Original article

A study of the incidence and factors associated with glioblastoma multiforme in Republic of Srpska

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Summary

Introduction. Glioblastoma multiforme (GBM) is a highly aggressive brain or spinal cord tumor, representing the most lethal form of brain tumors with a five-year mortality rate exceeding 90%. It constitutes approximately 60% of all primary brain tumors in adults and has an annual incidence of 2–3 new cases per 100,000 population. Although it predominantly affects adult patients, it can occur at any age. The aim of this study is to determine the incidence rate and factors (age, sex and outcome) associated with GBM in Republic of Srpska over a five-year period.

Methods. This retrospective observational cross-sectional study included a total of 97 male and female patients of all age groups from the territory of Republic of Srpska, who were pathohistologically diagnosed with GBM between January 1st, 2014 and December 31st, 2018. Data obtained from the National Registry for Malignant Neoplasms in Republic of Srpska, managed by the Public Health Institute and the Republic Institute of Statistics, were analyzed using Microsoft Excel.

Results. During the investigated period, GBM accounted for 15.13% of all reported brain tumors in Republic of Srpska with incidence rate of 8.45 per 100,000 population. The occurrence of this tumor was slightly higher in males, with a ratio of 1.2:1.0 compared to females. No cases were reported in patients under the age of 18. Among the reported cases, 65 persons (67.01%) were between 18 and 65, with incidence rate of 5.66 per 100,000 population, while 32 persons (32.99%) were over 65, with incidence rate of 2,78 per 100,000 population. Out of all patients diagnosed with GBM, 80 patients (82.47%) experienced a fatal outcome, while 17 patients (17.53%) survived.

Conclusion. GBM exhibits a high incidence compared to other brain neoplasms within Republic of Srpska, and it is characterized by an extremely high mortality rate, primarily affecting adult, working-age population (18–65 years).

Key words: glioblastoma multiforme, malignant neoplasm, brain tumor, incidence

Introduction

Glioblastoma multiforme (GBM), WHO grade IV, is a malignant brain and spinal cord tumor common in adults [1]. It is the deadliest form of brain tumors with the five-year mortality rate of more than 90% and represents about 60% of all primary brain tumors in adults with the annual incidence of 2–3 new cases per 100,000 population [2, 3, 4]. There are no published data

related to the incidence or prevalence of this tumor in the territory of Republic of Srpska and the countries in the region.

GBM is mostly present in adults with a median age of 64, but it can occur at any age, including childhood, with a slightly higher incidence in men compared to women (1.6:1), and the median survival is 12.6 months [2, 5].

GBM is clinically presented with headache, vomiting, epileptic seizures, hemiparesis, but also with psychiatric symptoms such as depression, anxiety, psychotic symptoms of schizophrenia (such as hallucinations, delusions, thought disorders), which can pose a problem in establishing diagnosis [6, 7].

The prognostic factors affecting survival include age, chemotherapy administration, total dose of radiation, location of the tumor in the brain or spinal cord and potentiality of complete tumor resection [8].

The most widely used non-invasive method for diagnosis is magnetic resonance (MR) with final confirmation of the diagnosis by biopsy [9].

The standard treatment approach is surgery followed by adjuvant radiotherapy and chemotherapy [10].

The aim of this study is to determine the incidence rate of GBM in the territory of Republic of Srpska, its appearance in relation to age, sex, and outcome (did the patient survive within the observational period).

Methods

This observational retrospective cross-sectional study included 97 male and female patients of all ages from the territory of Republic of Srpska, who were pathohistologically confirmed with the diagnosis of GBM. The observation period was from January 1st, 2014 to December 31st, 2018.

The data from the National Registry for Malignant Neoplasms in Republic of Srpska were used. The Public Health Institute of the Republic of Srpska and its regional centers maintain registries for malignant neoplasms in the belonging territories. The Public Health Institute consolidates data on malignant diseases for Republic of Srpska.

Sources regarding patients' data were reports of malignant neoplasms and copies of histological/cytological findings submitted by hospitals, clinics, institutes, histological-cytological, hematological and other laboratories. The National Registry for cancer does not collect information on the therapeutic procedures of patients with malignant neoplasms, but rather provides data on newly diagnosed cases of malignant neoplasms with data available at the time of diagnosis, which are defined on the malignant neoplasm registration form. Sources of mortality data were death certificates of the Republic Institute of Statistics, which were coded in the Service for Social Medicine, Health Organization and Economics of the Public Health Institute of Republic of Srpska.

Data on the total number of inhabitants in Republic of Srpska as of 2018 were collected from the Republic Institute of Statistics. Data were estimated based on the results of the Census of Population, which was conducted in October 2013, and based on annual results of the processing of statistics on natural and migratory population movements.

The X revision of the International Classification of Diseases, Book 1, ICD-10 and the International Classification of Diseases for Oncology – Third Edition, World Health Organization, 2000, Geneva, were used to code the diagnoses and histological type of malignant tumors. In the period from 2014 to 2018, there was a change and the release of a new classification of brain tumors, that is, in 2016 a new classification was released, which introduced molecular profiling of tumors [11]. Since 2021, the suffix multiforme, which has been dropped, is not used in the name of glioblastoma. Also, according to the new division of brain tumors from 2021, the presence of an

IDH mutation must be done for the diagnosis of GBM [12]. Due to the epidemiological approach to the study, this WHO brain tumor classification was not used.

The following data provided by the Institute of Public Health of Republic of Srpska, were used: patients age when the diagnosis was established, date of diagnosis, sex, outcome (survived or died by the time of data extraction), and place of residence. All patients were also divided by age: patients younger than 18 years, working-age population (18–65 years) and elderly population (over 65 years). Data of interest were extracted and processed in Microsoft Excel using statistical and mathematical formulas. Afterwards they were united in tables and graphs.

Results

Representation of GBM among all reported brain tumors in Republic of Srpska in the investigated period was 97 (15.13%) with incidence rate of 8.45 per 100,000 population of Republic of Srpska. The number of male persons suffering from GBM was 53 (54.64%) while 44 patients (45.36%) were females. Incidence rate of diagnosed males was 9.45 per 100,000 male population, and for females it was 7.49 per 100,000 female population. In the period from January 1st, 2014 to December 31st, 2018, there were no reports of patients aged under 18. There were 65 (67.01%) patients aged 18-65 with incidence rate of 5.66 per 100,000 population, of which 38 (39.18%) were men and 27 (27.84%) were women, and 32 (32.99%) patients were over 65, with incidence rate of 2,78 per 100,000 population, out of which 15 were men (15.46%) and 17 were women (17.53%).

Figure 1 shows the GBM distribution according to country regions and in relation to sex.
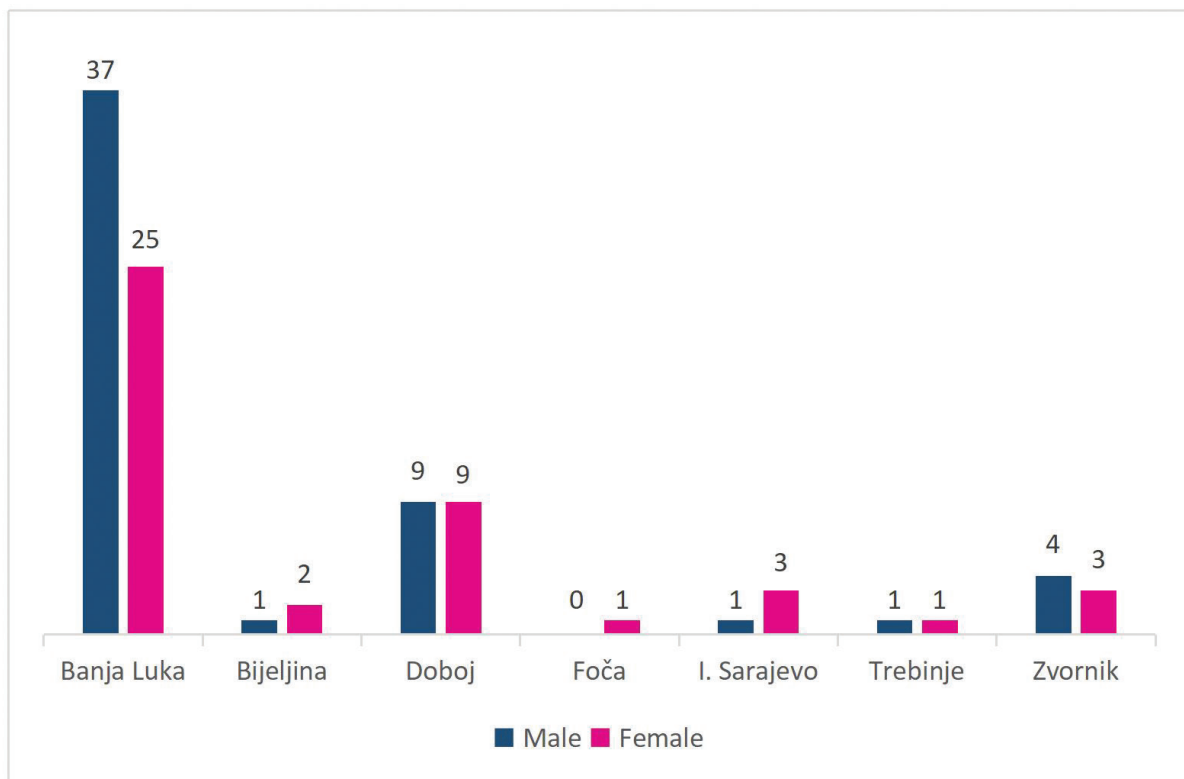
Figure 1. GBM distribution according to country regions and in relation to sex

Table 1 shows the data (male/female, age group, survived/died) of patients with GBM in the observed period divided by regions of Republic of Srpska.

Table 1. GBM patients by regions of Republic of Srpska

Region	N (%)	Sex		Survived (%)	Died (%)
		Male (%)	Female (%)		
Banja Luka	62 (63.92%)	37 (38.14%)	25 (25.77%)	12 (12.37%)	50 (51.55%)
Bijeljina	3 (3.09%)	1 (1.03%)	2 (2.06%)	0 (-)	3 (3.09%)
Doboj	18 (18.56%)	9 (9.28%)	9 (9.28%)	2 (2.06%)	16 (16.49%)
Foča	1 (1.03%)	0 (-)	1 (1.03%)	0 (-)	1 (1.03%)
Istočno Sarajevo	4 (4.12%)	1 1.03%)	3 (3.09%)	0 (-)	4 (4.12%)
Trebinje	2 (2.06%)	1 (1.03%)	1 (1.03%)	0 (-)	2 (2.06%)
Zvornik	7 (7.22%)	4 (4.12%)	3 (3.09%)	3 (3.09%)	4 (4.12%)
Total	97 (100%)	53 (54.64%)	44 (45.36%)	17 (17.53%)	80 (82.47%)
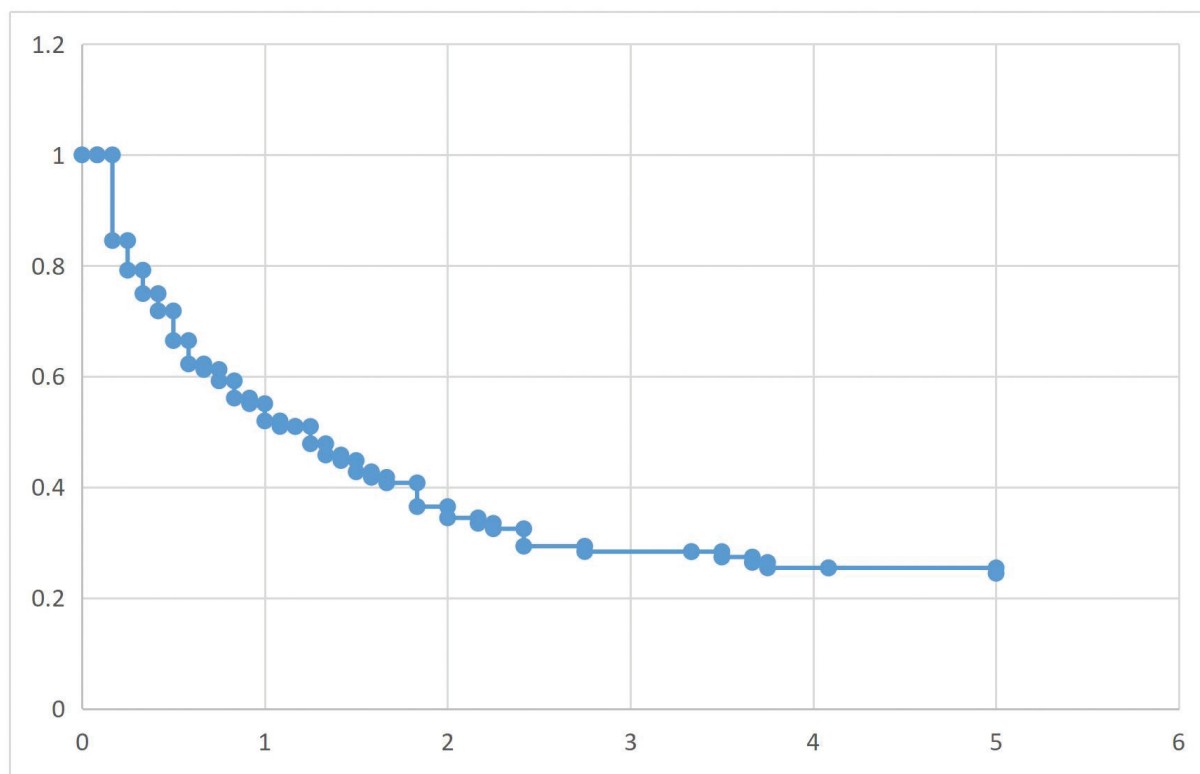
Figure 2. Kaplan Meier survival curve of patients with GBM in Republic of Srpska in the five-year period (January 2014–December 2018)

Figure 2 shows the five-year survival of GBM patients in Republic of Srpska during the observed period.

Discussion

According to our knowledge, this is the first cross-sectional study in Republic of Srpska on the incidence of GBM. GBM is one of the most aggressive malignancies and represents 14.5% of all brain tumors in the world [13], which corresponds to the percentage of GBM in the five-year period in the territory of Republic of Srpska in our research, which was 15.13%.

Many studies have shown that age significantly affects the occurrence of GBM, which was also confirmed by Kai et al. [13, 14] where 47.9% of persons diagnosed with GBM were >65 years old, and 46.3% of persons were in the age range of 40–64 years. According to Thakkar et al. [15] the median age of diagnosis is 64, while in study done by Koshi et al. [16] it was 59. In our study, the highest percentage of GBM was in the age range of 18–65 years (67.01%), with incidence rate of 5.66 per 100,000 population of Republic of Srpska, which represents working-age population.

Men to women ratio in our study was 1.2:1.0, while according to Li et al. the ratio was 1.3:1.0 [14]. Thakkar et al. estimated this ratio to 1.6:1.0 [15]. Cheo et al. also presented male predominance in patients diagnosed with GBM [17].

According to our study, the percentage of survival in Republic of Srpska was 17.53%. In Great Britain, as investigated by Brodbelt et al., the percentage was 15.3% [18], while according to Witthayanuwat et al. percentage was 13.8% [8]. Ghosh et al., in a single-center study established survival rates in the range of 8%– 12% [19].

Shortcomings

The shortcoming of this study is that the last processed data on GBM in the Registry for Malignant Diseases of the Public Health Institute of Republic of Srpska are from 2018. Because of the small sample of cross sectional data, it is very hard to determine the causal relationship between the examined factors and GBM. Due to the retrospective nature of the study, the results for the period from 2014 to 2018 would probably differ from those of present days, because the new division of brain tumors from 2021 has been valid, in which the presence of an IDH mutation must be done for the diagnosis of GBM.

Consclusion

GBM is the deadliest and one of the most common forms of brain tumors, and it occurs mostly in adults. We found that in the period January 1st, 2014 - December 31st, 2018, 97 cases of GBM were diagnosed and pathohistologically confirmed in Republic of Srpska, which was 15.13% of all reported brain tumors in the given period, with a slightly higher frequency of occurrence in males compared to females. The working-age population was the most affected, representing a significant socio-economic factor. Mortality was extremely high, and amounted to 82.47%.

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Studija učestalosti i faktori povezani sa glioblastomom multiforme u Republici Srpskoj

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Uvod. Glioblastoma multiforme (GBM) je visoko agresivan tumor mozga ili kičmene moždine, koji predstavlja najsmrtonosniju formu tumora mozga sa petogodišnjom stopom mortaliteta koja prelazi 90%. On čini oko 60% svih primarnih tumora mozga kod odraslih i ima godišnju incidenciju od 2 do 3 nova slučaja na 100.000 stanovnika. Iako pretežno zahvata odrasle pacijente, može da se javi u bilo kom uzrastu. Cilj ove studije je utvrditi stopu incidencije i faktore (godine starosti, pol i ishod) povezane sa GBM u Republici Srpskoj, u petogodišnjem periodu.

Metode. Ovom retrospektivnom opservacionom studijom presjeka obuhvaćeno je 97 pacijenata muškog i ženskog pola svih starosnih doba sa teritorije Republike Srpske, kojima je patohistološki dijagnostikovan GBM u periodu od 1.1.2014. do 31.12.2018. godine. Podaci dobijeni iz Nacionalnog registra za maligna oboljenja Republike Srpske, Instituta za javno zdravstvo i Republičkog zavoda za statistiku, analizirani su korišćenjem Microsoft Excel.

Rezultati. Tokom istraživanog perioda, GBM je činio 15,13% svih prijavljenih tumora mozga u Republici Srpskoj sa stopom incidencije od 8,45 na 100.000 stanovnika. Pojava ovog tumora bila je nešto češća kod muškaraca sa odnosom 1,2:1,0 naspram ženskog pola. Nije bilo prijavljenih slučajeva kod pacijenata mlađih od 18 godina. Među prijavljenim slučajevima, 65 osoba (67,01%) bilo je između 18 i 65 godina starosti sa stopom incidencije od 5,66 na 100.000 stanovnika, dok su 32 osobe (32,99%) bile starije od 65 godina sa stopom incidencije od 1,78 na 100.000 stanovnika. Od svih pacijenata kojima je dijagnostikovan GBM, kod 80 (82,47%) je zabilježen smrtni ishod, dok je 17 pacijenata (17,53) preživjelo.

Zaključak. GBM pokazuje visoku incidenciju u odnosu na druge neoplazme mozga u Republici Srpskoj, a karakteriše ga izuzetno visoka stopa mortaliteta sa zahvaćenošću prvenstveno odraslog, radno-sposobnog stanovništva (18–65 godina starosti).

Ključne riječi: glioblastoma multiforme, maligna neoplazma, tumor mozga, incidencija