

ORIGINAL RESEARCH

Epidemiological profile and incidence of brain tumors in Kosovo

Sefedin Muçaj^{1,2}, Naser Ramadani^{1,2}, Serbeze Kabashi-Muçaj^{1,3}, Naim Jerliu^{1,2}, Albiona Rashiti-Bytyci^{1,2}, Sanije Hoxha^{1,2}

¹ Faculty of Medicine, University of Prishtina, Prishtina, Republic of Kosovo;

² National Institute of Public Health of Kosovo, Prishtina, Republic of Kosovo;

³ Radiology Clinic, University Clinical Center of Kosovo (UCCCK), Prishtina, Republic of Kosovo.

Corresponding author: Naser Ramadani, MD, PhD,

National Institute of Public Health of Kosovo and Faculty of Medicine, University of Prishtina, Prishtina, Kosovo;

Address: Rr. “Instituti Shëndetësor”, 10000, Prishtina, Republic of Kosovo;

Telephone: +38138541432;

E-mail: naser.ramadani@uni-pr.edu

Abstract

Aim: Brain tumors (BT) are neoplasms developed in intracranial tissues and the meninges. The purpose of this study was to describe the epidemiological features of brain tumors diagnosed and treated at the University Clinical Center of Kosovo (UCCK), the only healthcare institution in Kosovo that diagnosis and treats malignancies.

Methods: A 3-year retrospective study (2019-2021) was carried out in the Neurosurgical Clinic, Radiology Clinic, and Institute of Pathology, of UCCK. Mann-Whitney test was used to compare age distribution between males and females.

Results: A total of 227 patients were treated for BT at the UCCK during the three-year period under investigation (that is 2019-2021). There were 119 males (52.4%) and 108 (47.6%) females. The incidence rate of BT for the year 2021 was 4.7/100,000 inhabitants. BT were most common in the age groups: >50 years (n=178, 78.4%), 25-50 years (n=33, 14.6%), whereas 13 cases (5.7%) were children from the age-group ≤ 14 years. Almost one third of the patients (33.9%) were from Prishtina region, followed by Peja region (18.5%) and Mitrovica region (13.2%). From the overall number of cases (n=227), 31.3% (n=71) were benign and 66.1% (n=150) were malignant tumors. The average age of brain tumor patients was 58.4 ± 18.3 years. The most prevalent histological type of BT was meningioma WHO gr. I (n=57, 25.1%) followed by glioblastoma WHO gr. IV (n=43, 18.9%) with similar appearances in both genders. Most often, tumors had supratentorial/intra-axial localization (63.4%).

Conclusion: Adults over 50 years old represent the most affected age-group for BT in Kosovo. Meningioma, and glioblastoma were the most frequent BT in Kosovo adults. Further studies are needed to assess the long-term outcome of patients with BT in Kosovo.

Keywords: brain tumors, epidemiology, Kosovo, incidence.

Introduction

Cancer is listed as the leading cause of death and a major obstacle for increasing life expectancy in every country all over the world (1). According to the World Health Organization (WHO) data, based on the publications of Globocan (International Agency for Research on Cancer), tumors are a major global public health problem, as they are the leading cause of deaths worldwide, causing 7.6 million deaths (13% of all deaths in 2008), while according to a WHO projection, cancer deaths represent a new increase in mortality, with an estimate of 13.1 million deaths in 2030 (1,2).

Brain tumors (BT) are a diverse group of neoplasms that grow from intracranial tissues (1,2). Brain tumors are classified into two types: primary and metastatic. Primary brain tumors form and grow in the brain. Metastatic brain cancers develop in other parts of the body and spread to the brain. Primary brain tumors can be classified as benign or malignant based on their capacity to penetrate surrounding tissue. In 2015, the global yearly incidence of primary brain tumors was projected to be 3.7 and 2.6 per 100,000 men and women, respectively, with developed countries (5.1/100,000) having a higher rate than developing countries (3.0/100,000) (3,4). Brain tumors make up 1.4% of all cancers and 2.4% of all cancer-associated deaths (3,4).

The incidence of brain tumors varies in different parts of the world, with a variable course. According to Global Burden of Disease Study 2016 (5), there were 330 000 (95% UI 299 000 to 349 000) incident cases of CNS cancer and 227 000 deaths globally; East Asia was the region with the most incident cases of CNS cancer for both sexes (108 000 [95% UI 98 000 to 122 000]), followed by western Europe (49 000 [37 000 to 54 000]), and South Asia (31 000 [29 000 to 37 000]) (5). The top three countries with the highest number of incident cases were

China, the USA, and India. (5) The annual global incidence standardized by the age of primary malignant brain tumors is ~ 3.7 per 100,000 for males and 2.6 per 100,000 for females (6,7). Rates appear to be higher in more developed countries (males, 5.8 and females, 4.1 per 100,000) than in less developed countries (males 3.0 and females 2.1 per 100,000). According to the latest statistical reports, the overall incidence of brain tumors for benign and malignant tumors combined is 18.71 per 100,000 persons/year. The most common benign brain tumor in adults is meningioma, with a higher incidence in women, and the most common malignant tumor is glioblastoma, with a higher incidence in adult men (8,9). Cancer disease is an increasingly important factor in the global burden of disease in the decades to come, with around 60% of all new cases that occur in developing countries all over the world (8,9). Aspects of cancer control should be seen in the context of a systemic and comprehensive approach, such as a cancer control plan or strategy. BT incidence assessment as well as the clinical benefits of early detection of BT are important considerations for policymakers (10,11), considering a BT screening program (12-15). Prevention and control of cancer, and in particular BT are among the most important scientific and public health challenges at present. Commitment needs to be made in each country to prevent, cure and alleviate cancerous diseases.

In Kosovo, there is a scarce data and limited studies on cancers (16-18), and especially on BT (18). Through this research we aim to contribute to informing policy making and responsible authorities regarding the course, incidence, and epidemiological profile of brain tumors in Kosovo. More specifically, this study aimed to determine the epidemiological features of BT diagnosed and treated at the University Clinical Center of Kosovo (UCCCK), the only tertiary care

institution in the country, according to several variables: years, age, gender, place of residence, and according to the type of tumor, anatomical localization, as well as the comparison of the course of BT over different time periods.

Methods

Study design

This was a 3-year retrospective study (2019-2021) carried out in the Radiology Clinic, Institute of Pathology and Neurosurgical Clinic of the University Clinical Center of Kosovo (UCCK). All patients hospitalized for the diagnosis of BT throughout the research period were included in the study. More specifically, this study included patients with BT examined and interpreted by Magnetic Resonance at the Radiology Clinic, with histopathological confirmation at the Institute of Pathology, and treated at the Neurosurgery Clinic at the UCCK in Prishtina, the only healthcare institution in the country that diagnoses and treats malignancies. We estimate that UCCK covers the vast majority of newly diagnosed patients with BT; therefore, the data collected may be considered representative for Kosovo.

Data collection

Due to deficiencies in the Kosovo Health Reporting System, patients' registers (hospitalization and outpatient registers) and records of the UCCK were used as the data source to identify the patients and then to obtain the data collection from their files. The data obtained included socio-demographic data (age, sex, residence and diagnosis), clinical presentation of each tumor type, histological type, WHO grading, and localization.

The reports of malignant diseases in the National Institute of Public Health of Kosovo (NIPHK), were used as well, for the purpose of the further analysis.

This research was carried out in line with the Helsinki Declaration. According to Kosovo legislation only bio-medical studies on human subjects require ethical permission and agreement to participate (19), but the use of personal data for research purposes requires no prior consent from the individual participants provided the data are anonymized before processing (20) which was the situation in this study. Personal data processing authorization was received from the UCCK's Personal Data Protection Office.

Statistical analysis

Descriptive data for 227 BT patients identified between 2019 and 2021 are presented. For this particular period, annual incidence crude rates per 100,000 people were estimated. Annual incidence rates at the Kosovo level were determined for accuracy by utilizing population data based on the 2011 census.

Data were analyzed using SPSS 23.0. Categorical variables were presented as frequency (n) and percentages (%). Continuous variables were expressed as mean \pm standard deviation (SD). Mann-Whitney test was used to compare age distribution between males and females. The course of new cases over years is presented through the respective equation and trend line.

Results

A total of 227 (n=227) patients were treated for BT at the UCCK during the three-year period under investigation (2019-2021). There were 119 males (52.4%) and 108 (47.6%) females. BT were most common in age groups: >50 years (n=178, 78.4%), 25-50 years (n=33, 14.6%), whereas 13 cases (5.7%) were children from the age group \leq 14 years. Almost one third of the patients (33.9%) were from Prishtina region, followed by Peja region (18.5%) and Mitrovica region (13.2%) (Table 1).

Table 1. General characteristics of the study population

Variables	N	%
Age (Years)		
≤14	13	5.7
15-24	3	1.3
25-50	33	14.6
≥50	178	78.4
Gender		
Female	108	47.6
Male	119	52.4
Regions of Kosovo		
Ferizaj	24	10.6
Gjakova	16	7.0
Gjilan	11	4.8
Mitrovica	30	13.2
Peja	42	18.5
Prishtina	77	33.9
Prizren	21	9.3
Unknown	6	2.6

Out of the total number of new cases of brain tumors reported (n=227), according to the years of diagnosis, the highest number was recorded in 2021 with 81 cases (35.7%), while the lowest number was recorded in 2020 with 67 cases (29.5 %). The highest incidence rate was recorded in 2021

(4.7/100,000 inhabitants), while the lowest incidence rate was in 2020 (3.9/100,000 inhabitants).

The average incidence rate for this period of time was 4.4/100,000 inhabitants (Table 2).

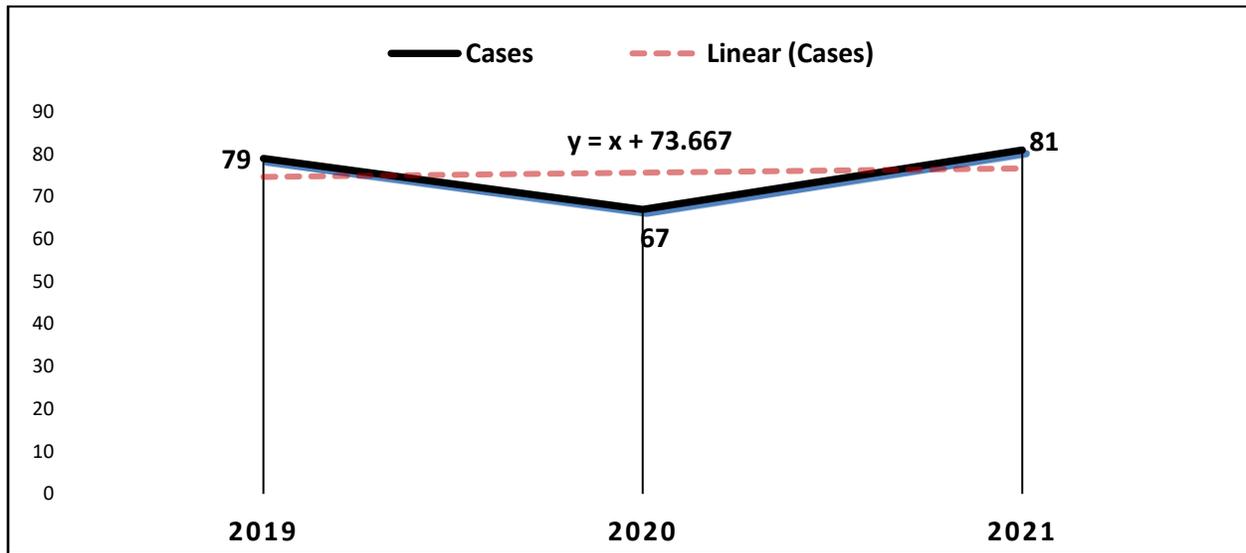
Table 2. Incidence of brain tumors by years, 2019-2021

Years	N (%)	Incidence / 100,000*
2019	79 (34.8)	4.5
2020	67 (29.5)	3.9
2021	81 (35.7)	4.7
Total	227 (100)	4.4

* Number of inhabitants in Kosovo according to the Kosovo Agency of Statistics (ASK 2011), approximately 1.74 million residents.

The course of linear trend of BT in Kosovo during the period 2019-2021 is presented in Figure 1.

Figure 1. The course of linear trend of brain tumors, according to the years 2019-2021



According to gender, the highest number was recorded in males with 119 cases (52.4%), to 108 cases (47.6%) among women (Table 3).

Table 3. Average age and gender of patients with brain tumors, 2019-2021

Parameter	Gender		Total
	Female	Male	
Number	108	119	227
Mean	57.5	59.1	58.4
SD	18.5	18.2	18.3
Min	5	3	3
Max	92	87	92

Mann-Whitney test: P=0.317

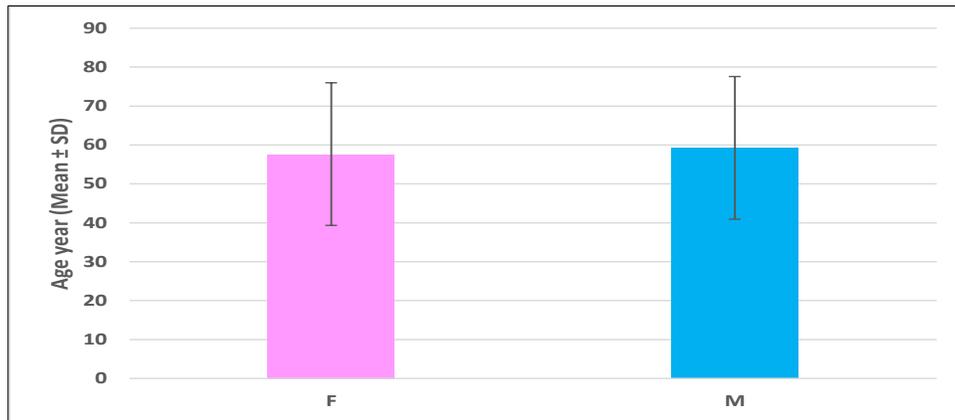
The average age by gender of the patients with BT in Kosovo during the period 2019-2021 is also exhibited in Figure 2.

The average age of patients with BT for the period 2019-2021 was 58.4±18.3 years. The youngest patient was 3 years old, and the oldest one was 92 years old. The average age of female patients was 57.5±18.5 years. The average age of male patients was 59.1±18.2 years. Mann-Whitney test did not indicate a

significant difference in the distribution of age by gender (P=0.317) (Table 3 and Figure 2).

Regarding malignant and benign tumors by gender, there was shown a significant difference (Chi-square test: P=0.001). Malignant tumors are more common in men and benign tumors are more common in women.

Figure 2. Average age by gender of patients with brain tumors, 2019-2021



According to the type of tumors, age groups, and gender, the highest number is recorded in the age group 55-59 years with 30 cases (13.2%), with more malignant tumors - 20 cases, than benign tumors - 10 cases, among them. The lowest number was recorded in the age groups 0-4 years, 20-24 years, and 25-29 years with only 1 case (0.4%) per each age group (Table 4).

According to the type of tumors (benign/malignant), the highest number was recorded as malignant tumors (n=150, 66.1%), with the most affected being the age group 65-69 years with 27 cases. The lower number was recorded in benign tumors with 71 (31.3%), with the most affected being the age group 70-74 years with 12 cases (Table 4).

Table 4. Types of tumors (Benign / Malignant), by age group and gender, 2019-2021

Type of tumors by gender and age groups	Age-groups																Total		
	0 - 4	5 - 9	10 - 14	15 - 19	20 - 24	25 - 29	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65 - 69	70 - 74	75 - 79	80 +	N	%
Benign	1	3	1	1			5	1	1	7	5	10	5	10	12	6	3	71	31.3
Female		2					1		1	6	4	8	3	6	9	4	1	45	19.8
Male	1	1	1	1			4	1		1	1	2	2	4	3	2	2	26	11.5
Malignant		4		1	1	1	2	4	5	7	17	20	21	27	12	19	9	150	66.1
Female		2				1	2	2	1	6	9	6	6	11	6	3	4	59	26.0
Male		2		1	1			2	4	1	8	14	15	16	6	16	5	91	40.1
Unknown		3	1								1						1	6	2.6
Female		2	1														1	4	1.8
Male		1									1							2	0.9
Total	N	1	10	2	2	1	7	5	6	14	23	30	26	37	24	25	13	227	100.0
	%	0.4	4.4	0.9	0.9	0.4	3.1	2.2	2.6	6.2	10.1	13.2	11.5	16.3	10.6	11.0	5.7	100.0	-

(Malignant and benign tumors by gender: Chi-test = 10.24, P = 0.001).

Regarding their localization, diagnosed brain tumors most often had supratentorial/intra-axial localization (63.4%), followed by supratentorial/extra-axial localization (22.5%), infratentorial/ intra-axial

localization (6.6%), Infratentorial / extra-axial localization (4.4%) and fewer were cases with supratentorial / intra-axial – extra-axial localization (2.2%). The ratio between supratentorial brain tumors and infratentorial

brain tumors was 89% to 11% (Report 8:1) (Table 5).

Table 5. Patients by tumor localization and gender, 2019-2021

Gender	Female	Male	Grand Total
Brain tumors by localization	Total (N=108)	Total (N=119)	(N=227)
Infratentorial /intra-axial	9 (8.3%)	6 (5.0%)	15(6.6%)
Infratentorial/extra-axial	7 (6.5%)	3 (2.5%)	10 (4.4%)
Supratentorial/extra-axial	33 (30.6%)	18 (15.1%)	51 (22.5%)
Supratentorial/ intra- axial	57 (52.8%)	87 (73.1%)	144 (63.4%)
Supratentorial/intra-axial – extra-axial	1 (0.9%)	4 (3.4%)	5 (2.2%)
Unknown	1 (0.9%)	1 (0.8%)	2 (0.9%)

Without statistical significance between genders and tumor location (Infratentorial/ supratentorial), (Chi test=0.235, P=0.125).

From the overall number of tumors classified according to the WHO grades (146 cases), the most common was meningioma WHO gr. I with (n=57, 25.1%) followed by glioblastoma

WHO gr. IV (n=43, 18.9%) with similar appearances in both genders. About 35.7% of the cases remained unclassified with respect to WHO grading (Table 6).

Table 6. Brain tumors according to WHO grading and gender, 2019-2021

Brain tumors according to WHO grading and gender	Female	Male	Total
Total= N (%)	N= 108 (%)	N= 119 (%)	N= 227 (%)
Adenomae Hypophysae	2 1.9	0.0	2 0.9
Astrocytoma WHO gr.I	1 0.9	2 1.7	3 1.3
Astrocytoma WHO gr.II	0.0	1 0.8	1 0.4
Astrocytoma WHO gr.III	2 1.9	1 0.8	3 1.3
Astrocytoma WHO gr.IV	0.0	1 0.8	1 0.4
Ciste	0.0	1 0.8	1 0.4
Craniopharyngioma WHO gr. I	1 0.9	0.0	1 0.4
Ependymoma WHO gr. I	1 0.9	2 1.7	3 1.3
Ependymoma WHO gr. IV	2 1.9	0.0	2 0.9
Glioblastoma WHO gr.II	0.0	2 1.7	2 0.9
Glioblastoma WHO gr.III	2 1.9	1 0.8	3 1.3
Glioblastoma WHO gr.IV	12 11.1	31 26.1	43 18.9
Glioma WHO gr II	1 0.9	1 0.8	2 0.9
Hemangioblastoma WHO gr.I	0.0	1 0.8	1 0.4
Hemangioblastoma WHO gr.III	1 0.9	0.0	1 0.4
Hemangioma	1 0.9	0.0	1 0.4
Medulloblastom WHO II	0.0	1 0.8	1 0.4
Medulloblastoma WHO IV	0.0	1 0.8	1 0.4
Meningeoma WHO gr.II	0.0	1 0.8	1 0.4
Meningioma WHO gr.I	38 35.2	19 16.0	57 25.1
Meningioma WHO gr.III	1 0.9	4 3.4	5 2.2
Neurinoma WHO gr. I	1 0.9	0.0	1 0.4
Oligodendroglioma WHO gr. II	3 2.8	3 2.5	6 2.6
Primitive Neuro-Ectodermal Tumors (PNET)	3 2.8	1 0.8	4 1.8
Unknown	36 33.3	45 37.8	81 35.7

Discussion

This study aimed to determine the epidemiological features of BT diagnosed and treated at the UCKK, the only tertiary care institution in Kosovo, according to an

array of characteristics including time period, age, gender, place of residence, and according to the type of tumor, anatomical localization, as well as the comparison of the

course of brain tumors over different time periods.

Our study is in line with previous studies conducted in other countries (21,22) and complies with the recommendations of the American Association of Neurological Surgeons (23). Yet, several potential limitations of this study should be mentioned including the time period under investigation (only three years), as well as the possibility of information bias (in particular, recording of cases and the diagnosis).

However, the UCKK covers the absolute majority of newly diagnosed patients with BT in Kosovo thereby providing generalizability of the findings for the whole country. Nonetheless, further studies are needed to assess particularly the long-term outcome of patients with BT in Kosovo.

The cancer registry is an essential part of any reasonable cancer control program and serves to report malignant diseases through the relevant malignancy application form (16-18). The Cancer Registry is an information system designed to collect, manage, and analyze data on people diagnosed with a malignant disease or malignant neoplasms (cancer).

Currently, the main headquarters of the Population Cancer Registry in Kosovo are located at the NIPHK and constitute the only Population Cancer Registry in Kosovo, but there is seemingly an underreporting from healthcare institutions. The installation of the new software CanReg5 at the NIPHK is done in order to increase the quality of analysis and data management for malignant neoplasms.

Conclusions

Adults over 50 years old represent the most affected age-group with BT in Kosovo. Meningioma, and glioblastoma were the most frequent brain tumors in adults.

Strengthening resources for central cancer registries, collecting and properly reporting data, that is timely, specific, and widely

consistent across Kosovo is needed to lay the ground for evidence-based research, as well as to advance the prevention of the BT and other central nervous system tumors, through early detection tumors as a future public health intervention.

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