Arch Iran Med. January 2020;23(1):1-6

http www.aimjournal.ir

ARCHIVES OF IRANIAN MEDICINE

Original Article

Open Access

Incidence of Malignant Brain and Central Nervous System Tumors in Golestan, Iran, 2004–2013

Marzieh Araghi, PhD[1]; Gholamreza Roshandel, MD, PhD[2*]; Susan Hasanpour-Heidari, MSc[2]; Abdolreza Fazel, MD[3]; Seyed Mehdi Sedaghat, MD[4]; Amirhoushang Pourkhani, MD[5]; Vahideh Kazeminejhad, MD[6]; Adalberto Miranda-Filho, PhD[1]; Freddie Bray, PhD[1]; Melina Arnold, PhD[1]

[1]Section of Cancer Surveillance, International Agency for Research on Cancer, 150 Cours Albert Thomas, Lyon, 69372 CEDEX 08, France
[2]Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
[3]Omid Cancer Research Center, Omid Preventive and Health Promotion Center, Golestan University of Medical Sciences, Gorgan, Iran
[4]Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[5]Department of hematology/oncology, Golestan University of Medical Sciences, Gorgan, Iran
[6]Cancer Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Abstract

Background: Brain and other central nervous system (CNS) tumors represent almost 3% of all new cancer cases worldwide and comprise a heterogeneous group of tumors with varying epidemiologic and clinical characteristics. The aim of this study is to present the distribution and trends in brain and other CNS cancer incidence in Golestan, Iran during a 10-year period.
Methods: Data on primary brain and other CNS cancers diagnosed between 2004 and 2013 were obtained from the Golestan population-based cancer registry (GPCR) dataset. We computed age-standardized incidence rates (ASRs) per 100 000 person-years. In order to assess changes in incidence over time, we calculated the estimated annual percentage change (EAPC) and corresponding 95% confidence intervals (CIs) to detect significant trends.
Results: Over the 10-year period (2004-2013), the incidence of brain and other CNS cancer was observed to increase for all ages (EAPC: 1.13, 95% CI: -6.06, 8.87). After 2008, the trends appear to have stabilized. Incidence rates were higher in males than females (ratio: 1.2) and glioblastoma was the most common tumor subtype (15.1% of all malignant tumors).
Conclusion: Trends and patterns in the burden of brain and other CNS cancer require careful monitoring alongside future research to increase our understanding of potential risk factors.
Keywords: Brain tumors, Central nervous system tumors, Epidemiology, Incidence rates
Cite this article as: Araghi M, Roshande G, Hasanpour-Heidari S, Fazel A, Sedaghat SM, Pourkhani A, et al. Incidence of malignant brain and central nervous system tumors in Golestan, Iran, 2004–2013. Arch Iran Med. 2020;23(1):1–6.

Received: May 11, 2019, Accepted: September 23, 2019, ePublished: January 1, 2020

Introduction

Malignant brain and other central nervous system (CNS) tumors are a group of rare and heterogeneous diseases which can be categorized into distinct pathological entities that display different biological behavior, treatment regimens and prognosis.[1] Unlike most non-malignant tumors, benign tumors of the brain and other CNS can be serious and life-threatening. The etiology of brain cancer is not well understood.[2-4] Probable genetic factors (Li-Fraumeni syndrome) and exposure to ionizing radiation have been associated with both benign and malignant brain and other CNS tumors.[5-8] Exposure to pesticides is found to increase the risk of death in farmers and non-farmers living in rural communities.[9-11] In contrast, no strong association has been found between the use of mobile phones and increased risk of glioma or meningioma.[12]

Close to 300 000 new cases of brain and other CNS tumors were reported worldwide in 2018, representing nearly 3% of all new cancer cases.[13] The incidence of brain and other CNS tumors varies significantly across countries and regions, ranging from 10.1 per 100 000 person-years in Latvia to 0.3 in Togo.[13] In the Middle East, Turkey ranks highest (6.5 per 100 000) with respect to the age-standardized incidence rate (ASR), with Iran (5.9 per 100 000) ranking second.[13] In general, higher incidence has been reported for men relative to women[4,14,15] and with increasing age, with the highest incidence rates observed among elderly populations. However, substantial variation exists in the epidemiology of histological subtypes of brain and other CNS tumors.[16,17] While gliomas are the most common primary brain tumor among adults,[15,18] embryonal tumors are most commonly observed in children.[19] In Iran, meningioma is reported to be the most common tumor among adults, while astrocytoma is reported to be the most common tumor in children.[20,21]

Increasing trends in the incidence of malignant brain and other CNS cancers have been reported over the last few decades in many countries.[22] The increase maybe as a result of improved diagnostic techniques.[7] Understanding the descriptive epidemiology of the cancer can yield fundamental information to inform public health decisions and actions. Previous efforts to quantify

*Corresponding Author: Gholamreza Roshandel, MD, PhD; Golestan Research Center of Gastroenterology and Hepatology, Sayyad Shirazi Hospital, Sayyad Shirazi Blvd., Gorgan, Iran. Tel: +98-911 375 73 27; Email: roshandel_md@yahoo.com

the incidence of brain and other CNS cancers in Iran are limited.[23-25] According to Cancer Incidence in Five Continents (CI5), brain and other CNS tumors are the seventh most common malignancy in Golestan.[26] The rural part of Golestan is a major consumer of pesticides, but no previous study has evaluated the impact of these substances on population health.

We aimed to present the burden of brain and other CNS tumors by age, sex, residential area (urban vs. rural) and histological type in Golestan and explore the environmental hypotheses using data from the Golestan Population-based Cancer Registry (GPCR) during its first 10-year of activity: 2004-2013.

Materials and Methods

Golestan is located in the South East littoral of the Caspian Sea in northern Iran. The province is divided into fourteen counties, 33 cities and 1051 villages. According to the latest census in 2016, Golestan has a population of about 1.9 million, representing about 2.3% of the total Iranian population. Half of its population lives in rural parts, the main agriculture area, while the other half resides in urban areas. The GPCR, established in 2001, has been a voting member of the International Agency for Research on Cancer (IARC) since 2007 and data has been included in Volumes X and XI of Cancer Incidence in Five Continents (CI5), indicating high data quality and completeness.[26]

For the current analysis, we selected all primary malignant brain and other CNS tumors (International Classification of Diseases, 10th edition (ICD-10) codes C70–C72), diagnosed between 2004 and 2013 from the GPCR database. ASRs per 100 000 person-years were computed using the world standard population.[27] In order to assess changes in incidence over time, we calculated the estimated annual percentage change (EAPC) and the corresponding 95% confidence intervals (CI) using the method proposed by Kim and colleagues[28] to detect significant trends. We calculated the EAPC using a generalized linear model (GLM) considering a Gaussian distribution for the ASRs. Under the assumption of linearity on the log scale, which is equivalent to a constant change assumption, the EAPC is calculated. EAPCs were considered statistically significant if the P value was less than 0.05. Analyses were carried out for all ages as well as for ages <50 years and ≥50 years to compare the trend between younger and older individuals diagnosed with brain cancer.

Additionally, the ICD-O-3 (2000) between 2004 and 2012 and the first revision of the ICD-O-3 (ICD-O-3.1; 2011) since 2013 were considered to define histological subtypes. The classification of the Central Brain Tumor Registry of the United States (CBTRUS)[29] was used to make histology groupings. The study protocol was reviewed and approved by the ethics committee of the Golestan University of Medical Sciences. Data analysis was conducted in Stata version 14.0 (StataCorp).

Results

In total, 850 malignant brain and other CNS tumors (480 in males and 370 in females) were reported to the GPCR during 2004-2013 (ASR = 6.1 per 100 000 person-years) (Table 1): 445 cases (255 in males and 190 in females, ratio: 1.3) in urban areas (ASR = 6.2) and 405 cases (225 in males and 180 in females, ratio: 1.2) (ASR = 5.9) in rural areas (Table 1).

Trends in incidence rates in urban and rural regions showed similar patterns until 2008 and somewhat diverging trends thereafter with slightly higher rates in urban relative to rural areas (Figure 1). The patterns of age-specific incidence rates were similar in urban and rural regions (Supplementary file 1, Figure S1). Over the 10-year period (2004–2013), the incidence of brain and other CNS cancers was observed to increase in Golestan for all ages but specifically, in those aged above 50 years and residing in urban areas (Figure 2), although the trends were not statistically significant (Table 2).

Overall, 38% and 13% of all brain and other CNS tumors were gliomas and embryonal tumors, respectively, while the proportion of unspecified malignant neoplasms was 48.5% (Figure S2). Glioblastoma was the most common malignant tumor (129 out of 850 cases; 15.2%), occurring mostly in older individuals (mean age ± standard deviation: 51.2 ± 16.2 years), followed by diffuse astrocytoma (98 out of 850 cases; 11.5%) and malignant meningioma (54 out of 850 cases; 6.3%) (Table 3).

Discussion

In this descriptive report of trends in the incidence of brain and other CNS cancers in Golestan during 2004-2013, we observed an upward trend in incidence, which was slightly more pronounced in urban compared to rural regions with stabilization in incidence rates since 2008. Moreover, our results showed that glioblastoma, diffuse astrocytoma, and malignant meningioma were the most common histological types. While previous studies[23,24] have investigated the epidemiology of CNS tumors in Iran, these studies have been limited to cases diagnosed in the hospital settings.

Globally, there is large variability in the burden of brain and other CNS cancers, suggesting a 5-fold difference between the regions with high (mainly in Europe) and the low (mainly in Asia) incidence rates.[22,26] Over the last few decades, the increasing trends in the incidence of brain and other CNS cancers suggested substantial burden for this cancer worldwide.[30] The incidence of 6.1, which we found in this study, is in line with findings from other studies that reported an estimate of 5.9 for Iran,[13,25] and it is higher than other countries in the Middle East such as Iraq (4.8 per 100 000) or Jordan (4.4 per 100 000).[13] While

Table 1. Number of New Cases and ASR Rates Per 100 000 Person-Years of Brain and Central Nervous System Cancers in the Golestan Province, Iran 2004-2013

Age	Year	Gender	Residential Area					
			Urban		Rural		Total	
			Cases	ASR (95% CI)	Cases	ASR (95% CI)	Cases	ASR (95% CI)
All Ages	2004-2008	Male	116	6.8 (5.4, 8.1)	124	7.6 (6.1, 9.0)	240	7.1 (6.1, 8.0)
		Female	87	5.8 (4.4, 7.0)	79	4.9 (3.7, 6.0)	166	5.3 (4.4, 6.1)
		Total	203	6.3 (5.3, 7.2)	203	6.2 (5.3, 7.1)	406	6.2 (5.5, 6.8)
	2009-2013	Male	139	7.1 (5.9, 8.4)	101	6.0 (4.7, 7.3)	240	6.6 (5.7, 7.5)
		Female	103	5.1 (4.0, 6.1)	101	5.5 (4.3, 6.6)	204	5.3 (4.5, 6.1)
		Total	242	6.1 (5.3, 7.0)	202	5.7 (4.9, 6.5)	444	5.9 (5.3, 6.5)
	2004-2013	Male	225	6.7 (5.8, 7.7)	255	7.0 (6.1, 8.0)	480	6.9 (6.2, 7.5)
		Female	190	5.4 (4.5, 6.2)	180	5.2 (4.4, 6.0)	370	5.3 (4.7, 5.8)
		Total	445	6.2 (5.6, 6.8)	405	5.9 (5.3, 6.5)	850	6.1 (5.6, 6.5)
<50 years old	2004-2008	Male	68	3.7 (2.8, 4.6)	74	4.1 (3.1, 5.1)	142	3.9 (3.2, 4.5)
		Female	43	2.5 (1.7, 3.3)	45	2.7 (1.9, 3.5)	88	2.6 (2.0, 3.1)
		Total	111	3.1 (2.5, 3.7)	119	3.4 (2.7, 4.0)	230	3.2 (2.8, 3.7)
	2009-2013	Male	72	3.4 (2.6, 4.2)	56	3.2 (2.3, 4.0)	128	3.3 (2.7, 3.8)
		Female	62	3.0 (2.2, 3.8)	56	3.1 (2.2, 3.9)	118	3.1 (2.5, 3.6)
		Total	134	3.2 (2.6, 3.7)	112	3.1 (2.5, 3.7)	246	3.2 (2.7, 3.6)
	2004-2013	Male	140	3.5 (2.9, 4.1)	130	3.7 (3.0, 4.3)	270	3.6 (3.1, 4.0)
		Female	105	2.7 (2.2, 3.3)	101	2.9 (2.3, 3.5)	206	2.8 (2.4, 3.2)
		Total	245	3.1 (2.7, 3.5)	231	3.3 (2.8, 3.7)	476	3.2 (2.9, 3.5)
≥50 years old	2004-2008	Male	48	19.0 (13.5, 24.4)	50	21.5 (15.3, 27.6)	98	19.8 (15.8, 23.9)
		Female	44	18.8 (13.1, 24.5)	34	13.6 (8.9, 18.3)	78	16.0 (12.3, 19.6)
		Total	92	18.9 (15.0, 22.9)	84	17.4 (13.6, 21.2)	176	17.9 (15.2, 20.6)
	2009-2013	Male	67	22.2 (16.7, 27.7)	45	17.3 (12.1, 22.6)	112	20.0 (16.1, 23.8)
		Female	41	13.5 (9.2, 17.7)	45	15.1 (10.6, 19.6)	86	14.3 (11.2, 17.4)
		Total	108	17.9 (14.4, 21.4)	90	16.1 (12.7, 19.5)	198	17.1 (14.6, 19.5)
	2004-2013	Male	115	21.1 (17.2, 25.1)	95	19.0 (15.1, 23.0)	210	20.0 (17.2, 22.8)
		Female	85	15.9 (12.4, 19.4)	79	14.3 (11.1, 17.6)	164	15.1 (12.7, 17.5)
		Total	200	18.6 (15.9, 21.2)	174	16.6 (14.1, 19.1)	374	17.5 (15.7, 19.3)

ASR, age-standardized incidence.

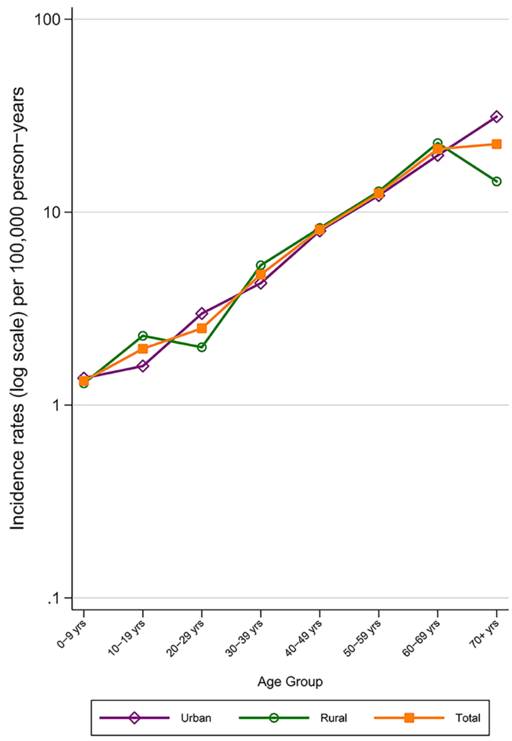

Figure 1. Trends in Brain and Central Nervous System Cancer Incidence (Per 100 000 Person-Years) in Golestan Province, Iran 2004-2013.

the underlying causes for the international differences in the frequency and distribution of brain tumors are largely unknown, they may be partly explained by variations in exposure to known and suspected environmental or lifestyle risk factors. These include dietary factors (cured meat consumption and low intake of vitamin C), as well as genetic diversities between racial/ethnic groups residing in different geographical regions. One cannot, however, discount differences in protocols and standards of case ascertainment, reporting, coding as well as diagnostic standards across cancer registries.[14]

Recent economic developments in Iran in urban areas may have led to inequalities in health by region in terms of access to health services. The observed increase in brain cancer among older individuals living in urban areas may have been a result of better access to diagnostic services, in particular CT and MRI examinations.[31] Although it is possible that the use of MRIs in the 1980s is associated with the observed increase in trends, there is no data to confirm this. There have been, however, broader changes in brain cancers classification as well as improvements in the diagnosis and reporting of these cancers over time. Moderate-to-high-dose ionizing radiation has been known and the only established environmental risk factor for

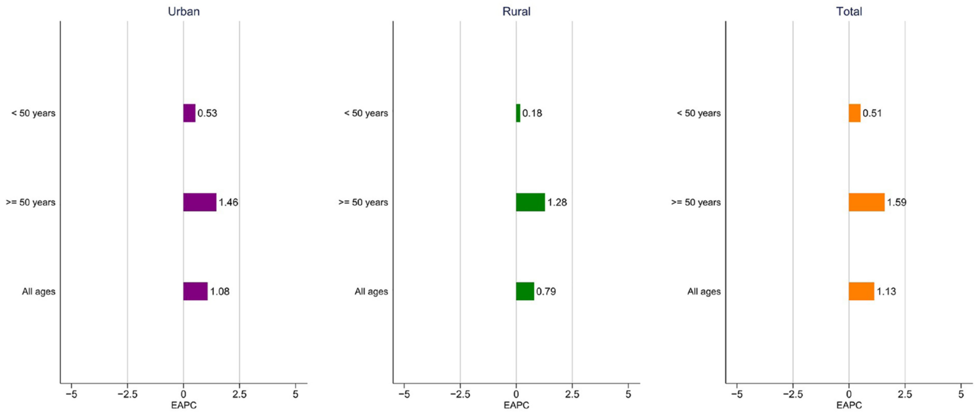

Figure 2. Estimated Annual Percentage Change (EAPC) in Age-Standardized Brain and Central Nervous System Cancer Incidence Per 100,000 in Golestan, Iran 2004-2013.

brain and other CNS cancers.[32,33] It has been shown that high doses of therapeutic radiation may increase the risk of developing brain and CNS tumors,[15,34,35] although the prevalence of therapeutic radiation is low in the general population. There is also a growing public concern regarding possible adverse health effects due to exposure to radiofrequency fields from mobile phones.[36] Recently, results from a large case–control study from 13 countries could not draw any strong conclusion about increased risk of brain cancer associated with mobile phone use.[12] Available epidemiological data also highlighted a role of pesticides as a primary concern, especially among farmers. In a meta-analysis of thirty-three studies on farmers, a 30% increase in the risk of brain cancer was reported (odds ratio: 1.30, 95% CI: 1.09, 1.56).[37] Yet, incidence rates were slightly lower in rural areas with higher levels of pesticide exposure when compared to urban areas.

Our results suggested higher incidence of malignant brain and other CNS tumors in males than females, which is in line with previous studies.[15] Although female sex hormones have been proposed by some investigators as protective factors against brain cancer, innate differences in the susceptibility of X and Y chromosomes to tumorigenic stimuli was also suggested as a possible explanation for higher rates of brain cancers among males.[38] Higher incidence in older age groups (≥50 years old) has been suggested to be linked to bioaccumulation of environmental toxic exposures that may increase the risk of brain and CNS tumors. Previously, in a study conducted in the United States, older age was associated with an increased risk of brain cancer (relative risk: 3.1, 95% CI: 3.0, 3.2), similar to residence in a metropolitan county (relative risk: 1.35, 95% CI: 1.31, 1.38).[39] Although

Table 2. Estimated Annual Percentage Change (EAPC) of Brain and Central Nervous System Cancers and Age Groups 2004-2013

Age Groups	Residential Area	EAPC	Lower Limit	Upper Limit
All ages	Urban	1.08	-6.03	8.72
	Rural	0.79	-6.41	8.55
	Total	1.13	-6.06	8.87
<50 years	Urban	0.53	-9.19	11.28
	Rural	0.18	-9.34	10.70
	Total	0.51	-9.13	11.18
≥50 years	Urban	1.46	-2.75	5.86
	Rural	1.28	-3.11	5.88
	Total	1.59	-2.74	6.11

EAPC, Estimated Annual Percentage Change.

Table 3. Number of New Malignant Tumors of the Brain and Central Nervous System by Histology, 2004-2013 in Golestan

Histology	Total	%	Mean Age ± SD
Tumors of neuroepithelial tissue			
Glioblastoma	129	15.1	51.2 ± 16.2
Diffuse astrocytoma	98	11.5	35.0 ± 17.4
Embryonal/primitive/medulloblastoma	35	4.1	20.8 ± 17.6
Ependymoma	17	2.0	26.2 ± 17.3
Anaplastic astrocytoma	16	1.8	32.6 ± 16.4
Oligodendroglioma	15	1.7	41.9 ± 10.3
Fibrillary astrocytoma	9	1.0	37.2 ± 18.3
Glioma	9	1.0	33.8 ± 21.5
Mixed glioma	7	0.8	39.5 ± 9.9
Anaplastic oligodendroglioma	5	0.5	40.0 ± 19.6
Other tumors of neuroepithelial tissue	17	0.5	35.7 ± 15.4
Tumors of cranial and spinal nerves			
Neurofibroma	5	0.5	35.8 ± 22.3
Schwannoma	5	0.5	38.0 ± 7.6
Meningioma	54	6.3	54.0 ± 20.2
Other mesenchymal, non-malignant and malignant	5	0.5	45.8 ± 11.1
Tumors of the hematopoietic system			
Malignant lymphomas	9	1.0	38.77 ± 23.0
Germ cell tumors			
Germinoma/teratoma	2	0.2	19.5 ± 12.0
Unclassified tumor			
Neoplasm, unspecified	413	48.5	49.4 ± 19.9
Total	850	100.0	—

SD, standard deviation

farmers with extensive exposure to pesticides have been shown to be at higher risk of brain cancer,[9,10] it may be concluded that the effects of pesticides are small, or the proportion of farmers is low, or there are more important risk factors in urban areas.

Consistent with current evidence,[40] our results showed that tumors of the meninges are more common among older individuals (≥50 years of age) and the mean age at diagnosis for incidence of embryonal/primitive/medulloblastoma and diffuse astrocytoma tumors was found to be 20 and 35 years, respectively. Worldwide, the most common tumor originating from the neuroepithelium, regardless of gender is glioblastoma.[19] In Golestan, for the period of 2004-2013, glioblastoma accounted for 15.1% of all brain and CNS tumors and 36.1% of all neuroepithelium tumors. This distribution is similar to that reported in the United States (2009-2013), where glioblastoma was reported to account for 14.9% of all brain and other CNS tumors and 46.6% of all neuroepithelium tumors.[41] Histologically confirmed diagnoses accounted for 52% of all brain and other CNS tumors in our study compared to 73% in the United States[42] and 86% in Japan.[42] This would suggest that a considerable number of the brain and other CNS cancers in the GPCR were registered without histological confirmation.

This study presents the GPCR findings on distributions and trends in brain and other CNS cancer incidence in Golestan. The potential misclassification of histological subtypes may occur due to the complexities in the tumor's pathological classification.[43] Considering the new brain and other CNS tumor classification (the 2016 World Health Organization [WHO] classification of tumors of the CNS),[44] which was introduced in 2007,[1] may improve case ascertainment and increase the accuracy of diagnosis and consequently, may result in improvement of the quality of the GPCR data. Due to small number of cases, we were not able to examine incidence patterns and trends by histology and for more granular age groups.

In conclusion, the results of this study indicate that brain and other CNS cancer incidence in Golestan may have stabilized since 2008. The slight increase in the incidence at older ages in urban regions may reflect differences in the distribution of risk factors, but may equally point towards differences in access to diagnostic services. Exposure to ionizing radiation has been proposed as the main risk factor for brain and other CNS tumors; however, the extent to which other genetic or environmental factors contribute to the variations is yet to be elucidated. Evidently, incidence trends of brain and other CNS cancers require careful monitoring; it is hoped that future research will increase our understanding of the underlying risk factors and increase the prospects for cancer control strategies.

Authors' Contribution

MaA, MeA, and AM conceived the study and contributed to study design, analysis and wrote the first draft of the manuscript. GR, SHH, AF, SMS, AP, and VK contributed to data collection and critically reviewed the manuscript. GR contributed to data preparation and analysis. FB contributed to drafting and finalizing the report. All authors read and approved the final manuscript.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The study protocol was reviewed and approved by the ethics committee of the Golestan University of Medical Sciences.

Acknowledgement

Authors would like to thank the staff of the GPCR as well as all physicians and personnel of healthcare centers throughout Golestan province for their collaborations in data collection. This study was supported by the Golestan University of Medical Sciences under contract 35-306385.

Supplementary Materials

Supplementary file 1 contains Figures S1- S2.

References

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol. 2007;114(2):97-109. doi: 10.1007/s00401-007-0243-4.
2. Ohgaki H. Epidemiology of brain tumors. Methods Mol Biol. 2009;472:323-42. doi: 10.1007/978-1-60327-492-0_14.
3. Rao JS. Molecular mechanisms of glioma invasiveness: the role of proteases. Nat Rev Cancer. 2003;3(7):489-501. doi: 10.1038/nrc1121.
4. Surawicz TS, McCarthy BJ, Kupelian V, Jukich PJ, Bruner JM, Davis FG. Descriptive epidemiology of primary brain and CNS tumors: results from the Central Brain Tumor Registry of the United States, 1990-1994. Neuro Oncol. 1999;1(1):14-25. doi: 10.1093/neuonc/1.1.14.
5. Bell DW, Varley JM, Szydlo TE, Kang DH, Wahrer DC, Shannon KE, et al. Heterozygous germ line hCHK2 mutations in Li-Fraumeni syndrome. Science. 1999;286(5449):2528-31. doi: 10.1126/science.286.5449.2528.
6. Nichols KE, Malkin D, Garber JE, Fraumeni JF Jr, Li FP. Germ-line p53 mutations predispose to a wide spectrum of early-onset cancers. Cancer Epidemiol Biomarkers Prev. 2001;10(2):83-7. doi: Published February 2001.
7. Schwartzbaum JA, Fisher JL, Aldape KD, Wrensch M. Epidemiology and molecular pathology of glioma. Nat Clin Pract Neurol. 2006;2(9):494-503. doi: 10.1038/ncpneuro0289.
8. Non-ionizing radiation, Part II: Radiofrequency electromagnetic fields / IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2011. Available from: https://monographs.iarc.fr/wp-content/uploads/2018/06/mono102.pdf.
9. Provost D, Cantagrel A, Lebailly P, Jaffre A, Loyant V, Loiseau H, et al. Brain tumours and exposure to pesticides: a case-control study in southwestern France. Occup Environ Med. 2007;64(8):509-14. doi: 10.1136/oem.2006.028100.
10. Samanic CM, De Roos AJ, Stewart PA, Rajaraman P, Waters MA, Inskip PD. Occupational exposure to pesticides and risk of adult brain tumors. Am J Epidemiol. 2008;167(8):976-85. doi: 10.1093/aje/kwm401.
11. Bohnen NI, Kurland LT. Brain tumor and exposure to pesticides in humans: a review of the epidemiologic data. J Neurol Sci. 1995;132(2):110-21. doi: 10.1016/0022-510X(95)00151-Q.
12. Grp IS. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. Int J Epidemiol. 2010;39(3):675-94. doi: 10.1093/ije/dyq079.

13. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi: 10.3322/caac.21492.
14. Darefsky AS, Dubrow R. International variation in the incidence of adult primary malignant neoplasms of the brain and central nervous system. Cancer Causes Control. 2009;20(9):1593-1604. doi: 10.1007/s10552-009-9404-1.
15. Fisher JL, Schwartzbaum JA, Wrensch M, Wiemels JL. Epidemiology of brain tumors. Neurol Clin. 2007;25(4):867-90. doi: 10.1016/j.ncl.2007.07.002.
16. Greig NH, Ries LG, Yancik R, Rapoport SI. Increasing annual incidence of primary malignant brain tumors in the elderly. J Natl Cancer Inst. 1990;82(20):1621-4; doi: 10.1093/jnci/82.20.1621.
17. Dahlrot RH, Poulsen FR, Nguyen NN, Kristensen BW, Hansen S, Holm NV, et al. Trends in tumors in the central nervous system in elderly in Denmark, 2008-2012. Acta Oncol. 2016;55(sup1):91-7. doi: 10.3109/0284186X.2015.1115123.
18. Ostrom QT, Bauchet L, Davis FG, Deltour I, Fisher JL, Langer CE, et al. The epidemiology of glioma in adults: a "state of the science" review. J Neurooncol. 2014;16(7):896-913. doi: 10.1093/neuonc/nou087.
19. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016;131(6):803-20. doi: 10.1007/s00401-016-1545-1.
20. Mehrazin M, Rahmat H, Yavari P. Epidemiology of primary intracranial tumors in Iran, 1978-2003. Asian Pac J Cancer Prev. 2006;7(2):283-8.
21. Mehrazin M, Yavari P. Morphological pattern and frequency of intracranial tumors in children. Childs Nerv Syst. 2007;23(2):157-62. doi: 10.1007/s00381-006-0198-0
22. Miranda-Filho A, Pineros M, Soerjomataram I, Deltour I, Bray F. Cancers of the brain and CNS: global patterns and trends in incidence. Neuro Oncol. 2017;19(2):270-80. doi: 10.1093/neuonc/now166.
23. Jafarzadeh N, Faal A, Izanloo A, Farrokhi F, Ziaolhagh R, Hashemian HR, et al. Epidemiology of Nervous System Tumors According to WHO 2007 Classification: A Report of 1,164 Cases from a Single Hospital. Int J Cancer Manag. 2018;11(4):e11462. doi: 10.5812/ijcm.11462.
24. Ameli NO, Haddadian A, Kamalian N. Incidence of intracranial tumours in Iran. Neurosurg Rev. 1979;2(2):67-71.
25. Jazayeri SB, Rahimi-Movaghar V, Shokraneh F, Saadat S, Ramezani R. Epidemiology of primary CNS tumors in Iran: a systematic review. Asian Pac J Cancer Prev. 2013;14(6):3979-85. doi: 10.7314/apjcp.2013.14.6.3979.
26. Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, et al. Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer. 2017.
27. Doll R, Payne P, Waterhouse J. Cancer Incidence in Five Continents, vol. I. Union Internationale Contre le Cancer, Geneva; 1966. doi: 10.1007/978-3-642-85849-9.
28. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3): 335-51.
29. Central Brain Tumor Registry of the United States. Statistical report. Primary brain tumors diagnosed in the United States in 2004-2005. Available from: http://www.cbtrus.org/.
30. Patel AP, Fisher JL, Nichols E, Abd-Allah F, Abdela J, Abdelalim A, et al. Global, regional, and national burden of brain and other CNS cancer, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(4):376-393. doi: 10.1016/S1474-4422.
31. Mabray MC, Barajas RF, Jr., Cha S. Modern brain tumor imaging. Brain Tumor Res Treat. 2015;3(1):8-23. doi: 10.14791/btrt.2015.3.1.8.
32. Bondy ML, Scheurer ME, Malmer B, Barnholtz-Sloan JS, Davis FG, Il'yasova D et al. Brain tumor epidemiology: consensus from the Brain Tumor Epidemiology Consortium. Cancer. 2008;113(7 Suppl): 1953-68; doi: 10.1002/cncr.23741.
33. Inskip PD, Linet MS, Heineman EF. Etiology of brain tumors in adults. Epidemiol Rev. 1995;17(2): 382-414.
34. Wrensch M, Minn Y, Chew T, Bondy M, Berger MS. Epidemiology of primary brain tumors: current concepts and review of the literature. Neuro Oncol. 2002;4(4): 278-99; doi: 10.1093/neuonc/4.4.278.
35. Braganza MZ, Kitahara CM, Berrington de Gonzalez A, Inskip PD, Johnson KJ, Rajaraman P. Ionizing radiation and the risk of brain and central nervous system tumors: a systematic review. Neuro Oncol 2012; 14(11): 1316-24; doi: 10.1093/neuonc/nos208.
36. Kundi M, Mild KH, Hardell L, Mattsson MO. Mobile telephones and cancer - A review of epidemiological evidence. J Toxicol Env Heal B 2004;7(5): 351-84; doi: 10.1080/10937400490486258.
37. Khuder SA, Mutgi AB, Schaub EA. Meta-analyses of brain cancer and farming. Am J Ind Med 1998; 34(3): 252-60.
38. McKinley BP, Michalek AM, Fenstermaker RA, Plunkett RJ. The impact of age and sex on the incidence of glial tumors in New York state from 1976 to 1995. J Neurosurg. 2000;93(6):932-9. doi: 10.3171/jns.2000.93.6.0932.
39. Deorah S, Lynch CF, Sibenaller ZA, Ryken TC. Trends in brain cancer incidence and survival in the United States: Surveillance, Epidemiology, and End Results Program, 1973 to 2001. Neurosurg Focus. 2006. 20(4):E1. doi: 10.3171/foc.2006.20.4.E1.
40. Leece R, Xu J, Ostrom QT, Chen YW, Kruchko C, Barnholtz-Sloan JS. Global incidence of malignant brain and other central nervous system tumors by histology, 2003-2007. Neuro Oncol. 2017;19(11):1553-64. doi: 10.1093/neuonc/nox091.
41. Ostrom QT, Gittleman H, Xu J, Kromer C, Wolinsky Y, Kruchko C, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2009-2013. Neuro Oncol. 2016;18(suppl_5):v1-v75. doi: 10.1093/neuonc/now207.
42. Kaneko S, Nomura K, Yoshimura T, Yamaguchi N. Trend of brain tumor incidence by histological subtypes in Japan: estimation from the Brain Tumor Registry of Japan, 1973-1993. J Neurooncol. 2002;60(1):61-9. doi: 10.1023/a:1020239720852.
43. Davis FG, Malmer BS, Aldape K, Barnholtz-Sloan JS, Bondy ML, Brannstrom T, et al. Issues of diagnostic review in brain tumor studies: from the Brain Tumor Epidemiology Consortium. Cancer Epidemiol Biomarkers Prev. 2008;17(3):484-9. doi: 10.1158/1055-9965.EPI-07-0725.
44. Hainfellner J, Louis DN, Perry A, Wesseling P. Letter in response to David N. Louis etal, International Society of Neuropathology-Haarlem Consensus Guidelines for Nervous System Tumor Classification and Grading, Brain Pathology, doi: 10.1111/bpa.12171. Brain Pathol. 2014;24(6):671-2. doi: 10.1111/bpa.12187.