Article published online: 2022-08-16

Original Article

Landscape, Presentation, and Characteristics of Brain Gliomas in Zimbabwe

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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 time.[3] Gliomas are tumors of the CNS arising from glial cells.[4] 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.[2,5] 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

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How to cite this article: Jokonya L, Musara A, Esene I, Mduluza-Jokonya TL, Makunike-Mutasa R, Rothemeyer S, *et al.* Landscape, presentation, and characteristics of brain gliomas in Zimbabwe. Asian J Neurosurg 2021;16:294-9.

Submitted: 22-Aug-2020 **Revised:** 23-Sep-2020
Accepted: 05-Jan-2021 **Published:** 28-May-2021

Access this article online

Website: www.asianjns.org

DOI: 10.4103/ajns.AJNS_404_20

Quick Response Code:

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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.[12] 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,

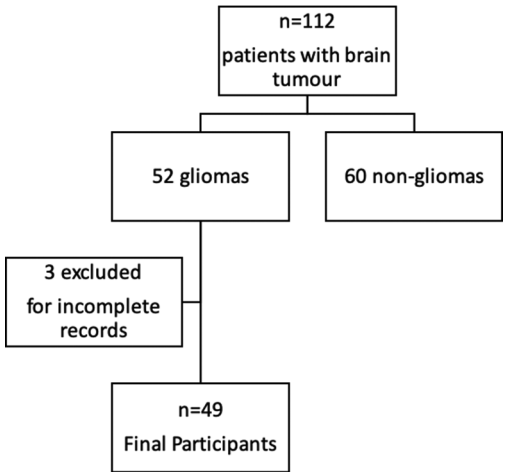

Figure 1: Trial profile

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 gangiogliomas. Of the astrocytic subclasification, 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].

Table 1: Participants demographics

Demographic variable	Frequency
Age (years), mean (SD)	41.8 (22.4)
Sex	
Male	47% (22)
Female	53% (25)
Race	
Black	85% (40)
Caucasian	15% (7)
Occupation	
Minor/student	26% (12)
Unemployed	23% (11)
Employed	51% (24)
Geographic location (province)	
Harare	57% (27)
Bulawayo	15% (7)
Midlands	9% (4)
Mashonaland west	6% (3)
Matabeleland south	4.3% (2)
Mashonaland central	2% (1)
Masvingo	2% (1)
Matabeleland north	2% (1)
Manicaland	2% (1)
Residence	
Urban	85% (40)
Rural	15% (7)

SD - Standard deviation

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

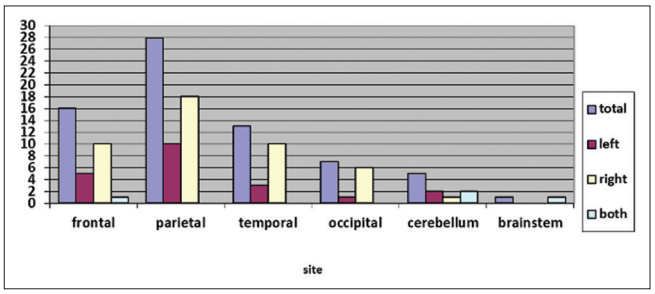

Figure 2: Tumor distribution in the brain

Table 2: Timeline for referral to neurosurgeons

	0-3 months	4-6 months	7-9 months	10-12 months	Total
Total	74% (32)	18.6% (8)	4.7% (2)	2.3% (1)	100% (43)

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

fact that most (67%) of the Zimbabwean population stays in the rural areas.[16] 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.[19] The significance of this mismatch will need to be further elucidated.

Table 4: Presentation

Variable	Frequency % (*n*)
Headache	89% (42)
Seizures	32% (15)
Memory loss	43% (20)
Weakness	64% (30)
Visual loss	38% (18)
Language deficit	9 % (4)
Cognition	19% (9)
Personality	17% (8)
Change in consciousness	43% (20)
Nausea and vomiting	51% (24)

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.[20,21] Black

people have been thought to be stoical in their pain threshold.[22] 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.[21] 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.[14,23-25]

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.[26]

Tumor characteristics

The histological type distribution was consistent with most literature.[1,14,17] 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.[27] 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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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