Research Article

PATTERN OF PRESENTATION OF GLIOMAS AND CLINICAL OUTCOME: AN INSTITUTIONAL DESCRIPTIVE STUDY

[1]Arbaz Gul Abro, [1]Aleena Azam, [1,2]Pardeep Kumar, [1]Tazeen Fatima, [1]Shaheer Ali Mughal, [1]Fayaz Mangi, [3]Riaz Ahmed Raja

[1]Clinical Research Division, Medical Research Centre, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro, Pakistan, [2]Bilawal Medical College, Jamshoro, Pakistan. [3]Department of Neurosurgery, Liaquat University of Medical & Health Sciences, Jamshoro Pakistan.

Correspondence:
Fayaz Ahmed Mangi
Clinical Research Division, Medical Research Centre
Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan
Email:
drmangi25@gmail.com

DOI
10.38106/LMRJ.2024.6.4-09
Received: 26.07. 2024
Accepted: 20.11.2024
Published: 30.12.2024

ABSTRACT:

Gliomas are common brain tumours presenting with aggressive clinical behavior. There is limited literature available to evaluate clinical pattern and survival outcome in Pakistani population. The patients were retrieved from Cancer Research Database, (a complete set of clinical data of cancer patients from 2008 till 2023, prospectively established and regularly updated). There were 139 patients of primary brain tumors. Most common histological type of glioma was GBM (36%) and there was male preponderance. Majority of patients presented with high grade IV and stage 4 tumors. Surgery was frequently used primary therapy while radiotherapy was most frequently give second line therapy. Out of 79 patients 63 died because of disease, median survival time was 6 months, age and grade did not appear to show any significant influence on survival. Our study showed that glioma has male predominant tumour with aggressive clinical pattern and poor overall survival. Further studies to understand biology and genetic pattern of glioma and development of targeted therapy is recommended so that clinical outcome of these patients can be improved.

Keywords: Glioma, Clinical presentation, Clinical outcome

INTRODUCTION:

Glioma is a tumor derived from glial cells; the supporting cells of the central nervous system (CNS); are the most common primary malignant tumor of the brain(1). These tumors arise within the substance of the brain and carry significant morbidity and mortality. World Health Organization (WHO) has classified glioma based on histology and molecular biology incorporating new markers of classification such as IDH mutation and 1p/18q co deletion etc(2).

As per recent global data of year 2020 by the global cancer observatory GLOBOCAN WHO, glioma emerged with an incidence of 308,102 cases globally with 168,346 cases in males and 139,756 cases in females and a 5 year prevalence of 837,152 cases globally(1). More than 54% of cases were reported from Asia (~166,925 cases), while 46% of cases were reported in other regions collectively in Europe, Latin America, North America, Africa, and Oceania(1). Reported mortality of glioma as per data of 2020 remains high with 251,329 deaths globally and 137,646 deaths solely in Asia reflecting the growing health burden of glioma(1). Glioma incidence is expected to rise from the current incidence to nearly 435,000 cases by the year 2040(1). In Pakistan glioma remains the 11th most common cancer in adults and the 9th most common cancer-causing deaths with reported cases of 4770 in 2020 with 3934 deaths, while the 5-year prevalence of glioma in Pakistan was reported to be 10,114 cases(1). Multiple studies across the globe have established patterns of distribution, overall survival and prognosis of different type of glioma in different populations(3–6). However, it showing geographical variation. Gliomas have been reported to have male preponderance with varying male to female ratio from 1.6:1 to nearly 2:1 in different populations with some studies

mentioning more than 50% patients of Glioblastoma Multiforme were males, similar results have been reported for Intracranial Ependymoma in pediatric population(7–11). Despite of extensive treatment regimen overall survival of glioma has not been so promising, with GBM demonstrating the worst clinical outcome. The studies have reported overall survival of 8.1 to 12 months for GBM and one study from Lombardia, Italy reported 18 months for newly diagnosed GBM (5,7,9-11).

However, better overall survival has been reported in pediatric population where Pilocytic Astrocytoma has shown survival of more than 60 months (12). According to the data reported from Karachi cancer registry CNS tumors are 14th most common malignancy in both genders (13). There is limited literature available reporting on clinical pattern of glioma with long term survival data. Thus this study was aimed to evaluate clinical pattern and survival outcome of patients presenting with glioma.

MATERIALS & METHODS:

This observational study was conducted at Cancer Research Laboratory, Clinical Research Division of Medical Research Center, Liaquat University of Medical & Health Sciences Jamshoro, Pakistan. The glioma patients were identified from Institutional database which was prospectively established and regularly updated from 2008 till date. A total of 139 patients who were registered with confirmed biopsy of glioma were included. Complete set of clinical information and histopathological characteristics were retrieved from clinical database while latest update of vital status was recorded on telephone call from patients and the family. Total of 79 patients responded to calls and were interviewed for recent follow-up update and included in survival analysis and 60 patients were lost to follow up as they could not be contacted thus they were only included in clinical pattern analysis. The overall survival was calculated from the date of diagnosis and death from any cause, while disease specific survival was calculated from date of diagnosis till death from glioma.

Statistical analysis:

The data was analyzed by using Statistical Package for Social Sciences (SPSS version 22.0, IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Continuous variables were analyzed and presented with median and Standard deviation (± SD), while categorical variables were analyzed and presented as frequency distribution and percentage. For comparison of categorical variables chi-square test was applied. Survival analysis was done by using Kaplan- Meier method with application of Log-rank test. A p-value of <0.05 was considered significant.

RESULTS:

A total of 139 glioma patients were identified out of which 65.5% (n=91) were males and 34.5% (n=48) were females. Median age of patients was 37 years (range 1-70 SD ± 17.6). Over 30 years was the predominant age group (Figure 1). In females predominant age group was ≤30 years while in males it was >30 years (p-value = 0.04, Figure 2).

Glioblastoma Multiforme was the most common histological type seen in 36% of cases, followed by malignant glioma (13.7%), oligodandroglioma of no special type (6.8%) and other types were observed in small number of cases. Considerably great majority was presented with stage IV (68%) followed by stage II (18.7%), stage III (12.9%) and only 6.5% were of stage I glioma. Grade IV was predominant, seen in 44.6% followed by Grade III (17.3%), Grade II (12.9%) and Grade I (5.8%). However, age and gender did not appear to show any significant association with stage and grade of the disease.

Treatment Pattern:

Out of 79 patients included in treatment and survival analysis 63 patients (79.7%) received surgery as primary treatment while 9 (11.4%) and 3 (3.8%) radiotherapy and chemotherapy respectively, while 3 (3.8%) patients received no primary treatment. While as second line treatment radiotherapy (62%) was given to majority of patients (Table 1).

Clinical Outcome

Median follow-up was 12 months. A total of 26 patients showed recurrence after primary treatment including 20 (25.3%) patients with local recurrence, 2 (2.5%) regional recurrence and 4 patients (5.1%) with distant metastasis. A

total of 16 patients died due to glioma with a median disease specific survival of 6 months (longest 103 months, Figure 3). Age and gender did not appear to show any significant influence on survival.

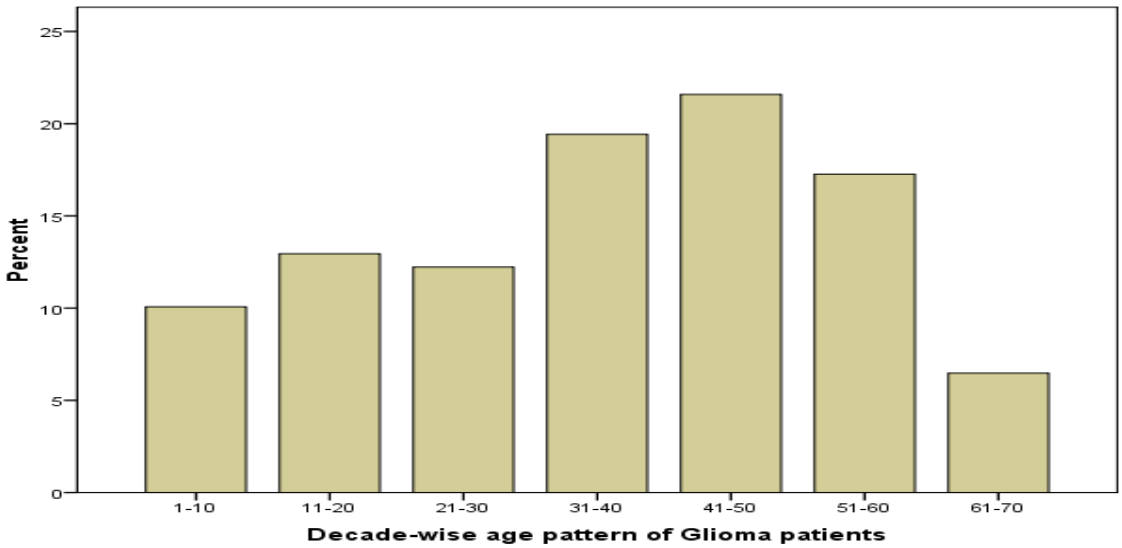

Figure 1. Age distribution of patients presenting with glioma

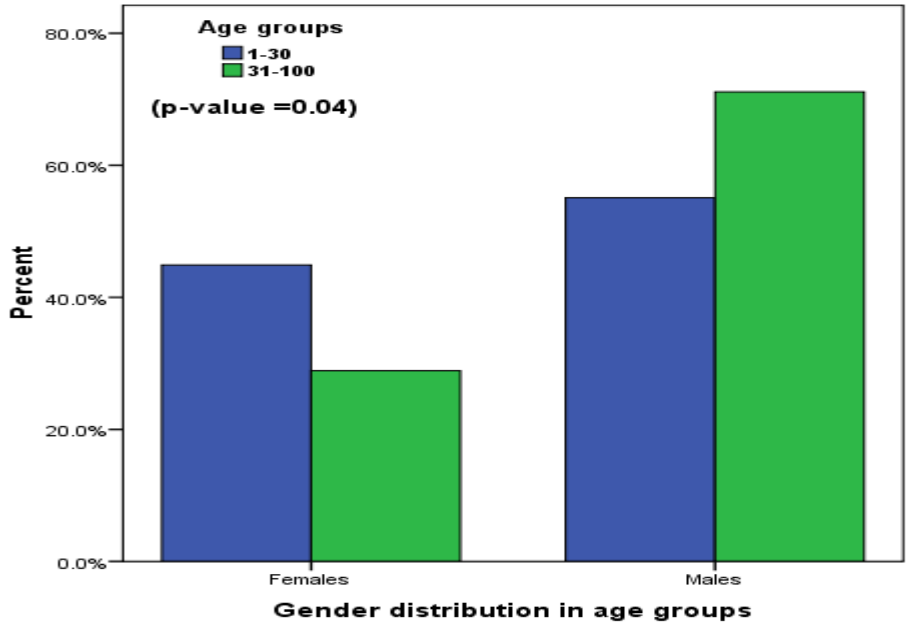

Figure 2. Age distribution in both genders: Male versus females in age groups ≤30 versus >30 years

Table 1. Pattern of treatment of glioma: primary treatment and second line treatment

Mode of treatment	First line n(%)	Second line n(%)
Surgery	63 (79.7)	7(8.9)
Radiotherapy	9(11.4)	49(62)
Chemotherapy	3(3.8)	6(7.6)
No Treatment	3(3.8)	17(21.5)

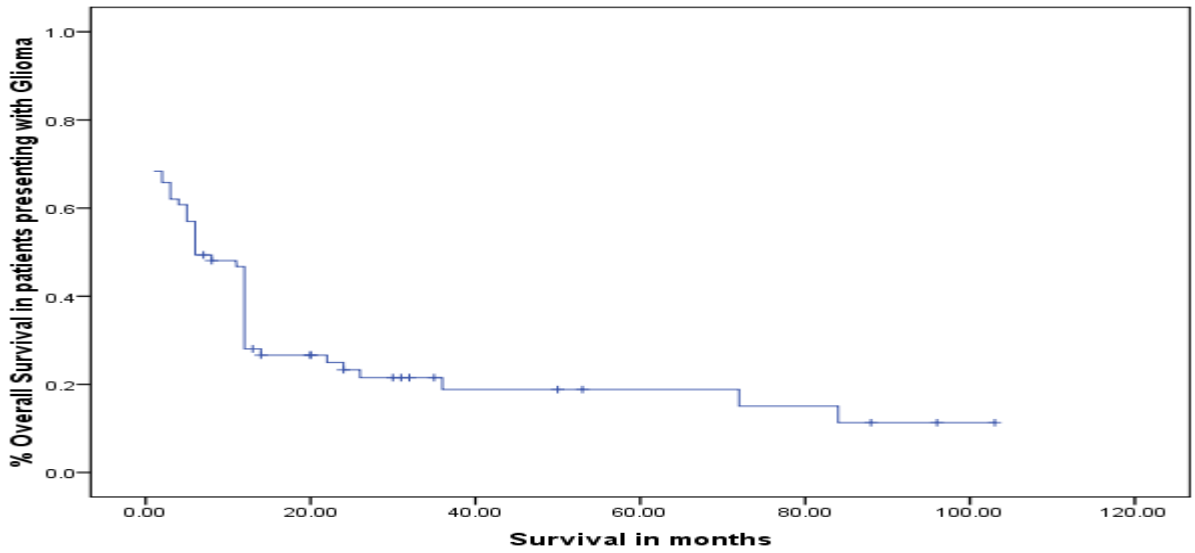

Figure 3. Overall survival of patients presenting with glioma

DISCUSSION

Gliomas are reportedly associated with poor survival outcome. The approach towards gliomas has been improving with advancement in treatment options and understanding of epidemiology. There is not much data available to understand pattern of glioma in Pakistan despite of the fact that a large chunk of annual glioma cases occur in Asia and glioma is one of top cancers in Pakistan(1). Our study is a contribution towards understanding glioma pattern in Pakistan. Relatively younger patients were observed in our study which is consistent with previously reported studies which identified that brain tumors were more common in age group of 20-39 years (14). A national study conducted by Pakistan society of neuro-oncology also reported similar results with the median age of diagnosis for males and females was 36 & 37 years respectively(15). Median age of diagnosis varies with variant of glioma and their grading as well as previously reported that the median age of diagnosis of brainstem glioma was 34 years, while from China the median age of diagnosis of glioma was 38 years, these international results are in consensus with our median age of diagnosis of glioma in Pakistan(16,17). Our results indicated male preponderance with 65.5% patients being male this is in line with various studies conducted across the globe(18,19). A large retrospective study conducted in 2019 also reported that 64% patients were males(20). An earlier Karachi based study conducted in 1999 demonstrated male preponderance as well reflecting that this pattern of glioma have remained unchanged with regard to gender(21).

In our cohort most common histological type was Glioblastoma Multiforme indicating that it contributes to the major chunk of gliomas, a retrospective study across 32 neurosurgical centers in Pakistan also reported similar results with 38% cases being of GBM(20). A Karachi based study also showed that GBM was most common histological diagnosis (33.5%). However, data from Surveillance, Epidemiology, and End Results (SEER) program of National Cancer Institute USA reported 54% of gliomas were GBM(22), which in much higher than the reported data from Pakistan. This may reflect even though GBM is one of most common variant of glioma in adults, in Pakistan its prevalence is lower in comparison to western world(22). In our cohort nearly 45% patients were having Grade IV tumors at the time of diagnosis and only 5.7% had Grade I this has also been reflected in earlier study conducted in Pakistan which demonstrated 39.38% patients had Grade IV tumors(20). This contrasts with one study conducted at DUHS Karachi which demonstrated that grade I tumors were most common 53.6% in their cohort(23). Large number of patients having high grade tumors in our case can be partially explained by late presentation and diagnosis of glioma and this is in conformation with international studies where they have identified Grade IV

tumors being most common such as one study reviewing cases over last 60 years have identified Grade IV tumors being most common(24).

The median overall survival time of our study population was 6 months (95% CI SD=1.361) this is comparatively lower with regards to national and international studies. However, there was scarce data available reported on overall survival of gliomas in Pakistan. Where there was only one retrospective study reported overall survival of 10 months for low grade gliomas(25). Most international studies have focused on type specific survival, an Italy based study showed survival of newly diagnosed GBM patient to be 12 months(5). Another French population based study demonstrated 6.8 and 11.2 months overall survival in patients of GBM aged <70 and >70 yrs. respectively(9). An study on rare adult brainstem glioma showed median survival of 5.4 years(16). Other Thailand based small scale study demonstrated comparatively better 18 months median survival for high grade glioma(26). The survival of the glioma reported to be poor ranging in few months(5,9,27). In our data age and grade did not appear to influence survival (p=0.105) but globally older age groups demonstrate even poor prognosis(9,28). As previously reported from National Cancer Data Base study of USA the median survival of only 6.31 months in patients of GBM older than 70 years(28). This may suggest direct towards aggressive biology leading to poor survival outcome even after optimum surgery followed by chemotherapy and radiotherapy.

Since this study was an institution based single centre study thus incidence was not measured. The sample size was small and given its retrospective nature many patients were lost from follow-up, is taken as limitation of the study. However, this is the large study with long term follow-up of the patients thus we were able suggest longest survival type which we consider as the strength of the study.

CONCLUSION

Glioma in our study demonstrated male predominance and GBM predominance in consensus with national and international reports. Overall it showed poor survival. Large scale studies with understanding of biology and genetic pattern are required followed by optimization of targeted therapy so that survival outcome of the patients can be improved.

Conflict of interest:

Authors declare that there is no conflict of interest

Funding:

This study was funded by Cancer Research Division of Medical Research Centre, Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan

REFERENCES:

1. Globocan [Internet]. 2020. Available from: https://www.uicc.org/news/globocan-2020-new-global-cancer-data#:~:text=GLOBOCAN 2020 is an online,for all cancer sites combined.
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021 Aug;23(8):1231–51.
3. Krex D, Klink B, Hartmann C, von Deimling A, Pietsch T, Simon M, et al. Long-term survival with glioblastoma multiforme. Brain. 2007 Oct;130(Pt 10):2596–606.
4. Badaoui N, Meyronet D, Cartalat-Carel S, Guyotat Jand Jouanneau E, d'Hombres A, Sunyach MP, et al. Patterns of care and survival of glioblastoma patients: acomparative study between 2004 and 2008 in Lyon, France. Rev Neurol. 2014 Feb;170(3):222–7.
5. Salmaggi A, Silvani A, Merli R, Caroli M, Tomei G, Russo A, et al. Multicentre prospective collection of newly diagnosedglioblastoma patients: update on the Lombardia experience. Neurol Sci. 2008 May;29(2):77–83.
6. Preston-Martin S, Staples M, Farrugia H, Giles G. Primary tumors of the brain, cranial nerves and cranial

meningesin Victoria, Australia, 1982-1990: patterns of incidence andsurvival. Neuroepidemiology. 1993;12(5):270–9.
7. Lutterbach J, Guttenberger R, Pagenstecher A. Gliosarcoma: a clinical study. Radiother Oncol. 2001 Oct;61(1):57–64.
8. Paulino AC, Wen B-C, Buatti JM, Hussey DH, Zhen WK, Mayr NA, et al. Intracranial ependymomas: an analysis of prognostic factors andpatterns of failure. Am J Clin Oncol. 2002 Apr;25(2):117–22.
9. Fabbro-Peray P, Zouaoui S, Darlix Amélieand Fabbro M, Pallud J, Rigau V, Mathieu-Daude H, et al. Association of patterns of care, prognostic factors, and use ofradiotherapy-temozolomide therapy with survival in patients withnewly diagnosed glioblastoma: a French national population-basedstudy. J Neurooncol. 2018 Dec;142(1):91–101.
10. Awwad S, Cull A, Gregor A. Long-term survival in adult hemispheric glioma: prognosticfactors and quality of outcome. Clin Oncol (R Coll Radiol). 1990 Nov;2(6):343–6.
11. Guilfoyle MR, Weerakkody RA, Oswal A, Oberg I, Jeffery C, Haynes K, et al. Implementation of neuro-oncology service reconfiguration inaccordance with NICE guidance provides enhanced clinical carefor patients with glioblastoma multiforme. Br J Cancer. 2011 May;104(12):1810–5.
12. Cyrine S, Sonia Z, Mounir T, Badderedine S, Kalthoum T, Hedi K, et al. Pilocytic astrocytoma: a retrospective study of 32 cases. Clin Neurol Neurosurg. 2012 Dec;115(8):1220–5.
13. Ahmed N, Bhurgri Y, Sadiq S, Shakoor KA. Pediatric brain tumours at a tertiary care hospital in Karachi. Asian Pac J Cancer Prev. 2007;8(3):399–404.
14. Pakistan Atomic Energy Commission. https://paec.gov.pk/Documents/Medical/PAECR_report_2018-19.pdf
15. Enam SA, Shah MM, Bajwa MH, Khalid MU, Bakhshi SK, Baig E, et al. The Pakistan Brain Tumour Epidemiology Study. J Pak Med Assoc. 2022 Nov;72(Suppl 4(11):S4–11.
16. Guillamo JS, Monjour A, Taillandier L, Devaux B, Varlet P, Haie-Meder C, et al. Brainstem gliomas in adults: prognostic factors and classification. Brain. 2001 Dec;124(Pt 12):2528–39.
17. Lin Z, Yang R, Li K, Yi G, Li Z, Guo J, et al. Establishment of age group classification for risk stratification in glioma patients. BMC Neurol. 2020 Dec;20(1):310.
18. Piñeros M, Sierra MS, Izarzugaza MI, Forman D. Descriptive epidemiology of brain and central nervous system cancers in Central and South America. Cancer Epidemiol. 2016 Sep;44 Suppl 1:S141–9.
19. Nasir S, Jamila B, Khaleeq S. A retrospective study of primary brain tumors in children under 14 years of age at PIMS, Islamabad. Asian Pac J Cancer Prev. 2010;11(5):1225–7.
20. Bajwa MH, Khalid MU, Shah MM, Shamim MS, Laghari AA, Akhunzada NZ, et al. Treatment patterns of glioma in Pakistan: An epidemiological perspective. J Pak Med Assoc. 2022 Nov;72(Suppl 4(11):S34–9.
21. Bhurgri Y, Bhurgri A, Hassan SH, Zaidi SHM, Rahim A, Sankaranarayanan R, et al. Cancer incidence in Karachi, Pakistan: First results from Karachi Cancer Registry. Int J Cancer. 2000 Feb;85(3):325–9.
22. Forjaz G, Barnholtz-Sloan JS, Kruchko C, Siegel R, Negoita S, Ostrom QT, et al. An updated histology recode for the analysis of primary malignant and nonmalignant brain and other central nervous system tumors in the Surveillance, Epidemiology, and End Results Program. Neuro-Oncology Adv. 2021 Jan;3(1).
23. Danish F, Salam H, Qureshi MA, Nouman M. Comparative clinical and epidemiological study of central nervous system tumors in Pakistan and global database. Interdiscip Neurosurg. 2021 Sep;25:101239.
24. Chen L, Zou X, Wang Y, Mao Y, Zhou L. Central nervous system tumors: a single center pathology review of 34,140 cases over 60 years. BMC Clin Pathol. 2013 Dec;13(1):14.
25. Bajwa MH, Anis S Bin, Yousaf I, Shah M. A 10-Year Survival-Trend Analysis of Low-Grade Glioma and Treatment Patterns from an LMIC. Asian J Neurosurg. 2023 Sep;
26. Noiphithak R, Veerasarn K. Clinical predictors for survival and treatment outcome of high-grade glioma in Prasat Neurological Institute. Asian J Neurosurg. 2017 Mar;12(01):28–33.
27. Dressler E V, Liu M, Garcia CR, Dolecek TA, Pittman T, Huang B, et al. Patterns and disparities of care in

glioblastoma. Neuro-Oncology Pract. 2019 Jan;6(1):37–46.

28. Amsbaugh MJ, Yusuf MB, Gaskins J, Burton EC, Woo SY. Patterns of care and predictors of adjuvant therapies in elderlypatients with glioblastoma: An analysis of the National CancerData Base. Cancer. 2017 Apr;123(17):3277–84.