Open access • Journal Article • DOI:10.1007/S11060-013-1054-1

Primary brain tumour epidemiology in Georgia: first-year results of a population-based study. — Source link

David Gigineishvili, Nino Shengelia, Giorgi Shalashvili, Sabine Rohrmann ...+2 more authors

Institutions: Tbilisi State University, University of Zurich

Published on: 21 Jan 2013 - Journal of Neuro-oncology (Springer US)

Topics: Population and Incidence (epidemiology)

Primary brain tumour epidemiology in Georgia: first-year results of a population-based study

Gigineishvili, David ; Shengelia, Nino ; Shalashvili, Giorgi ; Rohrmann, Sabine ; Tsiskaridze, Alexander ; Shakarishvili, Roman

Abstract: A population-based cohort study was initiated in Georgia in March 2009 to collect epidemiologic data of malignant and non-malignant primary brain tumours. During the first year, 473 incident cases were identified. For a population of 4.3 million, the annual incidence rate was 10.25 per 100,000 inhabitants, age-standardized to the year 2000 US population. Non-malignant tumours constituted about 66 % of all tumours. Males accounted for 40 % and females for 60 % of the cases. Crude incidence rates by histology were highest for meningiomas (2.92/100,000), pituitary adenoma (1.16/100,000) and glioblastomas (0.64/100,000), which was in agreement with the frequency of reported histology: meningiomas–45.2 %, pituitary adenoma–18.0 % and glioblastomas–9.9 %. The age-standardized incidence rates were higher among females than males for all primary brain tumours (11.05 vs. 8.44/100,000) as well as for individual histologies except for glioblastoma and several other neuroepithelial tumours. Some differences compared with 2004-2005 Central Brain Tumor Registry of the United States data may be explained by a higher percentage of unclassified tumours (37 %) in our study. We suggest further studies to clarify the nature of this discrepancy.

DOI: https://doi.org/10.1007/s11060-013-1054-1

David Gigineishvili[1], Nino Shengelia[1], Giorgi Shalashvili[1], Sabine Rohrmann[2], Alexander Tsiskaridze[1], Roman Shakarishvili[1]

Primary Brain Tumour Epidemiology in Georgia – first-year results of a population-based study

Affliations: 1- Department of Neurology & Neurosurgery, Faculty of Medicine, Tbilisi State University, Tbilisi 0112, Georgia

2-Division of Cancer Epidemiology and Prevention, Institute of Social and Preventive Medicine, University of Zurich, Zurich CH-8001, Switzerland

Corresponding Author: Prof. David Gigineishvili, Sarajishvili Institute of Neurology, Tevdore Mgvdlis str. 13, Tbilisi 0112, Georgia Tel: +995 593279079; Fax: +995 32 2347627
e-mail:epigeo@hotmail.com

Abstract

A population-based cohort study was initiated in Georgia in March 2009 to collect epidemiologic data of malignant and non-malignant primary brain tumours. During the first year, 473 incident cases were identified. For a population of 4.3 million, the annual incidence rate was 10.25 per 100,000 inhabitants, age-standardized to the year 2000 US population. Non-malignant tumours constituted about 66% of all tumours. Males accounted for 40% and females for 60% of the cases. Crude incidence rates by histology were highest for meningiomas (2.92/100,000), pituitary adenoma (1.16/100,000) and glioblastomas (0.64/100,000), which was in agreement with the frequency of reported histology: meningiomas – 45.2%, pituitary adenoma – 18.0% and glioblastomas – 9.9%. The age-standardized incidence rates were higher among females than males for all primary brain tumours (11.05vs.8.44/100,000) as well as for individual histologies except for glioblastoma and several other neuroepithelial tumours. Some differences compared with 2004-2005 Central Brain Tumor Registry of the United States (CBTRUS) data may be explained by a higher percentage of unclassified tumours (37%) in our study. We suggest further studies to clarify the nature of this discrepancy.

Key words: epidemiology, primary brain tumours, incidence, Georgian brain tumour registry

Background

Intracranial tumours account for 95% of primary Central Nervous System (CNS) tumours. Primary brain tumours are relatively rare compared with lung, breast, prostate and colorectal tumours. However, the mortality rate associated with them is quite high and brain tumours are a leading cause of cancer death in children under 15 years [1].

Brain Tumour Registries, although widely established, are still not established worldwide. Indeed, even in developed countries most cancer registries provide information only for malignant brain tumours [2-5]. In a light of the rarity of brain tumours, the focus on malignant brain tumours does not enhance systematic and detailed epidemiological data identification. Six-fold differences in the incidence of primary brain tumours have been reported in literature between countries worldwide and developed countries appear to have the highest rates of brain tumours, but the relevant studies from registries in developing countries are scarce [6-10] .

The aim of our study is to provide accurate and reliable information of incident cases of primary intracranial tumours in Georgia. The registration of primary brain tumour cases will establish a population-based Georgian Brain Tumour Registry, which will collect information of malignant and non-malignant brain tumours.

Material and method

We conducted a nation-wide prospective cohort study on primary brain tumours starting in March 2009. All registered neurosurgical departments and almost all neurodiagnostic departments and units contributed to the study as cooperative partners. Hospitals participating in the study represent at least 95% of the neurosurgery and neuroradiology activity in the country. Ethical approval was obtained from the Tbilisi State University Medical Faculty ethics committee.

Case ascertainment

The case identification was performed by: (a) searching of medical histories of Neurosurgery Departments; (b) searching of scan reports of Neuroimaging Departments and computer tomography (CT) and magnetic resonance imaging (MRI) units. The main part of the medical facilities is situated in three large cities (Tbilisi, Kutaisi and Batumi), which are checked by our representative once per three months.

All scan reports were reviewed by one neurosurgeon participating in the study. On the basis of the first radiological and follow-up scan (if existing) descriptions a diagnosis was established for each scan report. If the existing data was not sufficient to classify a tumour, the case was defined as unclassified. In the generated database each radiological case was matched with the data from the neurosurgical hospitals and if duplicated the surgical report was kept. If the neurosurgical diagnosis differed from the diagnosis assigned by the scan review, the case was reviewed by the neurosurgeon and the neurologist.

Secondary sources of case ascertainment included: (a) search of the operative protocol database in the Tbilisi neurosurgical departments for all patients coded as primary brain tumour; (b) search for all patients in the largest histopathology database in Tbilisi (serving up to 70% of surgical activities in the city) with a histological confirmation of a primary intracranial tumour. After all cases were identified and diagnosis assigned, the results were verified against histological database and in case of discrepancies in diagnoses from clinical department and histological database the histologically correct diagnosis was substituted.

Registration

All collected data were registered using a specially designed case reporting form. Filled in and completed printed reporting forms were stored, which, along with electronic records, formed Georgian Brain Tumour Registry database. Inclusion criteria were intracranial location of malignant and non-malignant tumour diagnosed after March 1, 2009. The date of diagnosis is defined as the date of neuroradiologic scan when the brain tumour was first detected. In accordance with the internationally recognized primary brain tumour standard definition, we have included into the study tumours located in the intracranial cavity and originated from the brain itself, meninges, cranial nerves, pituitary and pineal glands and craniopharyngeal duct [7, 11].

We excluded all cases of recurrent brain tumour and extracranial tumours with intracranial invasion from the study. In the reporting form demographic, histological and radiologic data were collected. On the basis of the new WHO 2007 histological classification of tumours of the central nervous system we have defined six main histology groups: neuroepithelial, tumours of cranial and paracranial nerves, tumours of meninges, lymphomas and hematopoetic tumours, germ cell tumours and sellar region tumours [12]. Registrants had to mark the histology group, subtype and type of tumour in the form. Tumour grade (I-IV) and behavior code (0, 1, 3), as specified in the International Classification of Diseases for Oncology, Third Edition (ICD-O-3), also has been registered. The tumour was

considered as non-malignant if the behaviour code was '0' (benign) or '1' (uncertain). Information regarding treatment is recorded as surgery with the indication of the operation type, chemo- and radiotherapy.

Statistical Analysis

Incidence rates, frequency and mean of parameters for the full cohort as well as within groups, selected by sex, age and histology, were calculated using STATA. The denominator used was the population of Georgia in 2009. Groups were compared by Student's t test and the χ^2 test for continuous variables and proportions, respectively. If a particular group consisted of less than 20 patients confidence intervals (CI) were not calculated. Age standardization was performed based on five-year age grouping across the whole age spectrum (total of 18 groups) and standardized to the US 2000 population in order to provide direct comparability of our incidence rates to those of the Central Brain Tumor Registry of the United States (CBTRUS) [13]. We have chosen CBTRUS statistics since it represents the largest and reliable dataset of primary brain tumours in the world.

Results

A total of 473 cases of newly diagnosed primary brain tumours were identified during one year, i.e. with the time period from March 1, 2009 to March 1, 2010. Males constituted 40% of cases. In 2009, Georgia had 4.3 million inhabitants [14]. The annual age-standardized incidence rate per 100,000 individuals was 10.25, while the crude incidence rate was 10.78 per 100,000 individuals. The mean age at diagnosis was 50 years (SD 17.96). In the population below 20 years of age only 38 cases were identified (8.8%). In 55.8% of the cases, the diagnoses were based on neuroradiological data, histological confirmation was received in 38.4%, and in the remaining 5.8% tumours were diagnosed clinically (unknown whether or not histologically confirmed due to absence of a pathology report in the medical record). Less than half of the patients (n=219) underwent neurosurgical intervention. Non-malignant tumours accounted for 66% of all cases with an age-standardized incidence rate of 3.57 per 100,000 individuals, while malignant tumours incidence rate was 1.82 per 100,000 individuals (crude incidence rates were 3.69 and 1.92 per 100,000 respectivelly). The most frequent tumours by reported histology were non-malignant meningiomas (45.2%, n=128), followed by tumours of sellar region (20.8%, n=59) (Figure 1). Gliomas, most aggressive malignant brain tumours (astrocytic, oligodendroglial, oligoastrocytic and ependimal origin), represent

20.8% of all brain tumours. Within this group, glioblastoma accounts for the majority of glioma, representing 48% of cases (Figure 2).

Crude incidence rates among histology groups are shown in Table 1. The highest rate was observed for tumours of meninges (3.21 per 100,000). Incidence rate of neuroepithelial tumours was 1.5 per 100,000, followed by tumours of the sellar region (1.34 per 100,000). Within specific histologies, incidence rates were distributed as follows: meningiomas (2.92 per 100,000), pituitary adenomas (1.16 per 100,000), glioblastomas (0.64 per 100,000) and neurinomas (0.64 per 100,000).

For all primary brain tumours combined and for selected histology groups, incidence rates were higher among females than males (Table 2). Age-standardized incidence rates were 11.05 per 100,000 (crude incidence 11.76 per 100,000) for females and 8.44 per 100,000 (crude incidence 8.75 per 100,000) for males. The difference between age-standardized incidence rates is statistically significant (IRR=1.31, 95% CI: 1.08; 1.58). Incidence rates ratio comparing females with males was substantially elevated for tumours of meninges (IRR=1.61, 95% CI: 1.14; 2.28). Incidence rates for specific histologies were higher in males only for several neuroepithelial tumours (glioblastoma, oligodendroglioma and medulloblastoma) and haemangioblastoma (Table 2).

Age-specific crude incidence rates for all tumours and selected histology groups are illustrated in Figure 3. Age-specific incidence rates were low for patients in late childhood and adolescence with prominent increasing tendency in adulthood and a peak within the age range of 65-74 years.

Discussion

The present study presents results of the first population-based study in the Caucasus region using the WHO 2007 histological classification of tumours of the central nervous system. Incidence and clinical and pathological features of primary brain tumours were assessed. The observed overall age-standardized incidence rate of primary brain tumours (10.25 per 100,000) is lower than recently published by CBTRUS in their 2009 statistical report of primary brain and CNS tumours diagnosed in 2004-2005 (18.16 per 100,000) and also lower than reported by the Austrian Brain Tumour Registry (ABTR) based on cases registered during 2005 (18.1 per 100,000) [7, 9]. Indeed, lower incidence rates were observed in our study for main histology groups and specific histology category. We suspect that the cause may be multifactorial. It should be noted, however, that a similar discrepancy was reported before

between the incidence of malignant tumours in developed and developing countries [15], furthermore even in some European countries incidence rates of primary intracranial tumours in a range between 8.5-14 per 100,000 were reported [8, 16, 17]. The active case ascertainment method used in our study does not exclude influences of several factors, which may result in missing of brain tumours cases. Firstly, low attention for subtle and obscure signs and symptoms of brain tumours from patients and/or treating physician along with lacking a strong health insurance may lead to a low utilization of healthcare resources. Secondly, unregistered migration of a population due to a high unemployment rate leads to an artificially increased denominator (i.e., the official population basis is higher than the "true" population number). Up to 22.9 percent of the total population of over 4.4 million was the international migrants number from Georgia estimated by the United Nations Population Division and the World Bank as of 2005 [18]. Thirdly, CT and MRI imaging systems are concentrated only in big cities and therefore the diagnostic methods are too expensive and inaccessible for rural population. Finally, so-called geographic variation factor probably could be taken into account, reflecting sociodemographic characteristics and environmental factors which may be associated with brain tumour risk factors.

The analysis of the brain tumour distribution by tumour behaviour and histology showed a high comparability of the rates in our study with the rates of the CBTRUS statistic, in particular the predominance of non-malignant over malignant tumours, with the most common histology being meningioma, followed by pituitary tumours, glioblastoma and neurinoma. Glioblastoma represent the most frequent type of gliomas. The main difference between the registries with respect to primary brain tumour frequency is that in our study pituitary adenoma was more common than glioblastoma, while in the CBTRUS report, pituitary tumours followed after glioblastoma. The comparison of incidence rates showed the highest incidence in tumours of the meninges in our data whereas in the American report, neuroepithelial tumours were the most prevalent neoplasms, followed closely by meningiomas.

A female preponderance was observed with regards to incidence rates in our study: meningiomas were more common in women, whereas the incidence rates for gliomas were higher in men. The observation was similar to that given in CBTRUS and ABTR reports, which may indicate the validity of our data. Moreover, age-specific rate curves for brain tumours combined among the registries were nearly identical with prominent increasing of the incidence rate after approximately 30 years and declining in those over 75 years. The incidence drop is clear in our and ABTR data, but less pronounced in CBTRUS report.

The study has limitations caused by the relatively low rate of histologically confirmed tumours (38.4%), whereas 69% of the brain tumours in CBTRUS report and 80.9% in the ABTR data were histologically verified. In other studies, however, comparable to our rate of histologically verified tumours (35-59%) have been reported [2, 16, 19]. It seems that achieving high rate of pathology verification is a similar issue for different tumour registries irrespective of economic status of county they represent.

We believe that a limited neurosurgical activity in elderly patients contributes to a higher number of neuroradiologically confirmed diagnoses. Similar hypothesis was proposed by Spanish investigators, observed 41% histologically unverified malignant primary brain tumour cases in data from the population-based cancer registry from Girona province [2]. One can speculate that due to a conservative treatment approach with very limited options of alternative therapies (at least outside Tbilisi) and higher rate of incurable tumours in elderly patients, brain tumours may be left surgically untreated and thus, unclassified. If the public attitude towards brain tumour management changes and non-surgical alternative therapies along with sophisticated neuroimaging tools become widely available, the proportion of detected malignant and non-malignant tumours will probably change by the decreasing of 'unspecified' category percentage. Further registration of newly diagnosed primary brain tumours is necessary to increase the representativeness of the registry and enhance monitoring of brain cancer morbidity and mortality rate. However, improving diagnostic accuracy and achieving highest histology verification rate should not be addressed only and mainly to registry personnel or particular clinical investigators, because of the tumour registry's primary goal is to collect and provide relevant information. We suggest that the presented data must help national health policy makers to detect problems and define correct strategy for improvement of pathology service along with the increase in accessibility and quality of health care for neurooncology patients, which in turn will affect reliability and quality of the cancer registry data. Besides mentioned purposes efforts should be directed on providing available financial resources and appropriate power for the Georgian brain tumour registry to completely setting up and function on a regular basis.

Acknowledgments

The authors thank Dr.Tatiana Mermanishvili (Head, Department of Neuropathology, City Hospital N5, Tbilisi, Georgia) for her valuable support in reviewing brain tumour cases in histopathology database.

This work was supported by grant from Shota Rustaveli National Science Foundation (GNSF/ST08/6-463). The funding organisation had no role in the design, conduct or analysis of this study, or in the preparation of this report.

Contributors: DG: study conception and design, designing data collection tools, data collection monitoring, statistics, cleaning and analysing the data, writing and critical revision of the paper. NS, GS: data acquisition, cleaning and analysing the data. SR: study design, statistics, revision of the draft paper. AT and RS: study conception and design and revision of the draft paper.

Ethics approval: Ethical approval was obtained from the Tbilisi State University Medical Faculty ethics committee.

Conflict of interest: The authors declare that they have no conflict of interest.

References:

1. Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, et al. (eds) (2004) SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2004/. Accessed 1 September 2012
2. Fuentes-Raspall R, Vilardell L, Perez-Bueno F, Joly C, Garcia-Gil M, Garcia-Velasco A, Marcos-Gragera R (2011) Population-based incidence and survival of central nervous system (CNS) malignancies in Girona (Spain) 1994-2005. J Neurooncol. 101(1):117-23
3. Cancer Research UK (2008) Brain and other CNS tumours - UK incidence statistics http://info.cancerresearchuk.org/cancerstats/types/brain/incidence/uk-brain-and-central-nervous-system-cancer-incidence-statistics. Accessed 1 September 2012
4. Centre for Cancer Control Research (2009) South Australian cancer statistics. Monograph number 11. Malignant brain tumours in South Australia http://www.cancersa.org.au/cms_resources/documents/Monograph_11_Brain.pdf. Accessed 1 September 2012
5. Sant M, van der Sanden G, Capocaccia R (1998) Survival rates for primary malignant brain tumours in Europe. European Journal of Cancer. EUROCARE Working Group Eur J Cancer 34(14 Spec No):2241-7
6. Katchy KC, Mallik AA, Al-Nashmi NM, Joseph E, Alexander S, Al-Ramadan A (2011) Intracranial tumors in Kuwait: a 15-year survey. J Neurooncol. 104(1):271-7
7. CBTRUS (2009) Statistical report: primary brain tumors in the United States, 2000–2004 published by the Central Brain Tumor Registry of the United States http://www.cbtrus.org/reports/2009-NPCR-04-05/CBTRUS-NPCR2004-2005-Report-.pdf. Accessed 1 September 2012
8. Dobec-Meic B, Pikija S, Cvetko D, Trkulja V, Pazanin L, Kudelic N, Rotim K, Pavlicek I, Kostanjevec AR (2006) Intracranial tumors in adult population of the Varazdin County (Croatia) 1996-2004: a population-based retrospective incidence study. J Neurooncol. 78(3):303-10
9. Wöhrer A, Waldhör T, Heinzl H, Hackl M, Feichtinger J et al. (2009) The Austrian Brain Tumour Registry: a cooperative way to establish a population-based brain tumour registry. J Neurooncol. 95(3):401-11
10. Pobereskin LH, Chadduck JB (2000) Incidence of brain tumours in two English counties: a population based study. J Neurol Neurosurg Psychiatry. 69(4):464-71

11. McCarthy BJ, Surawicz T, Bruner JM, Kruchko C, Davis F (2002) Consensus Conference on Brain Tumor Definition for registration. November 10, 2000. Neuro Oncol. 4(2):134-45
12. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (eds) (2007) World Health Organization Classification of Tumours of the Central Nervous System. Lyon: IARC
13. Day, Jennifer Cheeseman (1996) Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050, U.S. Bureau of the Census, Current Population Reports, P25-1130, U.S. Government Printing Office, Washington, DC http://www.census.gov/prod/1/pop/p25-1130/p251130.pdf. Accessed 1 September 2012
14. National Statistics Office of Georgia: Population. http://www.geostat.ge/index.php?action=page&p_id=473&lang=eng. Accessed 1 September 2012
15. Ferlay J, Shin HR, Bray F, Forman D, Mathers CD, Parkin D (2010) GLOBOCAN 2008 v2.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from: http://globocan.iarc.fr. Accessed 1 September 2012
16. Caldarella A, Crocetti E, Paci E (2011) Is the incidence of brain tumors really increasing? A population-based analysis from a cancer registry. J Neurooncol. 104(2):589-94
17. Liigant A, Asser T, Kulla A, Kaasik AE (2000) Epidemiology of primary central nervous system tumors in Estonia. Neuroepidemiology 19(6):300-11
18. Siar Sh (ed) Migration in Georgia: A Country Profile 2008 (2008) International Organization for Migration, Geneva, Switzerland
19. Cordera S, Bottacchi E, D'Alessandro G, Machado D, De Gonda F, Corso G (2002) Epidemiology of primary intracranial tumours in NW Italy, a population based study: stable incidence in the last two decades. J Neurol 249(3):281-4