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MEDICAL –GEOGRAPHIC ANALYSIS OF INCIDENCE AND MORTALITY FROM BRAIN TUMORS IN POPULATION OF CENTRAL SERBIA IN PERIOD 1999-2010

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ABSTRACT: *This paper gives an analysis of incidence and mortality from brain tumors in the population of Central Serbia during the period from 1999-2010. Using statistical methods it has been observed that mortality rates had increased for both, male and female population. The increasing trend of the incidence (new disease cases) has not been noticed. Among this, application of GIS software (Arc Map 10) was used in order to illustrate the spatial distribution of incidence and mortality from brain tumors in the observed populations. In case of male population, the highest concentration of new disease cases and deaths has been registered within Belgrade micro-region. Also, there is a higher concentration of the new cases and deaths in the western part of the analyzed region with comparison to the eastern part. When it comes to female population, high occurrence of new cases and deaths have been also registered within Belgrade micro-region. The higher occurrence of new cases among female population, detected in the western part of the Central Serbia region, does not represent the same tendency in the case of mortality. It has been noticed that most of the new cases (among both observed populations) are concentrated within areas of large urban centers: Belgrade, Niš and Kragujevac. Spatial distribution of the new cases affect the current health care system and the available medical technology in Serbia.*

Key words: *brain tumors, Central Serbia, incidence, medical geography, mortality*

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MEDICAL AND GEOGRAPHICAL RESEARCHES IN SERBIA AND WORLDWIDE

Medical geography studies the interaction between natural and social complex of geographical factors on the spreading of human diseases (Ђурђић, Смиљанић, 2006). Medical and geographical approach to the study uses concepts and methodologies of geographic disciplines during the research of health problems in the population. Based on the facts and theories, applying a variety of research techniques from the fields of natural and social sciences, medical geography approaches to its own, special perspective of studying the components of health and disease, with the use of spatial analysis (Figure 1) (Meade, Emch, 2010).

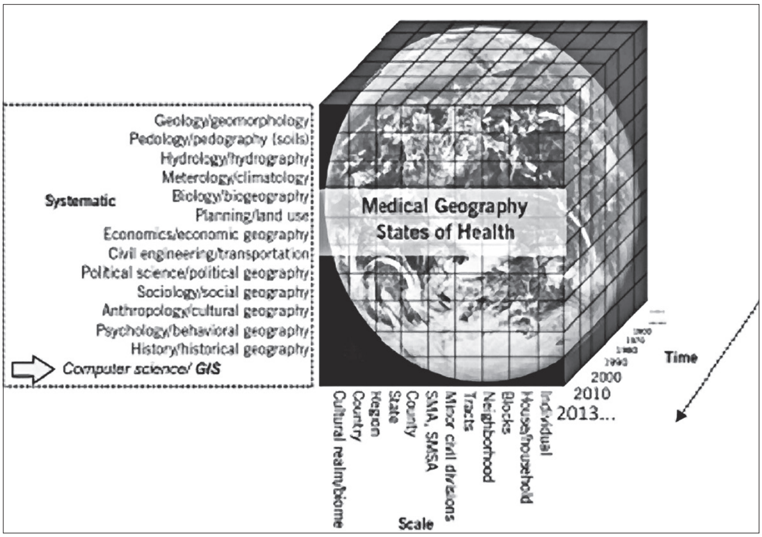


Figure 1. Position of medical geography in the science matrix
(modified after Meade, Emch, 2010)

General laws of geographical distribution of people diseases are studied by nosogeography in order to issue prognosis of possible occurrence of disease within a certain period of time (Ђурђић, Смиљанић, 2006). Spatial analysis of distribution of the disease is important from biomedical, economic, and a behavioral aspect (Johnes, Moon, 1991).

Developed countries are in advance in the medical and geographical approach to the study of diseases in regard to Serbia, where medical geography is still underdeveloped. This is supported by the fact of the existence of very few national scientific publications on this subject (e. g. Тополовић, Обрадовић, 2007; Ракић, 2007; Ђурђић, Смиљанић, 2006). However, more massive use of geographic information system (GIS) for spatial representation of diseases and conditions in the health sector (government, provinces, municipalities) in order to analyze the health status of the population contributes to its intensive development, popularization and applicative importance (Маринковић, 2010; Ракић, 2007).

BRAIN TUMORS IN CENTRAL SERBIA

The term *brain tumor* refers to the variation of different neoplasm, which each of them have their own biology, prognosis and treatment method (DeAngelis, 2001). These tumors are more closely defined as intracranial tumors, because all of them do not occur from the brain tissue (Schachter, 2004). Malignant brain tumors can be: (1) primary tumors and (2) distant metastases from malignant tumors (Black, 1999). It is characteristic that the tumor grows rapidly and invades healthy tissue which surrounds. Malignant cells can spread throughout the other areas of the brain or spinal cord. It is rare that a brain tumor metastasizes to another organ in the body (NCI, 2009). According to the International Classification of Diseases, conducted by the World Health Organization (WHO), malignant brain tumors are referred to under the code S71 (WHO, 2000).

European countries have the highest mortality rates of cancer, with more than 200 deaths per 100,000 habitants, on the first three places there are Hungary, Denmark and Croatia. Serbia, with a mortality rate of 251 per 100,000 habitants occupies a high 11th position (position shared with Slovenia) in the world (Маринковић, 2010). Malignant brain tumors are relatively rare tumors if we compare them with other malignant tumors and they are rarely causes of death (Пекмезовић et al., 2003).

According to the International Agency for Research on Cancer in Lyon, the number of new cases (incidence) is 1.9% worldwide, compared to all malignant diseases, and deaths (mortality) 2.3%.

The aim of this research study is to analyze the changing rates of incidence and mortality rates at the regional level by studying the data of the Cancer Registry of Central Serbia.

MATERIAL AND METHODS

Incidence and mortality data used in the study were collected from 12 reports issued by the National Cancer Registry of Central Serbia, for the period from1999 to 2010. Register works at the Institute of Public Health of Serbia “Milan Jovanović – Batut”. The population data of Central Serbia were obtained from the Federal Statistical Office.

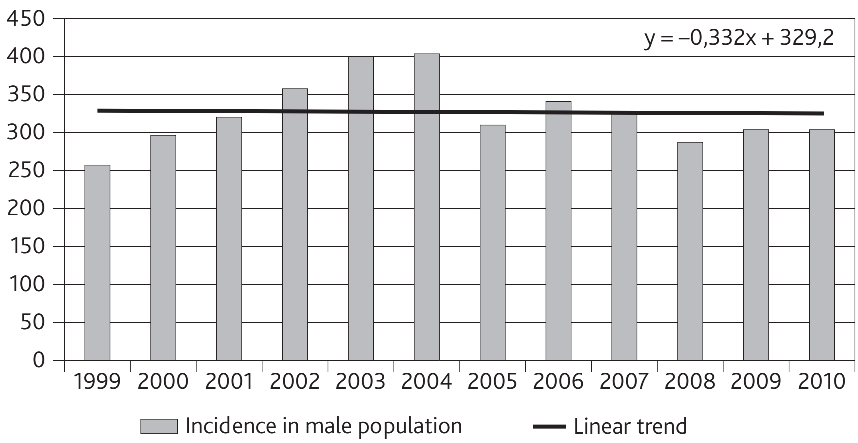
This paper presents the basic statistical methods used to analyze the data. Simple linear regression was used to determine the existence of trends in the researched time series. During the processing of the data it was used The Mann-Kendall test which is a nonparametric test for the trend detection in the researched time series (Kendall 1938, 1975; Mann 1945; Gilbert 1987; Libiseller, 2002). For statistical analysis, it was used the software package XLSTAT. In determining the significance of trends it was used the coefficient of significance of 95% ($\alpha = 0.05$). Using the software package Arc Map 10, it was shown the spatial distribution of incidence and mortality in Central Serbia for a period of from 1999 to 2010.

A TREND ANALYSIS OF INCIDENCE AND MORTALITY

Research of incidence and mortality from a brain tumor at the global level by the International Agency for Research on Cancer (Lyon) indicate that, at a global level by the end of the 2013th year, from a brain tumor, will be registered 3.8 new cases per 100,000 men, women, and die 2.9 from 100,000 men. In the case of the female population prognoses are 3.1 new cases per 100,000 women and 2.1 per 100,000 women will die[1].

In Central Serbia it was applied simple linear regression and trend analysis of incidence and mortality for both genders in the period from 1999 to 2010. When analyzing The Mann-Kendall test, two hypotheses were given H_0 and H_a. The hypothesis H_0 is granting the absence of trend, while hypothesis H_a is representing the existence of a trend in the analyzed series.

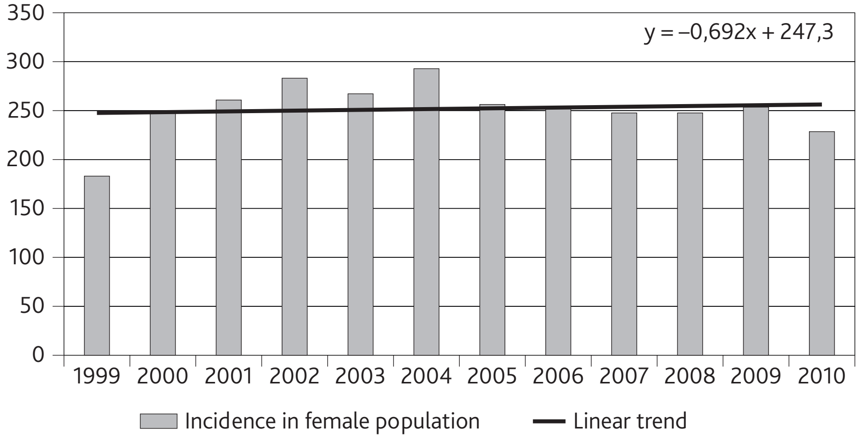
Graph 1 and the equation (*y*) show that there is no trend in the number of newly infected men from a brain tumor at a given time. Testing the hypothesis we verify the accuracy of the claims. Considering that the calculated *p* - value (probability) is greater than the significance level ($\alpha = 0.05$), we cannot reject the hypothesis H_0. The risk to reject the zero hypothesis is over 95 %, which shows that the trend in the analyzed series is not present.



Graph 1. Brain tumors incidence in male population in Central Serbia for the period 1999-2010

Graph 2 and equation (*y*) show that there is no trend in the number of new cases of women from a brain tumor at a given time. Testing the hypothesis we verify the accuracy of the claims. Considering that the calculated *p* - value (probability) is greater than the significance level ($\alpha = 0.05$) , we cannot reject the hypothesis H_0. The risk to reject the zero hypothesis is over 33 %, which shows that the trend in the analyzed series cannot be spotted.

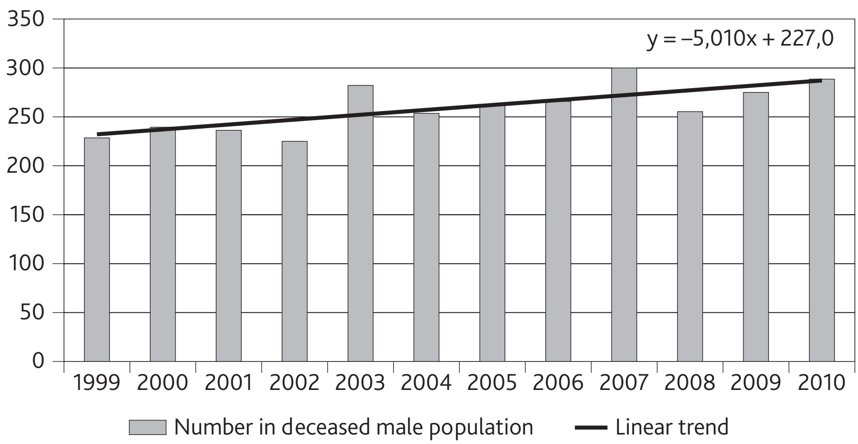
[1] http://globocan.iarc.fr



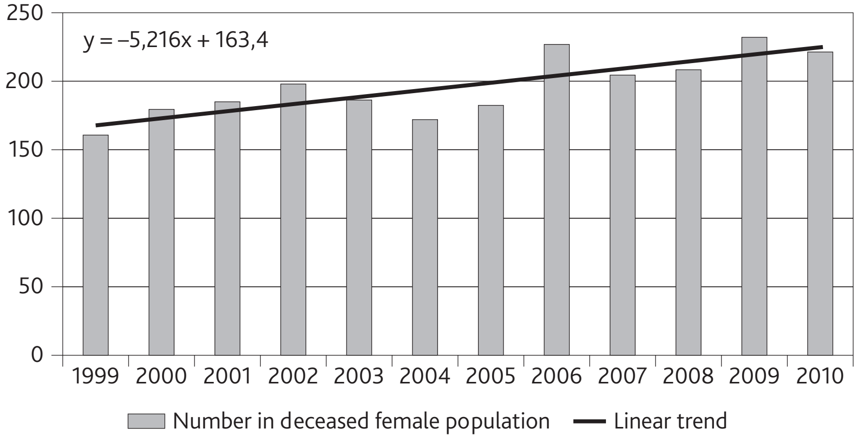
Graph 2. Brain tumors incidence in female population in Central Serbia for the period 1999-2010

Graph 3 and the equation (*y*) show that the trend in the number of men who died from a brain tumor in a given period exists. Testing the hypothesis we verify the accuracy of the claims. Considering that the calculated *p* - value (probability) is less than the significance level (α = 0.05), the hypotheses H_0 can be rejected and we can accept the alternative hypothesis Ha. The risk to reject the zero hypothesis is less than 1 %, which means that the probability that the trend in the analyzed series is of over 99 % positive.

Graph 4 and equation (*y*) show that the trend in the number of women who died from a brain tumor in a given period exists. Testing the hypothesis we verify the accuracy of the claims. Considering that the calculated *p* - value (probability) is less than the significance level (α = 0.05), the hypotheses H_0 can be rejected and we can accept the



Graph 3. Number of deceased in male population of brain tumors in Central Serbia for the period 1999-2010



Graph 4. Number of deceased in female population of brain tumors in Central Serbia for the period 1999-2010

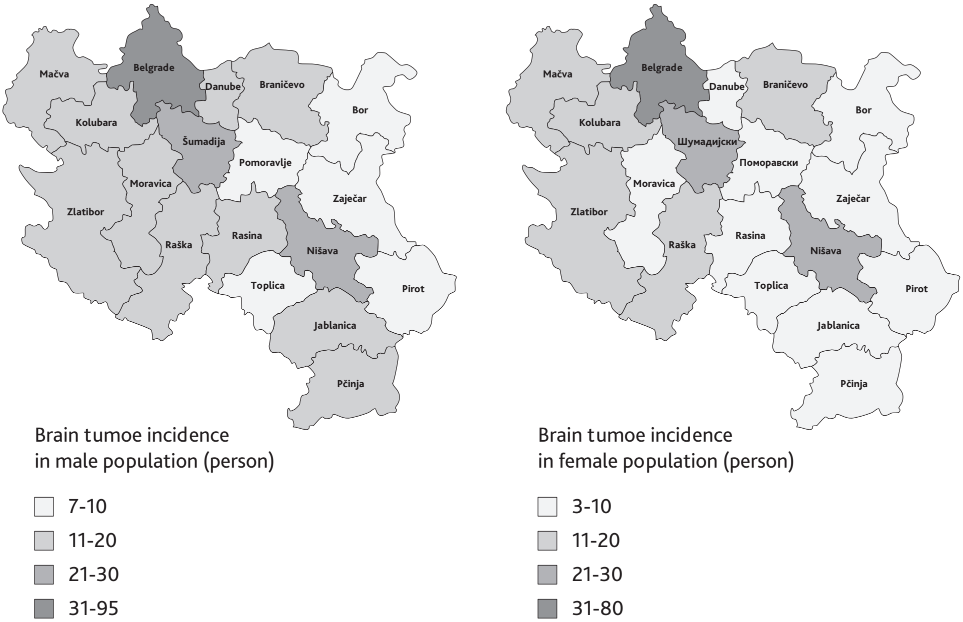
alternative hypothesis H_a. The risk to reject the zero hypothesis is less than 1 %, which means that the probability that the trend in the analyzed series is of over 99 % positive.

Brain tumors occur almost equally in men and women. However, some histologic types are specific to gender - *astrocytomas* and *gliomas* for men and for women - *meningiomas* (DeAngelis, 2001). Some authors believe that the introduction of computerized tomography - CT scan in routine practice in 1975 made a great contribution to the increase of the incidence of brain tumors (Helseth, 1995).

SPATIAL ANALYSIS OF INCIDENCE AND MORTALITY IN CENTRAL SERBIA

Using the software package Arc Map 10 the graphical visualization of the spatial distribution of incidence and mortality at the level of Central Serbia is provided.

Map 1 shows the spatial distribution of the incidence of brain tumors in the period from 1999 to 2010 in the male and female population. For men, the largest number of new cases is the territory of Belgrade (Belgrade micro region): 31-95 new cases per 100,000 men. In the second place, with an average of 21-30 cases per 100,000 inhabitants, there are Districts of Šumadija and Nišava. Western Region with Districts ofMačva, Kolubara, Morava, Zlatibor, Raška and Ras recorded a number of new cases (11-20 per 100,000) more than the eastern part, where Districts of Bor, Zaječar, Pomoravlje and Pirot recorded the lowest number of new cases (7-10 per 100,000). The exception of the eastern part represents Districts of the Danube Basin, Braničevo, Jablanica and Pirot where the number of new cases is the same as in the west (11-20 per 100,000). For women, the highest number of new cases is identical to the men where Belgrade is leading (31-80 per 100,000). Districts of Šumadija and Nišava are, also, in the second place as well as in men with 21-30 cases per 100,000. For women, the difference between the east-



Map 1. Spatial distribution of incidence from brain tumors (male and female population) in Central Serbia region for the period 1999-2010

ern and western part of the region is even more distinctive. Thus, the only exception in the western part of the region makes District of Morava with 3-10 new cases per 100,000, while the others around it have 11-20 new cases per 100,000 women (except District of Šumadija with 21-30 new cases per 100,000 women).

It can be seen that the greatest number of new men and women tied to the region of larger urban centers: Belgrade, Niš and Kragujevac. In further analysis we draw attention to the number of county residents (Table 1), which corresponds to the number of new cases.

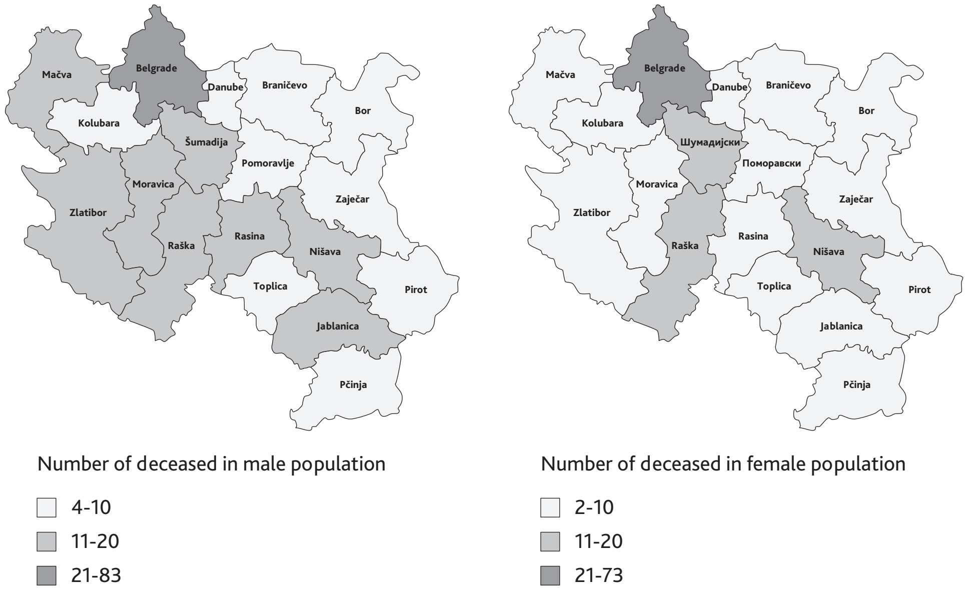
The majority of the population (for the period from 1999 to 2010) is in the City of Belgrade, while Niš is in the second place. Although Districts of Mačva and Zlatibor, in terms of population, are behind District of Nišava, we can notice fewer new cases in them compared to District of Šumadija. As the etiology of brain tumors insufficiently known (Пекмезовић et al., 2003), we cannot claim with certainty what the actual cause of these precedents at the district level. The only known risk factors for brain tumors are high doses of ionizing radiation which man can be exposed and selective cognitive and genetic disorders (Inskipetal, 1995). Still, these factors are present in a small percentage of new cases, while the majority of causes have unknown cause (Legleretal, 1999). Diets, as the consumption of alcohol and tobacco may not be related directly with an increased risk of disease (Inskipetal, 1995). What affects on the distribution image of new cases is, also, the current system of health care and technology available in the country (Lönnetal 2004; Institute of Public Health of Serbia 'Dr Milan Jovanovic – Batut').

Table 1. Population number by regions in Central Serbia based on population census in the years 1991 and 2002

District	2002	1991
Central Serbia	5,466,009	5,606,642
Belgrade	1,647,490	1,576,124
Nišava	381,757	389,838
Mačva	329,625	329,226
Zlatibor	313,396	332,470
Šumadija	298,778	303,484
Raška	291,230	293,311
Rasina	259,441	272,834
Jablanica	240,923	251,301
Pčinja	227,690	237,399
Pomoravlje	227,435	240,715
Morava	224,772	228,093
Danube	210,290	216,056
Braničevo	200,503	220,225
Kolubara	192,204	196,556
Bor	146,551	163,229
Zaječar	137,561	154,176
Pirot	105,654	115,970
Toplica	102,075	109,608

(Source: Упоредни преглед броја становника 1948, 1953, 1961, 1971, 1981, 1991, 2002. Републички завод за статистику, Београд, 2004)

Map 2 shows the spatial distribution of mortality from brain tumors in males and females for the period 1999-2010. In men, most of them of who died from a brain tumor are recorded in the City of Belgrade (31-83 per 100,000. Western Region of Central Serbia (Districts of Mačva, Zlatibor, Morava, Raška, Šumadija and Ras) are leading in mortality of men compared to the eastern, as well as incidence. An exception is District of Kolubara, which, like most of the county from the east (with the exception of Districts of Nišava and Jablanica), has the least number of deaths: 4-10 per 100,000. In women, most of them who died from a brain tumor in the studied period also were recorded in the city of Belgrade (21-73 per 100,000). The other three districts which are distinguished by a higher rate of mortality of patients are Districts of Šumadija, Raška and Nišava (11-20 per 100,000). All other districts have 2-10 deceased women per 100,000.



Map 2. Spatial distribution ofmortality from brain tumors (man and woman) in Central Serbia region for period 1999-2010

CONCLUSION

The incidence and mortality of brain tumors analysis of data in Central Serbia for the period 1999-2010 point to two general observations: (1) it is not recorded the trend of new cases of men and women, and (2) mortality in men and women shows a positive trend.

The spatial dispersion of new cases in Central Serbia shows that most new cases are recorded in Belgrade micro region (for both genders). The western part of the region of Central Serbia also has more new cases than the eastern. Most new cases are linked to the area of larger urban centers (Belgrade, Niš, Kragujevac).

The spatial dispersion of mortality in Central Serbia also shows that most deaths from brain tumors are in the micro region of Belgrade, for both genders. The western part of the analyzed region is leading compared to the eastern by the deceased men. In women, this image is a bit better, and connection between values of mortality with the western and eastern part of the region cannot be seen.

As the etiology of these tumors are mostly unknown, the greater is the importance of studying the spatial distribution, monitoring and detect eventual rules of appearance of disease in order to improve disease prevention and reduction of incidence.

The deficit of published papers in the field of medical geography talks about her lack of application and an unsatisfactory level of development in relation to the health of the population of Serbia. Research in this field may find wider application in improving the health care system of Serbia in respect of: maintaining and improving the health condition of the population, monitoring, identifying characteristics of each territory and certain population groups, review of health policies, strategies and technologies, and to improve health care management.

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