



Research article

Liquid Based Cytology Cervical Cancer Screening Program—Georgian Experience

Ekaterina Kldiashvili ^{1,*} and Sophio Bojgua ²

¹ Georgian Telemedicine Union (Association), Kostava str., 0171, Tbilisi, Georgia;

² New Vision University, Mikeladze str., 0159, Tbilisi, Georgia

* **Correspondence:** ekldiashvili@yahoo.com; Tel: +995-599-957328; Fax: +995-32-244-5542.

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 Papanicolau 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 case (0.08%), atypical squamous cells, cannot exclude high grade intraepithelial lesion (ASC-H) with 21 cases (1.63%) and atypical glandular cells of undetermined significance (AGUS) with 3 cases (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

1. 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 or 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% [1,4–12]. In a meta-analysis study [13] the sensitivity of cervical cancer screening performed by application of conventional smear was declared as 58% (range 11%–99%), with a specificity of 68% (range 14%–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 [14–17]. 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 [18–21].

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.

2. Materials and Method

One thousand two hundred ninety three cervical cytology samples have been analyzed in Georgia. These were 18–65 years old non-vaccinated for human papillomavirus (HPV), gynecologically asymptomatic females. The median age of screened group was 37 years. Specific inclusion criteria has not been used for patients recruitment. Informed consent has been obtained for all cytology smears. All smears were taken by usage of the ThinPrep reagents (Hologic). The cervical smear was obtained by rover cervical brushes and washed in sampling solution ThinPrep (Hologic). One package of sampling materials (cervical brush and vial with sampling solution ThinPrep) has been used per patient. After obtaining and before laboratory processing the samples were stored at room temperature. The delay time between obtaining of samples and their laboratory processing did not exceed 2 hours. The smears have been prepared on glass slides by the application of the ThinPrep 2000 Processor (Hologic) accordingly with the provided for gynecology samples instructions, the program #4 of the processor has been used. One glass slide has been prepared for each screened patient. Prepared wet smears have been fixed in absolute alcohol during 30 min and stained accordingly with Papanicolau staining protocol (<http://www.nottingham.ac.uk/pathology/protocols/papcytol.html>). The Bethesda 2001 System terminology (<http://nih/techrivier.net/bethesdaTable.php>) has been used for reporting of cervical smears. The average time required for processing and reporting of the sample was 4 hours (92.7% of cases). The Papanicolau stained smears were evaluated by light microscopy (Konus 5601-Biorex-2) under $\times 4$, $\times 10$, $\times 40$ and $\times 100$ objective lens. The stained smears have been archived accordingly with requirements to medical data storage and documentation specific to country of Georgia.

3. 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.

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

Table 2.

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

4. 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 psycho-social 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, Papanicolau, 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. 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 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) [22]. This is a comprehensive way to report cytologic peculiarities of the cervix by a simple diagnostic terms and the possibility to incorporate a descriptive diagnosis and evaluation of specimen adequacy [18–21].

Acknowledgments

The study has been performed during implementation of the project ‘Cervical Cancer Screening Using Telemedicine Resources in Georgia’ (#007G). This project was supported by 700 for Science and Hologic.

Conflict of Interest

There were no competing interests interfering with the unbiased conduction of this study.

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