ORIGINAL ARTICLE

Colposcopy and cytodiagnosis in the prevention of cervical malignancies

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Abstract

Background: *The aim of this study was to establish the value of cytology, colposcopy, and pathohistology in the prevention of cervical malignancies.*

Methodology*: A prospective study involving 750 patients hospitalized in the Obstetric-Gynecologic department during the period between January 2008 to January 2009 for different reasons in whom cervical dysplasia were noted on speculum examination or who showed typical clinical symptoms, direct biopsy was also obtained from 117 patients.*

Results: *272 of the 750 patients (36.27%) showed clinical symptoms of cervical pathology. Atypical epithelial changes noted during colposcopy were more frequent in patients 31-40 years of age (60 patients, 32.09%) and 41-50 years of age (59 patients, 31.55%).*

Histopathological changes were noticed in 19 cases (16.24%) of cervical dysplasia at different stages, six cases (5.13%) of carcinoma in situ, and three cases (2,56%) of invasive carcinoma.

Conclusions: *The correct clinical evaluation of cervical epithelial alterations enables a prompt diagnosis and the timely implementation of appropriate therapeutic measures.*

Key words*: colposcopy, cytodiagnosis, cervix.*

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Introduction

Morbidity and mortality from malignancies have increased rapidly in the last several decades. Worldwide, cervical cancer is the fifth most frequent malignant disease in women, ranking third, after endometrial and ovarian cancer, among malignant diseases of the female genitalia[1]. Sexual activity early in adolescence and promiscuity have been confirmed as risk factors.

Several epidemiological studies have stressed the relationship between cervical cancer and social background. In Jewish and Muslim women, the incidence of cervical cancer is much lower, due to the circumcision of their male partners[2]. Multiparity is also considered to be a significant factor in the risk of cervical cancer. Recently, there has been substantial evidence supporting the role of oncogenic serotypes of *Human Papilloma Virus* in the development of cervical cancer. Indeed, oncogenic serotypes of the virus have been identified in 99% of histopathological materials analyzed[3]. Additionally, chronic inflammation of the cervix stimulates regenerative processes and thus favors the development of malignancies, which are often located at the regenerative-transformation zone of the affected tissue[4].

In recognition of the fact that the cervix is a vulnerable organ, our study sought to underline the importance of early detection of pathological changes, using prophylactic methods such as cytodiagnosis and colposcopy. Cytodiagnosis has revolutionized the early diagnosis of precancerous diseases; when combined with colposcopy, its accuracy may reach 85-90%[5].

To reveal abnormalities in the cervical epithelium, PAP smears were used for cytological screening. This method has many advantages: it is fast, inexpensive, non-invasive, applicable in large numbers of patients, and has a specificity of 97% and a sensitivity of 56%. Although an abnormal result of PAP test does not necessarily mean cervical cancer, it is a sign of serious inflammation of the cervix or vagina[6]. Colposcopy is another diagnostic approach, allowing for a closer and more precise examination of the cervix. We recommend colposcopy for patients in whom there is some doubt regarding cervical dysplasia or cancer, as well as in those suspected of carrying an HPV infection, and in those with atypical squamous cells of undetermined significance (ASCUS) or repeated ASCUS[7]. As a final diagnostic method, material taken through biopsy, conization, fractionated curettage, or even hysterectomy should be submitted to histopathologic analysis[8].

Methodology

The study was carried out at the Clinic of Obstetrics and Gynecology, University Clinical Center, Kosovo, during the period between January 2008 and January 2009.

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The study population includes 750 patients, hospitalized in our Clinic for different reasons, in whom cervical alterations were noted during speculum examination or who showed typical clinical symptoms. A detailed medical history was obtained from each patient, after which external and internal examinations of the genitals, speculum examination of the vagina and cervix, bimanual examination, and in certain cases rectal and small pelvic examinations were performed.

The suspicion of pathogenic bacteria was evaluated by taking vaginal and cervical swabs from each patient. Additionally, a swab was taken from the vaginal portion of the posterior fornix, with particular focus on the transitory zone of cylindrical and planocellular epithelium, or from the part of the cervix in which a pathology was suspected, particularly the endocervix.

Cytological examination was performed by a cytologist, with the results classified using the Papanicolau system. The cytological analysis also considered patient data such as age, address, number of deliveries and miscarriages, age at menarche, duration of menstrual cycle, referred clinical diagnosis, and current medical treatment. The results of any previous cytological examination were sent to the cytologist for comparison and to monitor pathological alterations in the cervix. Data concerning other possible cervical interventions during previous deliveries and miscarriages, biopsies, and cervical conization were also included.

Testing for human papilloma virus (HPV) was not carried out because of the high cost, which could not be assumed by public health institutions, including our Clinic.

Patients with obvious inflammatory changes in the cervix were administered appropriate medical treatment. After resolution of the condition, cytological analysis was repeated.

All patients underwent colposcopy. In patients in whom the process was suspected to involve the endocervix, fractionated explorative curettage was conducted. All interventions were certified by histopathological analysis. Data was analyzed manually, statistical analyses of the results were conducted using the chi-squared (X^2) test, with a confidence interval of $p = 0.01$.

Results

The symptoms of patients with pathologic findings in the cervix are varied. Of the 750 patients, 272 patients or 36.27% had no clinical symptoms; 186 (24.80%) had bleeding, 82 patients (10.93%) were considered to be contact bleeding, 67 patients (8.93%) due to irregular bleeding. An abnormal bacterial flora was identified in 240 patients (82%). A rarer symptom was the finding of increased vaginal discharge, detected in 22 patients (2.93%). Table I shows that more than one-third of the patients were without symptoms or complaints, suggesting that premalignant changes have no pathognomonic symptoms that enables diagnosis of a malignancy or the suspicion of an occult, atypical premalignancy.

Colposcopic changes are divided into those with and without atypical epithelial changes. The presence of atypical epithelial changes is expected to lead to malignant alterations. Table I. provides information on all study patients who underwent colposcopy. Of these, no atypical epithelial change was present in 530 (70.67%) patients, whereas 187 (24.93%) had atypical epithelial changes in the cervix. Negative colposcopic changes in the sampled material were rare (33 patients, 4.40%).

Table II. shows the nature of the colposcopic changes according to the different patient age groups. Benign changes, without atypical epithelial findings, were present in all age groups, but were more frequent in patients between the ages of 31 and 40 (221 patients, 41.70%). Atypical epithelial changes noted on colposcopy were more frequent among patients aged 31-40 (60 patients, 32.09%) and 41-50 (59 patients, 31.55%). Atypical epithelial changes were not detected in any of the patients < 20 years of age. However, no significant difference in colposcopic findings with and without atypical changes according to age group could be established ($X^2 = 1.81$; $p > 001$).

Table III. presents details of the 187 patients in whom atypical changes were noted during colposcopic examinations. The most frequent atypical changes were mosaic (68 patients, 36.36%) and leukoplakia (50 patients, 26.74%). An atypical transformation zone was found in 22 patients (11.76%), whereas an iodine-negative zone was identified in only six patients (3.21%). The difference in the distribution frequencies based on the type of atypia was significant ($X^2 = 120.21$; $p < 0.01$). Again, none of the patients in the age group < 20 years had atypical epithelial changes.

Table IV. describes the patients with PAP I, II, and III findings, with most such patients in the age group 31-40 years. More precisely, this group contained 26 (43.33%) patients with PAP I, 195 (37.14%) with PAP II, and 51 (41.46%) with PAP III findings. Of all patients with PAP I, the fewest were in the age groups < 20 years (no patient) and 51-60 years (5 patients, 8.33%).

Table I: Classification of colposcopic results

Colposcopic changes	Total No.	%
Negative results	33	4.40
Without epithelial atypia	530	70.67
With epithelial atypia	187	24.93
Total	750	100.00

Table II: Colposcopic findings in the cervix, according to patient age group

Age group (years)		Colposcopic changes: Without epithelial atypia		With epithelial atypia		Negative		Total	
		No.	%	No.	%	No.	%	No.	%
< 20	No.	3	60.00	--	--	2	40.00	5	100.00
	%	0.57	--	--	--	1.07	--	0.67	--
21-30	No.	156	70.91	40	18.18	24	10.91	220	100.00
	%	29.43	--	21.39	--	12.83	--	29.33	--
31-40	No.	221	77.54	60	21.05	4	1.40	285	100.00
	%	41.70	--	32.09	--	2.14	--	8.00	--
41-50	No.	88	58.67	59	39.33	3	2.00	150	100.00
	%	16.60	--	31.55	--	1.60	--	20.00	--
51-60	No.	62	68.89	28	31.11	0	0.00	90	100.00
	%	11.70	--	14.97	--	0.00	--	12.00	--
Total	No.	530	70.67	187	24.93	33	4.40	750	100.00
	%	100.00	--	100.00	--	17.65	--	100.00	--

Table III: Distribution of colposcopic changes according to type of atypia and patient age group

Age group (years)	Type of atypia: Leukoplakia	Base	Mosaic	Atypical vascularity	Atypical Transformation Zone	Iodine-negative zone	Erosio vera	Total No.	Total %
<20	-	-	-	-	-	-	-	-	-
21-30	7	3	12	5	8	2	3	40	21.39
31-40	13	6	25	4	9	1	2	60	32.09
41-50	25	2	22	1	1	3	5	59	31.55
51-60	5	2	9	3	4	-	5	28	14.97
Total No.	50	13	68	13	22	-	15	187	100.00
Total %	26.74	6.95	36.36	6.95	11.76	3.21	8.02	100.00	--

Table IV: Cytological results of cervical examination according to age group

Age group (years)	PAP I No.	I %	II No.	II %	III No.	III %	IV No.	IV %	V No.	V %	Total No.	Total %
< 20	5	8.33	--	--	--	--	--	--	--	--	5	0.67
21-30	14	23.33	176	33.52	29	23.58	1	2.63	--	--	220	29.33
31-40	26	43.33	195	37.14	51	41.46	11	28.95	2	50.00	285	38.00
41-50	10	16.67	105	20.00	23	18.70	10	26.32	2	50.00	150	20.00
51-60	5	8.33	49	9.33	20	16.26	16	42.11	--	--	90	12.00
Total	60	100.00	525	100.00	123	100.00	38	100.00	4	100.00	750	100.00

Table V: Structure of histopathologically verified dysplasia in accordance with colposcopic atypia in patients who underwent biopsy for histopathology

Colposcopic atypia	Biopsy patients No.	%	Histopathologic diagnosis: Dysplasia seen on HP No.	%	Carcinoma in situ No.	%	Invasive carcinoma No.	%	Total No.	%
Leukoplakia	44	100.00	11	25.00	1	2.27	1	2.27	13	29.55
Base	12	100.00	2	16.67	1	8.33	1	8.33	4	33.33
Mosaic	14	100.00	3	21.43	1	7.14	1	7.14	5	35.71
Vascular atypia	8	100.00	1	12.50	1	12.50	--	--	2	25.00
Atypical Transformation Zone	22	100.00	1	4.55	1	4.55	--	--	2	9.09
Iodine-negative zone										
Erosio vera	3	100.00	--	--	--	--	--	--	--	--
Total	14	100.00	1	7.14	1	7.14	--	--	2	14.29
	117	100.00	19	16.24	6	5.13	3	2.56	28	23.93

Table V. shows the results of histopathological analysis in patients with suspicion of an abnormal cervical epithelium. Most of the analyses were done subsequent to obtaining the suspicious cytological results or the positive colposcopic results. Microscopic analysis is well-known to be the most effective method to diagnose atypical changes.

Apart from the material obtained during colposcopy, a biopsy (direct biopsy) sample was taken from 117 patients. Histopathological analysis of the biopsied tissue identified 19 patients (16.24%) with different levels of dysplasia, six (5.13%) with carcinoma in situ, and three (2.56%) with invasive carcinoma. The highest percentage of atypical epithelium was verified in the context of atypical colposcopy findings: leukoplakia, mosaic, base, and vascular atypia. Of the 44 patients with leukoplakia who underwent biopsy, dysplasia was verified at histopathology (HP) in 11 (25%); of the 14 patients with mosaic dysplasia, the findings were verified by HP in three (21.43%); of the 12 patients with base dysplasia, HP verified the results in two (16.67%); and of the eight patients with vascular atypia, dysplasia was verified by HP in one (12.50%). Atypical epithelium was verified histopathologically only very rarely when the findings consisted of either an atypical zone of transformation or erosio vera. Dysplasia could not be histopathologically verified in patients with iodine-negative zones of the cervix. Among all patients with colposcopic atypia, excluding those with iodine-negative zones, there was one case of carcinoma in situ, whereas invasive carcinoma was detected only in patients with leukoplakia, base, and mosaic findings.

Discussion

Correct evaluation of clinical and morphological atypia of the vaginal portion of the uterus is the basis of effective therapeutic and preventive measures[9]. Inflammatory changes noted on colposcopy, specifically atypical cervicitis, present with a wide range of morphological alterations in the cervical epithelium [10]. Clinical examination of the cervix is not sufficient to reveal atypical changes, because even if the epithelium is preserved, occult premalignant atypia and cancerogenic changes in the cervix may still be present. Usually, these changes are benign; mostly, they represent inflammation of the cervix and only rarely indicate premalignant atypia. Nonetheless, every pathological change in the cervix should be promptly diagnosed and the patient promptly administered therapeutic measures aimed at the total elimination of the atypia [11].

In this setting, the importance of colposcopy, cytology, and histology in the early detection of premalignant changes in the cervix is indisputable. In the prevention of cervical carcinoma, all females > 18 years of age, particularly those in the at-risk population, should undergo cervical screening [12]. Screening is essential for the detection and prevention of pathological preclinical

and clinical changes in the cervix, and especially of cervical carcinomas [13].

Nowadays, it is possible to discover carcinomas in the so-called preclinical phase, when the disease is asymptomatic. Cytological screening, offered in many countries throughout the world, has confirmed the importance of cytodiagnosis as the most effective medical weapon in the primary and secondary prevention of cervical carcinoma. However, screening clearly requires the full support of appropriately trained medical staff and considerable financial support[14].

Because of the position of the cervix and thus the relative ease of its evaluation, carcinoma of the cervix can often be detected even in the preinvasive form [15]; this is in contrast to other types of carcinomas in other female reproductive organs. The current detection methods are convenient, noninvasive, pose no risk to a woman's health, and are relatively cost effective. The level of accuracy in cytological examinations of the cervix is also important for the successful detection of premalignant and malignant changes. The percentage of false-negative results ranges from 1.1 to 26%. The latest American studies report ranges of 4.8-12.2% and 3.2-3.4%. False-negative findings may be largely due to improper collection and processing of the sample.

The best results are achieved when cytology and colposcopy are combined, because they complement each other. This increases the accuracy of diagnosis to 85% [16]. A disadvantage of colposcopy is that it does not provide information on the condition of the endocervix. In patients with suspicious or positive cytological results and negative colposcopy findings, endocervical curettage is necessary. Colposcopy can be used to identify the area of the endocervix from which a small sample of tissue (biopsy) should be removed for histological analysis.

Exfoliative cytology is a very practical method for detecting premalignant atypia and can be widely applied in the female population. Its advantage is that material can be taken from the cervical canal, which is not possible during colposcopy. This is an important consideration because 15-20% of all atypia are localized in the endocervix.

Application of the methods discussed in this report increases the detection of cervical carcinomas. Recent diagnostic methods enable the detection of atypical changes in the cervical epithelium, including various forms of basal hyperplasia and dysplasia, carcinomas in situ, and microcarcinomas[17]. These changes are associated with the pathological cervix. Patients with evidence of epithelial changes in the cervix, as demonstrated by colposcopy, should be followed carefully because the most effective treatment of carcinomas is during the preinvasive phase. The prevention of epithelial changes is clearly important and can be achieved by eliminating factors known to increase risk. It also requires knowledge of and the ability to interpret factors linked to the etiology of cervical carcinoma [18].

Many studies have reported an etiological dependency between number of deliveries and artificial abortions with cervical carcinomas. Others have examined the relation of cervical carcinoma with infection and birth trauma. Early sexual experience, pluriparity, and a high frequency of untreated inflammatory changes are among the many factors that may influence the presence and outcome of cervical changes [19].

Conclusions

Proper clinical evaluation of epithelial changes in the uterine cervix facilitates prompt diagnosis of cervical carcinoma and timely administration of necessary preventive and therapeutic measures.

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