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Professional paper

Cervical Cancer Screening in Serbia

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A B S T R A C T

Cervical cancer is the second most common female malignancy in Serbia, after breast cancer, with 1089 new registered cases and an age-standardized incidence rate of 27.2 per 100,000 women in 2002. It is the fourth leading cause of cancer death with 452 deaths and an age-standardized death rate of 7.2 per 100,000 women. Compared with other European countries, the incidence of cervical cancer in Central Serbia is the highest. Regional differences in incidence are pronounced in Serbia with the lowest age-standardized incidence rate (16.6 per 100,000 women) registered in the Mačvanski region and the highest in eastern Serbia and the region of Belgrade where the rates are double at 32.5–38.1 per 100,000 women. Cervical cancer prevention in Serbia has relied on opportunistic screening that is characterized by high coverage in younger and low coverage in middle-aged and older women. Screening of selected groups of women employed in large companies is performed annually by many regional hospitals but this approach has little effect on morbidity and mortality. Recently, the Ministry of Health nominated an Expert Group to develop and implement a national cervical cancer screening program. A number of pilot projects have been undertaken with the results used for development of a national programme for cervical cancer screening. This is expected to be finalized in 2007, and launched over a 3-years period in order to cover all women aged 25–64 in entire Serbia.

Key words: *cervical cancer, screening, Serbia*

Introduction

The aim of the present study was evaluate the burden of cervical cancer in Serbia and present the status of cervical cancer prevention. The sources used to develop this report were official the Statistical Office of Serbia and the Cancer Registry of Serbia, as well as the results of the studies and projects related to cervical cancer screening conducted in Serbia during the period of 2002–2007.

Global Situation

Cervical cancer is the second most common malignancy in women worldwide, with about 490,000 newly registered cases every year. There are large differences in the incidence rate which varies from 2.0 per 100,000 women in Syria to 87.3 per 100,000 women in Haiti (age standardized rates). The highest rates are observed in Eastern and Southern Africa, Melanesia, Caribbean and Central America; the lowest rates are observed in Eastern and Western Asia, Australia, Northern America, Northern and Western Europe[1].

Several factors contribute to regional differences in cervical cancer rates and their trends. Persistent infections with the Human papillomavirus (HPV) are a necessary but not sufficient cause of cervical cancer. HPV is primarily transmitted by sexual contanct but differences in sexual behavior cannot entirely account for the geographic variation in cervical cancer. The most important factor is the availability of screening. In many developed countries where screening has been in place for a number of years, a decline in cervical cancer incidence and mortality has been observed over the last 30 years.

Cervical Cancer – a Major Health Problem in Serbia

From 1973–1982, the European extremes in cervical cancer incidence were the German Democratic Republic with an incidence of 33.2 and Spain with the one of 4.1[2]. At that time, the incidence in regions of Central Serbia where the cancer registries were functioning properly was 14.7 to 18.2 per 100,000[3].

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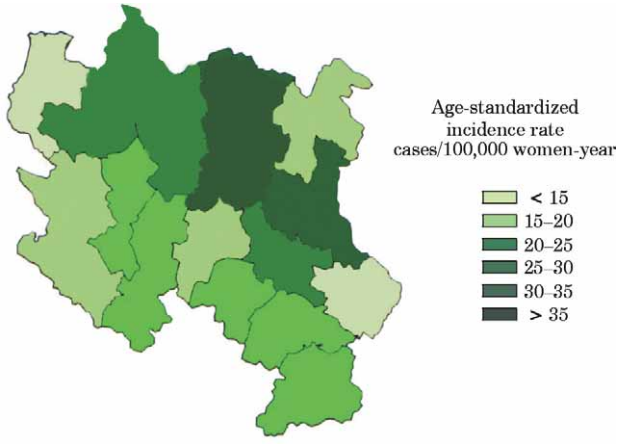

Fig. 1. Age-standardized cervical cancer incidence rates in Serbia, by regions, (per 100,000 women); average 27.3/100,000 women-year. Source: Cancer Registry of Serbia, 2002[6].

In 1995, the cancer registry in Central Serbia was reorganized with all new cases from Serbia's 16 regions registered centrally and the average age-standardized incidence rate for 1999 was 20.8/100,000 while the average standardized incidence rate for the European Union was 9.9[4]. Today, according to the data of the Cancer Registry of Central Serbia, cervical cancer is the second most common female malignancy after breast cancer with 1,089 new cases per year and the age-standardized incidence rate of 27.2 per 100,000 women in the year 2002[5]. However, there are also significant differences in cervical cancer incidence between the regions of Central Serbia (Figure 1). In 2002, the lowest age-standardized incidence rate (16.6 per 100,000 women) was registered in the Mačvanski region. The highest rates, more than twice higher, were registered in eastern Serbia, near the border with Romania, and in the region of Belgrade (32.5–38.1 per 100,000 women)[5].

When compared with data from European countries, the incidence of cervical cancer in Central Serbia is the highest in Europe. Similar high rates are observed in neighboring countries such as Romania, Albania and Bosnia & Herzegovina (Figure 2).

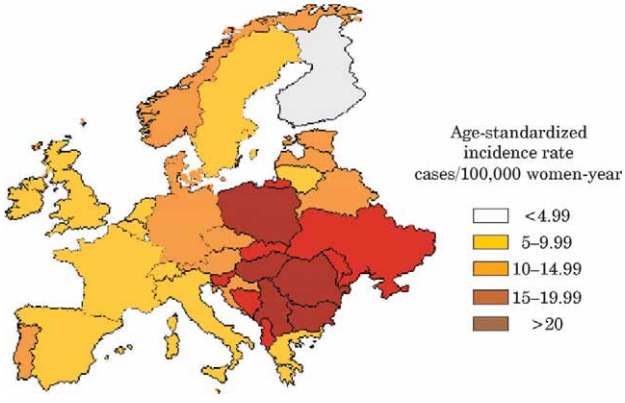

Fig. 2. Age-standardized cervical cancer incidence rates in European countries (per 100,000 women). Source: Ferlay J et al. Globocan 2002[1].

TABLE 1
COUNTRIES WITH HIGHEST CERVICAL CANCER MORTALITY RATES IN EUROPE (AGE-STANDARIZED MORTALITY RATES PER 100,000 WOMEN IN 2002)

Country	Age standardized mortality rate
Romania	13.0
Albania	9.8
Lithuania	9.0
Bulgaria	8.0
Bosnia & Herzegovina	8.0
Poland	7.8
Moldova	7.8
Macedonia	7.6
Latvia	7.4
Serbia	7.2
Hungary	6.7
Estonia	6.6
Russian Federation	6.5
Ukraine	6.4
Slovakia	6.1

Source: Ferlay J et al. Globocan 2002 and Statistical Office of Serbia[1]

In 2002, according to the data of the Statistical Office of Serbia, cervical cancer was the fourth leading cause of cancer death in females in Serbia with 452 deaths and the age-standardized death rate of 7.2 per 100,000 women[5]. As for mortality, Romania is the country with the highest mortality rate in Europe, while Serbian rate is significantly lower (Table 1). However, cervical cancer mortality depends on incidence and survival rates. As both Serbia and Romania have similar high incidence rates, difference in mortality could be explained by better availability and efficacy of cervical cancer treatment services in Serbia.

Age Distribution of Cervical Cancer in Serbia

The risk for cervical cancer increases with age. In Central Serbia very few cases are diagnosed before the age of 25. After that age, the incidence increases and reaches maximum in the 45 to 49 and 50 to 54 age groups[6] (Table 2).

Potential Target Population for Cervical Cancer Screening

Decisions on the target age group and frequency of screening are usually made at the national level, on the basis of local incidence and prevalence of cancer, HIV

TABLE 2
AGE DISTRIBUTION OF CERVICAL CANCER CASES IN CENTRAL SERBIA

Age group	No of cases	% of all cases	Age specific rate
0–14	0	0	0
15–19	1	0.1	0.6
20–24	1	0.1	0.6
25–29	23	2.3	12.4
30–34	40	4	22.7
35–39	75	7.5	42.9
40–44	108	10.8	56.7
45–49	162	16.1	75.3
50–54	173	17.2	77.9
55–59	105	10.5	66.3
60–64	89	8.9	55.4
65–69	93	9.3	52.2
70–74	77	7.7	46.5
75+	57	5.7	29.5

Source: Cancer Registry of Central Serbia 2003[7]

prevalence, availability of resources and infrastructure. WHO recommends that new programmes should start by screening women aged 30 years and more, and include women 25 to 29 only when the higher risk groups have been covered. Screening should not include women under 25 and for women over 65, screening is not necessary if they have had two previous negative smears[7].

The incidence of cervical cancer is high in all age groups from 35 to 69. The upper age limit of the target group should be set at least at the age of 64 so that there would not be many cases missed by screening in older age groups. On the other hand, lower age limit should be set at 30 so that as many lesions as possible would be discovered in precancerous lesions.

There is about 1,5 million women in the age group 30 to 59 and about 1,8 million women in the age group 30 to 64 in Serbia. With a three year interval, it would mean 0,5 or 0,6 million to be screened yearly.

Cervical Cancer Control Programme

A comprehensive, centalized screening programme for cervical cancer has never been implemented in Serbia and cervical cancer prevention has relied on opportunistic screening. This type of screening has been characterized by high coverage in younger and low coverage in middle-aged and older women. Screening of selected groups of women employed in large companies is performed annually by many regional hospitals. This approach, however, has had little effect on morbidity and mortality.

In spite of some efforts to initiate screening during the period between 1990 and 1999, the difficult situation in the country did not enable more organized approach. Besides the other effects on health service, the economic crisis left significant the consequences to general health:

- Economic resources for health were lowered.
- Investments for health were decreased (from € 150 per person in 1997 to less than € 50 in 1999).
- Prevention became inadequate.
- Overall mortality and morbidity increased.

In this situation, disease prevention through mass screening in central Serbia did not seem to be the primary problem and cervical cancer control in Serbia had unsatisfactory levels of effectiveness. This was primarily due to the absence of national strategy for cancer prevention, a lack of programme funds for cancer prevention or early detection, as well as an insufficient public and political awareness of the importance of cancer prevention. Primary prevention programs did exist but were carried out without well-defined methodology or objectives and without appropriate effectiveness analysis. As a consequence, a high proportion of cervical cancers were diagnosed when already well-advanced and metastatic, leading to a low probability of cure and high mortality rates.

Actions Against Cervical Cancer – Preparing the Foundation for Organised Cervical Cancer Screening

Beginning in the year 2000, the basic strategies applied to achieve the cervical cancer control in Serbia were focused on cancer prevention and early detection strategies. The main risk factors on the national level were defined and monitored. The efforts were made to improve the system for cancer registration. This could not be achieved without introduction of unique information system to help in overcoming communication problems on the local, regional and national level. To achieve these goals it was mandatory to increase the support of government, as well.

Becoming aware of the increasing incidence and mortality of cervical cancer in Serbia and the importance of early detection and treatment of this disease, the Ministry of Health nominated an Expert Group for the prevention and early detection of cervical cancer in 2003. The aim was to develop and implement national screening programme. It was expected that the systematic screening of non-symptomatic women would increase the proportion of localized tumors, but also the need of treatment resources for these cancers.

As a result, several projects have been completed to study the psycho-social aspects of cervical screening in this region and to improve the local screening infrastructure:

- A study conducted by the Institute of International Social Affairs in 2002 showed that an educational campaign on the importance of screening can increase participation by more than 60%[8].
- A survey sponsored by the Alliance for Cervical Cancer Prevention (ACCP) and conducted by Programme for

Appropriate Technology in Helath (PATH) in 2003–4, explored women's knowledge and perceived barriers towards cervical screening, so adequate campaigns can be designed.

The research was focused on urban women residing in the capital city and one major regional city. The study was comprised of qualitative (phase I) and quantitative (phase II) research. The main determining factors were the age and education of the women. The first phase has been realized through focus group discussions (62 women participated, recruited by network sampling) and in-depth interviews (conducted with 22 women)[9]. Data deriving from the qualitative study were used to develop a questionnaire on women's understandings and knowledge of cervical cancer. The survey was distributed to 800 women from a selected number of community health services[10].

The population sampled showed a broad lack of knowledge about the necessity of screening and shared attitudinal barriers with women in other regions. Results revealed that most of women do not regularly visit a gynaecologist, do not understand the purpose of Pap smear (even if they regularly have it), think that absence of symptoms means that they are healthy and do not need Pap smear, do not know the procedure of Pap smear, are often embarrassed about being examined (this was independent of the gynecologist's sex), believe that little can be done to prevent cancer and an unwillingness to talk about the illness. Education and economic status were not highly related to knowledge about cervical screening[10].

Thematic analysis identified that the interplay of social and personal barriers influenced women's poor presentation for screening. It found that the socio-economic situation prevented women from focusing on their health and it identified a number of problems with the delivery of health services in the region. Inadequate public health education, lack of patient-friendly health services, socio-cultural health beliefs, gender roles, and personal difficulties were the most salient barriers to screening[9].

The study findings suggest how, within the context of opportunistic screening, patient education maybe employed. The introduction of compulsory cervical cancer screening, suggested by some participants, may be a possible approach[9]. The success of public awareness campaigns elsewhere suggests that a media-centered approach could also have good results in Serbia. The lack of media attention noted in the study focus groups supports this conclusion.

In general, study findings was used to inform and facilitate the change in government's policy regarding cervical screening and to develop the public health campaign targeting cervical cancer.

- Clinical Center of Serbia was one of the partners in European Consortium for Cervical Cancer Education (ECCCE) project granted by European Commission and conducted from 2002–2004. This project has lead to the foundation of The European Cervical Cancer Association (ECCA). The ECCA was founded by 15 different organisations from across Europe, which included cancer charities, cancer treatment centres, university teaching hospitals and health education organisations. One of them was Clinical Center of Serbia. The ECCA was established specifically to co-ordinate a Europe-wide public health education programme that would raise awareness of cervical cancer and how it can be prevented. For the general public in Serbia the project was developing an educational programme to provide women with the information they need to reduce their risk of cervical cancer. This project has adopted the materials developed by ECCCE and ECCA. These materials are approved by Serbian Ministry of Health and widely distributed in Serbia through the network of regional health centres.
- Project »Improving Preventive Health Services in Serbia« (IPHSS) has started in September 2004. Its goal was to reduce the mortality by improving preventive health services. To achieve it, this project, funded by European Union, managed by European Agency for Reconstruction and realised by EPOS Health Consultants, targets both health professionals and women. IPHSS edited guidelines for prevention of cervical carcinoma elaborated in line with EU recommendations and will distribute them in 25 regional Serbian health centres[11]. It also supports the establishment of a national School for cytology. In parallel, IPHSS wishes to contribute to the education of women on the prevention of cervical cancer.
- A Pilot Programme for Cervical Cancer Screening was implemented 2004 in Branicevo, a region in eastern Serbia with a particularly high incidence of cervical cancer[12]. This project, supported by the French government and implemented by WHO, was the first organized screening programme in Serbia.

Screening Implementation

»Branicevo project« was the first organized screening in Serbia. In 2001, the French donor, the WHO and health authorities of the Republic of Serbia jointly agreed that the high mortality and incidence of cervical cancer in Serbia presents a major public health problem that needs urgent intervention. The French donor approved a grant for implementation of a pilot project for organized screening of cervical cancer that would serve as a basis for developing a national programme. The project management was entrusted to WHO Regional Office for Europe – WHO Country Office in Serbia (at the time Serbia and Montenegro) and was planned for implementation through the national health system (public health institutes and health service).

The project went through the following phases:

- Design of social mobilisation, action plan and implementation of social mobilisation.
- Setting up the Central Cytology Laboratory and the quality assurance system for cervical screening.

TABLE 3
THE DISTRIBUTION OF CERVICAL SMEAR RESULTS IN THE SCREENED POPULATION OF BRANICEVO REGION

Result of PAP smear	PAP I	PAP II	PAP IIIa	PAP IIIb L-SIL	PAP IIIb H-SIL	PAP IV	PAP V	Unsatisfacotry	Total
Number of women examined	554	11057	520	340	94	26	4	168	12,763
%	4.34	86.63	4.08	2.66	0.74	0.20	0.03	1.32	100.00

PAP – Papanicolaou, L-SIL – low grade squamous intraepithelial lesion, H-SIL – high grade squamous intraepithelial lesion

- Developing the Information Technology (IT) for screening.
- Training in software application and continuous on-site IT support.
- Regular weekly quality assurance visits to cytological laboratory.
- Setting up monitoring and evaluation system.
- Drafting of national strategy – process support.

Screening invitations were sent to 22,300 women aged 30–49 years in the Branicevo district and 12,763 women were screened. Sixty three high-grade squamous intraepithelial lesion (H-SIL) and 6 invasive cancers were detected in the screened population with the estimated cervical cancer incidence of 47.01 per 100,000 and 49.36 H-SIL lesions per 100,000 women (Table 3).

The specific project objectives were achieved:

- 60 % of target population (women aged 30–49 years of age) in the Branicevo district were screened for cervical cancer with cytological methods.
- Local Health experts were trained in methods of cytological screening and a system of quality assurance was set up.
- Bethesda system of cytological classification was successfully introduced into the practice.
- 16 % of all slides were re-screened through quality assurance system, all slides with positive findings at first screening and 10 % of slides assessed as negative at first screening.
- 95 % of matching between 1st and 2nd screening was identified.
- 1.32 % of slides were inadequate for cytology and had to be repeated.
- All women identified with pre-malignant lesions through the screening project were referred for full diagnostic procedure and required treatment.
- Effects of the pilot project on mortality for cervical cancer screening in the district will be monitored but will be visible only after a longer time period.

Conclusions

The results and experiences from the Branicevo pilot project have been used for development of a National programme for cervical cancer screening, which is expected to be finalized in 2007, and launched over a 3-years period in order to cover all Serbian women aged 25–64.

The development of national strategy is essential for the sustainability of the effects of the project in the pilot district and in Serbia in total. The Ministry of Health of Serbia had set up a National Committee for Prevention of Cervical Cancer, in July 2006. WHO will continue to provide technical support to the National Committee in 2007 (through its regular programme) until a National Programme for Cervical Cancer Screening and action plan for nation wide implementation over a 3-years period are fully developed.

In addition to supporting the development of the National Programme, the WHO also supported the National Cancer Registry so they were able to update the national cancer data-base. It is expected that in 2007, the National Cancer Registry will be able to start to monitor pre-malignant lesions of the cervix (from the pilot district) and when a national programme starts to be implemented to monitor pre-malignant cervical lesions nation wide. The Institute of Public Health (IPH) has been specifically supported to strengthen the Cancer Registry Department and to prepare and print Annual Cancer Registries for 2002 and 2003 (2004 and 2005 were prepared as well and will be published with internal resources of the IPH of Serbia in 2007).

At the end of 2006 the process of development of a National Programme for Cytological Screening of Cervical Cancer and preparing of a national action plan is fully under way. However, the operationalisation of the Programme and its implementation will depend on integration of this new public health programme into the financing mechanisms of the Serbian health system (combination of the national health insurance for individual services and Ministry of Health budget for the support to the public health component – social mobilisation, organisation of programme, programme monitoring and implementation).

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PROBIR RAKA VRATA MATERNICE U SRBIJI

SAŽETAK

Rak vrata maternice zauzima drugo mjesto među bolestima žena u Srbiji, odmah iza raka dojke, sa 1.089 registriranih novih slučajeva te dobno-standardiziranom stopom pojavnosti od 27,2 na 100.000 žena u 2002. g. Na četvrtom je mjestu po smrtnosti sa 452 smrtna slučaja te dobno-standardiziranom stopom smrtnosti od 7,2 na 100.000 žena. U usporedbi s ostalim europskim zemljama pojavnost raka vrata maternice u Centralnoj Srbiji je najviša. Regionalne razlike u pojavnosti ovog raka su jako izražene u Srbiji, sa najnižom dobno-standardiziranom stopom pojavnosti (16,6 na 100.000 žena) zabilježenom u području Mačvanski, a najvišom u istočnoj Srbiji te području Beograda gdje su stope pojavnosti dvostruko više (32,5–38,1 na 100.000 žena). Prevencija raka vrata maternice u Srbiji se temelji na oportunističkom probiru koji je karakteriziran visokom pokrivenosti mladih te niskom pokrivenosti starijih i žena srednjih godina. Probir odabranih skupina žena zaposlenih u velikim tvrtkama se provodi u mnogim područnim bolnicama jednom godišnje, međutim ovaj pristup ima mali utjecaj na bolest i smrtnost. Nedavno je Ministarstvo zdravstva imenovalo Grupu stručnjaka koja bi razvila i provela program probira raka vrata maternice na nacionalnoj razini. Provodi se velik broj pilot-projekata rezultati kojih se koriste za razvoj nacionalnog programa probira za rak vrata maternice. Očekuje se da će to biti dovršeno u 2007. g. te, kroz razdoblje od 3 godine, pokretanje programa probira koji bi pokrivao sve žene Srbije u dobi između 25 i 64 godine.