Landscape, Presentation, and Characteristics of Brain Gliomas in Zimbabwe

Abstract

Introduction: Gliomas are tumors of the supporting cells of the central nervous system. They have great heterogeneity in their clinical and pathological features as well as prognosis. There is paucity of glioma epidemiology data in Zimbabwe. We carried out a study to determine the landscape, presentation, and characteristics of brain gliomas in Zimbabwe.

Materials and Methods: A prospective cross-sectional study was conducted in Zimbabwe over a 2 years period to determine descriptive epidemiological data with regards to demographic distribution, presentation, and tumor characteristics. Consecutive patients from across the country with brain gliomas were recruited in the study. Results: A total of 112 brain tumors were diagnosed histologically. Of these 43.8% (n = 49) were gliomas and hence recruited in the study. The mean age of study participants was 40.3 years (standard deviation = 23.1 years), range 3–83 years. Male to female ratio (M:F) was 1:1. The study population consisted of 14% caucasians (n = 7), 83.7% black (n = 41), and 2% (n = 1) were of mixed race. Eighty-six percent (n = 42) of participants were from urban areas. The most common presenting complaint was headache in 87.8% (n = 43). The majority (61.2%) presented with a Karnofsky score ≥70%. Astrocytomas were the most common gliomas constituting 57.1% (n = 28), followed by ependymomas and oligodendrogliomas being 8.1% (n = 4) each. There was no statistical difference in the hemisphere of the brain involved (P = 0.475). Eight percent of the population were HIV positive (n = 4). Age above 60 years has an adjusted odds ratio of 13 for presenting with high-grade tumors. Conclusion: There is a disproportionately high number of gliomas among Caucasians, urban dwellers, and those gainfully employed. The prevalence of HIV in glioma patients is less than that of the general population.

Keywords: Brain glioma, brain tumors, epidemiology of brain glioma, Zimbabwe

Introduction

Brain tumors account for about 2% of all cancer deaths. The estimated global incidence of brain tumors is 8–10/100,000 population per year.[1,2] One in every 165 men and women will be diagnosed of a central nervous system (CNS) tumor in their life.[1] Gliomas are tumors of the CNS arising from glial cells.[10] They are the most common primary brain tumors, constituting 27% of all brain tumors with astrocytomas taking up 75% of these. Gliomas have been reported to be twice more common in White people than in Black people.[1,2]

The etiology of gliomas is unknown but it is associated with many risk factors. The most generally accepted risk factor is exposure to radiation. The presentation of gliomas is varied involving many different specialties.[2] The long-term prognosis of brain cancers has remained rather dismal despite major advancement in neurosurgical techniques and various treatment options.[2,3] In view of this, it is plausible to assume that further characterization of the epidemiological and risk factors for this disease may help in the early diagnosis and hopefully prevention of the disease.

Zimbabwe is a landlocked country in sub-Saharan Africa. It has a population of 13.59 million with the majority 67% being of rural abode. The population is predominantly black.[6] During the period of this study, there were only had six neurosurgeons in the country.

There are scanty data on the epidemiology of gliomas in sub-Saharan Africa[7–11] and currently none for Zimbabwe. It is therefore
imperative that a study be done to assess the burden and characteristics of the disease in Zimbabwe. This study will be a pilot point that will assist in the planning of future studies in glioma etiology.

Materials and Methods

Setting and commencement

A cross-sectional study was carried out in Zimbabwe for 2 years from April 1, 2014, to April 30, 2016. The catchment area for participants encompassed the entire country. All patients included in the study had a final histological diagnosis of brain glioma.

Case definition

Glioma included all glial cell origin tumors: Astrocytomas, ependymomas, oligodendrogliomas, and mixed glial tumors according to the World Health Organization grading system 2007. The diagnosis was by histology and immunohistochemistry was done for equivocal cases.

Study protocol

Routine surveillance of outpatients section, wards, theater, histology, and radiotherapy registers at Parirenyatwa hospital (only public hospital in Zimbabwe that offered neurosurgical services at the time of the study) was done to capture all glioma patients. Liaison was constantly made with all the neurosurgeons in the country (6 of them) including neurosurgeons at private health facilities to ensure that information about glioma patients were availed to the investigator. In addition, liaison was made with all the pathology laboratories in Harare so that information on all brain specimen/biopsy results in the country was accessed. This allowed access to data on all patients who had brain tumors operated on within Zimbabwe. The patients (or caregivers) were then followed up, interviewed and imaging and histology done was reviewed. Histological grading was done using the WHO grading system and immunohistochemistry was done for equivocal cases. The data collected were then entered. The patient’s ailments were managed as per hospital protocol and the study did not interfere with their standard management.

Authority to perform study

Permission to perform the study was obtained from the Joint Research and Ethics Committee at Parirenyatwa hospital. Written informed consent was obtained from all eligible patients.

Data management

A confidential data collection form was administered by the researchers. Data were then captured into a software package (Epi info) for analysis. Data were then exported to StataCorp, Collage Station, Texas, USA for further analysis and then conclusions were drawn. Data were analyzed using descriptive and regression statistics.

Results

Demographic data

All patients with a histological diagnosis of a brain tumor during the study was 112 [Figure 1]. Fifty-two of these were gliomas. Demographic data could not be accessed for 3 patients, hence was excluded from the study. Only 49 of the glioma patients were recruited into the study.

The mean age of the study population (49 patients) was 40.3 years (standard deviation [SD] = 23.1 years) with a range of 3–83 years. There was a bimodal distribution of ages with peaks at around 3 years and another between 40 and 50 years. There was a slight female preponderance of 53% (26/49) in the study population. There was no significant difference in age distribution between males (mean age = 38.3 years; SD = 21.4 years) and females (mean age = 42.1 years; SD = 24.8 years), P = 0.587 [Table 1]. Eighty-four percent (n = 41) were native Africans, 14% (n = 7) were Caucasian with only 2% (n = 1) being of mixed ethnicity. Eighty-five percent (n = 42) of the patients resided in urban setting versus 15% (n = 7) who were from rural areas. The majority of patients were from Harare (capital city), Zimbabwe [Table 1]. The majority of the patients presented early to the neurosurgeons [Table 2]. The prevalence of HIV infection among glioma patients was 8.3% (95% confidence interval [CI] 3.3–19.6).

Indicators for high-grade glioma in Zimbabwean patients

Gender, Karnofsky performance score at presentation, the presence of seizures did not have a bearing on grade of the tumor at 95% CI. Patients in the 40–60 years of age group where at 4 times odds of having high-grade gliomas, those above 60 years had 13-fold chance whereas those below 20 years where more likely to have low-grade gliomas [Table 3]. Chances of having high-grade glioma decreased with increased symptom duration for headache,
memory loss, and cognitive change. However, the chance for high-grade glioma increases with longer duration of focal deficit.

**Tumor characteristics**

Fifty-five percent of patients had tumors on the right hemisphere of the brain. The differences between the hemispheres of the brain involved was not statistically significant at $P = 0.475$. Three posterior fossa tumors (1 brainstem and 2 cerebellum) and 1 frontal tumor involved both the left and right hemisphere. Moreover, majority of the tumors spanned more than one lobe/region. The parietal region was the most common lobe involved in 57% ($n = 9$) of patients, followed by the frontal region 32% ($n = 16$). The temporal and occipital region were involved in 26.5% ($n = 13$) and 14.2% ($n = 7$) patients, respectively. The cerebellum was involved in 10% ($n = 5$) while only 2% ($n = 1$) had involvement of the brainstem. One patient had a tumor involving the corpus callosum [Figure 2].

The most common tumor type was astrocytomas constituting 57.1% ($n = 28$) of the study population, of these glioblastomas ranked highest, accounting for 12% of all gliomas. Ependymomas and oligodendrogliomas constituted 8.2% each ($n = 4$) while 2% ($n = 1$) were gangliogliomas. Of the astrocytic subclassification, the fibrillary type predominated (67.9%), followed by gemistocytic (21.4%) and pilocytic type (10.7%). The presentation was varied with the most common symptom being headache [Table 4].

**Discussion**

This study is the first in Zimbabwe to describe the distribution and characteristics of brain gliomas. Previously, the national cancer registry showed that the incidence of brain and CNS tumors in Zimbabwe was 1.6% however, they did not characterize the tumors.[13] The data in our study are representative of the whole country since it was performed at the only public neurosurgical unit in Zimbabwe during the study. Furthermore patients from private hospitals requiring radiotherapy would attend Parirenyatwa since it was the only center offering radiotherapy during the period of study. However, a notable limitation of the study was that some glioma patients from private hospitals who did not have radiotherapy ($n = 3$) were not be captured in the study (two had complete excision of low-grade glioma and the other demised before going for radiotherapy).

**Demographics**

Our study showed that gliomas exhibited a female preponderance of 53%, in contrast to other studies within Africa and globally show a male preponderance 60%.[14,15] Surprisingly, we noted that Caucasians constituted 14% of the glioma patients, despite that they constitute only 0.3% of the country’s population according to the 2012 Zimbabwean census.[16] Our data report a higher incidence of gliomas in Caucasians compared to Blacks and other race groups. These results are corroborated by previous reports showing that gliomas are more common in Caucasians.[1,17,18] One should bear in mind that Caucasians in Zimbabwe are more affluent hence are able to seek access to health care. The majority of our study participants resided in urban setting despite the...
fact that most (67%) of the Zimbabwean population stays in the rural areas. Nonetheless, whether this points toward a true increased incidence in urban city dwellers is possible but debatable. This may be a sampling bias as urban dwellers have better access to health care, health education, and proximity to medical facilities. Rural dwellers consult traditional and spiritual healers compared to urban dwellers. Hence, the glioma patient seeking alternative health care may not have been captured in our study. Nonetheless, for those that present to rural facilities, the referral system is generally efficient. However, other constraints are lack of transportation to tertiary facilities as well as to gain access to brain imaging facilities. The prevalence of HIV in the glioma patients was 8.3% while that in the whole country was 14.3% at that time. The significance of this mismatch will need to be further elucidated.

**Presentation**

In our study, the majority of glioma patients presented to a neurosurgeon within 1 month from the onset of symptoms. Financial constraints were cited as the most common cause of delayed presentation and were the main deterrent to the timely diagnosis of brain tumors. A significant number of patients with symptoms suggestive of a brain tumor seen during the study could not afford brain imaging. Notably 2% (n = 1) of participants were unemployed. This implies that only those that could afford treatment were enrolled in the study. Since Zimbabwe has a high unemployment rate this may reflect a sampling bias. The delay in presentation was attributed to the symptoms being minor and the patient hoped would go away on their own. Furthermore, symptoms such as memory loss and cognitive dysfunction were ascribed to age, while headaches credited to stress. There is a paucity of data on late presentation of glioma patients. In this study, medical officers were blamed for delayed referral mostly because of an incorrect initial diagnosis. One patient admitted to consulting traditional healers leading to the delayed presentation. Patients usually deny consulting traditional healers even when there is obvious tattoo (n’anga) marks that are used by traditional healers in their treatments.

The most common presenting symptoms was headache (87.8%), a feature that is considerably higher than the 48%–55% shown in previous studies. Black

### Table 3: Predictive clinical indicators for high-grade glioma regression analyses for the effect of gender, age, performance status, and duration of different presenting symptoms

| Features                  | Adjusted OR | 95% CI     |
|---------------------------|-------------|------------|
| Gender                    |             |            |
| Female                    | 1 (reference) | 1 (reference) |
| Male                      | 1.27        | 0.40-4.02  |
| Age (years)               |             |            |
| <10                       | 1 (reference) | 1 (reference) |
| 10-20                     | 0.13*       | 0.02-0.92  |
| 20-40                     | 0.41        | 0.09-1.82  |
| 40-60                     | 4.15*       | 1.15-14.92 |
| >60                       | 13.20*      | 1.51-115.35 |
| Performance status at presentation (%) |             |            |
| 0 (10)                    | 1 (reference) | 1 (reference) |
| 1 (20-40)                 | 1.11        | 0.20-6.15  |
| 2 (50-70)                 | 1.27        | 0.40-4.02  |
| 3 (80-100)                | 0.73        | 0.22-2.35  |
| Headache (months)         |             |            |
| None                      | 1 (reference) | 1 (reference) |
| <3                        | 3.80*       | 1.09-13.18 |
| 3-6                       | 4.00        | 0.75-21.35 |
| 7-9                       | 0.36        | 0.01-9.37  |
| >10                       | 0.11*       | 0.012-0.99 |
| Seizures (months)         |             |            |
| None                      | 1 (reference) | 1 (reference) |
| <3                        | 0.14        | 0.01-1.20  |
| 3-6                       | 2.62        | 0.25-27.18 |
| 7-9                       | 0.88        | 0.50-14.80 |
| >10                       | 0.10        | 0.01-2.09  |
| Memory loss (months)      |             |            |
| None                      | 1 (reference) | 1 (reference) |
| <3                        | 5.08*       | 1.16-15.39 |
| 3-6                       | 2.86        | 0.28-29.75 |
| 7-9                       | 0.36        | 0.01-9.37  |
| >10                       | 0.73        | 0.11-4.84  |
| Focal deficit (months)    |             |            |
| None                      | 1 (reference) | 1 (reference) |
| <3                        | 0.40        | 0.07-2.31  |
| 3-6                       | 0.84        | 0.05-14.26 |
| 7-9                       | 2.76        | 0.76-10.13 |
| >10                       | 3.9*        | 1.13-13.45 |
| Cognitive change (months) |             |            |
| None                      | 1 (reference) | 1 (reference) |
| <3                        | 6.2         | 0.28-13.69 |
| 3-6                       | 0.36        | 0.01-9.37  |
| 7-9                       | 2.40        | 0.20-28.45 |
| >10                       | 1.54        | 0.36-6.66  |

*Statistical significance at 5% (P<0.05). CI - Confidence interval; OR - Odds ratio
people have been thought to be stoical in their pain threshold. They may not complain of their pain until it becomes quite severe, and very few would present if they are not in pain. This may explain why at presentation most had severe headaches which may actually have led to their late presentation.

Seizure prevalence in our study population was less than that quoted in most literature. This may be attributed to a true lower incidence or a lack of patient education as simple partial seizures may go unnoticed or not even be reported. Some of the symptoms were particularly difficult to ascertain especially when the patient was not fully conscious and the caregivers were not sure about the symptoms. This is true especially for cognition, memory deficits or visual and sensory losses. The majority of the patients had a Karnofsky Performance Score equal to or >70% at presentation. This Karnofsky score is associated with independent function and a better prognosis following treatment.

**Indicators for high grade glioma**

Tumor grade was not affected by gender, Karnofsky score at presentation or presence of seizures. This was consistent with other studies. While fewer females may be affected by higher grade tumors, they tend to have poorer quality of lives when affected despite having better prognosis compared to males. However, gender had no bearing on the grade of tumor in our study. One may assume that higher grade tumors are more likely to present with a worse off performance score, our study did not show any association. Seizures did not show any association with tumor grade either. Age above 60 years was 13 times more likely to present with high grade and other studies confirm this as well.

High-grade gliomas in the Zimbabwean population were associated with a shorter duration of headache, cognitive change, and memory loss as presenting symptoms. This was in keeping with a study previously reported.

**Tumor characteristics**

The histological type distribution was consistent with most literature. The majority of the gliomas involved the right side of the brain, but it was not statistically significant ($P = 0.475$). Similar findings showing an equal involvement has been reported. In our study, the parietal followed by frontal regions where the most common sites of the tumor. One wonders whether this was not a sampling bias in that these sites are easily accessible surgically and hence its easy for a surgeon to decide to biopsy them earlier rather than later as opposed to deep seated ones which require more experienced surgeons and sophisticated equipment hence they may not be biopsied or operated on often. This is supported by the fact that only one brainstem glioma had a biopsy done versus the four others not biopsied.

**Study limitations**

The main limitation of the study was that it may have had a selection bias. There was little representation in the study population of the unemployed and rural dwellers despite the fact that they constitute the greater part of the country’s population. It is difficult to conclude whether gliomas are actually rare in this group or if it is merely a sampling bias. The selection criterion was such that only those that have access to health care and could afford it were sampled. The ideal would be an environment where health care is easily accessible and affordable for all, which was difficult in our setting.

Immunohistochemistry was only done routinely in private patients and for public patients only for difficult cases at an extra cost. It would be ideal to do immunohistochemistry on all samples since occasionally some pathological appearances may mimic each other, for example, lymphomas may mimic glioblastoma. The duration of the study was short hence a smaller sample size. Larger sample sizes would be needed to make meaningful conclusions.

A minority of the Zimbabwean population prefers to be treated in other countries, of these patients only those that were followed up locally were able to be captured in the study.

**Conclusion**

We report a higher prevalence of brain gliomas in Caucasians in Zimbabwe compared to other ethnic groups. Notably, these are the higher socio-economic group of people from urban centers. Furthermore, this prevalence was higher in females compared to males and tended to involve both hemispheres equally. Astrocytomas are the most common type. Financial constraints are the major cause of delayed presentation and for nonpresentation. There is need to improve health access for those of low socioeconomic status and those in rural areas.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Ostrom QT, Gittleman H, Liao P, Rouse C, Chen Y, Dowling J, et al. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2007-2011. Neuro Oncol 2014;16 Suppl 4:iv1-63.
2. Schneider T, Mawrin C, Scherlach C, Skalej M, Firsching R. Gliomas in adults. Dtsch Arztebl Int 2010;107:799-807.
3. SEER Cancer Statistics Review, 1975-2010 - Previous Version - SEER Cancer Statistics Review. Available from: http://seer.cancer.gov/archive/csr/1975_2010/. [Last Accessed on 2020 Aug 15].
4. Butler A, Passalaqua M. Contrast enhanced CT scan
supratentorial and radionuclide gliomas scan in. AJR Am J Roentgenol 1979;132:607-11.

5. Kanu OO, Hughes B, Di C, Lin N, Fu J, Bigner DD, et al. Glioblastoma Multiforme Oncogenomics and Signaling Pathways. Clin Med Oncol 2009;3:39-52.

6. Zimbabwe National Statistics Agency. Mashonaland West Province Report ZIMBABWE POPULATION; 2013. Available from: http://www.zimstat.co.zw/dmdocuments/Census/CensusResults2012/Mash_West.pdf. [Last Accessed on 2020 Aug 15].

7. Andrews NB, Ramesh R, Odjidja T. A preliminary survey of central nervous system tumors in Tema, Ghana. West Afr J Med 2003;22:167-72.

8. Ndubuisi CA, Ohaegbulam SC, Iroegbu LU, Ekuma ME, Mezue WC, Erechukwu UA. Histologically confirmed intracranial tumors managed at Enugu, Nigeria. J Neurosci Rural Pract 2017;8:585-90.

9. Olasode BJ, Shokunbi MT, Aghadiuno PU. Intracranial neoplasms in Ibadan, Nigeria. East Afr Med J 2000;77:4-8.

10. Ndubuisi CA, Mezue WC, Ohaegbulam SC, Chikani MC, Ekuma M, Onyia E. Neuroimaging findings in pediatric patients with seizure from an institution in Enugu. Niger J Clin Pract 2016;19:121-7.

11. Ndubuisi C, Ohaegbulam S, Chikani M, Muzue W, Mbadugha T, Okhuelegbe M. Some characteristics of gliomas managed at a Neurosurgery center in Nigeria. Niger Postgr Med J 2017;24:44-47.

12. 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;114:97-109.

13. ZNCR. Pattern of Cancer in Zimbabwe 2012 Annual Report; October, 2014. Available from: http://www.afcmr.org/attachments/article/83/ZNCR2012ANNUALREPORT.pdf. [Last Accessed on 2020 Aug 15].

14. Trabelsi S, H’mida-Ben Brahim D, Labid M, Mama N, Harrabi I, Tili K, et al. Glioma epidemiology in the central Tunisian population: 1993-2012. Asian Pacific J Cancer Prev 2014;15:8753-7.

15. Idowu O, Akang E, Malomo A. Symptomatic primary intracranial neoplasms in Nigeria, West Africa. J Neurol Sci (Turk) 2007;24:212-8.

16. ZIMSTATS. ZIMBABWE POPULATION Census 2012; 2012. p. 1-151. Available from: http://www.zimstat.co.zw/dmdocuments/Census/CensusResults2012/National_Report.pdf. [Last Accessed on 2020 Aug 15].

17. Sadetzki S, Zach L, Chetrit A, Nass D, Hoffmann C, Ram Z, et al. Epidemiology of gliomas in Israel: A nationwide study. Neuroepidemiology 2008;31:264-9.

18. Robertsona T, Gunter BC, Somese GW. Racial differences in the incidence of gliomas: A retrospective study from Memphis, Tennessee. Br J Neurosurg 2002;16:562-6.

19. Zimbabwe NAC, Zimbabwe, Care M of H and C. Zimbabwe National HIV and AIDS Strategic Plan (ZNASP) 2015-2018. Commitment towards Fast Tracking 90.90.90. Targets by 2020 and Ending AIDS by 2030. 2015; March, 2015-2018.

20. Batchelor TT, Curry WT. Clinical manifestations and initial surgical approach to patients with high-grade gliomas. UpToDate. 2015. Available from: http://www.uptodate.com/contents/clinical-manifestations-and-initial-surgical-approach-to-patients-with-high-grade-gliomas?source=search_result&search=high-grade+gliomas&selectedTitle=0-142%5Cnhttp://ekstern.infonet.regionsyddanmark.dk/files/Formularer/Upload/2013/03/cl. [Last Accessed on 2020 Aug 15].

21. Wong ET, Wu JK. Clinical presentation and diagnosis of brain tumors. UpToDate. 2011. p. 1-27. Available from: http://www.uptodate.com.com/contents/clinical-presentation-and-diagnosis-of-brain-tumors?source=search_result&search=brain+metastasis&selectedTitle=9-142%5Cnhttp://ekstern.infonet.regionsyddanmark.dk/files/Formularer/Upload/2013/03/cl. [Last Accessed on 2020 Aug 15].

22. Mphahlele NR, Kamerman PR, Mitchell D. Progression of pain in ambulatory HIV-positive South Africans. Pain Manag Nurs 2015;16:1-8.

23. Hess KR, Broglio KR, Bondy ML. Adult glioma incidence trends in the United States, 1977-2000. Cancer 2004;101:2293-9.

24. Niemelä A, Koivukangas, J, Herva R. Gender difference in quality of life among brain tumor survivors. J Neurol Neurophysiol 2011;2:1-5. [Doi: 10.4172/2155-9562.1000116].

25. 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;93:932-9.

26. Rasmussen BK, Hansen S, Laursen RJ, Kosteljanetz M, Schultz H, Nørgård BM, et al. Epidemiology of glioma: Clinical characteristics, symptoms, and predictors of glioma patients grade I-IV in the the Danish Neuro-Oncology Registry. J Neurooncol 2017;135:571-9.

27. Lönn S, Ahlborn A, Hall P, Fyechting M. Long-term mobile phone use and brain tumor risk. Am J Epidemiol 2005;161:526-5.