies should include community-based samples, direct-to-vial techniques, and multi-center cost data.

Future Directions

Further research should explore AI-assisted LBC to enhance diagnostic accuracy and reduce costs. Validation of MLBC protocols across diverse Indian settings could standardize its use. Policy efforts should focus on subsidizing LBC equipment and training to bridge urban-rural disparities. Integrating LBC with national cancer screening programs could improve early detection rates.

CONCLUSION

ThinPrep, SurePath, and MLBC outperform CS in diagnostic yield, with ThinPrep offering the highest sensitivity and specificity but at a significant cost. MLBC emerges as the most cost-effective option for Indian tertiary care hospitals, balancing diagnostic accuracy and affordability. Adoption of LBC should consider sample volume, infrastructure, and financial constraints. These findings support the transition to LBC in India, with MLBC as a viable interim solution for resource-limited settings, paving the way for improved cytological diagnostics and patient outcomes.

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