

Liquid Based Cytology Cervical Cancer Screening Program – Georgian Experience

Sophio Bojgva¹ and Ekaterina Kldiashvili²

¹New Vision University, Tbilisi, Georgia

²Georgian Telemedicine Union (Association), Tbilisi, Georgia

Corresponding author: Ekaterina Kldiashvili, Ph.D., Executive Director, Georgian Telemedicine Union (Association) 75 Kostava str., 0171 Tbilisi, Georgia, Tel: 95599957328; E-mail: ekldiashvili@gmail.com

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Abstract

Objective: The study aimed to evaluate liquid based cytology as a tool for cervical cancer screening in Georgia.

Materials and methods: 1293 cervical cytology samples have been analyzed in Georgia. The samples had been collected and processed by the usage of materials and equipment provided by Hologic. Prepared smears were post-fixed in 96% ethanol and stained accordingly with Papanicolaou protocol. The Bethesda 2001 system terminology was employed for reporting and diagnoses of cervical smears.

Results: The negative for intraepithelial lesion or malignancy (NILM) category was equal to 1156 cases (89.40%). Other categories in decreasing order were atypical squamous cells of undetermined significance (ASCUS) with 104 cases (8.04%), low grade squamous intraepithelial lesion (L-SIL) with 8 cases (0.62%), high grade squamous intraepithelial lesion (H-SIL) with 1 cases (0.08%), atypical squamous cells, cannot exclude high grade intraepithelial lesion (ASC-H) with 21 case (1.63%) and atypical glandular cells of undetermined significance (AGUS) with 3 case (0.23%). Cellularity was lower in liquid based cytology (LBC) as compared with conventional smears (CS). Also, nuclear overlap was significantly less observed compared to CS. The smear background was notably cleaner and cell morphology was better evaluated in LBC. In terms of *Trichomonas* and *Candida* detection, LBC was superior compared to CS. Doderlein lactobacilli were seen in significantly lesser amounts and were mainly situated in close vicinity to the squamous epithelial cells. Due to lack of pretreatment, the degree of inflammation was better assessed in CS.

Conclusion: Our experience shows that LBC is superior to CS in the evaluation of cell morphology and detection of certain microorganisms such as *Trichomonas* and *Candida*. The degree of inflammation is better assessed with CS.

Keywords: Liquid based cytology; Conventional smear; Cervical cancer; Papanicolaou

Introduction

Cervical cancer is the severe health care problem. According with global statistics, cervical cancer is on the second place by the frequency and on the third by mortality among the cancers of reproductive system [1–3]. 527,000 newly diagnosed cases of cervical cancer and 265,000 deaths due to this health care problem were recorded in 2012 by World Health Organization. Most part (85%) of cervical cancer incidence and mortality occurred in developing countries [2], those are characterized by the absence of ineffective and irregular screening programs [2,3]. The cytological screening is the main screening approach for cervical cancer [2,3]. The Papanicolaou stained conventional smear can be used for cervical cancer screening purposes, but some authors [2] complained on low diagnostical sensitivity because of false positive and false negative results. The amount of false-negatives varies from 2% to 50% [1,4–6]. In a meta-analysis study [7] the sensitivity of cervical cancer screening performed by application of conventional smear was declared as 58% (range 11% to 99%), with a specificity of 68% (range 14% to 97%).

Liquid-Based Cytology (LBC) method has been applied by Cytic Corporation (USA) for cervical cytology smears obtaining and collection in the 1990s. The method has been approved by the United States Food and Drug Administration in 1996 and introduced for cervical cancer screening as an alternative of the conventional smear. LBC method enables suspension of the cells in liquid medium and preparation of cellular monolayer [8-15]. Nowadays two methodologies and solutions of LBC are widely available: ThinPrep (Hologic, Marlborough, MA, USA) and BD SurePath (BD Diagnostics – TriPath, Burlington, NC, USA).

LBC is characterized by the improved sensitivity and specificity in comparison with conventional smear. The method is ensuring the better fixation and excellent preservation of nuclear details. Atypical cells are obvious; they aren't obscured by another cells or background. Furthermore, LBC method is characterized by the low rate of unsatisfactory

samples. The application of LBC for cervical cancer screening in countries with middle and low income is limited due to the financial restrictions, conventional smear is still the basic method of cervical cancer screening in developing world [16].

As it was the case that LBC method by usage of ThinPrep was introduced in Georgia, the aims of this study were to evaluate the feasibility of ThinPrep as a methodology in terms of ease of installation, procedure, interpretation and cost.

Materials and Methods

1293 cervical cytology samples have been analyzed in Georgia. The samples had been collected and processed by the usage of materials and equipment provided by Hologic. Prepared smears were post-fixed in 96% ethanol and stained accordingly with Papanicolaou protocol. The Bethesda 2001 system terminology was employed for reporting and diagnoses of cervical smears. Cervical smears were taken in the West Georgia, but they were diagnosed in the capital, Tbilisi. The samples have been transported by express post every two weeks from the region to the capital. The collected samples were stored at room temperature. The smears were prepared in the laboratory located in the capital, Tbilisi. Prepared

smears were post-fixed in 96% ethanol and stained accordingly with Papanicolaou protocol. The Bethesda 2001 system terminology was employed for reporting and diagnoses of cervical smears. Informed consent has been obtained for all cytology smears.

Results

One thousand two hundred ninety three cases were analyzed in our study. All cases were the cellular monolayer; nuclei overlap has not been seen. 1156 cases (89.40%) were reported as the negative for intraepithelial lesion or malignancy (NILM), atypical epithelial cells were seen in 134 (10.37%) cases, and glandular cell atypia was reported in 3 (0.23%) cases (**Table 1**). Among cases with reported abnormal cervical cytology the following reports were written: atypical squamous cells of undetermined significance (ASC-US) - 104 cases (77.61%); atypical squamous cells, cannot exclude high grade squamous intraepithelial lesion (ASC-H) - 21 cases (15.67%); low grade squamous intraepithelial lesion (LSIL) - 8 cases (5.97%); high grade squamous intraepithelial lesion (HSIL) - 1 case (0.75%). These results are given in **Table 2**.

Table 1 Negative for intraepithelial lesion or malignancy (NILM), atypical epithelial cells were seen in 134 (10.37%) cases, and glandular cell atypia was reported in 3 (0.23%) cases.

Category/ Number of Cases	Negative for intraepithelial lesion or malignancy	Atypical epithelial cells	Glandular cell atypia
Totally – 1293 cases (%)	1156 (89.4%)	134 (10.37%)	3 (15.53%)

Table 2 Atypical squamous cells of undetermined significance.

Category/ Number of Cases	ASCUS	ASC-H	LSIL	HSIL
Totally – 134 cases (%)	104 (77.61%)	21 (15.67%)	8 (5.97%)	1 (0.75%)

Discussion

The article presents a result of LBC based cervical cancer screening pilot study in Georgia. One thousand two hundred ninety three cases were analyzed in this study. It is obvious that LBC is effective and appropriate method for cervical cancer screening. Furthermore, the pilot study aimed standardization of reporting of cervical cancer screening results. Cancer is a top priority health care issue in Georgia. Cervical, breast, colorectal and prostate cancer screening programs are available in the country, but due to some psychosocial factors, limitations and barriers patients are attending the office of medical doctor only in the case of urgent necessity. As a result, more than half of all cancer cases are diagnosed in the late stages. It has been revealed, that different classification systems (e.g., the Bethesda System

2001, Papanicolaou, Cervical Intraepithelial Neoplasia - CIN) are used in Georgia to communicate results of cytology tests. This is the most important factor of misunderstanding in the chain of medical service. It is obvious, that the cytology screening of cervical cancer is the effective screening test utilized in health care. It can be realized by application of conventional smear, or through application of LBC technology depending on the budget.

Conclusion

It has been concluded that the LBC based cervical cancer screening is more comfortable than conventional smear based one. Monolayer smears are easier for interpretation; cells with atypia are not obscured by other of cells or background (inflammation, blood and etc.). Furthermore, the amount of

unsatisfactory for interpretation smears is minimal; in the frames of our pilot we have not unsatisfactory samples. However, for LBC test to be effective, three things must occur:

1. Sampling should be adequate and proper.
2. Sample processing, review and reporting should be proper and standardized.
3. Reporting terminology should be standard and understandable for the clinician.

Regarding terminology it should be emphasized, that the most informative and adequate is the Bethesda 2001 System (TBS) [16]. This is a comprehensive way to report cytological peculiarities of the cervix by a simple diagnostic terms and the possibility to incorporate a descriptive diagnosis and evaluation of specimen adequacy [17,18].

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