

## **A comparative analysis of chosen lesions of the uterine cervix in the population of women in Podlasie Province**

Borsuk A.<sup>1\*</sup>, Pryczynicz A.<sup>1</sup>, Niewiarowska K.<sup>1</sup>, Cepowicz D.<sup>2</sup>, Niksa M.<sup>1</sup>, Hawryluk M.<sup>1</sup>, Korniluk A.<sup>1</sup>, Famulski W.<sup>3</sup>

<sup>1</sup> Department of General Pathomorphology, Medical University of Białystok, Poland

<sup>2</sup> 2nd Department of General and Gastroenterological Surgery, Medical University of Białystok, Poland

<sup>3</sup> Department of Medical Pathomorphology, Medical University of Białystok, Poland

### **ABSTRACT**

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**Purpose:** In Poland, cervical screening tests are performed in the group of women aged 25 to 59 years. The aim of the study was to evaluate the usefulness of the Bethesda System in assessing cervical smears.

**Methods:** Results of gynecological cytologies performed in the UPDC in the period of 01 August 2011 – 31 July 2012 were analyzed. Of the material, cases subjected to histopathological analysis in correlation with cytological outcome were chosen.

**Results:** Of 19,887 patients who underwent cytology, 603 had atypical epithelial cells. In 83/603 cases, histopathological specimens were available for analysis.

The level of cytological and histopathological compatibility was the highest in the HSIL group (75%), being the lowest in patients with LSIL (40%). It should be emphasized that in HSIL cases, histological specimens showed no evidence of normality.

**Conclusions:** The level of cytological and histopathological compatibility was the highest in the HSIL group (75%). The compatibility was the lowest in the LSIL group (40%). It should be emphasized that in HSIL cases, histological specimens showed no evidence of normality.

**Key words:** cervical cancer, Bethesda system, cytology

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\*Corresponding author:

Agnieszka Borsuk

Department of General Pathomorphology

Medical University of Białystok,

ul. Waszyngtona 13, 15-269 Białystok, Poland.

Tel/Fax: +48 85 7485996

e-mail: agnieszkaborsuk@wp.pl

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## **INTRODUCTION**

In Poland, cervical cancer remains a most common neoplasia in women. One of the major tests for its early detection is cytology, being indispensable for assessing the clinical condition of the normal and pathological uterine cervix. Over the past 15 years, enormous progress has been made to assess samples obtained from exfoliative cytology of the uterine cervix. Until recently, the Papanicolaou classification system was commonly applied to evaluate cervical smears. However, the diagnostic conclusions gave superficial descriptions of smear cells [1, 2]. In 1988, the cytological classification with a multi-stage assessment according to the Bethesda System was recommended. The protocol is constantly complemented and its latest version functions as the Bethesda System of 2001. The classification consists of 4 basic parts: 1/ assessment of the technical condition of the smear, 2/ general evaluation of the smear for the presence of endothelial pathology, 3/ determination of the types of inflammatory and endothelial lesions, and 4/ indication for further management of a patient. The newer system of gynecological smears takes into consideration a number of non-neoplastic pathological lesions, i.e. inflammatory, repair and hormonal abnormalities [3, 4].

The above classification introduces a two-stage division in squamous intraepithelial lesions: 1/ LSIL (low grade squamous intraepithelial lesion), a low-grade HPV-related pathology and/or corresponding to CIN I, and 2/ HSIL (high grade squamous intraepithelial lesion (CIN II/CIN III) [5,6].

There are two categories of ambiguous pathological lesions, namely ASCUS (atypical squamous cells of undetermined significance) and AGUS (atypical glandular cells of undetermined significance). In 2001, The Bethesda system was slightly modified: the ASCUS lesions were divided into atypical squamous cells of undetermined significance (ASC-US) and those that cannot exclude high-grade SIL (HSIL ASC-H) [6]. In the Bethesda System cervical smears are stained using the Papanicolaou technique. The above method distinctly stains the cell nucleus, chromatin and nucleoli, and allows distinction between malignant and benign cells. Also fungi and bacteria are stained [7].

A detailed description of a smear allows monitoring of the course of pathophysiological conditions of the uterine cervix, comparative assessment of its lesions and cytological control of the therapy.

The aim of the study was to compare abnormal cytological findings in specimens from

the uterine cervix with histopathological tests in the same patients.

## **MATERIALS AND METHODS**

Cytological smears of the uterine cervix diagnosed from 01 August 2011 to 31 July 2012 in the University Pathomorphology Diagnostic Centre (UPDC) in Białystok were assessed. A total of 19,887 cytological smears were analyzed. In all the study cases, the Papanicolaou staining procedure was used, followed by the Bethesda System. Abnormal epithelial cells were found in 603 cases. However, the exfoliative cytology findings were confirmed histopathologically only in 83 cases, which were further investigated.

The research method involved the analysis of histopathological documentation of individual cases applied to determine the correlation between cytological and histopathological outcome. The study was approved by the Bioethics Committee, Medical University of Białystok.

## **RESULTS**

In 2010, 686 499 cytological smears were performed in Poland [8]. In Podlasie Province, 28 608 women were examined, accounting for only 29% of the annual population covered by the screening program. The figure is highly unsatisfactory, since all women aged 25-59 were personally invited. As this type of action was undertaken for the first time in the last 50 years, it is still believed to improve women's attendance rates. Cytology-positive cases accounted for 3.2% of all the smears analyzed in UPDC in the study period. A small number of abnormal cytological results may suggest that it is still the "healthy" part of the population attending prophylactic examinations whereas women who can be potentially affected seem to ignore the screening program. Improved awareness and knowledge among the population can promote participation in prophylactic examinations.

Abnormal epithelial cells were found in 603 cases, accounting for 3.2% of the study population (Tab.1). The lesions were found to affect squamous cells (586 cases) and glandular cells (17 cases). The study group included 415 diagnosed cases of ASCUS, 118 LSIL, 37 ASC-H, 15 HSIL, 1 squamous cell carcinoma and 17 cases of abnormal glandular epithelial cells (AGC).

Of the 603 patients with abnormal cytology, specimens from only 83 patients were sent for histopathological testing. Samples from uterine cervix disc were used for further diagnostic investigations. Correlation was assessed between

cytological and histopathological diagnosis in 83 cases. Among them, 38 cases of ASCUS, 12 cases of ASC-H, 25 cases of LSIL and 8 HSIL were diagnosed.

**Table 1.** Types and number of atypical cytology findings over the study period between 01 August 2011 and 31 July 2012.

DIAGNOSIS ACCORDING TO THE BETHESDA SYSTEM	NUMBER OF PATIENTS N= 603	PERCENTAGE SHARE (%)
ASCUS	415	68.86%
ASC-H	37	6.13%
LSIL	118	19.56%
HSIL	15	2.48%
Cancer	1	0.16%
AGC	17	2.81%
TOTAL	603	100%

Table 2 presents the percentage contribution of the histological results of the specimens collected from patients with cytological diagnosis of ASCUS. The inflammatory lesions and/or erosion accounted for 52.36% of the results, CIN I lesions for 34.22%, CIN II for 7.89%, CIN III for 2.63%, adenocarcinoma for 2.63%. There were 12 patients with ASC-H cytological results. Inflammatory lesions and erosions were predominant (41.68%), CIN I was found in 8.34% of cases, CIN II in 16.66%, CIN III in 16.66%, squamous cell carcinoma and adenocarcinoma in 16.66%. Some authors reject the diagnosis of ASC-H as ambiguous. The cytological finding described as “atypical squamous epithelial cells of

undetermined significance that cannot exclude high-grade lesions” may refer to a viral infection-related pathology or CIN I, CIN II and CIN III [12].

The histopathological results confirmed the ambiguity of ASC-H diagnosis. In 6 cases, the cytological findings had to be verified. The specimens, in which cytological and histopathological findings were different, underwent retrospective assessment (these were ASCUS – adenocarcinoma, ASC-H – inflammatory lesion/erosion). In each of these cases the women were in the perimenopausal age, and the smears showed features of sub-atrophy and extensive inflammation, which hindered proper assessment.

Another group of patients consisted of 25 women with the cytological diagnosis of slight dysplastic endothelial lesions corresponding to CIN I and human papilloma virus infection, the so called LSIL (low grade squamous intraepithelial lesion).

Table 2 presents the numerical contribution of the respective histological findings from specimens obtained from patients with cytological diagnosis of LSIL HPV/CIN1. The inflammatory lesions and/or erosion accounted for 40%, CIN I – 40%, CIN II – 16% and CIN III – 4% of these cases. Eight women had abnormal cytological findings corresponding to high grade dysplastic endothelial lesions (CIN II/CIN III), the so called HSIL (high grade SIL). In 6 women, histopathological investigation revealed CIN III (75%), whereas 2 women (25%) were diagnosed with squamous epithelial cell carcinoma. The analysis of the results showed a very high correlation between cytological and histopathological findings. As many as 75% of CIN III type lesions were detected.

**Table 2.** The percentage and numerical contribution of histopathological findings from samples obtained in cytology.

HISTOPATHOLOGICAL DIAGNOSIS = 83						
CYTOLOGICAL DIAGNOSIS N=83		INFLAMMATION/EROSION	CIN I	CIN II	CIN III	CANCER/ Adenocarcinoma
	ASCUS 38/83	52.63% 20/83	34.22% 13/83	7.89% 3/83	2.63% 1/83	2.63% 1/83
	ASC-H 12/83	41.68% 5/83	8.34% 1/83	16.66% 2/83	16.66% 2/83	16.66% 2/83
	LSIL 25/83	40% 10/83	40% 10/83	16% 4/83	4% 1/83	0% 0/83
	HSIL 8/83	0% 0/83	0% 0/83	0% 0/83	75% 6/83	25% 2/83

## DISCUSSION

Cancer of the uterine cervix is a challenge for doctors. In Poland, each year the number of the reported cases is approximately 13 per 100,000 of the population [9]. The prophylactic measures undertaken to improve the unfavorable situation involve screening programs, such as smear tests allowing early disease detection. Abnormal cytological diagnosis is confirmed and complemented with colposcopy with biopsy and histological investigations. In 2007, a total of 686,623 smears were done, including 27,941 in Podlasie Province as part of the Population Program of Cervical Cancer Early Detection [10]. Until September 2010, a total of 686,499 cervical smears were performed in Poland and 28,608 in Podlasie Province. Despite the cervical cytology campaign encouraging women to take advantage of free Pap smear screening services financed by the National Health Fund by sending personal invitations, no significant increase has been noted in the number of performed cytologies.

In patients with cytological diagnosis of ASCUS, inflammatory lesions and/or erosions constituted the largest group (52.63%), but also other abnormalities were found, including CIN I (34.22%), CIN II (7.89%) and CIN III (2.63%). Similar results have been reported by a study on uterine cervix pathologies in Lubuskie Province [11].

Patients with LSIL (low grade squamous intraepithelial lesion) accounted for 30.12% of the study group. The cytological diagnosis of LSIL in cervical smears was confirmed in 40% of the cases (CIN-I), the other 40% of histological diagnoses were inflammatory lesions and/or erosion. The findings are comparable with those reported by other authors [11]. Endothelial lesions of CIN II and CIN III were confirmed in 16% and 14%, respectively. Importantly, no in situ cancer was seen in any of the cases.

The diagnoses of HSIL accounted for the smallest number of abnormal cytologies (9.66%). The cytological results correlated with histopathological findings of CIN III in 75%. Also other authors have revealed a 76.92% compatibility with HSIL [12]. The remaining 25% referred to epithelial squamous cell carcinoma. Significantly, in no case there was evidence of normality. The 75% cytological and histopathological compatibility is high and comparable with data reported by other authors [13-15].

Discrepancies between the cytological and histological diagnoses are estimated at 2 - 28% [15]. Results are considered incompatible when the diagnoses differ by 2 levels in the sequence of ASCUS – CIN I – CIN II – CIN III – carcinoma. With a more strict discrepancy criterion, i.e. one-level difference as in our study, the compatibility

percentage can be higher. In ASCUS cases (atypical squamous cells), the correlation outcome is similar to those reported by other authors [11]. Inflammatory lesions and/or erosion accounted for 52.63%, CIN I for 34.22%, CIN II for 7.89% and CIN III for 2.63%. Thus, the 40% of histopathologically confirmed LSIL is a satisfactory outcome, whereas the 75% of HSIL cases confirmed in cervical specimens is comparable with literature data.

When histopathological investigations reveal more advanced lesions than those found in smears, cytological specimens need to be verified. If no diagnostic errors are found then smear collection technique should be controlled.

Preliminary cytological findings are highly correlated with final histopathological diagnosis. The success of the screening programme depends on a large number of women benefiting from the program, proper diagnostics and appropriate treatment of uterine cervical lesions.

## CONCLUSIONS

1. The level of cytological and histopathological compatibility was the highest in the HSIL group (75%).
2. The compatibility was the lowest in the LSIL group (40%).
3. It should be emphasized that in HSIL cases, histological specimens showed no evidence of normality.

### Conflicts of interest

The authors declare no conflict of interest.

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