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ORIGINAL ARTICLE

Mortality from cervical cancer in Serbia in the period 1991-2011

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Summary

Purpose: *The aim of this study was to analyze trends of death rates for cervical cancer (CC) on territory of The Republic of Serbia in the period 1991-2011.*

Methods: *In this descriptive epidemiological study, unpublished data of the Statistical Office of the Republic of Serbia were used for the analysis of mortality due to CC among women in Serbia, from 1991 to 2011. Three different types of rates were calculated: crude, age-specific and age-adjusted rates. The age-standardized rates were calculated by the direct method of standardization using the World Standard Population as standard. The trends were assessed by joinpoint linear regression analysis. An average annual percentage change (AAPC) and the corresponding 95% confidence intervals (CI) were computed for trends.*

Results: *The average age-standardized CC mortality rate (ASCCMR) was 7.03 per 100,000. The lowest value of the ASCCMR was at the beginning of the observed period (6.05 per 100,000) and the highest was 8.17 per 100,000 in 2008. The age-adjusted CC mortality rates have been continuously and significantly increasing (AAPC=+0.7, 95% CI=0.3-1.1, p<0.05). In all age groups we found increasing trends, except in the age group of 65-74 years.*

Conclusion: *Since ASCCMR has been steadily increasing during the period observed, reducing these rates is highly warranted. To achieve this target, an organized CC screening program is essential.*

Key words: *cervical cancer, mortality, trends*

Introduction

With standardized annual mortality rate of 6.8 per 100,000 women and 266,000 deaths, estimated in 2012, CC is the fourth most common cause of death from all malignant diseases among women worldwide [1].

Statistics shows that 88% of all deaths attributable to CC appear in less developed countries [2]. In developed countries, the widespread use of screening programs has dramatically reduced the mortality rates of CC [3]. Based on the information presented by the International Agency for Research on Cancer (IARC) in 2012, Serbia is in the third place for the mortality, after Romania and Moldova [4].

According to unpublished data of the Cancer Registry of the Institute of Public Health of Serbia "Dr Milan Jovanović Batut", in 2011, the CC standardized mortality rate was 6.9 per 100,000 women [5]. With contribution of 5.5% in central Serbia and 5.94% in Vojvodina, CC was the fourth most frequent cause of death from cancer among the female population in Serbia [5,6].

The aim of this study was to estimate death rates for CC on the territory of the Republic of Serbia and their trends during the period 1991-2011.

Methods

This study represents a descriptive epidemiological analysis of CC mortality rates among women in the Republic of Serbia for the period 1991-2011.

Data on women who died of CC (code 180-revision 9 and code C53 revision 10 of the International Disease Classification) were obtained from the Statistical Office of the Republic of Serbia (used for the analysis of mortality due to CC in Serbia in 2011).

The population data related to the total number of women of the Republic of Serbia (excluding the Province of Kosovo and Metohia), as well as the number of women by age groups were obtained from the popula-

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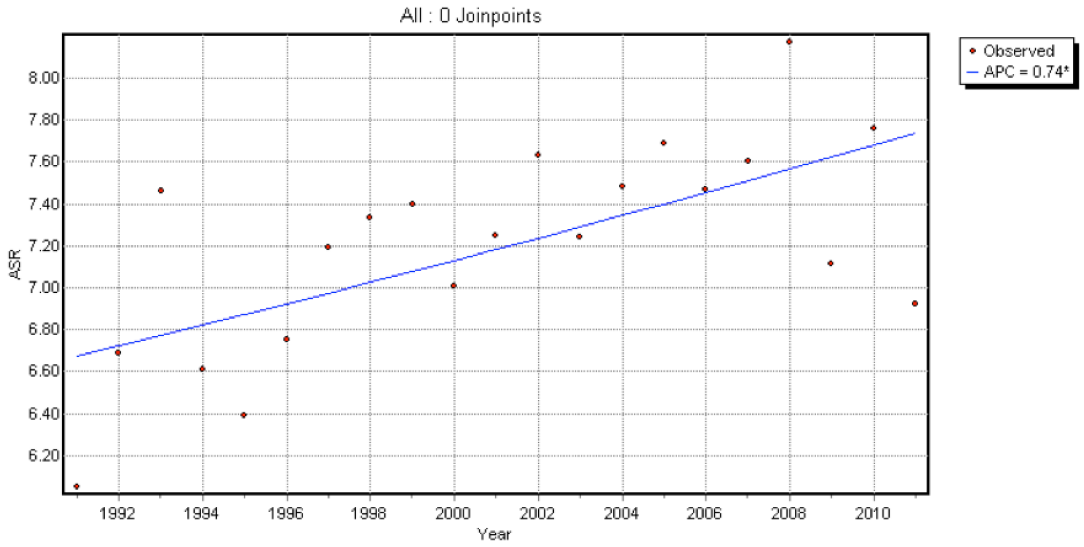

Figure 1. Joinpoint regression analysis of cervical cancer mortality in the Republic of Serbia in the period 1991-2011 ASR: age-standardized mortality rates (per 100,000); standardization by World Population; APC-annual percent change: *The APC is statistically significantly different from zero (two-sided p<0.05)

tion censuses in 1991, 2002, and 2011. The estimates of population for the inter-census years, from the Statistical Office of the Republic of Serbia, were used.

The age groups ≤34 years were not included, because there were too few cases to allow calculation and analysis for mortality rates.

Three different types of rates were calculated: crude, age-specific and age-adjusted rates. The age-standardized rates were calculated by the direct method of standardization using the World Standard Population as standard (according to the methodology described by Segi) [7,8].

Statistics

In order to detect statistically significant change in linear trends of the CC mortality rates, we used joinpoint linear regression analysis. This provides measuring the trends with the Annual Percent Change (APC) and Average Annual Percent Change (AAPC) and their respective 95% confidence intervals (95%CI) [9].

Joinpoint analyses were performed using the Joinpoint regression software (version 3.5.4, August 2012), available through the Surveillance Research Program of the US National Cancer Institute.

Results

In the observed period (1991-2011), 7209 women have died from CC in Serbia. The average age-standardized CC mortality rate (ASCCMR) was 7.03 per 100,000. The smallest ASCCMR of 6.05 (per 100,000) was at the beginning of the observed period and the highest was 8.17 (per 100,000) in 2008. The age-adjusted CC mortality rates have been continuously and significantly increased (AAPC=+0.7, 95% CI=0.3-1.1, p<0.05) during the observed period (Figure1).

Table 1. Cervical cancer mortality in Serbia in the period 1991-2011

Year	*N*	*Crude rate*	*ASR*
1991	280	9.50	6.05
1992	308	10.44	6.69
1993	342	11.59	7.46
1994	315	10.67	6.61
1995	297	10.07	6.39
1996	315	10.68	6.75
1997	330	11.61	7.19
1998	348	12.28	7.33
1999	355	12.58	7.40
2000	327	11.62	7.01
2001	337	12.00	7.25
2002	368	13.12	7.63
2003	355	12.69	7.24
2004	358	12.82	7.48
2005	370	13.28	7.69
2006	359	12.92	7.47
2007	384	13.87	7.60
2008	389	14.10	8.17
2009	358	13.02	7.11
2010	367	13.39	7.76
2011	347	12.71	6.92

ASR: age-standardized rate (per 100,000), using World Standard Population

The absolute number of deaths, crude death rates and age-standardized mortality rates are shown in Table 1.

Table 2. Joinpoint regression analysis of cervical cancer mortality in the Republic of Serbia[§] in the period 1991-2011

Age groups (years)	*AAPC (95%CI) 1991-2011*	*Years*	*APC (95%CI) for specified periods*
35-44	-0.0 (-1.3 to 1.2)		
45-54	+1.7 * (0.8 to 2.6)		
55-64	+1.7 * (0.1 to 3.3)	1991 - 1993	+12.3 (-0.3 to 26.5)
		1993 - 1999	-2.6 (-5.1 to 0.1)
		1999 - 2008	+4.8 * (3.4 to 6.2)
		2008 - 2011	-5.0 (-10.5 to 0.8)
65-74	-1.0 * (-1.7 to -0.2)		
≥75	+0.7 (-0.3 to 1.7)		

*Joinpoint significantly different from zero (p<0.05); AAPC: average annual percentage change, APC: annual percent change, CI: confidence interval, [§]excluding the data for the autonomous province of Kosovo and Metohia

Differences in trends of age-specific mortality rates were not so visible in middle-aged women (45-54 years). Significant increasing mortality trend was observed during the whole study period (+1,7% per year; 95% CI 0.8 to 2.6) (Table 2).

Among women aged 55-64 years, 4 patterns of changes in CC mortality rates were observed: a marked increase (by +12.3% per year) from 1991 to 1993, was followed with decrease (- 2.6% per year) in the period 1993-1999. The second significant increase (+4.8%, per year; 95% CI 3.4 to 6.2; p<0.05) was in the period 1999-2008 and ended with a decline of -5.0% per year in the period 2008 to 2011 (Table 2).

Only in the group of women aged 65-74 years the mortality rates decreased significantly over the entire study period (-1.0% per year, 95% CI -1.7 to -0.2) (Table 2).

In the oldest women (≥75 years), slight, but insignificant increase of CC mortality (0.7% annually, 95% CI -0.3 to 1.7) was recorded (Table 2).

Discussion

CC is a major public health problem in many countries worldwide. In Serbia,the highest recorded mortality rate was in 2008, but in the last 3 years, a decline of death rate was observed.

In the whole 21-year study period, in Serbia, the average value of standardised CC mortality rate was 7.03 per 100,000, which is similar to those in Central and Eastern European countries (7.0 in Bulgaria, 7.5 in Lithuania, and 7.9 in the Republic of Moldova). Opposing these results, low age-standardized mortality rates were observed in the North-West and the South parts of the Balkan region (Slovenia: 3.0/100,000, Croatia: 3.2/100,000, Bosnia and Hercegovina:2.7/100,000, Albania and Greece: 1.8/100,000) [1].

As for the trend of CC mortality rates in Serbia throughout the whole observed period we showed a steady increase (APC=0.7% per year). An earlier study by Denic et al. showed similar results for CC mortality in central Serbia, the greater part of the Republic of Serbia [10]. Similar results were shown in the study by Arbyn et al. with constantly increasing rates in Latvia, Lithuania, Romania and Bulgaria, linked to historical lack of organized screening program. Stable mortality rates were recorded in Estonia [11].

On the contrary, the Northern European countries where screening programs have been established during the last century (Denmark, Finland, Sweden and the UK), decreasing trends were observed. The negative slope of the trend was very steep (APC = –15.6%) in the first years of analysis in Finland, but became less pronounced subsequently (APC= –4.7%). Ireland showed a modest regularly decreasing trend (APC=–1.1, 95% CI–1.4 to -0.7%, without significant joinpoint) [12].

In Canada, mortality rates dropped from 13.5 to 2.2 per 100,000 (83% in total) between 1952 and 2006, which is in correlation with high levels of participation in the cervical screening program that started in the 1970s [13].

Adding to this pattern, a Taiwanian study showed that increasing death rates recorded in the period 1981-1995 until the implementation of the CC screening program in 1995, were followed by the two-fold decrease of rates during 1996-2010 [14].

Concerning age-related trends, our study showed significant increase of death rates of +1.7% per year in two age groups: 45-54 years and

55-64 years.

Similarly, in Romania, mortality rates started to increase in the age group 30–39 after 1975, in the age group 40–49 after 1985 and in the age group 50–59 after 1995. In Estonia and Latvia, mortality rates increased in the age groups 40-59 years. In Bulgaria, mortality trends were rather stable with a tendency to rise in age groups of 30–59 years [11].

Opposite trends were found in the Netherlands' study, where a significantly decreasing mortality trend for the age groups 30-34 and 35-39 years was shown [15]. Similarly, in Bulgaria and Romania, slightly decreasing rates for women aged 55 or older were demonstrated [11].

Based on some encouraging international experiences [18,19], a CC screening program in Serbia will hopefully reduce mortality rates. The decreasing trends could be expected to begin in about 10 years after the introduction of a nationwide organized early detection preventive program with wide coverage.

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