

Gliomas: Analysis of Disease Characteristics, Treatment Timelines and Survival Rates from Two Tertiary Care Hospitals of India

Abstract

Context: Gliomas are a heterogeneous group of relatively rare cancers that have an important public health-care implication due to their high levels of mortality and morbidity. While standard management guidelines are available, their implementation in a resource-limited scenario needs greater scrutiny. **Settings and Design:** This is a retrospective analysis of disease characteristics, treatment parameters including the time to imaging and time to treatment, and overall survival (OS) at 1 and 5 years in patients of brain gliomas. **Subjects and Methods:** Demographic, clinical, and follow-up data of histologically proven glioma patients that received radiotherapy (RT) between 2009 and 2013 at two tertiary care hospitals of India were collected and analyzed. **Statistical Analysis:** Kaplan–Meier curves were used to compare OS at 12 and 60 months. Cross-tabulation and Pearson's Chi-square test were used to study the association of study variables with survival. **Results:** One hundred and nine patients were included. The mean age was 45 years and males were three times as common as females. Astrocytomas were the most common histology with Grade IV astrocytomas comprising 48% of the total. The OS at 12 and 60 months was 79.8% and 24%, respectively, for the entire cohort. The average time taken for brain imaging from onset of symptoms was 24 days, while the time to surgery and the time to start RT were 18 and 44 days, respectively. Old age and ability to tolerate treatment were shown to affect survival at 1 year from diagnosis, though tumor histology and grade had an apparent impact on long-term prognosis. **Conclusions:** Hospital registries are an important source of demographic and clinical information on less common cancers such as gliomas. Increasing awareness among the general public and sensitization of primary health-care apparatus are critical for early diagnosis and treatment.

Keywords: Astrocytoma, brain tumor, glioma, radiotherapy

Introduction

Brain tumors are a group of infrequent adult malignancies contributing to 1%–3% of all cancers across the globe and in India.^[1–3] However, due to the associated high mortality rate, adverse effects on quality of life, and high incidence in young- and middle-aged populations, it is a significant burden on public health care with a powerful negative stigma in the sociocultural environment.

Detailed and exhaustive epidemiological data are available from brain tumor registries in the more advanced countries and population- and hospital-based registries in the developing nations.^[3–7] Central nervous system (CNS) tumors are an extremely heterogeneous group of disorders, which include tumors from varied sites (brain, spinal cord, and meninges),

histopathologies (gliomas, embryonal tumors, and nerve sheath tumors), and clinical courses and prognoses classified together.^[8] Difficulty in obtaining tissue diagnosis from lesions located in eloquent areas of the brain, lack of consistency in histological definitions of tumors, and inclusion of benign conditions in brain tumor registries (meningiomas, pituitary adenomas, and craniopharyngiomas) are other reasons why generation and comparison of epidemiological data of different regions should be done with a cautious approach.^[1] To develop meaningful and useful epidemiological and clinical data, it is pertinent that studies are carried out on specific and well-defined subgroups of brain tumors.

There are several consensus management guidelines available from the Western countries about the management and follow-up of gliomas depending on

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histological and clinical factors.^[9,10] While these protocols are widely accepted in academic discussions, there is significant heterogeneity and limited information about their timely implementation in a developing country with limited resources.^[11]

In our study, we have tried to focus on the demographic and clinicopathological spectrum of only one type of malignant brain tumor patients, namely, gliomas, treated at our two institutes. We have also tried to record and evaluate the timelines of patient presentation, diagnosis, and treatment in a tertiary care cancer center catering to a wide diaspora of the population across different socioeconomic strata.

Subjects and Methods

Clearance from the institutional ethical committee was obtained before the start of the study. Diagnosis, treatment, and follow-up records of all histologically proven cases of cranial gliomas registered at two tertiary care centers in Northern and Western India, respectively, over 5 years between 2009 and 2013, were examined and the data were collected. Besides demographic data, we also collected data on presenting symptoms, site of tumor within the brain, size, and laterality of tumor (right, left, or bilateral). The largest dimension of the tumor on preoperative magnetic resonance imaging (MRI) brain scan was used to determine its size in millimeters. Only the gross lesion, without surrounding edema, was considered for this measurement. Tumor histopathology and grade were also recorded as per the 2007 WHO classification of CNS tumors.^[12]

The type of surgery was classified as per the neurosurgeon's intraoperative notes. The surgeries were classified into gross total resection (GTR), if all visible tumor was removed, partial resection (PR), if only part of the visible tumor was excised, and biopsy (Bx) if only sampling of the tumor tissue for histopathological analysis was carried out. The data were also recorded for evidence

of residual tumor on postoperative brain imaging. The radiotherapy (RT) data were collected in terms of the modality used (two-dimensional RT or three-dimensional conformal RT [3DCRT] or intensity-modulated RT [IMRT]) and whether the patient was able to complete the planned RT schedule or not. The chemotherapy (CT) data gathered were on schedule, sequencing (concurrent or adjuvant), and drugs used.

We also attempted to determine the time taken by the patient to reach every level of medical management from diagnosis to surgery to adjuvant therapy. We measured and calculated the average duration taken by each patient from the onset of symptoms to first neuroimaging. This was referred to as DOI. Similarly, duration from first neuroimaging to surgery (DIS) and from the first surgery to start of radiotherapy (DSR) was also measured and the average values were calculated. The relevant dates were collected from the recorded history given by the patient or his/her caregiver at the time of the first presentation of the disease.

Only patients with a minimum follow-up of 12 months were included in the study. Frequency tables and histograms were used to analyze distribution of variables in the study group. Overall survival (OS) at 12 and 60 months was calculated for the entire cohort using Kaplan–Meier plots. The Pearson's Chi-square test was used to assess if an association existed between the OS at 12 months and age (above or below 60 years), gender, tumor grade, modality of RT, adjuvant CT, and presence or absence of residual tumor after surgery. The status of the disease at 12 months after first surgery was also assessed and divided into the following groups: complete remission, partial response, progressive disease (PD), and dead (D). All statistical analyses were carried out using IBM (International Business Machines Corporation, Armonk, NY, USA) Statistical Package for the Social Sciences (SPSS) 20 software.

Table 1: Age, gender, grade, and histopathological distribution of tumors

Tumour	Male			Female			Total		
	<i>n</i>	%	Mean Age (Years)	<i>n</i>	%	Mean Age (Years)	<i>n</i>	%	Mean Age (Years)
Astrocytoma	70	65.1%	44.9	24	22%	50.5	94	86.2%	46.3
Grade I	2	1.8%	35.5	0	0	–	2	1.8%	35.5
Grade II	22	20.2%	36.5	8	7.3%	37	30	27.5%	36.7
Grade III	8	7.3%	37.5	1	0.9%	70	10	8.3%	41.1
Grade IV	38	34.9%	51.9	15	13.8%	56.3	53	48.6%	53.1
Oligodendro-glioma	2	1.8%	44.5	4	3.7%	39.3	6	5.5%	41
Grade II	2	1.8%	44.5	1	0.9%	36	3	2.8%	41.7
Grade III	0	0	0	3	2.8%	40.3	3	2.8%	40.3
Mixed Oligo- Astrocytoma	6	5.5%	32.5	1	0.9%	29	7	6.4%	32
Grade II	4	3.7%	33.5	0	0	–	4	3.7%	33.5
Grade III	2	1.8%	30.5	1	0.9%	29	3	2.8%	30
Ependymoma	2	1.8%	34	0	0	–	2	1.8%	34
Grade II	1	0.9%	35	0	0	–	1	0.9%	35
Grade III	1	0.9%	33	0	0	–	1	0.9%	33
TOTAL	80	73.4%	43.7	29	26.6%	48.2	109	100%	44.9

Results

A total of 109 histologically proven glioma patients received RT at our centers during the study period and were included for analysis. The mean age of patients at the time of diagnosis was 44.8 years with only 17 patients above the age of 60 years (15.6%). The number of male cases was nearly three times as many as female cases (80:29). Table 1 shows the age and distribution of different glioma types encountered in our study.

Figure 1 displays the patterns of presenting symptoms in our study. Headache was the most common one, followed by generalized seizures. Facial paresthesias, behavioral changes including emotional lability, and amnesia were some of the uncommon presentations. One patient was detected to have a glioma incidentally during an annual follow-up MRI of the brain done for an old history of seizure disorder. Fifty-five (50.5%) patients presented with more than one symptom.

The tumor size, as measured in our study, ranged from 18 mm to 91 mm with the mean dimension being 51.3 mm. The distribution of tumor size among all patients as a bell curve histogram is shown in Figure 2a. The

average tumor sizes across histological grades and sites are shown in Figure 2b and c, respectively.

The site and laterality scattering of the tumors is shown in Figure 3a and b, respectively. Histologically, astrocytomas (86.2%) were the most common, of which Grade IV glioblastoma (GBM) made up 48.6%. On the other end of the spectrum, only 2 (1.8%) tumors were pathologically classified as Grade I. One was a pilocytic astrocytoma, while another was a pleomorphic xanthoastrocytoma. The histopathology and grade division of tumors are displayed in Table 1 and Figure 3c, d.

In terms of management, only patients who had undergone surgery and adjuvant RT were included in the study. The types of surgical resections are shown in Figure 4a. 43% were classified as GTR with all visible tumor excised. However, on postoperative neural imaging, only 31% of the scans showed no residual tumor [Figure 4b], leading to a 12% mismatch between surgical and radiological findings.

Fifty-one patients received radiation treatment on linear accelerators using 3DCRT treatment planning and delivery, while 52 received treatment on telecobalt machines with two-dimensional treatment planning and delivery. Six patients received IMRT on linear accelerators. The RT doses prescribed were as per the prevalent standard treatment recommendations and ranged from 54 Gy for Grade I and II to 60 Gy for Grade III and IV tumors at 1.8–2 Gy per fraction. 93.5% of patients were able to completely receive the planned RT dose [Figure 4c and d].

Sixty-one patients received concurrent CT in the form of temozolomide (TMZ) along with RT. 49 of these were patients of GBM. Four patients of GBM did not receive concurrent CT due to old age (>70 years) or poor performance status and could not complete planned RT either. The other 12 patients who received concurrent CT included 9 with grade III tumors and 3 of grade II astrocytomas.

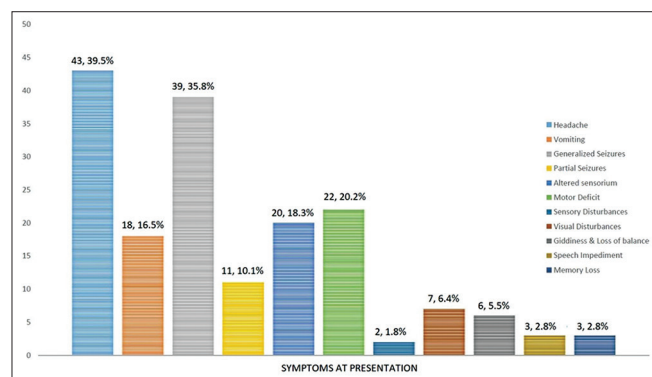


Figure 1: Distribution of presenting symptoms in the study population

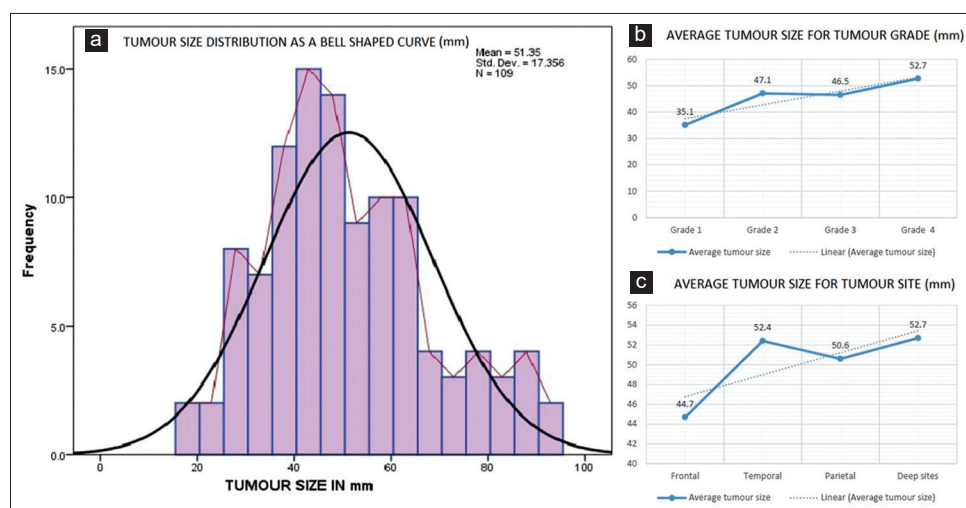


Figure 2: (a) Distribution of tumor size as a bell-shaped curve. (b) Grade wise distribution of average tumor size. (c) Site-wise distribution of average tumor size

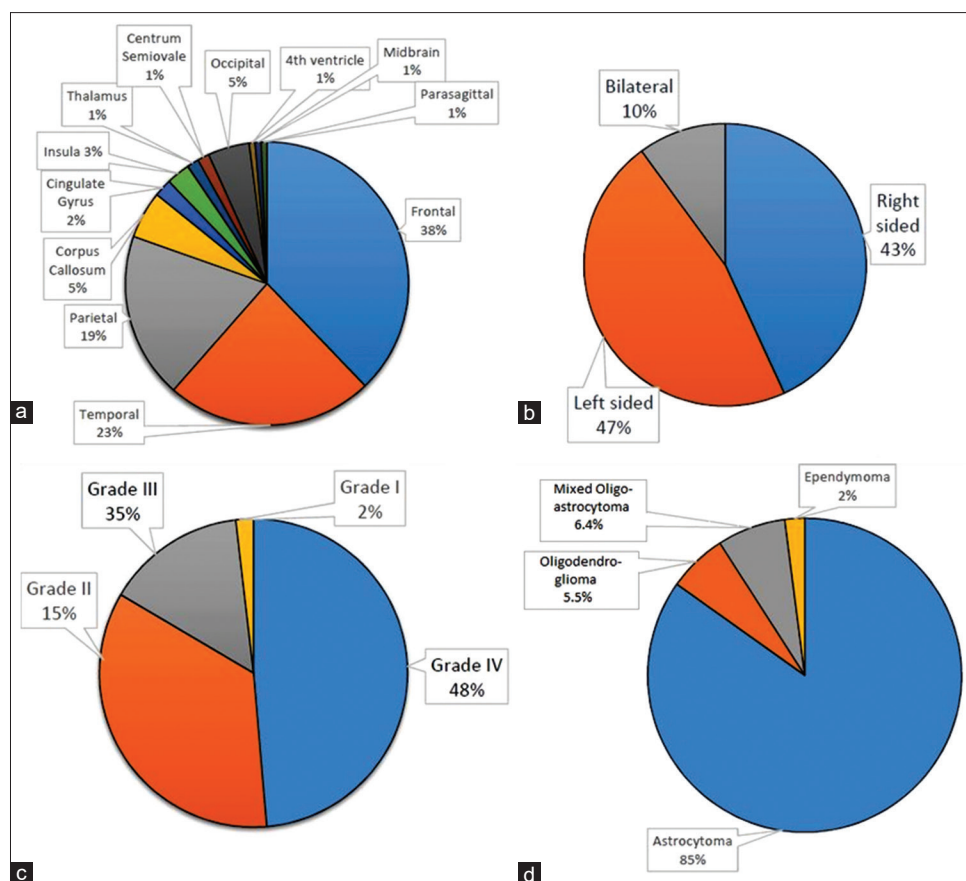


Figure 3: (a) Distribution of tumor sites. (b) Distribution of tumor laterality (right/left/bilateral). (c) Distribution of tumor grade. (d) Distribution of tumor histopathology

Sixty-eight patients were offered adjuvant CT. Of these, 42 were GBM patients. None of the 11 GBM patients who did not receive adjuvant CT survived more than 14 months with 10 dying within 10 months of diagnosis. The 26 non-GBM patients who received adjuvant CT included 14 Grade III and 12 Grade II tumors. The adjuvant CT schedule consisted of six cycles of TMZ every 21 days in 66 patients, which all but eight patients were able to complete. Two patients of anaplastic oligodendrogliomas (ODGs) received 6 cycles of procarbazine, lomustine, and vincristine (PCV) as adjuvant CT. The treatment timelines of the entire study cohort are presented in Figure 5. The survival plots of OS at 12 months and 60 months are displayed in Figures 6 and 7, respectively, while Figure 8 shows the disease status of the study population at 1 year from the first surgery.

Discussion

In a developing country like India, meticulous and authentic hospital-based registries can play a vital role in supplementing population-based cancer registries in generating useful epidemiologic and clinicopathological data of diseases such as cancers. This enrichment of information can contribute toward understanding disease patterns and planning and development of health-care policies.^[13]

Among malignant brain tumors, gliomas are the most frequently encountered in both adult and pediatric

population, representing 38%–67% of primary brain cancers in various Indian studies.^[5–7] Between 25.4%–59.5% of these are high-grade astrocytomas, mostly GBMs. Histologically, gliomas arise from nonneuronal glial tissues which have supportive and protective roles in the CNS. They include astrocytomas, oligodendrogliomas, ependymomas, and mixed gliomas. Pathological features such as increased cellularity, mitotic activity, degree of nuclear atypia, presence of necrosis, and neovascularization are used to grade the tumors from I to IV. Molecular and genetic markers such as ATRX, IDH mutations (1 and 2), p53, O6-MGMT methylation, and 1p19q codeletion are used to classify the tumors and assist in therapeutic decisions. Management of these cancers consists of maximal safe surgical resection followed by adjuvant therapy in the form of RT with or without CT.^[14] Prognosis and expected survival of patients are variably affected by age, performance status, clinical features, histology, molecular markers, and extent of surgical resection. GBMs and elderly patients consistently do poorly, while patients who undergo complete removal of tumor have the longest survivals. Expected survival rates in gliomas can be starkly contrasting, ranging from a 10-year survival of >90% for a completely resected Grade I tumor to a 2-year survival of about 3% for the dreaded Grade IV GBM.^[14]

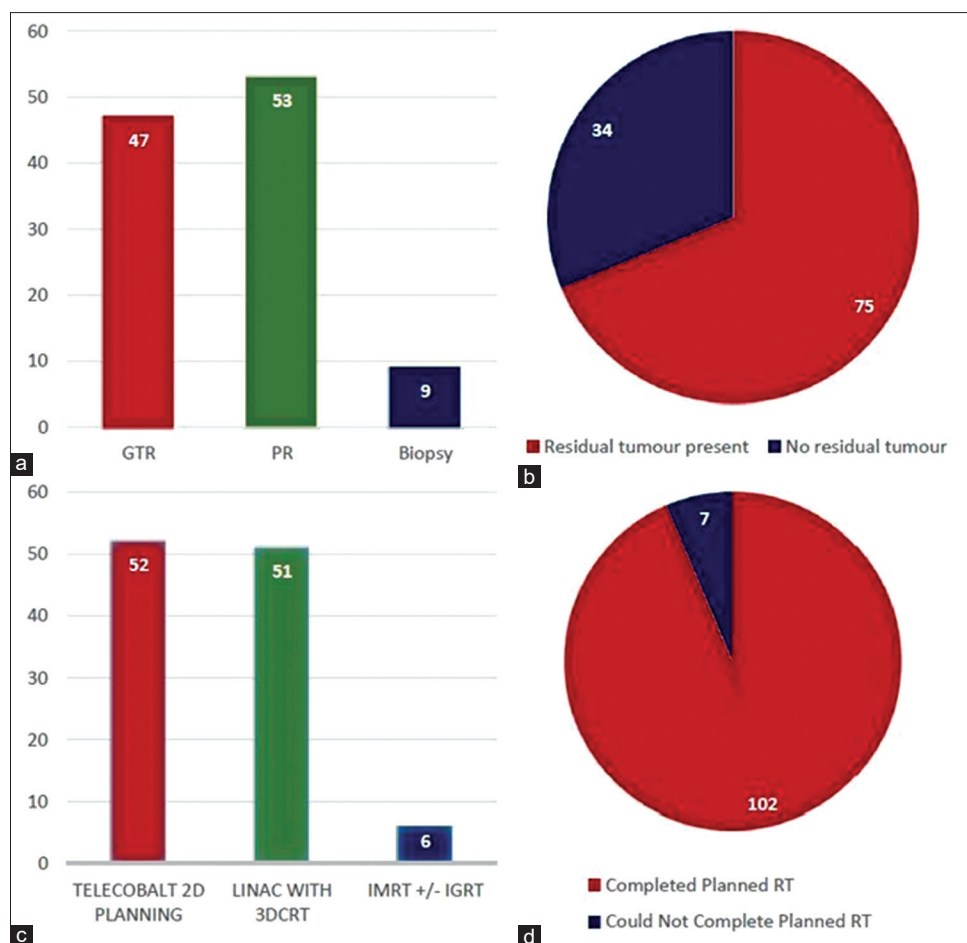


Figure 4: (a) Types of Surgical procedure done. (b) Ratio of patients with residual tumor after first surgery. (c) Type of radiotherapy modality used. (d) Ratio of patients who completed planned radiotherapy treatment

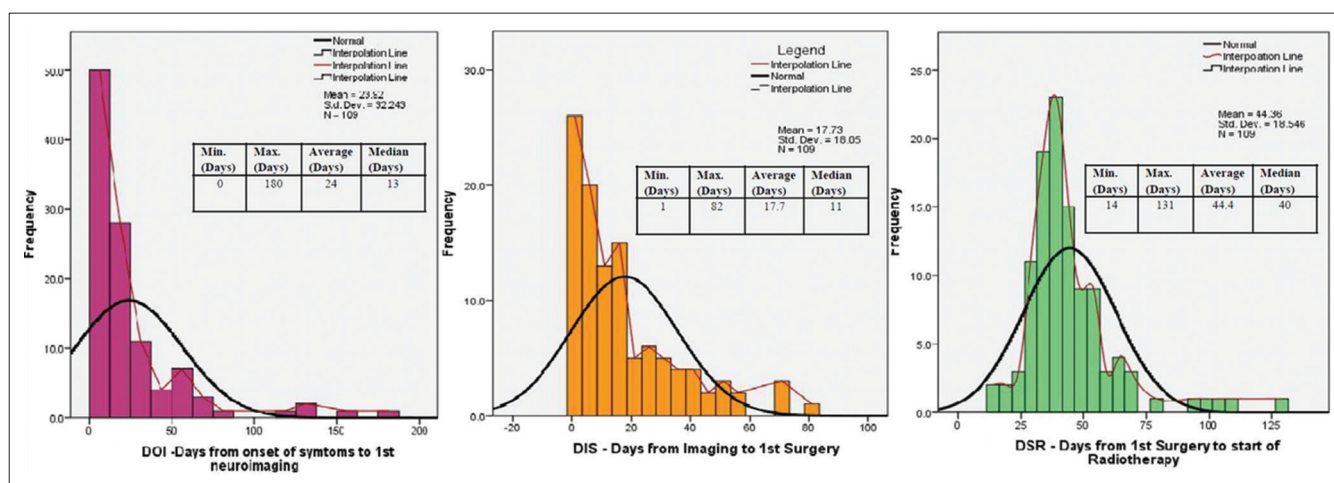


Figure 5: Distribution of treatment timelines in the study cohort. Time taken to reach every level of medical management from first brain imaging to surgery to adjuvant radiotherapy

Primary brain tumors have been called a disease of middle-aged men. The CBTRUS data show a male: female ratio of 1:1.38, but this is primarily due to the inclusion of meningiomas, which are much more common in women.^[4] In Indian studies, the gender ratios consistently show a greater predilection of brain tumors for the male sex. For GBMs,

the male: female ratio from CBTRUS is reported as 1.57:1, while in a South Indian study, it is as high as 2.4:1. Genetics likely play a role in this gender bias. Sun *et al.* have reported that the inactivation of the RB tumor suppressor gene is seen twice more commonly in men than women.^[15] Environmental factors such as greater exposure to pesticides,

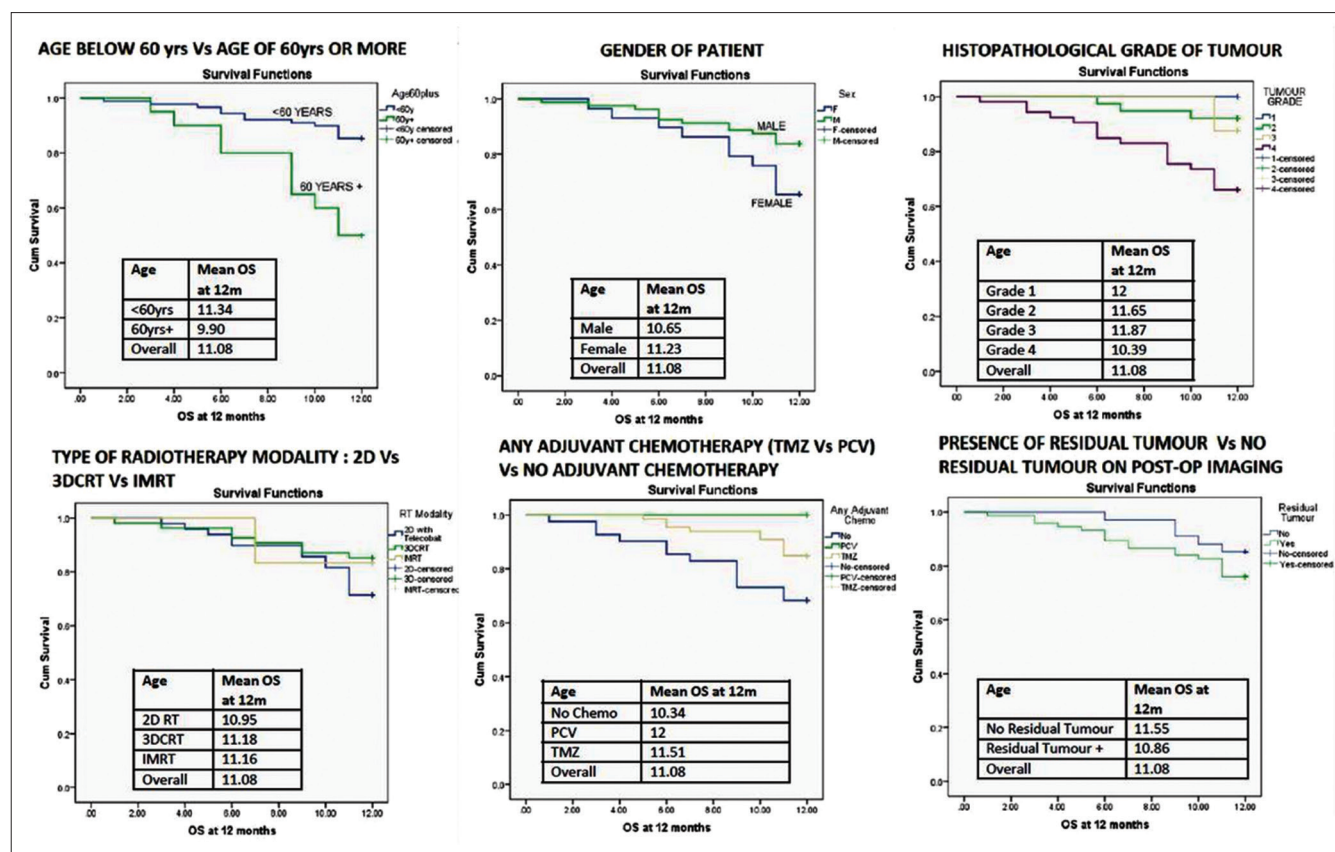


Figure 6: Survival curves at 12 months of follow-up

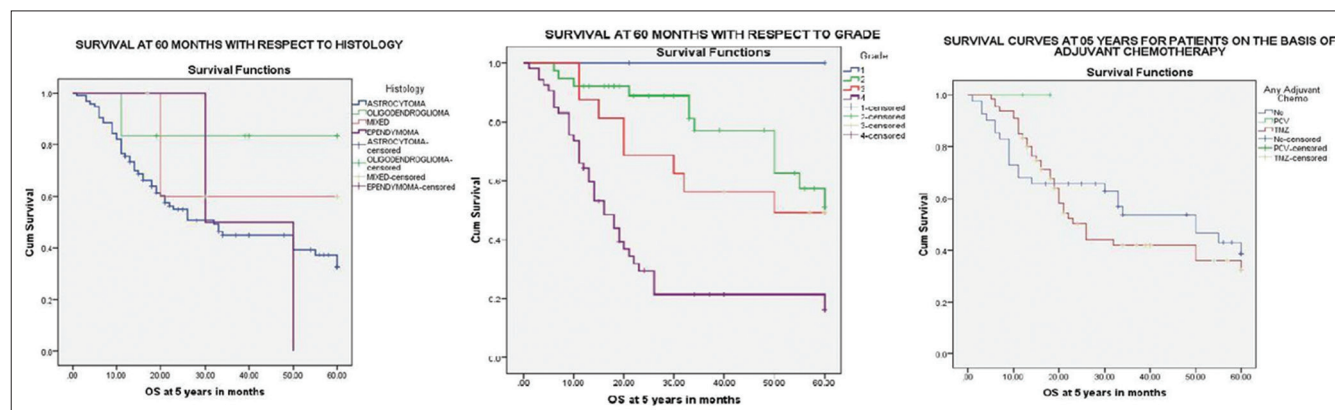


Figure 7: Survival curves at 60 months of follow-up

industrial chemicals, and other carcinogens among men may also be contributory. In our study, the males outnumber the females by a factor of 2.75:1. An additional factor among others for this exceptionally high ratio is probably the fact that our clientele primarily consists of military personnel, the majority of whom are male. On comparing OS at 12 months [Figure 6], we see that females have a poorer survival rate than males in our study. This could probably be due to the older average age of the females compared to the males in our study. However, more importantly, the proportion of malignant gliomas (Grade III and IV) in females is slightly higher (69%) than in males (61%) [Table 1].

In our study cohort, the patients' ages spanned 6 decades from 18 to 74 years with an average being 44.8 years (43.7 for men and 48.2 for women). Other Indian series have also identified the decades of the 40s and 50s as having highest brain tumor incidence.^[5,7] Only 15.6% of our study patients were above the age of 60 years. The average age of glioma presentation in India is a decade earlier than the West, which is reflective of the higher proportion of younger adults in our population as well as of the lower life expectancy compared to the developed nations.^[6,7] Variations in genetic makeup and lifestyle are also possible contributors to this phenomenon. This trend is also seen in cancers of the breast, kidney, and colorectal.

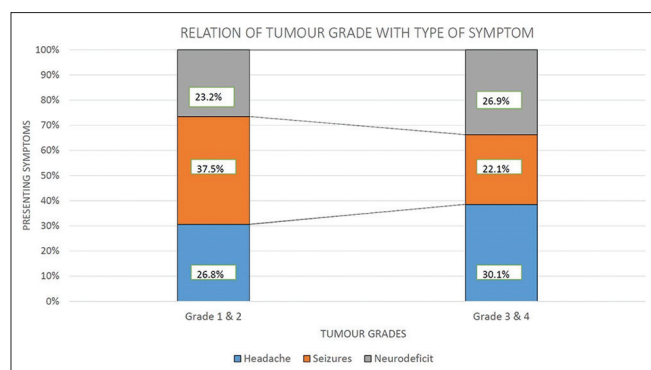


Figure 8: Association of tumor grade with symptoms

Among astrocytomas in our cohort, the mean age of presentation increased from 36 years for low-grade tumors to 51 for high-grade ones [Table 1]. Jaiswal *et al.* have stated that the proportion of Grade IV tumors affecting a population increases with age, while that of grade I tumors reduces simultaneously. The peak age of incidence of GBM was found to be the highest among all CNS tumors in the study from Delhi's PBCR.^[5,7] OS at 12 months was much poorer for older patients (>60 years) [Figure 6], which is an established phenomenon.^[14] The reasons are a mixture of poor tolerance of surgery and adjuvant therapy as well as the higher proportion of high-grade tumors in the older age group.

Headache was the most common presenting symptom [Figure 1] in our series with 43 (39.5%) cases. 7 (6.4%) of these had no other symptoms, while in 16, it was associated with vomiting. As per neurological textbooks, headache can be seen in 50% of patients of primary brain tumors with about 8% such cases having it as the solitary presenting symptom. The slightly lower percentage in our study is possibly because of noninclusion of benign tumors such as meningiomas which more often present with headache. Partial or general seizures are seen in 30%–90% brain tumors, and our figures (39, 35.9%) are commensurate with that, though the percentage of low-grade gliomas presenting with seizures (37.5%) is much lower than what is described in the literature (up to 85%).^[16]

It is classically hypothesized that the higher grade, fast-growing tumors tend to present as headaches due to rapid rise in intracranial tension. Low-grade, insidious tumors present more often as seizures and are more often associated with neurodeficit. In Figure 6, we can see that in our study too, the low-grade tumors had a higher percentage of patients presenting with seizures (37.5%) than headache (26.8%), while for high-grade tumors, the ratio is reversed (22.1% had seizures and 30.1% had headache). The proportion of cases with neurodeficit was similar in low- (23.2%) and high-grade (26.9%) tumors.

When we looked at brain sites involved by the tumors [Figure 3a], the most common ones were the frontal (38%), temporal (23%), and parietal (19%) lobes.

These are the most commonly affected sites, excluding the meninges, in the CBTRUS data as well as the TMH study.^[4,6] The occipital was affected in only 5% of cases, while the other, more deeply located sites (insula, corpus callosum, and thalamus), were affected in about 15% of cases. We had only two cases of ependymomas, one of which arose from the fourth ventricle, while the other affected the frontal and parietal lobes. In about 27% of cases, more than one site in the brain was affected.

Inskip *et al.* have commented that neither laterality of the brain is seen significantly more in the incidence of gliomas or other brain tumors.^[17] However, they observed that in 489 gliomas, aphasia and behavioral disturbances were more common in patients with left-sided lesions. In our series also [Figure 3b], the left-to-right ratio was very close to 1 (1.09) with 10% of tumors present in bilateral hemispheres at presentation. Interestingly, all three patients presenting with speech disturbances and 5 out of 6 presenting with behavioral changes had lesions on the left side of brain affecting frontal, parietal, or temporal lobes. Involvement of the 'dominant' hemisphere, thus, can have implications on clinical presentation.

The tumor size at the time of presentation in our cohort varied from 18 to 91 mm with an average of 51.3 mm. We also compared average tumor sizes [Figure 2c] between four subsites: frontal, temporal, parietal, and deep areas of the brain (corpus callosum, cingulate gyrus, centrum semiovale, insula, and thalamus). Twenty-nine cases involving more than one subsite and 2 involving occipital lobe were excluded for this analysis. Frontal lobe lesions were found to be the smallest at the time of detection which is probably due to the early occurrence of symptoms in lesions of this site. In low-grade gliomas, a preoperative tumor diameter of ≥ 6 cm has been proven to be a high-risk feature for tumor recurrence.^[18] In high-grade malignant gliomas, on the other hand, size does not seem to be associated with prognosis.^[19] In a study by Dempsey *et al.* of 70 patients with recurrent malignant gliomas, unidimensional or bidimensional tumor measurement was not found to have a significant association with survival, but volumetric tumor size was predictive of it.^[20] In our study, the average tumor size is seen to increase with increasing grade [Figure 2b]. High-grade tumors have aggressive biology and are fast growing and consequently larger at the time of diagnosis. Thus, larger tumor size, even on unidimensional measurements, may point toward an aggressive tumor biology, with lesser possibility of complete excision and poorer expected survival.

Histopathologically, the majority of tumors in our study were astrocytomas (86.2%). This is similar to other Indian and Western studies, where astrocytomas comprise between 21.5% and 66.5% of all brain tumors (the denominator often includes benign tumors also). Among only primary brain cancers, their percentage ranges from 53.7% to

71.2%.^[4-7] The higher proportion of these tumors in our study is probably because we selected only those cases who received RT after surgery. Among astrocytomas, the most common type of tumor overall was GBM (48.7%) similar to other brain tumor series where they range from 38 to 59.5%^[4,14,16] [Table 1 and Figure 3c, d].

Oligodendrogliomas and mixed oligoastrocytomas were both around 6% each in our study, while ependymomas were only 2 (1.8%). All the 6 ODGs and 7 mixed oligoastrocytomas (OAs) underwent molecular testing for 1p19q chromosomal codeletion with 3 testing positive (all 3 received CT). Between 2009 and 2013, other molecular studies were not routinely done at our center. Six out of 11 tested GBM patients were found to have positive silencing of O6-methylguanine-methyl-transferase and 6 of 12 patients of Grade II astrocytoma showed a mutation in Isocitrate dehydrogenase (IDH) 1 or 2.

Histopathological origin and grade are two of the most important factors affecting disease prognosis and patient survival.^[14] Figures 6 and 7 show that when comparing OS at 12 and 60 months, Grade IV tumors consistently do the worst and Grade I tumors the best. This fact is commonly known and accepted. Tumors with Grades II and III can also similarly be arranged on a spectrum of worsening survival rates with increasing grade. In our study, grade III tumours were doing better than grade II tumours at 12 months. This is explained by the fact that 35% of Grade III tumors in our cohort are ODGs and Mixed Oligoastrocytomas (MOAs), while only 21% of Grade II tumor are nonastrocytomas [Table 1]. Histologically, astrocytomas do worse than all other tumor types. On following the survival curves further, we see that after 12 months, Grade III tumors have a worse survival than grade II tumors till the two curves meet at 60 months. The survival curve for different histologies at 5 years is shown in Figure 7. As expected, astrocytomas have the worst prognosis, though numbers of other tumor types are not sufficient for their survival pattern to be reliably studied.

The average duration from symptom onset to cross-sectional neuroimaging (DOI), taken by the patients in our study, was 24 days. This, in essence, can be considered the time to radiological diagnosis. In a family practice study of the National Health Service from the UK, the average time taken for diagnosis of primary brain tumors was also 24 days, with a range between 7 and 65 days.^[21] The timelines are similar as in all our cases neural imaging led to diagnosis. The various indigenous factors that would have contributed to the increase in DOI in our study are limited access to specialist health services in rural and peripheral areas, incongruous geographical distribution of population and health-care services, neglect of symptoms by patients, and dependency on traditional forms of medicines. On comparing symptoms, the average DOI of patients suffering from headache alone was 29 days. The

presence of seizures reduced the average to 23.4 days, while hemiparesis or other neurodeficits reduced it to 6.3 days. This reflects the seriousness attributed by the general population to various neurological symptoms.

The average time from imaging to surgical intervention (DIS) was 18 days. While 41% of patients underwent first surgical intervention within a week of brain imaging, 62% had undergone surgery by 15 days. However, 21% were operated upon after more than a month of their imaging. The factors affecting this delay include time taken for the patient to reach a center with neurosurgical, anesthesia and critical care resources, patient or next of kin's initial unwillingness for surgery, a diagnostic dilemma about etiology of the lesion, and localization of lesion in an eloquent area of the brain requiring a deliberate approach. Brain tumors often present in the emergency department with clinical scenarios of raised intracranial pressure, mass effect, and brain herniation requiring urgent surgery. While this seems to be universally true for aggressive high-grade tumors, the advantage of early overdelayed surgery in low-grade, slow-growing tumors is less clear with contrasting evidence available.^[22,23]

Gross total excision of gliomas is associated with improved survival and best prognosis compared with incomplete resection in both low- and high-grade tumors.^[23-25] However, this is often difficult due to the infiltrative nature of these tumors and due to involvement of the deeper and eloquent areas of the brain. In our study, as per intraoperative appearance, the GTR percentage was 43%, but a complete absence of residual tumor on postoperative imaging was seen in only 31% of cases. More recently, GTR rates of 76%–96% have been described in literature when using advancements such as 5-aminolevulinic acid imaging and intraoperative mapping/monitoring.^[26,27] A potential confounder in our study is the fact that the timing and modality of postoperative imaging were extremely heterogeneous. CT or MRI was variably used between 24 h and 2 weeks postsurgery and could have possibly affected the interpretation. Figure 6 depicts a poorer survival at 12 months for patients with residual tumor after surgery though it was not statistically significant.

The average time taken from the date of first surgery to start of radiotherapy (DSR) was 44 days. Delay in RT up to 48 days has not shown to affect survival in high-grade gliomas.^[28] A Cochrane review of low-grade gliomas receiving early or delayed RT has also found no difference in OS between the two strategies though progression-free survival (PFS) was longer in patients receiving early adjuvant RT.^[29] The standard protocol at our centers is to start RT at 30 days postsurgery. The reasons for the delay in starting RT beyond 30 days included redo surgery due to large residual tumor, poor wound healing or recovery of the general condition of patient postsurgery, delay by the patient to report to RT center within time, the time required

for treatment planning, and rarely, machine downtime due to preventive or corrective maintenance. Only 7 out of 109 patients (6.4%) were not able to complete their planned RT due to poor performance status or disease progression.

Nearly half of our patients were treated on Cobalt-60 teletherapy machines using 2D treatment planning. India is a developing nation with an enormous gap in the need and availability of health resources. Our country has 180 functional telecobalt machines, mostly in government institutes like ours.^[30] Often, it is the only accessible machine for cancer treatment for economically challenged clientele when even relocation of the patient to a center with a Linear Accelerator (LINAC) is not feasible. The survival curves shown in Figure 6 compare survival at 12 months of patients treated by different RT modalities. The OS is lower for 2D RT than for the conformal techniques, but the difference is not significantly large. A possible bias affecting this study may be that patients with older age and poorer general health were more often treated with 2D planning and telecobalt while the younger, fitter patients were more often treated with conformal RT to reduce the possibility of long-term sequelae. Though this was confirmed by the treating physicians, it could not be quantified numerically. Comparison of late sequelae of RT and its influence on the quality of life between 2D and 3D/IMRT would have been an important question to ask, but has not been addressed by our study.

Use of concurrent and adjuvant TMZ or PCV based CT along with RT has now become standard of care for high-grade gliomas, especially GBM.^[31] CT has also shown to be advantageous in improving PFS and OS when used in low-grade gliomas,^[32] but is less often utilized in our clinical setting. On comparing the survival curves [Figures 6 and 7], we see that patients receiving CT have better survival than those not receiving it at 12 months. This is interesting because the majority of patients receiving CT in our group are GBM who should have the worst prognosis. Sure enough, we see that the survival worsens for patients on CT at 18 months compared to those not receiving CT with both curves finally meeting at 60 months.

Finally, the disease status of patients at the end of 12 months is displayed in Figure 9. 20% of the patients were dead while 7% had PD. This is reflective of the high percentage of high-grade gliomas in our study. The only factors which were found to have a statistically significant association with OS at 12 months were age above 60 years (worse for older patients, $P = 0.000$) and completion of planned RT dose (worse for those not completing RT, $P = 0.000$). The effect of old age on survival has been discussed earlier. Inability to complete RT was likely due to poor performance status and general condition which would have affected survival also. Histology, grade, and residual disease did not show a statistically significant impact on

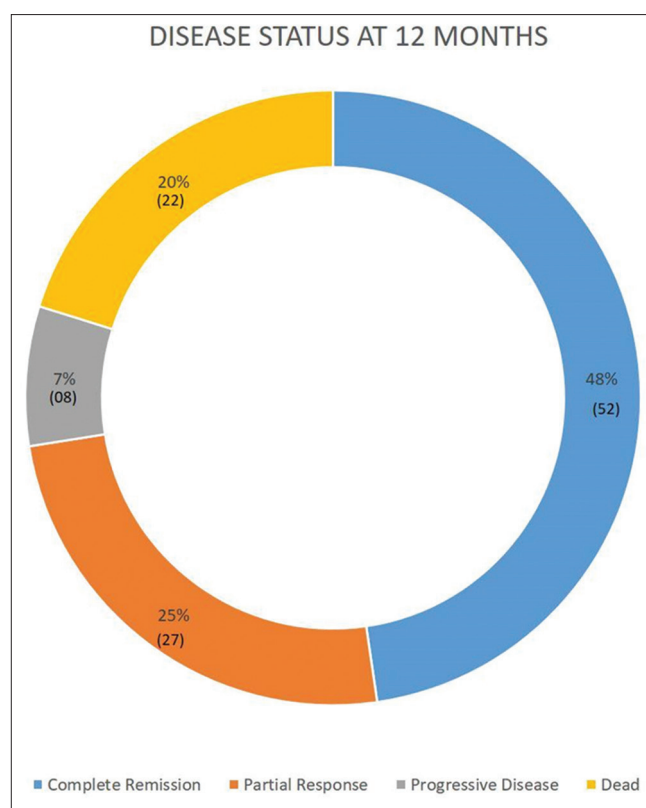


Figure 9: Disease status distribution of the study population at 12 months of follow-up

survival probably because of the relatively small study population and short follow-up of 12 months. Statistical testing could not be carried out at 5 years follow-up due to the high rate of loss to follow-up (30%) of patients.

Conclusions

The study is limited by the fact that it is retrospective and researchers have had to depend on recorded clinical, treatment, and follow-up data. The study cohort is relatively small and the available follow-up period for statistical analysis is short. Only patients in whom RT was delivered were included while comparisons have been made with institutional brain tumor registries which also include cases where RT is not offered. Brainstem gliomas could not be included in the study due to the lack of histopathological confirmation. Nonetheless, several relevant findings have been made.

Hospital registries are an important source of demographic and clinical information on less common cancers such as gliomas. High-grade astrocytomas are the most common variety of gliomas. 24 days is the average time taken to seek medical attention after appearance of symptoms. Old age and ability to tolerate treatment were shown to affect survival at 1 year from diagnosis though tumor histology and grade have an impact on long-term prognosis. Increasing awareness among the general public and sensitization of primary health-care apparatus are critical for early diagnosis and treatment.

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Conflicts of interest

There are no conflicts of interest.

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