ORIGINAL ARTICLE

Correlation of Cervical Smear and Pathohistological Findings

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ABSTRACT

Introduction: In endeavor to suppress the cervical carcinoma there are several possible approaches including measures of primary and secondary prevention. So far effects of these measures on the number of cases and mortality rate of cervical carcinoma were modest. Only exception is organized testing based on cytological exam of the cervical smear – Pap test, which has proven to be highly effective in reducing the number of cases and mortality of cervical carcinoma in countries with this program. **Goal** of this research is analysis of correlation between abnormal cytological test results and pathohistological diagnosis of all patients in the analyzed period. **Material and methods:** Research is descriptive, analytical, comparative, and partly epidemiological. Results of cytological and pathohistological diagnostic in the period between January 1, 2009 and December 31, 2011 were used for analysis. All analyzed patients had colposcopy exam and Pap test, and patients with abnormal results of this test underwent cervical biopsy for pathohistological diagnostics. **Results:** We came to following results and conclusions: total number of L-SIL and H-SIL (PAPA III) results was 395 (6.20%) in comparison to total sample of 5894 (92.44%) patients. There is a statistically significant difference in relation to PHD result of cervical biopsy after L-SIL and H-SIL (PAPA II and IV), and highest statistical margin is in relation of CIN II changes to cytological findings, issued at Clinic of Obstetrics and Gynecology and other health institutions. We come to conclusion that the highest percentage of patients with L-SIL and H-SIL findings is in age group between 0-29 years old. Statistical analysis has shown a positive trend in number of younger patients with L-SIL and H-SIL (PAPA III and IV), with average age of patients in 2011 being 31.12±9.12 years old.

Key words: Pap test, biopsy.

1. INTRODUCTION

Cytological methods are applied starting from the mid-19th century, when the researchers found abnormal cells in body fluids such as urine, sputum, exudates and gastric fluid.

Papanicolaou (1928) in New York announced the era of modern diagnostic cytology, when he published an article titled "A new diagnosis of cancer". Despite skepticism at the beginning of cytopathological era, the use of this method that is popularly known as "Pap" test is accepted as the most appropriate screening test for early detection of cancer and precancerous states of uterine cancer (1).

Exfoliative cytology analyzes spontaneously exfoliated cells from the skin, mucous and serous membranes. Cytodiagnostics of the vaginal-cervical-endocervical (VCE) smear by volume is the largest in exfoliative cytology, since it covers both the healthy and sick women. The smears include epithelial and non epithelial cells (2,3). In the universal effort for combating cervical cancer are available several possible approaches, including measures of primary and secondary prevention. So far, most of the effects of these measures on the incidence and mortality of cervical cancer were modest. The only exception seems to represents organized screening based on the use of cytological examinations of the cervix (Pap test), which proved to be highly effective in reducing the incidence and mortality of cervical cancer in countries where it is implemented. Reduction of mortality caused by cervical cancer in the United States and other developed countries is significant, and this is due to the successful early diagnosis. Squamous intraepithelial lesions are detected in adolescents, young adults and adults. The peak incidence is at the age of about 30 years. Similarly, invasive carcinoma occurs earlier, in the third decade of life with a peak frequency at about 40 years, or 10-15 years later (4).

Cytodiagnostics of conventional cervicovaginal smears or "Pap test" for half of a century is the basic method of secondary prevention of cervical cancer, which is applied at the same time as a classic test of choice for the detection of lesions and a differential-diagnostic method for predicting the histological diagnosis (5). In an effort to reduce potential errors and increase the overall sensitivity of the screening, during the past years has developed several new techniques that have been proposed as a complementary method to conventional "Pap test". These include HPV DNA typization (6). There is an assumption that

	2009		2010		2011		Total	
	N	%	N	%	N	%	N	%
L-SIL; (PAP III)	101	4.34	186	9.50	135	6.46	395	6.20
H-SIL (PAP IV)	25	1.07	20	1.02	15	0.72	27	0.42
Normal cytological findings	2202	94.59	1752	89.48	1940	92.82	5894	92.44
Total	2328	100.00	1958	100.00	2090	100.00	6376	100.00

Table 1. The frequency of the L-SIL and H-SIL (Pap III and Pap IV) findings in relation to other cytological findings (Pap test)

Age groups	2009		2010		2011		Total	
	N	%	N	%	N	%	N	%
≤29	89	45.88	129	55.13	104	51.74	322	51.19
30-59	96	49.48	99	42.31	92	45.77	287	45.63
≥60	9	4.64	6	2.56	5	2.49	20	3.18
Total	194	100.00	234	100.00	201	100.00	629	100.00

Table 2. The age groups of patients with L-SIL and H-SIL (Pap III and IV) cytological findings

during the last 25-30 years has increased the frequency of diagnosis of carcinoma in situ, and in part because of the efficiency of cytologic examination (7).

In the history of medicine, the only case of reduced incidence and mortality, as well as human malignancies is cervical cancers without medical intervention (8).

2. GOAL

The aim of the research is to analyze the correlation between the abnormal cytological findings and histological diagnosis in all patients during the observed period.

3. MATERIAL AND METHODS

The study was descriptive-analytical, comparative, partly epidemiological, and mainly clinical applicative. The study involved all patients who meet the criteria for inclusion in the study. Used are the results of cytological and histological diagnosis in the period from January 1, 2009 to December 31, 2011.

In all subjects had previously done colposcopic examination and Pap test, and in patients with abnormal findings was also performed cervical biopsy for obtaining histopathological diagnosis.

Colposcopy was performed using the Olympus colposcope. The Pap test is taken from the front and rear lip and cervical canal. From the sample taken is made the cytological smear, which is fixed on a microscopic slide and stained by the method of Pap-Nikolai. After staining was performed microscopic analysis of morphological characteristics of the cells in the course of which are detected signs of cervical inflammation, causes infection, benign and malignant cells and other pathological changes.

After the punch biopsy changes in the cervix, the samples were forwarded to the Department of Pathology at the further processing.

For statistical analysis of the data obtained was used software package *SPSS for Windows.* In the analysis of the results obtained, the following statistical methods were used: for continuous variables in the study as the first analysis of symmetry (normality) of their distribution by Kolmogornov-Smirnov and Shapiro-Wilk test. Since the distribution of continuous variables significantly deviated from normal (Gaussian) distribution, mean values and a measure of dispersion, for their comparison is used the median and interquartile range and nonparametric test (ANOVA), normal and ordinal variables in the study were analyzed by χ2 test and in the lack of expected frequencies used Fisher's exact test. The statistical analysis used the Pearson χ2 test for difference distribution of nominal and ordinal data.

4. RESULTS

Table 1 shows the frequency of dysplasia (L-Sil and H-SIL) in relation to the normal cytological findings.

Mann-Whitney test showed a statistically significant difference in the frequency of L-SIL and H-SIL (Pap III) findings in relation to the period covered by this study. In 2010 was recorded the highest percentage compared to the total number of L-SIL and H-SIL (Pap III) findings, Z=-4.913, p=0.004.

Distribution of respondents by age group is displayed on Tables 2 and 3.

Analysis of respondents by age groups compared to the period covered by this study has been determined that the highest percentage of patients was with L-SIL and H-SIL (Pap III and IV) findings for the age group under 29 years. The percentage and frequency of L-SIL and H-SIL (Pap III and IV) findings in women of older age groups linearly decreases and the lowest is in the age group 60-69 years.

ANOVA test showed that there was no statistically significant difference in the average age of patients with L-SIL and H-SIL (Pap III and IV) findings in relation to the tested year, F=3.86, p=0,21. Statistical analysis showed a positive trend in terms that younger respondents have L-SIL and H-SIL (Pap III and IV) cytological findings, so that the average age of respondents in 2011 was 31.12±9.12 years.

	Mean	SD	SEM	95% Confidence Interval for Mean		Min	Max.
				Lower Bound	Upper Bound		
2009	33.85	10.46	0.74	32.39	35.32	19.00	69.00
2010	33.14	10.51	0.68	31.80	34.48	19.00	68.00
2011	31.12	9.12	0.65	29.82	32.42	19.00	66.00
Total	32.75	10.14	0.40	31.95	33.54	19.00	69.00

Table 3. The average age of patients with L-SIL and H-SIL (Pap III and IV) cytological findings in relation to the period covered by the survey

| | | | Year | | | Total |
			2009	2010	2011	
Biopsies	Clinic of Obstetrics and Gynecology	N	126	206	80	412
		% within biopsies	30.6%	50.0%	19.4%	100.0%
		% within years	63.6%	86.2%	41.7%	65.5%
	Other	N	72	33	112	217
		% within biopsies	33.2%	15.2%	51.6%	100.0%
		% within years	36.4%	13.8%	58.3%	34.5%
	Total	N	198	239	192	629
		% within biopsies	31.5%	38.0%	30.5%	100.0%
		% within years	100.0%	100.0%	100.0%	100.0%

Table 4 shows the total number of biopsies that are performed in the analyzed period.

Table 4. Number of the performed biopsies in case of L-SIL and H-SIL (Pap III and IV) findings, performed at the Clinic of Obstetrics and Gynecology and in other institutions, on annual basis.

Pearson Chi square test showed a statistically significant difference in the incidence of cytologic findings of L-SIL and H-SIL (Pap III and IV), set by the cytologist at the Clinic of Obstetrics and Gynecology and other institutions, χ^2=93.85, p=0.000.

The highest percentage of women who underwent cervical biopsy had CIN I findings (n=283), followed by CIN II (n=165), CIN III (n=152). Histopathologic findings of CIN II and CIN III were the most frequent in 2010.

Pearson Chi square test showed a statistically significant difference in the prevalence of histopathological diagnosis in relation to the total number of the performed biopsies. The most common finding was CIN I, while there is a small percentage difference in the incidence of CIN II and CIN III diagnosis, χ^2=15.68, p=0.016.

| | | | Biopsies | | Total |
			CoOaG	Other	
PHD	CIN I	N	161	122	283
		%	56.9	43.1	100.0
	CIN II	N	98	67	165
		%	59.4	40.61	100.0
	CIN III	N	137	15	152
		%	90.1	9.87	100.0
Total		N	396	204	600
		%	66,00	34.00	100.0

CoOaG=Clinic of Obstetrics and Gynecology

Table 5. Histopathological diagnosis after a biopsy of the cervix

5. DISCUSSION

The incidence of cervical cancer is unacceptably high. It is believed that about 80% of all cases occur in less developed countries, because prevention programs are either non-existent or poorly implemented.

There is a general opinion that organized national screening programs using Pap test produce the best results. This is best illustrated by data from Finland, where organized screening results were exceptional, reducing the incidence from 14.8/100,000 in 1963 to 2.8/100,000 in 1992, reducing the total incidence by 69.6% (9).

Due to the simplicity of implementation, VCE smear cytology is considered to be the best technique for screening. It is important to note that on the basis of cytology is not made a definitive diagnosis, it is always necessary to respect the protocol. Results may be false positive and false negative in range from 10 to 35%. A particular problem is definitely false negative results (10).

The course of this research led to the following results.

The highest percentage of L-SIL and H-SIL (Pap III) findings was during 2010 and it was (186) 9.5%, and the lowest in 2009, where there was (101) 4.34%. In this period, the total number of L-SIL and H-SIL (Pap III) findings amounted to 395 (6.20%) compared to other cytological findings–5894 (92.44%).

Analysis of respondents by age group compared to the years covered by this study has been determined that the highest percentage of patients with L-SIL and H-SIL (Pap III and IV) findings was in the age group under 29 years. The percentage and frequency of L-SIL and H-SIL (Pap III and IV) findings in women of older age groups linearly decreases and is lowest in the age group from 60-69 years.

Brotherton JM. and associates (11), in their study, "Does HPV type 16 or 18 in the prevalence of cervical intraepithelial neoplasia grade 3 lesions vary by age? An important issue for postvaccination surveillance", stated that among the 317 women who were enrolled in the study, with diagnosis CIN III, 70% of them aged 16-25 years, was detected HPV, 16.59% in women age aged 26-35 years and 48% in women older than 36 years.

The study "Gynecologic malignancy in Tuzla Canton" by Fatusic and colleagues report that in the period from 1993-2006, 27.11% of all women with cervical cancer is younger than 30 years (12).

This situation can be attributed to insufficient information, the motivation of young women for regular gynecological examinations, as well as the absence of national screening program.

According to the literature, the very frequency of cervical dysplasia and occurrence of HPV declines in percentage with age, so our results do not differ statistically from the research of other authors.

ANOVA test showed that there was no statistically significant difference in the average age of patients with L-SIL and H-SIL (Pap III and IV) findings in relation to the tested years.

Statistical analysis showed a positive trend that younger respondents have L-SIL and H-SIL (Pap III and IV) cytological findings, so that the average age of respondents in 2011 is 31.12±9.12 years.

Analyzing the number of the performed biopsies on the L-SIL and H-SIL (Pap III and IV) findings, set at the Clinic of Gynecology and Obstetrics and in other institutions on an annual basis, we came up with the following results.

Of the total number of the performed biopsies on the Clinic of Gynecology and Obstetrics, University of Sarajevo–629, cytological L-SIL and H-SIL (Pap III and IV) finding was in 412 (65.5%) respondents who directly came to the Clinic of Gynecology and Obstetrics, and in 217 (35.5%) of respondents cytological L-SIL and H-SIL (Pap III) finding was set at other medical institutions. The highest percentage of cervical biopsy due to L-SIL and H-SIL (Pap III and IV) findings was made in the 2010, 38% (239), and approximately the same number was made in 2009 and 2011. The highest percentage of biopsies due to L-SIL and H-SIL (Pap III and IV) that was set in other medical institutions was made in 2011–112 (51.6%).

On this basis we can say that there is statistically significant difference in the frequency of cytologic findings of L-SIL and H-SIL (Pap III and IV), set at the Clinic of Gynecology and Obstetrics and other institutions by the cytologist. The highest percentage of women who underwent cervical biopsy had CIN I findings (n=283), followed by CIN II (n=165), CIN III (n=152). Histopathologic findings of CIN II and CIN III were the most common in 2010. In relation to the total number of the performed biopsies there was a statistically significant difference in the incidence of histopathological diagnosis. The most common finding CIN I, and the difference between CIN II and CIN III diagnosis was in a small percentage.

In a study conducted by Kirschner et al. is stated that from the 290 analyzed cervical biopsies diagnosed with intraepithelial cervical neoplasia, 276 of them were HPV positive. HPV16 and HPV18 were found in about 75% of cervical intraepithelial lesions of high-grade in population of Denmark, and these two genotypes are considered as causes of at least 61.9% cases (13).

In the study "Correlation of cervical cytology and histology" conducted by Saha et al., 2004-2005, which included 43 patients, 22 of them with benign lesions, 8 LSIL, 9 HSIL and 1 ASCUS, came to the conclusion that the Pap test is in a statistically significant correlation with biopsy results (14). In the course of our research, analyzing the relationship between histopathologic diagnoses after cervical biopsy in relation to the place of setting the diagnosis, we reached the following results.

Of the total number of patients with CIN I (n=283) at the Clinic of Gynecology and Obstetrics was diagnosed in 56.9%, and with a diagnosis of CIN I diagnosed in other institutions was 43.1%. With CIN II at the Clinic of Gynecology and Obstetrics was 59.4%, and from other institutions 40.6%. While the total number of women with CIN III (n=152) at the Clinic of Gynecology and Obstetrics was 90.1%, and women who were diagnosed at other clinics was 9.9%. This results show that there is a statistically significant difference compared to the PHD biopsy of the cervix after L-SIL and H-SIL (Pap III and IV) cytologic findings, and that the largest statistical difference is in case CIN III changes in relation to the cytological findings, issued on the Clinic of Gynecology and Obstetrics and other medical institutions.

6. CONCLUSION

In this study, which was conducted at the Clinic of Gynecology and Obstetrics, Clinical Center of Sarajevo University from January 1, 2009 to December 31, 2012, were included a total of 2328 patients. We came to the following conclusions: The total number of L-SIL and H-SIL (Pap III) findings amounted to 395 (6.20%) compared to other cytological findings–5894 (92.44%). The frequency of H-SIL (Pap IV) was not statistically different in the observed period. The highest percentage of women who underwent cervical biopsy had CIN I findings (n=283). Histopathologic findings of CIN II and CIN III were the most common in 2010. There is a statistically significant difference compared to the PHD biopsy of the cervix after L-SIL and H-SIL (Pap III and IV) cytologic findings, and that the largest statistical difference in CIN III changes is in relation to the cytological findings, issued at the Clinic of Gynecology and Obstetrics and other health care institutions. The highest percentage of patients with L-SIL and H-SIL (Pap III and IV) findings was in the age group under 29 years. The percentage and frequency of L-SIL and H-SIL findings in women of older age groups linearly decreases and is lowest in the age group of 60-69 years.

CONFLICT OF INTEREST: NONE DECLARED

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