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A Comparative Study of Conventional Pap Smear and Liquid-Based Cytology

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ABSTRACT

Background: Cervical cancer is a major health issue globally, particularly in developing countries where it remains a leading cause of cancer-related deaths among women. In Georgia, it ranks as the fifth most frequent cancer among women overall and the third among women aged 15–44 years. Approximately 1.60 million women aged 15 years and older in Georgia are at risk of developing cervical cancer. Annually, about 327 women are diagnosed, and 204 die from the disease. Screening for cervical cancer is crucial for reducing incidence and mortality rates. While the conventional Pap smear has been the primary screening method, its limitations in sensitivity and sample adequacy have led to the development of liquid-based cytology (LBC).

Materials and Methods: This study analyzed 1000 cervical cytology samples from women aged 18–65 years in Georgia, who were gynecologically asymptomatic and not vaccinated for HPV. The median age was 37 years. Informed consent was obtained for all participants. Samples were collected using ThinPrep reagents (Hologic) and processed within 2 h. Smears were prepared using the ThinPrep 2000 Processor, fixed in absolute alcohol for 30 min, and stained according to the Papanicolaou protocol. The Bethesda 2001 System terminology was used for reporting. Smears were evaluated by light microscopy and archived per Georgian medical data requirements.

Results: The study found significant differences between the two screening methods. LBC showed a higher rate of satisfactory smears and better detection rates for negative for intraepithelial lesion or malignancy—NILM (89.4% vs. 80.3% for conventional Pap smear). Unsatisfactory smears were significantly lower with LBC (1.33% vs. 7.33%). Detection rates for atypical squamous cells of undetermined significance (ASCUS), atypical squamous cells, cannot exclude high grade squamous intraepithelial lesion (ASC-H), low grade squamous intraepithelial lesion (LSIL), and high grade squamous intraepithelial lesion (HSIL) were also improved with LBC, indicating higher diagnostic accuracy.

Conclusion: LBC outperforms the conventional Pap smear in cervical cancer screening by providing higher sample adequacy, better detection rates, and greater diagnostic accuracy. Implementing LBC more widely in Georgia could enhance early detection rates and reduce cervical cancer incidence and mortality, particularly in high-risk populations. These findings support the adoption of LBC as a superior screening method in clinical practice.

1 | Introduction

Cervical cancer poses a significant health challenge worldwide, particularly in developing countries where it remains a leading cause of cancer-related deaths among women. In Georgia, cervical cancer is the fifth most frequent cancer among women overall and the third most frequent among women aged 15–44 years [1]. The country has approximately 1.60 million women aged 15 years and older who are at risk of developing cervical cancer. Annually, about 327 women are diagnosed with cervical cancer, and 204 succumb to the disease [1].

Screening for cervical cancer is a crucial preventive measure that significantly reduces both incidence and mortality rates [2]. The conventional Pap smear has been the cornerstone of cervical cancer screening for decades [3]. However, its limitations in sensitivity and sample adequacy have prompted the development of liquid-based cytology (LBC) as a more effective alternative [4]. LBC was introduced to address these limitations and improve the detection rates of cervical abnormalities [5].

The prevalence of high-risk Human Papillomavirus (HPV) types, particularly HPV 16 and 18, which are responsible for 69.2% of invasive cervical cancers in Georgia, further underscores the need for effective screening methods [1]. Given that approximately 1.1% of women in the general population harbor cervical HPV-16/18 infections at any given time, enhanced screening methods are critical for early detection and intervention [1].

This study aims to compare the efficacy of LBC with the conventional Pap smear in a large sample from a tertiary care center in Georgia, focusing on sensitivity, specificity, and sample adequacy. By examining these parameters, the study seeks to provide comprehensive insights into the effectiveness of both screening methods.

2 | Materials and Methods

This study was conducted in Georgia, analyzing 1000 cervical cytology samples from women aged 18–65 years who were gynecologically asymptomatic and not vaccinated for HPV between April 14, 2019, and December 14, 2019. The median age of the screened group was 37 years. Exclusion criteria included pregnancy, postpartum period, sexual inactivity, history of hysterectomy, and prior treatment for cervical intraepithelial neoplasia (CIN) or cervical cancer. Detailed medical histories and symptoms were meticulously recorded for each participant, although HPV status was not routinely available due to limited access of the Georgian population to molecular testing. Samples were collected using an Ayers spatula for the conventional Pap smear and a cervex brush for LBC. The samples were processed and stained using the Papanicolaou method [6], and results were reported based on the Bethesda 2001 System [7] terminology.

To assess the diagnostic accuracy, 64 patients with abnormal cytology findings on conventional Pap smear (categorized as ASC-H, LSIL, or HSIL) underwent cervical biopsy. Among these

64 cases, only 25 also had corresponding abnormal cytology detected by LBC, while 39 cases were abnormal by conventional Pap smear alone. Biopsy results served as the reference standard for evaluating the concordance and diagnostic performance of each method.

The statistical analysis of this study involved a comparison of LBC and the conventional Pap smear using chi-square tests to evaluate the significance of differences between the two methods. Ethical clearance was secured from the Bioethics International Committee of the Petre Shotadze Tbilisi Medical Academy (identification code: 20042019/2, Tbilisi, Georgia). All procedures adhered to the Helsinki Declaration of 1975, revised in 2013, with participants receiving comprehensive study information and providing written informed consent before inclusion.

3 | Results

The results presented a clear picture of the differences between the two screening methods (Table 1).

The statistical analysis, using chi-square tests, revealed significant improvements with LBC (Table 2).

To assess the diagnostic accuracy of the two cytological methods, cervical biopsies were performed in 64 women who exhibited abnormal cytological findings on the conventional Pap smear, categorized as ASC-H, LSIL, and HSIL. Among these 64 patients, only 25 also had abnormal cytology detected through LBC, while the remaining 39 cases appeared normal on LBC but abnormal on conventional cytology. Biopsy results revealed that in the 25 cases where both LBC and conventional Pap smear detected abnormalities, 23 were confirmed as true positives through histopathological examination, reflecting a 92% concordance with biopsy. In contrast, among the 39 patients with abnormal Pap smear findings only, 32 were confirmed histologically, resulting in an 82.1% concordance rate for conventional Pap smear alone in the discordant group. When focusing specifically on HSIL cases, both this diagnose cases detected by LBC were biopsy-confirmed, demonstrating 100% concordance. For conventional Pap smear, 22 cases were classified as HSIL, and 16 of these were confirmed histologically, yielding a 72.7% confirmation rate.

4 | Discussion

The results from this study strongly suggest that LBC outperforms the conventional Pap smear in several key areas [4]. One of the most striking advantages of LBC is the reduced rate of unsatisfactory smears [5]. In our study, the unsatisfactory rate for conventional Pap smears was 7.33%, compared to only 1.33% for LBC. This reduction aligns with findings from previous studies, which have similarly reported that LBC improves sample adequacy [8–10]. The clear background and even distribution of cellular material in LBC samples contribute significantly to its higher diagnostic accuracy [11]. Additionally, LBC samples take less time to screen and allow for HPV testing

TABLE 1 | Cytology findings.

Category	Conventional pap smear		Liquid-based cytology	
	(n = 1000)	Percentage (%)	(n = 1000)	Percentage (%)
NILM (negative for intraepithelial lesion or malignancy)	803	80.3	894	89.4
ASCUS (atypical squamous cells of undetermined significance)	125	12.5	79	7.9
ASC-H (atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion)	24	2.4	17	1.7
LSIL (low-grade squamous intraepithelial lesion)	18	1.8	6	0.6
HSIL (high-grade squamous intraepithelial lesion)	22	2.2	2	0.2
AGC (atypical glandular cells)	8	0.8	3	0.3

on residual samples, making this method not only more efficient but also more comprehensive [12]. These factors make LBC a superior tool for cervical cancer screening, particularly in settings where early detection is paramount.

The adequacy of samples collected using LBC was significantly higher than those collected using the conventional Pap smear [13]. This improved adequacy not only enhances diagnostic accuracy but also reduces the need for repeat testing, which can be stressful for patients and costly for healthcare systems. The detection rates of epithelial abnormalities were higher with LBC. LBC's ability to detect a higher percentage of NILM cases compared to the conventional Pap smear underscores its superior sensitivity [4, 14–17]. This is crucial for early identification of premalignant and malignant lesions, which can significantly improve patient outcomes.

The diagnostic differences observed between conventional Pap smear and LBC may be influenced by multiple factors, including age-related epithelial changes, hormonal status, and sampling technique [4]. In our study, although cytological results were not stratified by age, a trend was observed in which younger women (aged 18–35) were more frequently categorized as NILM, while abnormalities such as ASCUS and LSIL were more common in the 36–50 age group. These differences may be explained by transformation zone accessibility in younger patients, atrophic cellular changes in perimenopausal women [18], or sampling variability inherent in conventional smear collection. Moreover, LBC's superior cellular preservation and clearer background may enhance interpretation, particularly in borderline or age-sensitive lesions [19].

The biopsy data provided essential insight into the comparative diagnostic accuracy of LBC and the conventional Pap smear. The results demonstrated that when both cytological methods identified abnormalities, the likelihood of histopathological confirmation was markedly high. Specifically, the 92% concordance rate in these dual-positive cases affirms that LBC, when abnormal findings are present, strongly correlates with true pathological changes. In contrast, cases where only the conventional Pap smear suggested cytological abnormalities showed a lower concordance rate with biopsy findings (82.1%), indicating a tendency toward overcalling or detecting borderline lesions not consistently verified histologically [20]. This is particularly relevant in the context of ASCUS and LSIL, where interobserver variability and sampling affects may lead to inconsistent interpretations. Importantly, the 100% biopsy confirmation of HSIL cases detected by LBC underscores its higher specificity, especially in identifying clinically significant, high-grade lesions [21]. By comparison, HSIL cases identified by the conventional Pap smear showed a 72.7% confirmation rate, suggesting a higher potential for false positives. These findings support the growing evidence that LBC enhances diagnostic precision by minimizing sample inadequacy, improving cellular preservation, and providing clearer smear backgrounds. It reduces the likelihood of false-positive results and ensures that significant lesions are accurately flagged for further evaluation [22]. In resource-limited settings such as Georgia, where HPV testing is not yet widespread, the use of LBC can improve the balance between early detection and overdiagnosis, ultimately enhancing the effectiveness and efficiency of national cervical cancer screening

TABLE 2 | Statistical significance.

Category	Conventional pap smear (%)	LBC (%)	p value
Unsatisfactory smears	7.33	1.33	< 0.001
Detection of NILM	80.3	89.4	< 0.001
Detection of ASCUS	12.5	7.9	< 0.01
Detection of HSIL	2.2	0.2	< 0.01

programs. Many high-income countries have transitioned from cytology-based screening to primary HPV testing [23], owing to its higher sensitivity and ability to detect persistent high-risk infections before morphological changes appear. In countries such as the Netherlands, Australia, and the UK, Pap smear testing has been phased out or significantly downscaled as part of national programs. However, in Georgia, the healthcare system continues to rely on cytology, predominantly conventional Pap smears, as the primary method for cervical cancer screening. This reliance stems from economic constraints, infrastructure limitations, and a lack of universal access to HPV DNA testing. While the Pap smear has historically played a pivotal role in reducing cervical cancer incidence, its limitations in sensitivity, reproducibility, and sample adequacy are well recognized [24]. In this context, transitioning from conventional Pap smear to LBC represents a practical and impactful intermediate step [3, 4]. LBC not only enhances diagnostic accuracy, as demonstrated in this study, but also allows for HPV triage testing from residual material when resources permit. This is particularly relevant in Georgia, where opportunistic screening rather than organized population-based programs is the norm. Implementing LBC as the standard method could bridge the gap between existing practice and future integration of molecular testing, ultimately contributing to better cervical cancer prevention outcomes.

5 | Conclusion

In conclusion, LBC has demonstrated superior performance in cervical cancer screening compared to the conventional Pap smear. LBC offers higher rates of satisfactory smears, better detection of NILM, and greater overall diagnostic accuracy. Implementing LBC more widely could improve early detection rates and reduce cervical cancer incidence and mortality, particularly in high-risk populations.

Author Contributions

Kldiashvili Ekaterina: conceptualization, investigation, writing – original draft, writing – review and editing, supervision. **Khuntsaria Irakli:** investigation, formal analysis. **Kekelia Elene:** investigation, formal analysis. **Mamiseishvili Ana:** investigation, formal analysis. **Abuladze Mariam:** investigation, formal analysis.

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Ethics Statement

Ethical clearance was secured from the Bioethics International Committee of the Petre Shotadze Tbilisi Medical Academy (identification code: 20042019/2, Tbilisi, Georgia). All procedures adhered to the Helsinki Declaration of 1975, revised in 2013, with participants receiving comprehensive study information and providing written informed consent before inclusion.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data sets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Transparency Statement

The lead author, Kldiashvili Ekaterina, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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