



Mortality rate of lip, oral cavity and pharynx malignant tumors in Serbia within a period 1991–2009

Stopa mortaliteta od malignih tumora usne, usne duplje i ždrela u Srbiji u periodu 1991–2009. godine

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Abstract

Background/Aim. Lip, oral cavity and pharynx malignant tumors account for 3.7% of all cancer deaths worldwide, with significant geographic variations in frequency and distribution. The aim of this descriptive epidemiologic study was to analyze the mortality rate of lip, oral cavity and pharynx malignant tumors in Serbia proper within a period 1991–2009. **Methods.** Mortality rates standardized directly using the world population as the standard were used in data analysis. Linear trend and regression analyses were used to analyze rate trends in mortality. **Results.** The Serbian population demonstrated an increase in the mortality of lip, oral cavity and pharynx malignant tumors ($y = 3.32 + 0.03x$; $p = 0.002$; average annual percent change = + 0.8). The male population showed a significant increase in mortality trend ($y = 5.90 + 0.03x$; $p = 0.020$; % change = + 0.9), while the female population did not show a significant increase in mortality. The male/female cancer mortality ratio was 5.5:1. Mortality rates for lip, oral cavity and pharynx cancer increased with age in both genders, with rates being the highest in the population aged 85 and older. Increasing trends of lip, oral cavity and pharynx cancer mortality were observed in males aged 50–54; the average annual percent change was + 7.4 % (95% CI, 6.2–9.0). The population of both genders aged 55–59 demonstrated an increase in lip, oral cavity and pharynx cancer mortality, the increase being + 1.8% (95% CI, 1.4–2.2) in men and + 34.3% (95% CI, 28.4–40.2) in women. **Conclusion.** The increasing trend in lip, oral cavity and pharynx cancer mortality points to the necessity to investigate etiology and improve primary and secondary prevention measures.

Key words:

mouth neoplasms; pharyngeal neoplasms; serbia; mortality; risk factors.

Apstrakt

Uvod/Cilj. Maligni tumori usne, usne duplje i ždrela uzrok su 3,7% svih smrtnih slučajeva od raka u svetu, sa značajnim geografskim varijacijama u učestalosti i distribuciji. Cilj ove deskriptivne epidemiološke studije bila je analiza mortaliteta od malignih tumora usne, usne duplje i ždrela u Srbiji u periodu od 1991. do 2009. godine. **Metode.** U analizi podataka korišćene su standardizovane stope mortaliteta, dobijene metodom direktne standardizacije sa populacijom sveta kao standardom. Linearni trend i regresiona analiza korišćeni su za analizu trenda mortaliteta. **Rezultati.** U populaciji Srbije zabeležen je porast mortaliteta od malignih tumora usne, usne duplje i ždrela ($y = 3,32 + 0,03x$; $p = 0,002$; prosečna godišnja procentualna promena = + 0,8). Kod muškaraca je zabeležen značajan trend porasta mortaliteta ($y = 5,90 + 0,03x$; $p = 0,020$; % promena = + 0,9), dok kod žena nije utvrđen značajan porast mortaliteta. Odnos mortaliteta među polovima (muškarci/žene) bio je 5,5 : 1. Stope mortaliteta od malignih tumora usne, usne duplje i ždrela povećavale su se sa starošću kod oba pola, pri čemu su stope bile najviše u populaciji starijih od 85 i više godina. Trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela uočen je kod muškaraca starosti 50–54 godine: prosečna godišnja procentualna promena iznosila je + 7,4% (95% IP = 6,2–9,0). U populaciji oba pola u uzrasnoj grupi 55–59 godina zabeležen je trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela, pri čemu je porast iznosio + 1,8% (95% IP = 1,4–2,2) kod muškaraca i + 34,3% (95% IP = 28,4–40,2) kod žena. **Zaključak.** Trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela ukazuje na neophodnost etioloških istraživanja i unapređenja mera primarne i sekundarne prevencije.

Ključne reči:

usta, neoplazme; farinks, neoplazme; srbija; mortalitet; faktori rizika.

Introduction

The International Association of Cancer Registries in the most recent estimate reports 128,000 deaths from oral cavity cancer (including lip cancer) and 147,000 pharyngeal cancers in 2008 worldwide¹⁻³. Oral cavity and pharynx cancers account for 3.7% of all cancer deaths in the world. Geographic variations in mortality were observed³⁻⁵.

Globally, the highest lip, oral cavity and pharynx cancer mortality rates for both males and females are found in Melanesia (11.3 per 100,000 people), South-Central Asia (9.1), and South-East Asia (8.8)^{1,3}. The lowest death rates are found in Central America (1.3), North America (1.5) and Australia/New Zealand region (1.9). Nearly 80% of lip, oral cavity and pharynx cancer cases (216,425 cases) occur in developing countries (150,820 men *versus* 65,605 women)^{1,3}. The greatest number of deaths (70.1%) was recorded in Asia, almost 50% of which occurred in India.

These cancers are more than twice as common in men as in women^{5,6}. Most people of both genders, diagnosed with oral cavity and pharynx cancer are older than 50 years⁵. In the United States, from 1975 through 2002, age-adjusted mortality rates were higher among males than females and highest for black males⁷. By the mid 1980s, mortality rates were declining for white and Afro-American males and females, but however disparities persist^{7,8}. In the United States the lowest mortality rates were recorded in Latinos⁸. The age-adjusted death rate for cancer of the oral cavity and pharynx was 2.4 per 100,000 men and 0.7 per 100,000 women per year in 2005–2009 in the US Latinos, with a significant declining trend (average annual percentage change was - 3.6% in males and - 1.5 % in females). Though oral and pharyngeal cancer mortality in Europe has declined in the last decade in men, there are still rises in a few Central and Eastern European countries, reaching exceedingly high rates in Hungary and Slovakia, which now have the highest rates on a European scale^{9,10}.

The aim of this descriptive epidemiologic analysis was to estimate death rates for lip, oral cavity and pharynx cancer and their secular trends in the population of Serbia over a period 1991–2009.

Methods

This descriptive epidemiologic study used data on individuals who had died of lip, oral cavity and pharynx malignant tumors (codes 140–149 revision 9 and C00–C14 revision 10 of the International Classification of Diseases to classify death, injury and cause of death), all malignancies (revision 9 codes 140–209 and revision 10 codes C00–C97), symptoms and undefined states (revision 9 codes 780–799 and revision 10 codes R00–R99), and all causes of death (revision 9 codes 001–999 and revision 10 codes A00–Z99) collected by the Statistical Office of the Republic of Serbia, which receives death certificates and compiles mortality data by gender, age, year, and cause of death. The research included the entire population of the Republic of Serbia (all ages), excluding the Province of Kosovo, from 1991 to 2009. Data for internally displaced

2009. Data for internally displaced persons and refugees were included in the population of Serbia, but could not be set aside as a special contingent. Data on the number and composition of the population of the Republic of Serbia by gender and age were obtained from the population censuses (1991 and 2002 national censuses) for the years 1991 and 2002, and for inter-census years estimates published by the Statistical Office of the Republic of Serbia. The age-standardized rates (per 100,000 people per year) were calculated by direct standardization, using the World Standard Population as proposed by Jensen et al.¹¹.

An estimate of the linear trend of the age-adjusted lip, oral cavity and pharynx cancer mortality rates was obtained by fitting Poisson regression models to the data observed over the period 1991–2009. Two-sided *p* values were reported and considered to indicate statistical significance when they were less than 0.05. Age-specific mortality rates were computed for 5-year age groups. Percent changes of mortality rates were calculated as a percent difference between the adjusted rates of the two successive years and then as an average of these changes for the entire observation period. Confidence intervals (CI) for the average age specific rates were assessed with 95% level of probability.

All statistical analyses were conducted using the Statistical Package for the Social Sciences software (SPSS Inc, version 19.0, Chicago, IL, USA).

Results

Over the 19-year observation period, in the Republic of Serbia, excluding the Province of Kosovo, a significant decrease in total mortality was observed ($y = 799.31 - 7.78x$; $p = 0.000$; % change = - 0.7), with a significant increase in deaths from all malignant tumors ($y = 119.69 + 1.18x$; $p = 0.000$; % change = + 1.0) (Figure 1). Mortality rate of lip, oral cavity and pharynx malignant tumors increased ($y = 3.32 + 0.03x$; $p = 0.002$; % change = + 0.8). The nonsignificant declining trend ($y = 63.33 - 0.83x$; $p = 0.151$; % change = - 0.2) was observed for mortality in which the causes of death were symptoms, signs and abnormal clinical and laboratory findings.

In the same period, mortality of lip, oral cavity and pharynx malignant tumors significantly increased among males ($y = 5.90 + 0.03x$; $p = 0.020$; % change = + 0.9), whereas the increase in mortality among women was not statistically significant (Figure 2). On average, men died of lip, oral cavity and pharynx malignant tumors 5.5 times more frequently than women.

Trends analysis of age adjusted mortality rates of oral cavity cancer (including lip cancer) showed a significant increase ($y = 1.79 + 0.02x$; $p = 0.001$; % change = + 1.1) in the population of Serbia (Figure 3), with an increase in both genders ($y = 3.20 + 0.03x$; $p = 0.010$; % change = + 0.9 in men, *versus* $y = 0.57 + 0.02x$; $p = 0.038$; % change = + 4.6 in women). On the other hand, mortality rates of malignant pharyngeal tumors have not decreased significantly (Figure 4).

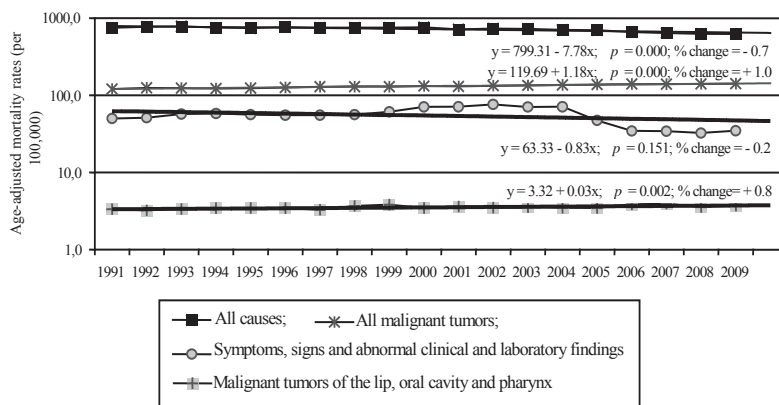


Fig. 1 – The mortality rates of the chosen causes in Serbia, excluding the Province of Kosovo, in 1991–2009

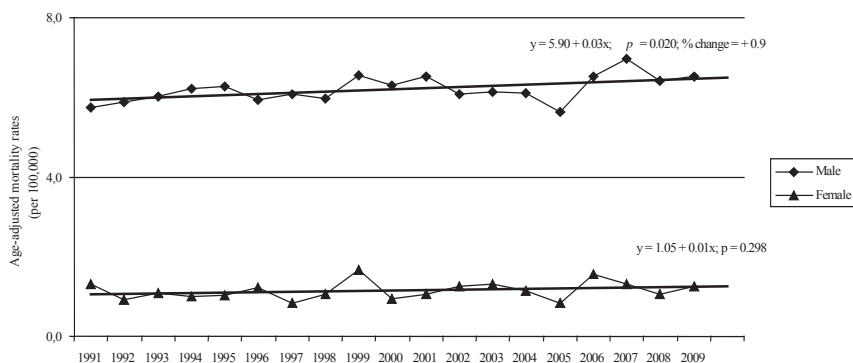


Fig. 2 – The mortality rates of malignant tumors of the lip, oral cavity and pharynx by gender in Serbia, excluding the Province of Kosovo, in 1991–2009

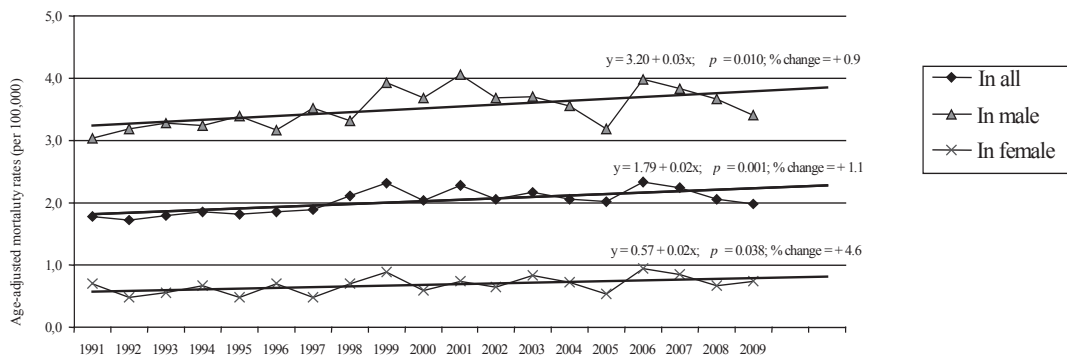


Fig. 3 – The mortality rates of malignant tumors of the lip and oral cavity by gender in Serbia, excluding the Province of Kosovo, in 1991–2009

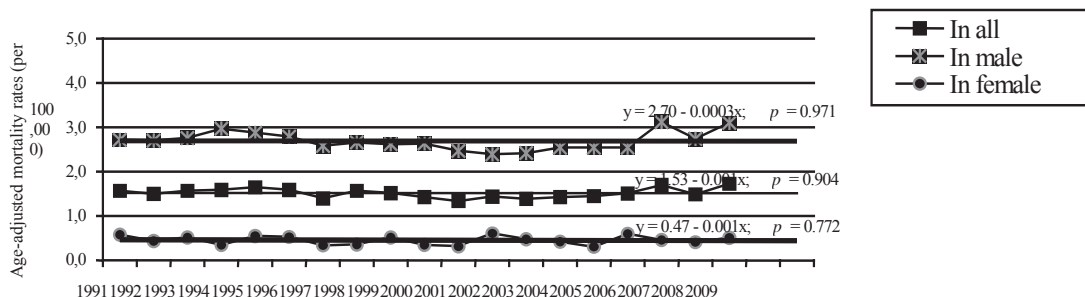


Fig. 4 – The mortality rates of malignant tumors of the pharynx by gender in Serbia, excluding the Province of Kosovo, in 1991–2009

Lip, oral cavity and pharynx cancer mortality rates increase with age and are highest in people aged 85 and older (Table 1). Low mortality rates were recorded in both men

(14.4), and the lowest mortality rates (approximately 1 per 100,000) are recorded in Israel, Kuwait and Cyprus^{2,3}. Countries with female population mortality rates higher than

Table 1
The average age-specific mortality rates and linear trend in lip, oral cavity and pharynx malignant tumors in Serbia, excluding the Province of Kosovo, in 1991–2009

Age (years)	Age-specific rates (per 100,000)	Linear trend	<i>P</i>	Average annual percentage change (95% CI)
Male				
≤ 19	0.05	†		
20–24	0.02	†		
25–29	0.21	†		
30–34	0.28	†		
35–39	1.24	†		
40–44	4.31	†		
45–49	11.88	†		
50–54	18.16	$y = 15.04 + 0.31x$	0.049	+7.4 (6.2–9.0)
55–59	25.82	$y = 22.03 + 0.38x$	0.003	+1.8 (1.4–2.2)
60–64	27.94	†		
65–69	29.51	†		
70–74	28.04	†		
75–79	26.77	†		
80–84	29.25	†		
85+	33.43	†		
Female				
≤ 19	0.05	†		
20–24	0.04	†		
25–29	0.17	†		
30–34	0.22	†		
35–39	0.34	†		
40–44	0.93	†		
45–49	1.45	†		
50–54	2.73	†		
55–59	3.26	$y = 0.56 + 0.95x$	0.027	+34.3 (28.4–40.2)
60–64	3.74	†		
65–69	4.44	†		
70–74	6.51	†		
75–79	9.09	†		
80–84	13.86	†		
85+	20.56	†		

† None of the regression analysis models corresponded to mortality data for this age group; CI – confidence interval

and women aged under 45. In terms of gender, age-specific rates were notably higher among males than among females, and the differences were highest for the age 45–64. In the observation period, a significant increase in the number of deaths caused by lip, oral cavity and pharynx cancer was recorded in people aged 55–59, the increase being + 1.8% (95% CI, 1.4–2.2) in men and + 34.3% (95% CI, 28.4–40.2) in women. The male population also demonstrated an increase of 7.4 % (95% CI, 6.2–9.0) in deaths caused by lip, oral cavity and pharynx cancer in a younger age group (50–54 years of age). None of the regression analysis models corresponded to mortality data for other age groups.

Discussion

Lip, oral cavity and pharynx cancer rates varied considerably among countries^{2–4, 7}. The highest standardized male population death rates in 2008 were recorded in Hungary (19.4 per 100,000 individuals), Slovakia (15.6) and India

5 per 100,000 individuals are Bangladesh, Pakistan and India, and countries with the rates less than 1 per 100,000 individuals are countries of North and South America, Australia, New Zealand and Northern and Western Europe.

In the period 1991–2009, the average standardized mortality rate of lip, oral cavity and pharynx cancers in Serbia was 6.2 per 100,000 in men and 1.2 per 100,000 in women. These mortality rates place Serbia among the countries with medium mortality values. Serbian male and female mortality rates are more similar to mortality rates of Central and Western European countries rather than to those of Eastern and South European countries^{3, 12}.

In last decades, the USA records a decline in deaths of oral cavity and pharynx cancers in all races (white, Afro-American, Asian/Pacific Islander, American Indian/Alaska Native, Latinos), for both sexes, although disparities persist^{7, 8}. Oral cancer mortality has been rising appreciably in most European countries up to the late 1980s, essentially for men^{6, 10}. From 1990 to 2004, the European Union records a decline in mortality of approximately 7% in men and an in-

crease of nearly 16% in women^{9,13}. However, in some countries, such as Hungary, Romania, Slovakia and Czech Republic, an increase in oral and pharynx cancer mortality in both men and women is recorded. Oral cancer mortality in men has been declining since the late 1980s in most western countries, although some persisting upward trends were recorded in Denmark, United Kingdom, England and Wales, and Scotland. These trends should be essentially interpreted in terms of patterns and changes in exposure to alcohol and tobacco in Central and Eastern Europe^{4,9}.

For the youngest age categories in the Serbian population, mortality rates were generally less than 1 per 100,000 individuals per year; however, after about the third decade of life, rates began to increase notably, with the sharpest increases seen for males. Lip, oral cavity and pharynx cancer mortality rates in 11 countries (USA, Asian and European countries, and Australia) during the period 1990–2006, were from 3 to 10 times higher in males than in females⁵. The reason for this may be that men had been more likely to use tobacco and alcohol in the past^{4,7,10}. Among females, few differences in mortality rates were observed for all the countries studied with the exception of China (Hong Kong)⁵. Although the age-standardized rates in China (Hong Kong) have evidently decreased over the period, they were still 5 times higher for both genders.

Oral cavity cancer mortality rates ranged from 12.1 per 100,000 among males and 5.9 among females in Melanesia, 6.3 among males and 3.6 among females in South-Central Asia, to less than 1 for both genders in North America, Northern and Western Europe, and Australia/New Zealand^{1,3}. The highest pharyngeal cancer mortality rates in 2008 were recorded in South-Central Asia and Southern Africa (7 per 100,000 among males and approximately 2 per 100,000 among females). The lowest pharyngeal cancer mortality rates (1 per 100,000) for both genders were recorded in North America, Northern and Western Europe, and Australia/New Zealand. In India, among all malignant tumors, lip, oral cavity and pharynx cancer mortality rates have a leading position in the structure of mortality when considering the entire population (9.7 per 100,000) and the male population alone (14.4), while they rank number 3 in female population (5.4)^{1,3}. In India, pharyngeal cancer death was more frequent than oral cavity cancer death in men (7.6 versus 6.8), while in women oral cavity cancer mortality rates were twice as high as those of pharyngeal cancer.

Some potential explanations for this apparent differences among the countries may be discrepancies in the disease early detection and availability of the improved treatment methods. However, numerous epidemiological studies indicated that the increase was attributed primarily to changes in the patterns of smoking and alcohol use (especially among women) in recent decades; in addition, nutritional, lifestyle and other factors^{3,14}. The difference in rates between black and white population is attributable to racial differences in patterns of alcohol intake, especially among current smokers, as well as to higher risks associated with alcohol intake among blacks^{7,10,15}. A Swedish population-based case-control study showed that risk factors for oral

and oropharyngeal squamous cell carcinoma were poor oral hygiene, dental status (defective and missing teeth), oral mucosal lesions, alcohol and tobacco use, human papilloma virus (HPV) infection, and lifestyle-related factors¹⁶. The findings in England and Wales¹⁷ about a positive correlation between liver cirrhosis and intraoral cancer suggested that rising alcohol consumption is more closely related to increasing intraoral cancer incidence and mortality than smoking, most notably among younger males since the early 1970s.

In India¹⁴, tobacco chewing emerged as the strongest risk factor for oral cancer, while the strongest risk factor for pharyngeal cancer was tobacco smoking in current smokers. Oral tobacco products (snuff or chewing tobacco) are related to cancers of the cheek, gums, and inner surface of the lips. In Southeast Asia, South Asia, and some other areas of the world, many people chew betel and/or gutka^{18,19}. Several studies have found that a diet low in fruits and vegetables is related to an increased risk of oral cavity and oropharyngeal cancers^{20,21}.

The rising rate of HPV related cancers is thought to be due to changes in sexual practices in recent decades, particularly to the increase in oral sex²². The International Agency for Research on Cancer conducted a multicenter case-control study of oral cavity and oropharyngeal cancer in nine countries, where HPV DNA was detected in biopsy specimens of 3.9% of oral cavity cancers with valid polymerase chain reaction (PCR) results and 18.3% of oropharyngeal cancers²³.

Mortality rates in the Republic of Serbia for which symptoms, signs and ill-defined states were indicated as causes of death suggest that caution must be present when interpreting statistical data on mortality in international comparisons. However, it is not likely that these had a significant impact on the increasing trend of lip, oral cavity and pharynx cancer mortality, for which the increasing trend ($y = 3.31 + 0.02$; $p = 0.033$) was also observed for the 1991–2003 period, when mortality rates of undefined death causes also demonstrated a considerable increasing trend ($y = 47.23 + 1.93$; $p = 0.000$).

A similar increasing trend of the mortality of lip, oral cavity and pharynx malignant tumors (average annual percent change = + 0.8) and the mortality of all malignant tumors (average annual percent change = + 1.0) in Serbia can be only partially explained by the lack of organized programs for primary and secondary prevention, especially during the recent decades which characterised the economic sanctions against Serbia, the war and the 1999 NATO bombing of Yugoslavia. Other than, it was not possible to give specific information about internally displaced persons and refugees, although they may have a different exposure, which could be of great importance for understanding the trends in mortality of malignant tumors. Despite changes in recent years, the most significant exposures to risk factors for malignant tumors in Serbia are still higher than in developed countries. The prevalence of smokers in the adult population has decreased from 40.5% in 2000 to 33.6% in 2006, while a third of young people in the 15–19 age group consumed alcoholic beverages²⁴. In Serbia,

an increase in the number of deaths of lip, oral cavity and pharynx malignancies and of all malignant tumors was observed for the period from 1991 to 2009, is pointing to the need to conduct analytical epidemiologic studies to help identify risk factors for lip, oral cavity and pharynx malignant tumors in the Serbian population.

Conclusion

Lip, oral cavity and pharynx cancer mortality rates place Serbia among the countries with medium mortality

values. The increasing trend in lip, oral cavity and pharynx cancer mortality points to the necessity to investigate etiology and improve primary and secondary prevention measures.

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