Implementation of secondary preventive practice important for cervical cancer among women who use oral contraception

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SUMMARY

Background: *In the course of the previous 50 years, demographic trends in Serbia have been quite unfavorable and there is the epidemiological transition. The aim of the study was to examine the factors that influence women's decision to take oral contraceptives (OC) and to examine preventive measures for the cervical cancer.*

Method: *We analyzed data that were collected in a cross-sectional study National Health Survey in Serbia in 2006, which was based on a nationally representative population sample. Our subsample included 2,378 women aged from 20 to 49 years.*

Results: *The results of this multivariate analysis confirmed the association of the OC usage with socio-demographic factors, such as marital status and region of living. Respondents from Vojvodina took OC more often than those from Belgrade (OR= 0.48, 95% CI, 0.30-0.78) and Central Serbia (OR=0.42, 95% CI 0.29-0.61). The results of adjusted multivariate analysis showed that the level of education, place of living, and region were significantly associated with secondary preventive measures for the cervical cancer (regular check-ups and Pap tests). Secondary preventive measures are more frequently used among less educated participants who live in the urban areas and in the region of Vojvodina, compared to the more educated women from rural areas and living in the capital Belgrade.*

Conclusion: *Our study did not confirm association of OC usage with secondary preventive measures for the cervical cancer.*

Key words: *Uterine Cervical Neoplasms; Contraceptives, Oral; Papanicolaou Test*

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INTRODUCTION

The main factors with negative impact on women's reproductive organs are number of sex partners, early sexual activities, no application of the contraceptive measures, unplanned and unwanted pregnancies, low socioeconomic and educational status, and health care factors (1-4). Basic form of the birth control in developing countries is application of modern methods of contraception (5-6). However, research suggests that traditional contraceptive methods such as coitus interruptus, non-fertile days, and abortion are the most common ways of the family planning in Serbia. The *National Health Survey* study results from 2006 show that 36.9% of women in the reproductive age and with regular partners practice unreliable methods of contraception (6). In the previous 50 years, particularly since the last decade of the previous century, demographic trends have been quite unfavorable in Serbia and there is an epidemiological transition.

Numerous epidemiological studies have been performed to determine association of OC usage and development of the cervical cancer. Some studies dealing with the same problem have not positively confirmed possible increased risk (7, 8). However, evidence suggests that both current and previous OC users are at the increased risk of the cervical cancer being reduced after OC withdrawal (7).

After the breast cancer, cervical cancer is the third most common malignancy in Serbia with the standard incidence rate of 24.1 per 100,000 women (9). Mortality rate due to this cancer reaching 9.2 per 100,000 women is in Serbia high and it is the third highest in Europe, after Romania (10). Systematic review of 28 studies including 12,531 women with the cervical cancer has shown that relative risk of its occurrence increases if the time of its usage prolongs (10). All included studies show that the OC users belong to the risk group when cervical cancer is concerned and for that reason they are advised to be screened in shorter time intervals. In Serbia until 2013, not considering pilot projects in some regions, there was no organized screening for the cervical cancer but only opportune one (gynecological examination and Pap smear) was implemented (11). Cervical cancer develops slowly over a long period and it can be effectively treated only if diagnosed in its early phase. Alarming fact is that in Serbia, according to the *National Health Survey* study from 2006 that included women older than 20 years, 6.3% of them had never visited a gynecologist. Sociodemographic factors were significantly associated with secondary preventive measures for the cervical cancer (screening) in Serbia. Younger women with higher educational level and higher socioeconomic status more often used preventive gynecological measures (6). Aim of the study was to examine in Serbia the factors that influence women's decision to take OC as a method of contraception and to examine secondary preventive measures as a protection from the cervical cancer.

METHOD

We analyzed data that were collected in a cross-sectional study *National Health Survey* in Serbia in 2006 (without data on Kosovo and Metohija), which was based on a nationally representative population sample. It was carried out by the Ministry of Health of the Republic of Serbia with financial and professional support from the World Bank, the WHO Regional Office for Europe (State Office of Serbia), and the Institute of Public Health of Serbia *Dr Milan Jovanovich Batut.* This is a cross-sectional study that includes randomly selected representative population sample of 14,522 women aged 20 years and more (6). In order to provide statistically reliable estimates of the health

indicators at the national level, a stratified two-stage randomized sample of all registered households in Serbia was firstly formed according to the population census from 2002. Out of 7,673 randomly selected households, 6,156 were interviewed within the period September-October in 2006. Within the included households, there were 7,664 women aged 20 years and older. Information concerning the socio-demographic and socio-economic characteristics and preventive measures were obtained from the interviews such as face-to-face, self-administered questionnaire, or by the trained interviewers. Here are analyzed characteristics of 2,343 women aged 20 to 49 years who have answered questions referring to the OC usage as a method of the family planning.

Variables

Three groups of data relevant to the usage of OC as a contraception method were analyzed: women's socio-demographic characteristics, reproductive behavior, and application of the secondary preventive measures. The following sociodemographic variables were analyzed: participants' age (shown in a ten-year intervals from 20 to 49 years of age); marital status (married, single /single comprises of single, living alone, divorced, and widow/); education (primary, secondary, higher or university level); type of the settlement (urban, rural), region (Vojvodina, Central Serbia, Belgrade), and socio-economic status measured by the household welfare index (Wealth Index). According to the obtained values of the well-being index, respondents were classified into five socio-economic categories or quintiles: the poorest, poor, medium, rich, and the richest. Analyzed variables related to reproductive behavior were the number of children (0, 1, 2, 3 or more) and the number of abortions (0, 1, 2, 3 or more). Analyzed variables with regard to application of secondary preventive measures were the frequency of regular gynecological examinations (once a year, less than once a year) and when the last Pap test was performed (within the last 12 months before the survey, more than 1 year ago). All analyzed data were shown and correlated with the OC usage (regular, occasional, no) (no=0; regularly or occasionally (1).

Statistical analysis

Descriptive statistics were used in presentation of analysis referring to the selected data. Frequency distributions of selected variables are shown in relation to the OC usage (yes, regularly or occasionally, no) and significance of differences was tested by using the chi-square test. For the minimum level of statistical significance $p<0.05$ was used, when $p<0.01$ was defined as statistically significant.

In order to calculate the relationship between dependent and independent variables we performed univariate logistic regression analysis and results are presented as odds ratios (OR) with 95% confidence interval (95% CI). Variables showing high significance after the univariate analysis were additionally tested by the multivariate analysis. Association between secondary preventive measure {dependent variables: regular gynecological examinations within the last 12 months (once a year/rarely) and the Pap test within the last 12 months (yes, no)} and the OC usage (independent variables) was tested by the multivariate (adjusted) logistic regression analysis. Multivariate (adjusted) logistic regression model was created by adding all socio-demographic variables in the model (place of living, region, and education) as well as to the OC usage.

The analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study included women aged from 20 to 49 years (mean age 34 years, 8±8.75 years).

Table 1 shows frequency and results of the univariate logistic regression referring to the socio-demographic characteristics and reproductive behavior of respondents. Marital status did influence upon decision to take OCs.

Table 1. Socio-demographic characteristics and reproductive behavior of respondents for the use of OC

Women's characteristics	*Total number of women*	*Yes (occ/always) no. (%)*	*Odds ratio (95% CI)*	*P value*
Age group (years)				
20-29	675	52 (7.7)	1.00	
30-39	838	56 (6.7)	0.86 (0.58-1.27)	0.444
40-49	830	48 (5.8)	0.73 (0.49-1.10)	0.138
Marital status				
Married	1924	121 (6.1)	1.00	
Single*	355	34 (9.6)	**1.62 (1.08-2.42)**	**0.017**
Education				
Elementary school	457	28 (6.1)	1.00	
Secondary school	1503	92 (6.1)	1.00 (0.65-1.55)	0.990
University degree	381	36 (9.4)	1.60 (0.96-2.67)	0.070
Type of settlement				
Urban	1292	89 (6.9)	1.00	
Rural	1051	67 (6.4)	0.92 (0.66-1.28)	0.620
Region				
Vojvodina	577	63(10.9)	1.00	
Belgrade	448	30 (6.7)	**0.59 (0.37-0.92)**	**0.021**
Central Serbia	1318	63 (4.8)	**0.41 (0.28-0.59)**	**<0.000**
Wealth index				
Poorest	340	19 (5.6)	1.00	
Poorer	487	32 (6.6)	1.19 (0.66-2.13)	0.564
Middle	469	31 (6.6)	1.20 (0.66-2.15)	0.552
Richer	543	32 (5.9)	1.06 (0.59-1.90)	0.850
Richest	504	42 (8.3)	1.54 (0.88-2.70)	0.133
Number of children	2314	156 (6.7)		
0	359	24 (6.7)	1.00	
1	462	22 (4.8)	0.71 (0.39-1.29)	0.26
2	1207	78 (6.5)	0.97 (0.60-1.55)	0.88
3 and more	242	24 (9.9)	1.48 (0.82-2.67)	0.19
Number of Abortion	1945	124 (6.4)		
0	1007	58 (5.8)	1.00	
1	368	22 (6.0)	1.04 (0.63-1.73)	0.878
2	281	25 (8.9)	1.60 (0.98-2.60)	0.060
3 and more	289	19 (6.6)	1.15 (0.67-1.97)	0.606

* Single comprises of single, living alone, divorced, and widow

Table 2. Secondary preventive measure from the cervical cancer for the use of OC

Women's characteristics	*Total number of women*	*Yes,* occ / always *no. (%)*	*Odds ratio (95% CI)*	*P value*
Attending regular examinations		84 (8.1)	1.00	
Once a year	1035	71 (5.7)	**0.68 (0.49-0.95)**	0.023
Less than once a year	1247			
Time of last PAP test		41(6.9)	1.00	
Within the last 12 months	592	115 (6.6)	0.94 (0.65-1.37)	0.768
More than 1 years ago	1749			

It was shown that the majority of OC users were single women (OR= 1.62, 95% CI, 1.08-2.42). Regarding education, college educated respondents more often take OCs as a method of the birth control when compared with those having primary level of education (OR=1.60, 95% CI 0.96-2.67).

Respondents from the rural areas, compared to those from the urban ones, used OCs less frequently (OR=0.92, 95% CI 0.66-1.28). As for regional differences, significantly smaller number of respondents used the OCs in Central Serbia (OR=0.41, 95% CI 0.28-0.59) and Belgrade (OR=0.59, 95% CI 0.37-0.92) when compared with women in Vojvodina. Women's financial status was not a factor showing any effect on the OC usage among our respondents.

Only women who had two abortions, used OCs 1.6 times more often in comparison with those who did not have any abortion (OR=1.60, 95% CI 0.98-2.60).

Table 2 shows results of the univariate logistics regression referring to the application of secondary preventive measures as a protection from the cervical cancer. Respondents who use OCs do not apply more often preventive gynecological measures in comparison with those who do not apply them. Only respondents who use OCs, infrequently go to gynecological examinations - less than once a year, in comparison with those who have control examinations once a year (OR=0.68, 95% CI, 0.49-0.95).

Table 3. Multivariate logistic regression analysis for the use of OC

Women's characteristics	*Odds ratio (95% CI)*	*P value*
Marital status		
Married	1.00	
Single	**1.63 (1.06-2.49)**	**0.024**
Education		
Elementary school	1.00	
Secondary school	0.89 (0.57-1.40)	0.628
University degree	1.27 (0.73-2.20)	0.392
Region		
Vojvodina		
Belgrade	1.00	
Central Serbia	**0.48 (0.30-0.78)**	**0.003**
	0.42 (0.29-0.61)	**<0.000**
Attending gynecological examinations		
Once a year	1.00	
Less than once a year	0.72 (0.51-1.01)	0.060

Table 3 shows results of the multivariate analysis of all independent variables showing statistically significant difference after univariate analysis: marital status, education, region, gynecological examinations. Results of

Table 4. The use of preventive secondary gynecological practices and socio-demographic factors: multivariate (adjusted) logistic regression analysis Use of OC

	Regular check-ups in the last 12 months Yes (n=1038) versus No (n= 1250)		**PAP test in the last 12 months Yes (n=591 versus No (n= 1750)**	
	Multi AOR (95%CI)	P value	Multi AOR (95%CI)	P value
Use of OC				
Yes (occ/always)	1.00		1.00	
No	0.73 (0.46-1.15)	0.170	1.22 (0.72-2.06)	0.467
Place of living				
Rural	1.00		1.00	
Urban	1.47 (1.17-1.85) *	**<0.000**	1.33 (1.02-1.75) *	**0.035**
Region				
Vojvodina	1.00		1.00	
Belgrade	0.59 (0.41-0.85) *	**0.005**	0.67 (0.40-0.87) *	**0.008**
Central Serbia	1.00 (1.17-1.85) *	**0.008**	1.34 (1.00-1.80) *	**0.051**
Education				
Elementary	1.00		1.00	
Secondary school	0.41 (0.31-0.54) *	**<0.000**	0.67 (0.48-0.92) *	**0.014**
University	0.32 (0.22-0.46) *	**<0.000**	0.36 (0.24-0.54) *	**<0.000**

*p<0.01
AOR - adjusted for all other variables (place of living, region, education)

this multivariate analysis have confirmed association of the OC usage with socio-demographic factors, such as marital status and region of living. Respondents from Vojvodina take OCs more often than those from Belgrade (OR= 0.48, 95% CI, 0.30-0.78), and Central Serbia (OR=0.42, 95% CI 0.29-0.61).

Multivariate (adjusted) logistic regression model was used to analyze predictors of secondary preventive practices, regular check-ups, and Pap tests. Model was created by adding all socio-demographic variables together in the model (place of living, region, education) as well as to the OC usage. Results of adjusted multivariate analysis showed that level of education, place of living and region were significantly associated with secondary preventive measures for the cervical cancer (regular check-ups and Pap tests). Secondary preventive measures were more frequently used by less educated respondents, who lived in the urban areas and in the region of Vojvodina, compared to the more educated women from rural areas and living in Belgrade (Table 4).

DISCUSSION

The aim of this study was to examine association between the OC usage and secondary gynecological preventive measures among women being in their reproductive age in Serbia. In this way, we created a profile of the OC users in Serbia by analyzing the nationally representative sample of women (5). We analyzed women's socio-demographic characteristics and the application of secondary preventive gynecological measures of importance for protection from the cervical cancer. It was found out that OC users were more often married and were living in Vojvodina. In addition, they had attended regular gynecological control examinations once a year. Results did not find out any association between secondary preventive gynecological measures (regular controls and Pap test within the last 12 months) and OC usage, but level of education, place of living and region were significantly associated with secondary preventive measures for the cervical cancer. Secondary preventive measures were more frequently used by less educated respondents, who lived in the urban areas in Vojvodina.

Women's financial status was not a factor associated with OC usage. According to Krings et al., women who take OCs are more often highly educated and have private health insurance or a higher economic status (12). There was no difference with regard of age structure of women who were either using OCs or not. In the study of Skjeldestad et al., pill is the dominant form of contraception for women of all age groups in Norway (13). Results from the representative sample of Canadian women in the reproductive period showed that OCs are predominantly used method of contraception (14).

There were no differences in usage of the OCs for women from both rural and urban areas. Regarding regional differences, respondents from the Central Serbia and Belgrade took OCs less frequently than those from Vojvodina did. Study conducted by Shulovich et al., has also shown that there are great differences among regions in Serbia regarding the use of contraceptives, being conditioned by the cultural heritage, economic situation, health education and religion (15). The study of Tobar et al., confirmed considerably smaller number of women from the rural areas in the USA who take OCs. Parallel analysis of contraceptive methods in developed countries such as USA, although with different approach to the health institutions when compared with ours, has shown that there is no significant differences in the OC usage by women living in rural regions and those living in cities (16). In the study of Eaker et al., women from the rural areas in Sweden also take OCs less often than those from the urban ones and the absence of the Pap testing may be some of reasons for that (17). Our study did not find out that reproductive behavior associated with the decision to take OCs. Only women who have had two abortions, in comparison with those who have not had any abortion, use OCs more often as a method of family planning. In the study of Rasević and Sedlecky, there is a great number of abortions in Serbia. The most important reasons are easily approachable medical services for abortion, lack of knowledge of contraception, hostility toward modern contraceptive methods and limitations in the family planning program (18). The following secondary preventive measures for the cervical cancer have been examined: frequency of the regular gynecological examinations and time of the last Pap test. The study has not confirmed that responders who use OCs, in comparison with those who do not use them, more frequently apply secondary preventive gynecological measures. The study by Castellsagué and Muñoz has pointed out importance of secondary preventive measures for the cervical cancer in OC users (19). Some studies, unlike ours, have found out more frequent preventive measures application in the OC users (20-22). The study by Park SJ and Park WS have found to women under hormone therapy were significantly more likely to get Pap tests and check-ups (23). Some studies have confirmed risk of the cervical cancer in the OC users (24), and they have demonstrated that risk of the invasive cervical cancer increases such as the OC usage prolongs (25-27). Moreno and col. have shown that women who had never used OCs as well as those who had used them for less than 5-year interval were not at an increasing risk of the cervical cancer (7). Association of OC usage, with HPV infections and the cervical cancer has been confirmed. However, numerous studies have found out that much time can elapse from exposure to hormones, to the invasive cancer development. Development of the vaginal cancer in girls whose mothers were taking diethylstilbestrol during pregnancy was also confirmed (28-31). All these results emphasize that greater awareness of the OC usage as well as of other modern methods of contraception in both girls and women should be treated as priority (19, 32). For this reason regular gynecological controls and Pap screening for the cervical cancer prevention in the OC users in Serbia is of particular importance. It is not only the task of the health care services, but also the task of community in general, schools and mass media.

CONCLUSION

This study did not confirm association of OC usage with secondary preventive measures for the cervical cancer. The users of OC in Serbia did not apply measures of secondary prevention against cervical cancer more often than women who did not use this form of prevention. Results showed that level of education, place of living and regions were significantly associated with secondary preventive measures for the cervical cancer (regular check-ups and Pap tests).

We believe that this study will be beneficiary in creation of policy for implementation of the organized screening program for the cervical cancer and its application in the routine practice.

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Conflict of Interest

We declare no conflicts of interest.

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