

RESEARCH ARTICLE

Differences in Risk Factors for Cervical Dysplasia with the Applied Diagnostic Method in Serbia

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Abstract

Background: In the etiology of cervical cancer not only HPV infection is important, but also other factors such as demographic influences and sexual and reproductive health attitudes, as well as others related to preventive measure usage (or non usage). The aim of this study was to examine factors associated with cervical dysplasia in asymptomatic women who were examined by routine cytology and cervical biopsy for early detection of cervical cancer. **Materials and Methods:** Socio-demographic and other characteristics were obtained from medical files of 85 examinees with pathologic cytologic findings (Pap test) and histopathologic (HP) findings after biopsy. **Results:** According to the Pap test result, a greater probability for development of cervical dysplasia was noted with examinees having a larger number of sexual partners (OR= 5.01, 95% CI 1.04-24.10), and those who are afraid of the Pap finding. Risk factors for development of cervical dysplasia according to the bioptic finding were early beginning with sexual activities, presence of any STD in personal medical history and fear of the Pap test finding. **Conclusions:** The only risk factor found to be important for both methods was fear of the Pap testing finding.

Keywords: Cervical dysplasia - risk factors - cytology - Pap smear - histopathology - Serbia

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Introduction

In etiology of the cervical cancer not only HPV infection is important, but also other factors, such as demographic factors, sexual and reproductive attitudes, as well as factors related to preventive measures usage (non usage). Initiating sexual activity in the early age, the number of sexual partners during the lifetime and positive medical history of the sexually transmitted diseases (STD) has been also confirmed as important risk factors (Bosch et al., 2002; Reich, 2005). In addition to the risky sexual behaviour, there are factors such as the number of deliveries and abortions, as well as to early deliveries and abortions (Bosch et al., 2002; Reich, 2005). Usage of the oral contraceptives (OC) and smoking increase the risk of the cervical cancer (Castellsague and Munoz, 2000; Kjellberg et al., 2000; Smith et al., 2003; Gadducci et al., 2011). As well as not complying to the regular gynecological examinations (in countries organizing opportune screening) (Cuzick et al., 2008; Clement and Mansour, 2013) or not responding to the screening (Uysal and Birsal, 2009). In some countries risk factors were examined in relation to the cytologic finding (Papa test) (Patil et al., 2006; Ritter et al., 2009; Indarty et al., 2013),

while in other studies histopathologic (HP) finding in the bioptic material represented the “golden standard“ for evaluation of the cervical carcinoma risk factors (Boicea et al, 2012; Poomtavorn et al, 2013). Cytologic analysis in combination with colposcopy as complementary method for early detection of the cervical cancer enables high level of sensitivity and specificity (Karimi-Zarchi et al., 2013), but final diagnosis of this carcinoma is to be made on the basis of histopathologic finding from the bioptical sample, or by endocervical curettage (Apgar and Brotzman, 2004).

The aim of this study is to examine factors associated with cervical dysplasia in asymptomatic women who were examined by methods for early detection of the cervical cancer, namely, by the routine cytology and cervical biopsy.

Materials and Methods

This was a descriptive-analytical diagnostic study that included examinees aged 18-69 years who were for any reason examined by their chosen gynecologist in two primary health care centers in Serbia in the period of January 1 to March 31, 2013.

Evaluation of the risk factor differences concerning

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development of the cervical cancer was carried out by two diagnostic methods, that is, by the routine cytology and biopsy of the cervix uteri. Cytologic results are presented by the Bethesda classification.

Data on the Pap test were obtained from the medical documentation of 525 examinees. In 435 of them Pap finding was normal (ASC-US) and in 90 (17.14%) of examinees abdominal cytologic finding was positive. Out of those 90 examinees who had positive cytologic finding, in 85 the target biopsy was undertaken, while in 5 examinees local vaginal therapy was applied. This study represents analysis of characteristics obtained from medical files of those 85 examinees with pathologic cytologic finding (Pap test) and histopathologic (HP) finding after performed biopsy (Figure 1).

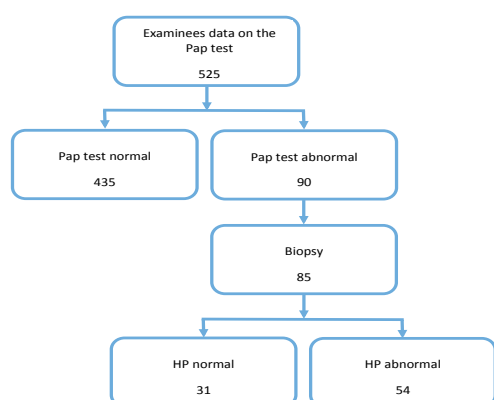


Figure 1. Examinees Data on the Pap test

Data on the socio-demographic characteristics and sexual and reproductive behaviour were obtained by using specially designed and previously tested questionnaire. Data on the used diagnostic methods for early detection of changes in the cervix uteri were obtained from the patients' medical documentation. Questionnaire contained three groups of variables: socio-demographic variables, variables related to behaviour associated with the risk of the cervical cancer development and variables related to the usage of diagnostic method for this change.

Socio-demographic characteristics included following variables: age, partnership status (married, single (unmarried), divorced, widow), self-evaluation of the financial status (very bad, bad/good, excellent), educational level (primary, secondary/high) and number of deliveries (0, 1, 2, 3 and more), Group of variables related to sexual behaviour contains data on the first sexual intercourse (<18 or ≥18), total number of the sexual partners during the life span (>4 or ≤4), consistent usage of the condom (yes or no). One part of the questionnaire were related to Pap testing (fear of results, regular control examinations, other).

Data related to diagnostic methods for the cervical carcinoma were obtained from the medical files. These data included: interval between the Pap testing; the frequency of testing (once a year, once in two years, less frequent), Pap test finding (ASC-US, L-SIL, H-SIL and AIS) and HP finding of the bioptic sample (benign/CINI, II, III, CIS). Committee for Ethics of the Medical Faculty

Table 1. Demographic and Socio-Economic Characteristics, Characteristics Related to Behaviour and Characteristics Related to Use of Preventive Practices of the Respondents According to the Abnormal Pap Test and Histopathology

Characteristics		Abnormal Pap test			Histopathology		
		L-SIL No (%)	H-SIL No (%)	p	Benign No (%)	CIN/CIS No (%)	p
Age	40.13 (10.7)*			0.124			0.536
Partnership status	Single/divorced/ widowed	41 (67.2)	7 (29.2)	0.001**	22 (71.0)	26 (49.1)	0.050**
	Married/common law	20 (32.8)	17 (70.8)		9 (29.0)	27 (50.9)	
Education	Elementary	8 (13.1)	2 (8.3)	0.801	5 (16.1)	5 (9.4)	0.526
	High school	37 (60.7)	16 (66.7)		17 (54.8)	35 (66.0)	
	College/university	16 (26.2)	6 (25.0)		9 (29.0)	13 (24.5)	
Self-assessed socio-economic status	Unsatisfactory	15 (24.6)	15 (62.5)	0.001**	7 (22.6)	22 (41.5)	0.078
	Satisfactory	46 (75.4)	9 (37.5)		24 (77.4)	31 (58.5)	
Ever smoking	Yes	46 (75.4)	23 (95.8)	0.030**	19 (61.3)	49 (92.5)	<0.000**
	Never	15 (24.6)	1 (4.2)		12 (38.7)	4 (7.5)	
Current smoking	Yes	36 (59.0)	18 (75.0)	0.168	12 (38.7)	41 (77.4)	<0.000**
	No	25 (41.0)	6 (25.0)		19 (61.3)	12 (22.6)	
Parity	<3	48 (78.7)	14 (58.3)	0.057	25 (80.6)	36 (67.9)	0.207
	≥3	13 (21.3)	10 (41.7)		6 (19.4)	17 (32.1)	
Abortion	0	18 (34.0)	1 (4.5)	0.008**	10 (35.7)	9 (19.6)	0.123
	≥1	35 (66.0)	21 (95.5)		18 (64.3)	37 (80.4)	
Age of first sexual intercourse	<18	33 (55.0)	22 (87.5)	0.005**	9 (29.0)	44 (84.6)	<0.000**
Number of partners	<4	37 (60.7)	3 (13.6)	<0.000**	20 (64.5)	20 (38.5)	0.022**
	≥4	24 (39.3)	19 (86.4)		11 (35.5)	32 (61.5)	
Consistent use of condoms	Yes	2 (3.9)	0 (0.0)	0.346	2 (8.0)	0 (0.0)	0.049**
	No	49 (96.1)	22 (100.0)		23 (92.0)	47 (100.0)	
History of STD***	Yes	19 (31.7)	14 (58.3)	0.037**	6 (20.0)	26 (49.1)	0.008**
	No	41 (80.3)	10 (19.7)		24 (46.6)	27 (53.4)	
Undertaking pap test	Once a year	33 (54.1)	2 (8.3)		19 (61.3)	16 (30.2)	
	For one or two years	23 (37.7)	10 (41.7)		9 (29.0)	24 (45.3)	
	Rarely	5 (8.2)	12 (50.0)		3 (9.7)	13 (24.5)	
Pap reason	Fear	10 (16.4)	11 (45.8)		2 (6.4)	19 (35.9)	
	Regularly	47 (77.0)	10 (41.7)		26 (83.9)	30 (56.6)	
	Other	4 (6.6)	3 (12.5)		3 (9.7)	4 (7.5)	

*mean (SD); **p<0.01; ***STD-sexually transmitted diseases

Table 2. Multivariate Analysis According to the Abnormal Pap Test and to the Histopathology

Characteristics		Multivariate analysis			
		Pap		Histopathology	
Partnership status	Married/common law	1.00		1.00	
	Living alone	1.78 (0.51-6.24)	0.366	0.62 (0.14-2.85)	0.541
Ever smoking	Yes			1.00	
	Never			0.12 (0.01-1.01)	0.051
Number of partners	<4	1		1	
	≥4	5.01 (1.04-24.10)	0.045**	0.67 (0.1-4.48)	0.676
History of STD***	Yes	1.00		1.00	
	No	0.84 (0.13-5.64)	0.861	0.12 (0.02-0.78)	0.026**
Age of first sexual intercourse	<18	1.00		1.00	
	≥18	0.46 (0.10-2.10)	0.316	0.03 (0.06-0.19)	<0.000**
Undertaking pap test	once a year			1.00	
	For one or two years			5.57 (0.61-33.97)	0.138
	Rarely			0.56 (0.04-7.53)	0.661
Pap reasons	fear	1.00		1.00	
	Regularly	0.49 (0.25-0.98)	0.043**	0.09 (0.00-0.87)	0.043**

*OR (95%CI); **p<0.01; ***STD-sexually transmitted diseases

in Belgrade approved this study (No 29.1- 13) realised within the period 01.01.2013- 31.03.2013.

Statistical analysis

Statistical analysis included descriptive and modeling statistics. Descriptive statistical methods (relative numbers, mean values and standard deviations, SD) were used for distribution analysis of variables of interest: socio-demographic factors, sexual behaviour, and practices related to Pap testing. Distributions of the chosen variables incidence were categorized according to the findings from the Pap test (L- SIL, and H-SIL) and HP of the bioptic sample (benign/CINI, II, III, CIS). Statistical significance of difference was tested by the hi square test, where p<0.05 and p<0.01 were used as statistically high level of significance.

Outcome variables were both pathologic Pap and HP finding. Association between independent and outcome variables were tested by univariate and multivariate logistic regression analysis, and results were expressed through odds ratios (OR) with 95% of the confidence interval (95%CI). Deterministic model was designed to examine association of every risk factor with abnormal both Pap test and HP biopsy finding in addition to control of all other risk factors.

Results

Table 1 presents socio-demographic characteristics of examinees, variables related to examinees' behaviour and determinants related to (non) usage of preventive measures by examinees according to the abnormal Pap test and HP finding. Partnership and socio-economic status show statistical significance for results of both methods.

According to the Pap test result, greater probability for development of cervical dysplasia had women who are having larger number of sexual partners, or those who are afraid of the Pap finding. Risk factors for development of cervical dysplasia (according to the bioptic finding) were: early beginning with sexual activities; presence of any STD in personal medical history, and fear of the Pap test finding (Table 2).

Discussion

This study has shown that there are significant differences among the risk factors of the development of cervical dysplasia, depending on the applied diagnostic methods for early detection of these changes. Results have been obtained by routine cytologic diagnostics and by target biopsy of the cervical changes, and then mutually compared.

According to the results of the Pap test, greater probability for development of cervical dysplasia is having larger number of the sexual partners and having fear of the Pap finding. According to the bioptic HP findings, risk factors for development of cervical dysplasia are: early beginning with sexual activity, presence of STD in personal medical history and fear of the Pap test findings. In this study, risk factor important for both diagnostic methods and their compared results refer to barriers against going to Pap testing. Women afraid of the Pap testing finding have greater probability to develop premalignant cervical changes. Many studies have shown that good communication with health professionals is an important factor that influence women's decision for preventive examination (Vivilaki et al., 2005; Matejic et al., 2008; Dugandzija et al., 2012). Role of nurses and midwives in prevention of the cervical cancer is also important (Duval et al., 2009; Gottvall et al., 2009; Kent et al., 2010). Studies dealing with knowledge level of nurses and students of the health care concerning risk factors of the cervical cancer have shown that even health professionals do not have satisfactory level of that knowledge (Baer et al., 2000; Suwała et al., 2012). According to results from this study single women, divorced or widows, compared with those having marital status or constant sexual partner, have greater probability for pathologic Pap test finding, but not for pathologic HP one. There are numerous evidences that living in marriage or with a constant partner reduced the risk for development of the cervical cancer (Billstrom et al., 2013; Labeit et al., 2013; Jiang et al., 2013). This study has confirmed well known fact that early sexual activity is an important risk factor for pathologic finding of the Papa test, but not for the pathologic HP finding. Studies showed that for

women having the first intercourse before 16 or 18 years of age relative risk of the cervical cancer is 2-16 times greater in comparison with those who started with sexual activity later in life (ICSI, 2005; Deacon, 2000). Presence of STD in personal medical history is the risk factor of development of cervical dysplasia according to HP findings, but not according to the Papa test finding. Role of STD and infections transmitted by the sexual contact in occurrence and development of the cervical cancer is not completely explained (Smith et al., 2002; 2004). Higher incidence of the cervical cancer was confirmed in patients having some of STD, that is, in those who were treated at clinics for genital diseases (Kanno et al., 2005; Datta et al., 2011). Risk factors related to behaviour were examined most often of all other risk factors of the cervical cancer. Risk factors related to sexual behaviour such as the number of sexual partners during the life span, sexual activities in early age and existence of STD in personal medical history can be associated with higher risk of the cervical cancer (Bosch et al., 2002; International Collaboration of Epidemiological Studies of Cervical Cancer, 2009). There are proofs confirming association of the HPV infection as the most frequent etiologic factor of the cervical cancer. Number of sexual partners also represents high risk of the cervical carcinoma development (Rong et al., 2002; Chan et al., 2002; Natphopsuk et al., 2012; Hoque et al., 2013).

There is a significant association of the number of deliveries and abortions as well as of deliveries in adolescent age with the cervical cancer (Castellsague and Munoz, 2000; Chankapa et al., 2011; Thulaseedharan et al, 2012). Of all contraception methods representing the risk factors of the cervical carcinoma, usage of oral contraceptives was most frequently analysed and as a protection factor, persistent usage of condoms. This study confirmed that persistent usage of condoms is not the risk factor and in Serbia a small number of women use pills so that their effect was not analysed (National Health Survey for the population of Republic of Serbia 2006; Antic et al., 2013). Risk of the cervix uteri carcinoma is in positive correlation with the time period of oral contraceptives (OC) usage (Castellsague and Munoz, 2000; Smith et al., 2003; Kjellberg et al., 2008).

In future, study on the risk factors should be undertaken in the same group of examinees after three or five-year period including both Pap and HP findings follow-up. It would be of great help if results of that study could be implemented into the screening programmes for the cervical cancer prevention.

In conclusion, there are significant differences in the risk factors of development cervical dysplasia in dependence of diagnostic methods (routine cytology and cervical biopsy). The only risk factor found to be important for both methods refers to barrier against Pap testing (fear of the Pap test finding).

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