



# The Usefulness of Papanicolaou Test in the Cytomorphological Evaluation of Squamous Cell Abnormalities of the Cervix

BRIEF  
REPORT

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ABSTRACT

Papanicolaou or Pap test as a screening method is a suitable method in the prevention of cervical cancer. The aim of the present study was to detect the prevalence of various cervical cytology results in the squamous epithelial tissue of the endocervix and endometrium in women, aged 18–70 years, according to the 2014 Bethesda system. This was a hospital-based cross-sectional study conducted on 16,790 Pap smears prepared from women aged 18–70 years between January 2017 and December 2017. The evaluation of the results is hospital based and not the whole country. Diagnosis of atypical squamous cells of undetermined significance was made in 72 (12%) cases. Atypical squamous cells as a HSIL was seen in 36 (6%) cases, human papillomavirus infection in 26 (4%) cases, low-grade squamous intraepithelial lesion as a CIN 1 in 27 (5%) cases and as a CIN 2 in 13 (2%) cases, and high-grade squamous intraepithelial lesion (HGSIL or HSIL) or CIN 3 in 5 (1%) cases. The prevalence of various epithelial abnormalities as glandular epithelial cell abnormalities was determined in 20% of women (119 cases), and it was 50% (298 cases) in other abnormalities. According to these results (high prevalence of epithelial cell abnormalities in cervical smears due to I–XII), Pap test as a screening method should begin at the age of 18 years. This screening test can detect abnormal cervical cells before they turn into malignant neoplasm or can be used as a good screening method to detect the earliest signs of carcinogenesis.

**Keywords:** Cervix, Papanicolaou test, LSIL, HSIL, epithelial abnormalities

## INTRODUCTION

According to the increase of incidence of malignant diseases, early diagnosis, therapy, and treatment are the most important. Analyzing the cells and their ratio is particularly important for determining and approving the physiological or pathophysiological mechanisms. Cytodiagnostics as a method is based on the analysis of the cell size, diameter, cytoplasm content, nuclear size, cell membrane construction, fixation of the material staining, and their ratio (1).

The aim of cytology and their used principles and methods is to observe the normal or modified processes that occur at cell level (1). The use of these principles and methods makes it possible to accurately determine all the changes of the cells. By using suitable high-quality appliances and reagents, proper staining, and advanced microscopy, cell analysis can be performed. For this purpose, it is necessary to prepare the slides to be monitored correctly and efficiently. The microscopic preparation itself is prepared in an appropriate manner according to certain confirmed protocols. The cytology can be exfoliative and aspirational (2, 3). Aspiration cytology uses aspirate, the cells for analysis are obtained with puncture using a fine needle, and based on the negative pressure generated during the procedure, the cells are injected from the tissue in which they are located (2). Exfoliative cytology as a part of clinical cytology uses the cells that are desquamated from body surfaces especially the cells from different layers of epithelial tissues. For that purpose, the cells are microscopically examined (their morphology, structure, dimensions, and staining), and different changes or malignancy in the cells is detected or confirmed by the presence of abnormal or atypical cells as a result of some infection, inflammation, or parasitic infestations. Exfoliative cytology uses simple, quick and non-invasive techniques and collects the material from the mouth, urine, sputum, abdominal, pleural, or peritoneal fluid, and vaginal secretion (3). In contrast to the cells in exfoliative cytology, the cells in aspiration cytology have preserved morphology and structure, and in this context, changes are more easily visualized and confirmed (2).

Cytological techniques are fast, simple, and cheap, and they are acceptable from the patients. Papanicolaou or Pap smears as a material are prepared in the procedure as a mechanical exfoliation, when the cells are scraped from the cervix with a spatula (4). Papanicolaou test (abbreviated as Pap test) as a method is very useful for the early detection of cervical cancer. This test was named after George Papanicolaou (1883–1962), an American scientist and academic teacher with Greek origin. Pap test examines the possible changes in cervical

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**Table 1.** Categorization of cases according to the results of cervical cytology using a PAP test from January (I) to December (XII)

	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	SUM
Negative	520	1155	1150	1138	1213	1087	1208	1255	1660	2054	2255	1499	16194 (96%)
Positive													596 (4%)
ASC-US	11	4	4	5	8	8	6	5	5	9	5	2	72 (12%)
ASC-H	1	1	1	1	9	5	2	5	1	3	5	2	36 (6%)
HPV	1	4	0	3	3	1	2	3	2	0	1	6	26 (4%)
CIN 1 (LGSIL)	1	3	1	5	4	1	0	1	2	4	4	1	27 (5%)
CIN 2 (LGSIL)	1	1	2	0	0	0	1	2	0	0	3	3	13 (2%)
CIN 3 (HGSIL)	0	3	0	0	0	0	0	0	1	1	0	0	5 (1%)
AGC	11	8	3	9	22	25	6	24	8	2	0	1	119 (20%)
Abnormalities	26	24	11	23	46	40	17	40	19	19	18	15	298 (50%)
SUM													16790

PAP: Papanicolaou test (abbreviated as Pap test); ASC-US: Atypical squamous cells of undetermined significance; ASC-H: Atypical squamous cells cannot rule out high-grade squamous intra-epithelial lesion; HPV: Human papillomavirus; CIN: Cervical intraepithelial neoplasia; LGSIL: Low-grade squamous intraepithelial lesion; HGSIL: High-grade squamous intraepithelial lesion; AGC: Atypical glandular cells; SUM: Summation/ in mathematics

cells. The Pap test may indicate whether there is infection in abnormal cervical cells or detect the earliest signs of carcinogenesis. In addition, Pap smear can detect infections and evaluate a visible lesion or abnormal cervical cells that can later alter into malignant cells (4, 5). Treatment of infections and precancerous conditions of the cervix can prevent the development of cancer. According to the 2018 data, current estimates indicate that 151 women are diagnosed with cervical cancer, and 59 die from the disease annually. Cervical cancer ranks as the sixth most frequent cancer among women in Macedonia and the third most frequent cancer among women between 15 and 44 years old (6). Visiting a gynecologist should be approximately 10–20 days after the first day of the menstrual cycle. At least 2 days before visiting a gynecologist or before performing the test, women should not use vaginal creams, medications, tampons, powders, or deodorants, have sex, or douche. The examination is painless, but for some women, it is an unpleasant experience. The gynecologist, with a brush or spatula, collects the cells from the cervix, and a sample material (smear) is spread thinly on a microscope slide and sent to a cytological laboratory for testing. PAP test as a technique is a part of liquid-based cytology (4). The stain in this technique passes through various modifications, from conventional Pap methods to rapid and modern technique with only an intention to reduce the time taken for staining (7, 8). In R. Macedonia, Pap test as a screening method is performed on women around 18 years old until the age of 70 years old. The aim of the test is to detect precancerous or cancerous cells or other abnormal, atypical cells in the squamous epithelial tissue of the endocervix and endometrium caused by human papillomavirus (HPV, a sexually transmitted disease), bacterial infection, or parasitic infestations. According to the 2014 Bethesda system (9), interpretations of the results can be as follows:

- Negative for intraepithelial lesion or malignancy,
- Positive for epithelial cell abnormalities (squamous cell or glandular),
- Other malignant neoplasms.

The aim of the present study was to detect the prevalence of various precancerous or cancerous cells or other abnormal, atypical cells in the squamous epithelial tissue of the endocervix and endometrium in women in Macedonia, aged 18–70 years, according to the 2014 Bethesda system.

## MATERIALS and METHODS

All participants were informed of the nature and purpose of the research. Only those participants who provided consent are included in the study. The study was approved by the ethics committee of the Faculty of Medical Sciences (12/20/2017, case no. 2002-288/27) in accordance with the Declaration of Helsinki and with the principles of good clinical practice.

This was a hospital-based cross-sectional study conducted on 16,790 Pap smears, prepared from women in Macedonia aged 18–70 years, at the Clinic for Gynecology and Obstetrics in Skopje, between January 2017 and December (I–XII) 2017 (Table 1). The most common infections of the patients are infections with *Trichomonas vaginalis*, *Gardnerella vaginalis*, and *Candida albicans*. Abnormal results are reported according to the 2014 Bethesda system (8, 9), and they include negative results for intraepithelial lesion and positive results for squamous cell abnormalities, evaluated as atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells as a HSIL (ASC-H), low-grade squamous intraepithelial lesion (LGSIL or LSIL), high-grade squamous intraepithelial lesion (HGSIL or HSIL), and squamous cell carcinoma glandular epithelial cell abnormalities (AGC).

The basic morphological criteria in which the degree of lesion is diagnosed are differentiation of the cells, the degree of maturation, and stratification of the epithelium, nuclear morphology, and mitotic activity (7, 8, 9). According to the 2014 Bethesda system (9), we detect atypical epithelial cells dissimilar with other cells, but without dyskaryosis. These cells were contained within group in the ASC-US, and they are the most important because they can be followed by the development of malignant tumor cells (8, 9).

## RESULTS

The evaluation of the results is hospital based and not the whole country. In the present study, 16,790 PAP smears were examined in our cytology lab. Of the 16,790 PAP smears, 96% were negative. The age range of the patients was 18–70 years. The mean age was  $26.5 \pm 10.73$  years. The majority of cases were in the age group of 30–39 years (35.25%). The mean age of patients with LSIL was  $25.8 \pm 15.2$  years. The youngest patient was 18 years. Cervical cancer has been diagnosed in women under the age of 35 years. Categorization of cases according to the results of cervical cytology using a Pap test is confirmed in Table 1. ASC-US was diagnosed in 72 (12%) cases. ASC-H was seen in 36 (6%) cases, HPV infection in 26 (4%) cases, LGSIL or LSIL as a CIN 1 in 27 (5%) cases and as a CIN 2 in 13 (2%) cases, and HGSIL or HSIL as a CIN 3 in 5 (1%) cases. The prevalence of various epithelial abnormalities as AGC was determined in 20% of women (119 cases), and it was 50% (298 cases) in other abnormalities.

## CONCLUSIONS

The present study observed a high prevalence of epithelial cell abnormalities in cervical smears in our set-up. Pap smear examination is widely accepted as a screening method in countries such as Macedonia, where the population is predominantly rural with low socioeconomic status and poor health outcomes, and where marriage at an early age is common. According to these results (high prevalence of epithelial cell abnormalities in cervical smears due to I–XII), PAP test as a screening method should begin at 18 years old, and this screening test can detect abnormal cervical cells before they turn into malignant neoplasm or can be used as a good screening method to detect the earliest signs of carcinogenesis. Treating these atypical or abnormal cells in the endocervix and endometrium can prevent carcinogenesis and most cases of cervical cancer. By implementing and introducing PAP test as a cytological screening method in women between 18 and 70 years, it can significantly reduce the risk and incidence of cervical cancer.

**Ethics Committee Approval:** The study was approved by the ethics committee of the Faculty of Medical Sciences (12/20/2017, case no. 2002-288/27) in accordance with the Declaration of Helsinki and with the principles of good clinical practice.

**Informed Consent:** Written informed consent was obtained from participants in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Conceived and designed the experiments or case: LB, NV. Performed the experiments or case: LB. Analyzed the data: LB, NV. Wrote the paper: LB, NV. All authors have read and approved the final manuscript.

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