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Trends in clinico-epidemiology profile of surgically operated glioma patients in a tertiary care center over 12 years—through the looking glass!

Suyash Singh¹, Harsh Deora², Azfar Neyaz³, Kuntal Kanti Das⁴, Anant Mehrotra⁴, Arun Kumar Srivastava⁴, Sanjay Behari⁴, Awadhesh Kumar Jaiswal⁴ and Sushila Jaiswal^{3*}

Abstract

Background: Hospital-based cancer registries can provide information on the magnitude and distribution of cancers in a given hospital. Hospital-based brain tumor registry data, focusing on glioma, from a tertiary care rural neurological center is lacking in the scientific literature. This data can be useful in understanding the need for research and funding required for these specific brain tumors.

Data of patients operated for glioma, at our institute, was collected between January 2004 and December 2015. Patients' clinical details and histopathological diagnosis were recorded. Data were analyzed and compared with that of previously published literature, and inferences were drawn on patterns of reporting and epidemiology.

Results: A total of 1450 cases of glioma, with a mean age of 39.3 (\pm 17.36 SD) years with males (66.6%) comprising more population as compared to females. Majority of patients 70.8% (n = 1027) belong to the economically active age group of country (18–60 years). Majority of cases (41.4%) were glioblastoma with the next common tumor (22.8%) being diffuse astrocytoma (n = 331) followed by pilocytic astrocytoma (6.2%) and oligodendroglioma (4.5%) in that order. While our data followed similar trends with other Indian data the average age of glioma was a decade younger to what is quoted earlier in Indian and international studies.

Conclusion: This data for glioma gives a glimpse of the prevalence of this tumor in a primarily rural population and highlights the need for a National Brain Tumor Registry with the need for the development of evidence-based policymaking and enhanced research into this particular ailment.

Keywords: Hospital-based brain tumor registry, High-grade glioma, Diffuse astrocytoma, Prevalence, Rural population

Background

Glioma constitute 38.7% of CNS tumors, with the high-grade (grades III and IV) variants comprising 59.5% and low-grade (grades I and II) varieties approximately 33.1%. The tumor possesses high morbidity and thus subtends a high economic burden to the country.

Overall, the glioblastoma (40%), followed by metastatic tumors (20%) and meningioma (15%) are the most prevalent CNS tumors in the adult [1]. Majority of the previous series have focused on brain tumors as a whole, but herein, we have focused our interest on histopathologically proven cases of glioma only. Therefore, our study presents an undiluted picture of prevalence and trend over the last 12 years. There is an increase in the incidence of glioma possibly due to better diagnostic armamentarium or increasing carcinogens around us in

* Correspondence: sushilapath@yahoo.com

³Department of Pathology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, UP 226014, India

Full list of author information is available at the end of the article

the atmosphere [2]. Even with all possible adjunct treatment modalities, the survival of patients is poor with high functional and neurological morbidity. The prognosis of these tumors depends largely on histopathology, apart from age and molecular markers. The exact prevalence of these tumors in developing countries, especially in India, is difficult to determine due to lack of data registry like CBTRUS. In this article, we have highlighted the prevalence and trend, discussed the descriptive epidemiology and distribution of glioma in patients operated at our institute in the past 12 years in the background of WHO classification 2007. Understanding the trend helps caregivers in early detection and management of glioma [3].

Methods

A total of 1450 cases of glioma, operated in Neurosurgery Department from January 2004 to December 2015, were retrieved from our database of Department of Pathology. The diagnoses in all the cases were made on histological examination of processed tissue. Fixing, dehydration, and clearing followed by impregnation with wax were the processing procedure for all the sections. The wax blocks were cut in 5–6 μ sections and stained by hematoxylin and eosin stain. All the cases were classified and termed according to the revised World Health Organization (WHO) classification 2007. Patient age, gender, year of surgery, histopathological diagnosis, and WHO grade were entered into a database. Non-neoplastic and inflammatory lesions including non-gliomatous tumors, bony tumors, and benign lesions like meningioma, vestibular schwannoma, arachnoid cysts, colloid cysts, and epidermoid cysts were excluded. The cases with incomplete histopathological reports were excluded from the analysis ($n = 32$). The gender data were not available in 84 patients (5.7%) and the grade data were not available in 11 patients (0.75%). Institutional ethical clearance for retrospective analysis of data was taken prior to study. Individual consent for using clinical and radiological material for publication from all the patients is taken at time of admission, as per our departmental protocol. The relative frequency of tumors and the distribution of age and sex were analyzed using Statistical Package for the Social Sciences (SPSS) International Business Machines Corporation (IBM) version 22.0.

Results

Mean age of patients in our study was 39.3 (± 17.36 SD) years ranging from 2 years to 85 years. Seventy-five percent of patients were below 53 years. 15.3% ($n = 222$) pediatric patients were below 18 years of age whereas 13.9% ($n = 201$) patients were above 60 years of age. Therefore, the majority of patients 70.8% ($n = 1027$)

belong to the economically active age group of country (18–60 years) with a maximum prevalence in the third and fourth decades (39%).

In our study, the prevalence of glioma was found more in males (66.6%) as compared to females. The gender distribution among different age groups also showed male preponderance. 70.5% males affected below 18 years, 69.7% males between 19 and 50 years and 72.8% above 50 years. Since the included cases were before 2016, the WHO 2007 classification has been followed for them. Majority of cases (41.4%) were glioblastoma on histopathology ($n = 601$).

The next common tumor (22.8%) was diffuse astrocytoma ($n = 331$), pilocytic astrocytoma (6.3%), and oligodendroglioma (4.5%) in that order. Anaplastic astrocytoma comprised 7.0% ($n = 102$) and oligoastrocytoma was 4.8% ($n = 65$). It is important to note that oligoastrocytoma is extremely rare after the 2016 classification and thus this prevalence rate may now vary. Other rare tumors reported were gliosarcoma (2.6%), anaplastic ependymoma (2.3%), pilomyxoid astrocytoma (0.3%), subependymoma (0.3%), glioblastoma cerebri (0.1%), giant cell glioblastoma (0.3%), ependymoma (0.3%), and angiocentric glioma (0.1%).

When we analyzed our data, according to WHO 2007 grading of glioma, we found that 7.1% belong to WHO grade I, 32.7% belong to grade II, 15.4% belong to grade III, and 44.8% belong to grade IV. On comparing the distribution of WHO grade among different age groups, we found a significant difference ($p < 0.001$) [using chi-square test] suggesting that grade IV tumors are common at late age groups (more than 50 years) (Fig. 1). Seventy-six percent of patients with age more than 50 years had their histopathology being WHO grade IV, with mean age of patients with histopathology being glioblastoma was 48.6 years (Fig. 2). 41.7% of patients ($n = 91$) and 28% of patients ($n = 61$), below 18 years, belong to WHO grades II and I subsequently. Similarly, 39.3% of patients ($n = 316$) and 37.4% of patients ($n = 301$), between age 19 and 50 years, belong to WHO grades II and IV. The distribution of WHO grade among males and female genders was similar throughout the population ($p = 0.66$) with 45.5% of the male population and 43.2% of females having WHO grade IV histopathology as the most common grade.

On analyzing the number of cases operated each year, we found that there were exponential increases in cases. There was a steep rise in the referral of patients from 2007 to 2011 where 58.3% ($n = 846$) patients of glioma were referred. In the last 4 years, the referral pattern was persistent to high with 36.9% ($n = 537$) patients. The pattern of referral suggests an increasing prevalence of glioma patients in the last 12 years (Fig. 3).

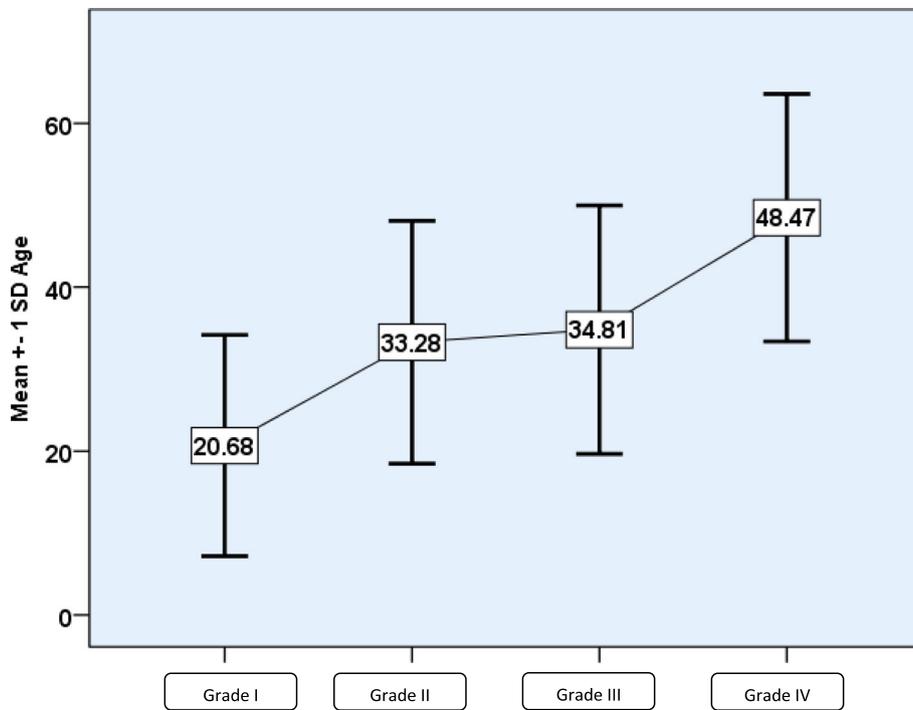


Fig. 1 Relation of WHO grade of tumors with age of patients in our study. The higher grade tumors presented at elder age (mean 48.47) as compared to low grade tumors (who presented at mean age of 20.68)

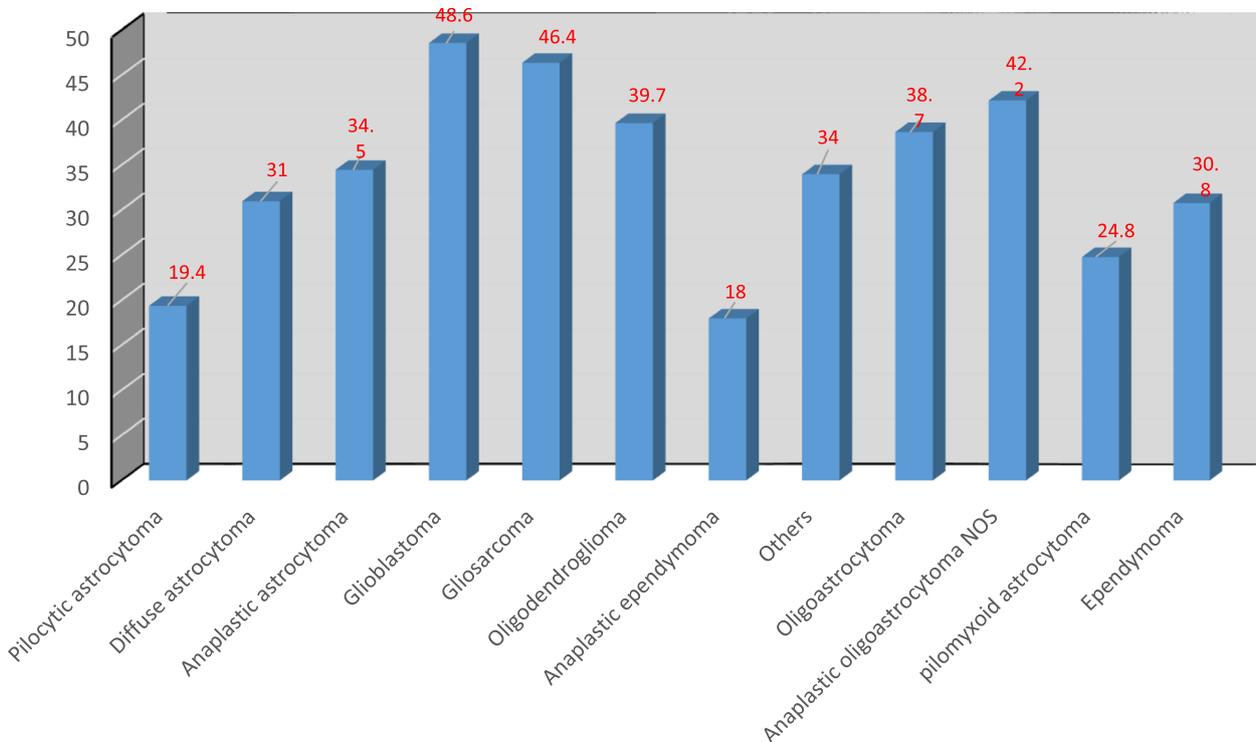
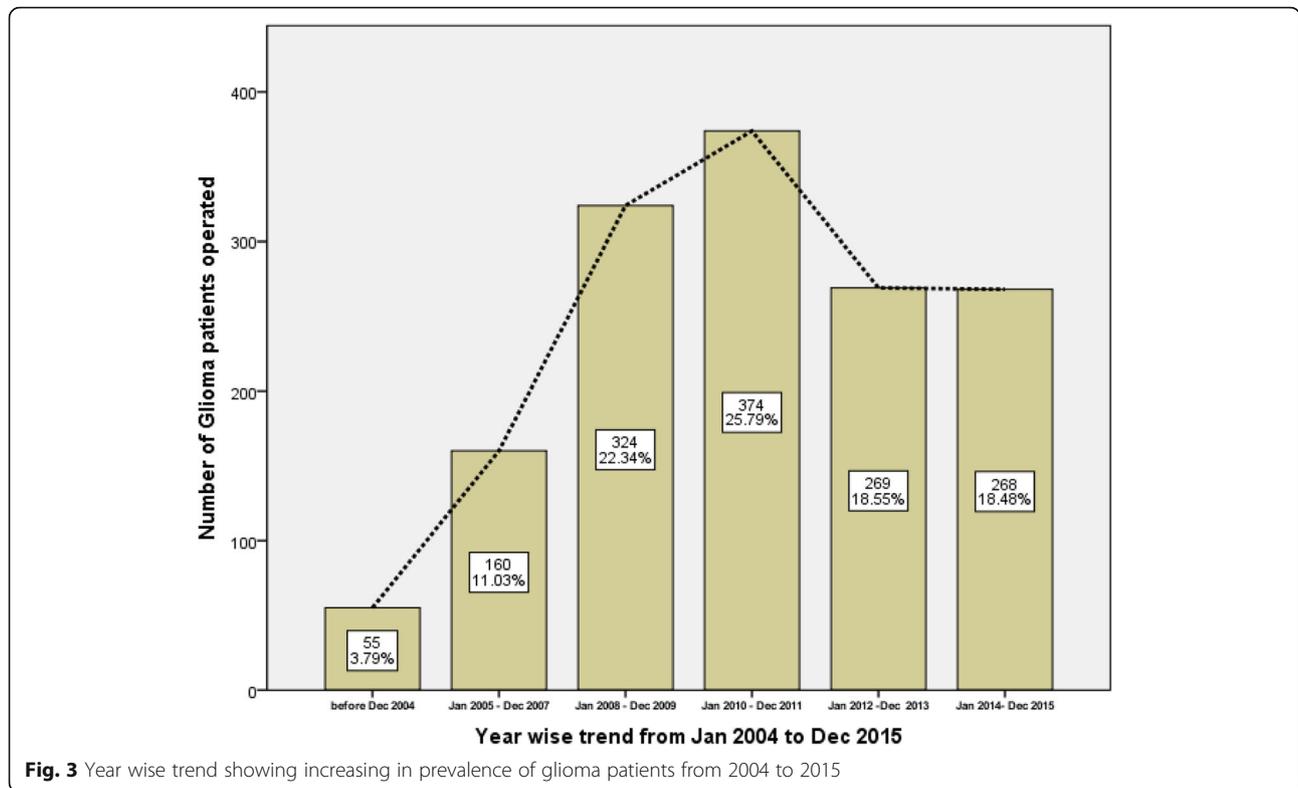


Fig. 2 Bar showing mean age of patients with various histopathologies in our study



Frontal lobe was the most common site in our series with 29% of cases ($n = 421$). The next common sites were temporal lobe (13.6%) and cerebellar hemisphere (8.6%). Other sites were parietal lobe (7.5%), ventricular ($n = 60$), thalamic ($n = 32$), spinal ($n = 64$), optichypothalamic ($n = 44$), brainstem ($n = 27$), corpus callosum ($n = 27$), perisylvian ($n = 38$), and insular ($n = 18$). When we observed the histopathological distribution of cases in our series we found that glioblastoma was

commonly found in frontal and temporal lobe whereas diffuse astrocytoma was commonly found in frontal lobe and cerebellar regions. Pilocytic astrocytoma was common in the cerebellar and suprasellar regions. Anaplastic astrocytoma (WHO grade III) and anaplastic oligodendroglioma were also common in frontal lobes (Table 1). Most common histopathology in thalamic, ventricular, insular, hypothalamus, and brainstem region was diffuse astrocytoma whereas the most common

Table 1 Histopathological wise distribution of age and gender in our study ($n = 1450$)

Histopathology	n	%	Mean age	SD	R	Male %	Preferred location	Age group			
								0-20	21-40	41-60	Above 61
Pilocytic astrocytoma	92	6.3	19.4	12.2	3-74	70.3	Cerebellum	61	24	6	1
Diffuse astrocytoma	331	22.8	30.9	15.2	2-80	70.5	Frontal	93	151	76	11
Anaplastic astrocytoma	102	7.0	34.5	14.1	6-34	73.0	Frontal	20	47	32	3
Glioblastoma	601	41.4	48.5	15.1	7-85	71.6	Frontal	28	150	297	128
Gliosarcoma	38	2.6	46.4	14.8	15-71	72.2	Temporal	3	9	20	6
Oligodendroglioma	65	4.5	39.7	10.9	10-61	63.5	Frontal	4	31	29	1
Anaplastic Ependymoma	33	2.3	18.0	11.3	5-48	67.7	Intraventricular	23	8	2	0
Oligoastrocytoma	69	4.7	38.6	12.5	2-58	74.6	Frontal	5	32	32	0
Pilomyxoid astrocytoma	9	0.6	24.7	18.7	5-54	77.8	Ventricle	4	3	2	0
Anaplastic NOS	86	5.9	42.2	12.4	8-72	62.8	Frontal	4	36	41	5
Ependymoma	5	0.3	30.8	20.4	8-56	100	Frontal	2	1	2	0
Others	19	1.3	34.0	20.0	6-75	-	-	-	-	-	-

n number of patients, % percentage, SD standard deviation, R range

histopathology in the suprasellar region was a pilocytic astrocytoma.

Discussion

The glial tumors of the central nervous system have overall poor survival with high morbidity. There are acceptable cancer registry systems like the CBTRUS (Central Brain Tumor Registry of the United States) in developing countries, where adequate government funds are available; but there is no such database in developing countries. In a developing country, where an economical fund is lacking and educational level is low, the population-based registry system is difficult to establish. Additionally, the previous series provide descriptive data of all brain tumors. A focused study, with large sample size, provides a better trend of such fatal disease. Gousias et al. studied the prevalence of glioma in the south European region and found that the age of presentation was comparatively higher [4]. Environmental and racial factors may influence the pattern of glioma. In our study, we have tried to incorporate similar studies from other neurosurgical centers of southeast Asian subcontinent regions (SEAR) from also. Reasons for non-adoption of a registry-based system may include poor referral or improper/non-existent surveillance system. Our data comprises all glioma patients; still, those patients who got primary radiotherapy were excluded. Our institute is one of the largest referral centers; therefore, our study largely reflects a proportionate prevalence to projected population.

Other similar studies from SEAR show meningioma being common in females and glioma common in males. Similar studies show male preponderance in glioma patients. In a similar Indian study by Jaiswal J et al. ($n = 4295$) and Tambi et al. ($n = 510$), who included all the patients of primary intracranial tumors, found the fourth decade, as the most common age group [1, 5]. The grade IV tumors, glioblastoma, were more prevalent in older age groups. There was a significant difference ($p < 0.05$) among the distribution of grades and age of patients in our study. The average age in our study is a decade younger to what is quoted in western literature (CBTRUS) and other Indian studies [6]. The results show more propensity of glioma among the younger population. Such trends of early onset of disease are coming forward for other cancers also and young patients with malignant disease are increasing throughout the world. A comparative WHO grade wise analyses would provide better results. This tendency might be because of better diagnostic armamentarium.

Among the pediatric population, pilocytic astrocytoma was the most common. We did not include medulloblastoma in our series. The study from Jaiswal J et al., including all CNS tumors, found that astrocytomas (25.1%),

followed by embryonal (20.6%) and ependymal tumors (14.8%), are commonly found at pediatric age group [1].

In our study, 7.1% belong to WHO grade I, 32.7% belong to grade II, 15.4% belong to grade III, and 44.8% belong to grade IV. The distribution showed slightly different result compared to previous data where 36.3% tumors in the registry were classified as WHO grade I, 11.4% as grade II, 20% as grade III, and 18.9% as grade IV tumors. But those studies included benign tumors also.

When we compared year-wise cases operated, we found an exponential increase in the second half of the timeline. This may be due to awareness and bed availability in formative years of institute. As the hospital grew, case turnover and referral increased simultaneously. Results from Ahsan J et al. and Thambi R et al. also noticed similar fact with a year-wise distribution of cases showing an increase in a number of cases. Chen L et al. found that growth rate had reached 106 to 139% in the three most recent years of his study [7].

Glioblastoma followed by diffuse astrocytoma was the most common histopathology in our study. Other studies from India also found glioblastomas as the most common tumor (38%) but followed by anaplastic oligodendrogliomas (24.5%) as second most common. We had lesser number of anaplastic oligodendrogliomas cases (5.6%) as compared to previous data. The study from south India showed glioblastoma NOS-grade IV was the most common histological subtype (58.5%) followed by diffuse astrocytoma NOS, grade II (26.9%). A similar study by Manoharan et al., including 1989 cases, found 21.5% glioblastoma [8]. A study by Nibhoria S et al., including 100 cases, showed the most common tumor being anaplastic astrocytoma and glioblastoma as the second common, but sample size limits their substantiality [9]. The difference maybe because of a variable number of "older age group" patients in each study. The spectrum of patients in our study was almost similar distributed throughout all age groups. According to the CBTRUS data, glioblastoma (17.7%) and anaplastic astrocytoma (2.1%) were the most common malignant tumors in adults [6]. The most common site affected was frontal lobe followed by temporal lobe, which was in accordance with other studies also [1, 6, 10–16]. We had a wider spectrum of cases including thalamic tumors, ventricular, and opticohypothalamic tumors. Rare gliomas including angiocentric glioma, giant cell glioblastoma, gliosarcoma, and desmoplastic ganglioglioma had a higher prevalence compared to previously reported.

Limitation of our study

Our study is a single institutional study, including only operated cases excluding patients who underwent up-front radiotherapy. In the initial formative years of the

Table 2 Distribution of glioma in rural/urban areas of India on basis of histopathology

Series	Pilocytic Ast	Diffuse Ast	Anaplastic Ast	OGD	Mixed Ast	Glioblastoma	Neuroblastoma	Epd	Anaplastic Epd	Lymphoma	NST	Unspecified
Urban												
Manoharan N (Delhi)	411/1989		83/1989		505/1989	428/1989	31/1989	43/1989		12/1989	18/1989	332/1989
Jalali R (Mumbai)	36/656	48/656	49/656	19/656	19/656	102/656	60/656	46/656		NR	-	23/656
Narmadha R (Chennai)	158/890			40/890	-	163/890	16/890	42/890		9/890	103/890	-
Mondal S (Kolkata)	54/130			11/130	-	-	7/130	5/130		1/130	9/130	-
Rural												
Ghangoria S (Indore)	16/65			NR	-	-	NR	5/65		NR	5/65	-
Thambi R (Kottayam)	128/510			2/510	12/510	NR	NR	7/510		5/510	71/510	-
Jaiswal J (Bangalore)	235/1800	23/1800	128/1800	53/1800	57/1800	598/1800	NR	201/1800		NR	NR	-
Chawala N [§] (Rohtak)	43/77			0	-	-		3/77				
Present study	92/1450	325/1450	99/1450	65/1450	69/1450	600/1450	NR	10/1450	33/1450	-	-	-

^{**}In the study from Jaiswal J, from Bangalore, they separately mentioned anaplastic OGD, anaplastic oligoastrocytoma, and anaplastic astrocytoma, with a separate mention of oligoastrocytoma. Some other studies considered them as mixed glioma or unspecified. So, this part was confusing and a prospective study with WHO 2016 classification may better provide exact prevalence

[§]Chawala n et al. quoted 44.18% were grade II while grade III and grade IV constituted 20.9% in their study. The distribution was different as grade IV glioma in other studies were predominant

institute, the data do not represent the population so may represent disproportionate results. Our hospital is a government institution, deals mainly the lower socioeconomic class in the society, limiting the number of cases included. A multi-centric population-based study or CBTRUS like recording system would be more substantial. We did not study the etiological associations in our patients; Gousias et al. found a positive association between the risk of glioma and a history of traumatic brain injury, while no significant association was found for alcohol consumption, smoking and use of mobile phones [4]. Another limitation in our study is the 'referral bias'. The average age in our study is a decade younger than that reported in the western literature. Moreover, contrary to the western literature, wherein, the low-grade tumors (grade I or II) are known to be more prevalent in younger age groups, these tumors comprise 39.8% of the present study vs. 47.7% in the literature. In this study, we used WHO 2007 classification as this is a retrospective study and the cases enrolled are of the period when WHO 2016 classification was not available.

Need for "National glioma or Brain Tumor Registry (BTR) and tumor bank

The referral pattern in India is such that, even government hospitals of urban area, get patients from rural nearby rural regions. So the data, although, published from an urban region, might represent a subgroup of rural patients (Table 2). A better way is to include patients from private/corporate hospitals also. This problem represents an unmet need of national cancer registry for the country. Since most studies have reported only operated cases this skews the data tremendously. Again, Jaiswal J et al. separately mentioned anaplastic oligodendroglioma, anaplastic oligoastrocytoma, and anaplastic astrocytoma [1] with a separate mention of oligoastrocytoma. Some other studies considered them as mixed glioma or unspecified. Hence, a uniform reporting system with a single classification system followed is urgently needed to avoid this confusion. Perhaps, the WHO 2016 has solved this for us by deciding the grade as per the immune-histochemistry (IHC) rather than just by the morphology. Then again, there is the issue of availability. Even at our center, IHC markers are difficult to acquire for each case due to monetary constraints or availability. The problem becomes worse for brain stem gliomas as there are not enough tissue samples even for research purposes [12]. Stereotactic biopsy of these cases at the minimum may be a solution to the immediate problem before any long-term solution is found. Using IHC markers in all cases, even biopsies and ensuring that every case is added to a central registry from each center even if un-operated, is a plausible answer. It is advisable to maintain an institutional/

departmental tumor bank, wherein, all tumor tissues should be stored for any future research.

Conclusion

Our study in single institutional retrospectively analyzed large-scale descriptive database, focusing on glioma, rather on the complete spectrum of brain tumors, which models population-based prevalence from northern India. Glioblastoma being the most common, with the maximum propensity of glioma in the third and fourth decades. The study also highlights increasing tumor burden in developing country since the last decade with the trend of early age presentation.

Abbreviations

CNS: Central nervous system; WHO: World Health Organization

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Authors' contributions

SS, SJ, and HD helped in the conception and design. SS and HD drafted the manuscript. AN, KKD, AM, AKS, SB, SJ, and AKJ critically revised the manuscript. All authors reviewed the final version of the manuscript and approved for submission.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due [not applicable] but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Individual written consent of patients was taken for the use of clinical data for publication as per our departmental protocol. Sanjay Gandhi Post Graduate Institute of Medical Sciences Institute Ethical Clearance (IEC 2012-168-MD-EXP17) has been taken.

Consent for publication

The inform consent was taken from all the patients for publication (as per our department policy we take such consent from all the patients at time of admission).

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Neurosurgery, All India Institute of Medical Sciences, Raebareilly, UP, India. ²Department of Neurosurgery, National Institute of Mental Health and Neurosciences, Bangalore, India. ³Department of Pathology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, UP 226014, India. ⁴Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, UP 226014, India.

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