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Original Article

Clinico-demographic Profile of Malignant Gliomas at a Tertiary Cancer Centre

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Abstract

Background: Gliomas have traditionally been classified as astrocytic, oligodendroglial, oligoastrocytic (mixed), or ependymal tumors based on light microscopic features as defined in the World Health Organization (WHO) classification of the central nervous system tumors of 2007. The WHO additionally assigns each tumor a histologic grade, ranging from WHO Grade I to WHO Grade IV, reflecting the range from low to high grade of malignancy. Historically gliomas have been shown to be associated with certain risk factors. There are analyses correlating these factors with race/ethnic group, gender, age, life style, and dietary habits in adult gliomas and various subtypes of gliomas.

Aims and Objectives: The aim of the study was to analyze the clinicodemographic profile of gliomas at a tertiary care center.

Materials and Methods: Clinical profile of thirty patients was analyzed in the years 2018–2020 with respect to various demographic parameters.

Results: Male gender and advancing age seem to be risk factors associated with glioma incidence.

Conclusion: We have concluded that advancing age and female gender are two important determinants which are effecting the clinic-demographic outcome. For other parameters we need large cohort of patients.

Key words: Malignant Gliomas, Clinico-Demographic Profile, Outcome

INTRODUCTION

Gliomas are neuroepithelial tumors originating from the supporting glial cells of the central nervous system (CNS). They range in behavior from benign low-grade gliomas (LGGs), amenable to resection or observation, to aggressive histologies such as diffuse intrinsic pontine gliomas and supratentorial glioblastomas (GBMs) with nearly uniform poor prognoses despite aggressive therapy. They account for 29–35% of the CNS tumors in adolescents and young adults (AYA), with approximately two-thirds being LGG and the remaining being high-grade glioma (HGG).[1] Neoplasms of the CNS are the most frequently encountered solid tumors of childhood, but are less common in AYA.

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NCCN categorizes gliomas on the basis of the World Health Organizations (WHOs) morphologic classification as Grade I - Pilocytic astrocytoma, pleomorphic xanthoastrocytoma (PXA), ganglioglioma, and suependymal giant cell astrocytoma, Grade IIb- diffuse astrocytoma, and oligodendroglioma, Grade III - Anaplastic astrocytoma and oligodendroglioma, and Grade IV - GBM.

Incidence of gliomas varies across all age groups. Their types and grades are predominant in specific age groups with certain grades predominant in particular age groups. Pilocytic astrocytoma occurs mostly in children and young adults under age 20.[2] Likewise PXA is a rare brain tumor, most commonly affecting children and young adults.[3] Diffuse astrocytomas and oligodendrogliomas represent the third most common type of glioma, comprising 4–15% of all gliomas and can be classified by degree of malignancy into Grade II and Grade III, according to the WHO classification. These are seen mostly in young and middle aged adults.[4] GBM multiforme, which is the most common malignant tumor of the CNS considering all ages, accounts for nearly 50% of all primary malignant CNS

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tumors. The average age at diagnoses has been reported to be sixth or seventh decade of life.[5]

In a Danish national population based analysis the male: Female ratio did not differ significantly between various grades of gliomas[6] whereas in another analysis on gliomas patients across all age groups, the population comprised 58.3% male patients and 41.7% female patients. The ratio of males to females was 1.4:1.[5]

Genetic factors that contribute to glioma etiology are poorly understood[7] however segregation analyses and other genetic models suggest that inherited factors may contribute to 5–12% of all brain/CNS cancers.[8] Cancers other than glioma in family members also may be related to glioma risk and usually are not taken into account in heritability estimates. Risk of glioma has been somewhat elevated among adults who report a relative with a cancer of the brain/nervous system.[8]

Although cigarette smoking and alcohol drinking increase the risk of several cancers and certain components of cigarette smoke and alcohol can penetrate the blood-brain barrier, it remains unclear whether these exposures influence the risk of glioma.[9] A Japanese analysis found a significant inverse association between coffee consumption and brain tumor risk in subjects who consumed ≥3 cups/day. No association was seen between green tea and brain tumor risk suggesting that coffee consumption might reduce the risk of brain tumor, including that of glioma, in the Japanese population.[10]

This study suggests that there is no association between meat or iron intake and adult glioma.[11] A number of occupations and industries have been inconsistently associated with the risk of brain cancer. Among men, the industries and/or occupations that had a significantly increased risk for employment of more than 10 years included roofing, siding, and sheet metalworking; newspaper work; rubber and plastics products, particularly tires and inner tubes. Among women, significant excess risk was observed for occupations in agricultural services and farming, apparel and textile products, electrical and electronic equipment manufacturing, various retail sales, record-keeping, and restaurant service. Workers in industries with a potential for gasoline or motor exhaust exposures experienced a non-significant excess risk of brain glioma.[12]

Radiation-induced gliomas though relatively rare, are a well-characterized entity in the neuro-oncologic literature. Retrospective analyses in pediatric populations after therapeutic intracranial radiation have shown a clear increased risk in glioma incidence, that is both patient age- and radiation dose/volume-dependent. Data in adults are more limited but show heightened risk in certain groups exposed to radiation. In both populations, there is no evidence linking increased risk associated with routine exposure to diagnostic radiation.[13]

MATERIALS AND METHODS

This was a retrospective, analytical study conducted in the Departments of Radiotherapy GMC Srinagar, Jammu and Department of Neurosurgery Government Super Speciality Hospital, Jammu from January 2018 to December 2020. Data of each patient were collected from registration counter Radiotherapy department, SMHS Hospital and Medical Records Department Susper-Speciality Hospital Jammu. All patients who were enrolled for the analysis had histopathological documentation of a malignant brain tumor through either a decompressive surgery or a biopsy from the representative site. Data were then analyzed for clinico-demographic information such as age, gender, residence, dietary habits, tobacco consumption, alcohol intake, presenting symptoms, and signs. These parameters were then correlated with each other. Histological grading was done as per the WHO grading system. Grading was done on morphological basis only. Genetic analysis was not done as many patients had declined the proposal due to financial implications associated with the test.

RESULTS

This study included 30 patients who had histologically proven malignant glioma.

Patients were evaluated for headache, vomiting, and seizures which were the most common modes of presentation, seen in more than 80% of the patients. Computed tomography brain was the first investigation carried out, coupled later with contrast enhanced magnetic resonance imaging (MRI) brain for the suspected cases. Fronto-parietal was the most common location of the tumor seen in nearly 50% patients. Of 30 patients analyzed 24 were subjected to decompressive surgery or subtotal resection, whereas in five only biopsy could be taken and one patient was treated on the basis of radiological features, in view of high operative risk due to eloquent site of the lesion. Post-operative period was uneventful in 24 of the thirty patients (80%). In six patients, there were minor post-operative complications which were addressed conservatively. Majority (>70%) of the patients (22 of 30) had HGGs (the WHO Grade III or IV) and warranted some kind of adjuvant treatment (Radiation therapy/Chemotherapy) for which patient was referred to radiation oncology department. Patients were followed up at 6 months whence 18 patients reported improvement in clinical condition while as six patients still had intermittent presenting symptoms. Four patients had deteriorated at 6 months and two patients were reported to have died [Table 1].

Male to female ratio was 2:1 [Table 2]. The age distribution varied from 18 to 76 years with the youngest patient being a female one. The age and gender distribution is shown in Table 2. Majority of the patients were more than 40 years of age (60%). Age group <40 years constituted 40% of patients of which 10% were males. Moreover, majority of the females were in the age group of >60 years. Family history was not significant; only three patients had family history of brain tumor. Only eight patients had history of tobacco consumption and all patients were of same ethnic background. Majority of patients were of rural background (80%). None of the patients had any history of radiation exposure in the past or in the near past. Only five patients were strict vegetarian and the rest were Mixetarian. Over 30% of the patients had some sort of medical comorbidity.

DISCUSSION

Gliomas account for 24% of brain tumors in adults and as a group are the second most common brain tumors in adults.[14] GBM is the second most frequently reported primary intra-cranial tumor and the most common malignant tumor of the CNS when considering all ages. GBM accounts for 15.4% of all primary brain tumors and 45.6% of primary malignant brain tumors. This disease is less common in children, comprising ~2.9% of all brain and CNS tumors reported among 0–19 year olds, and 3.2% of all brain and CNS tumors reported among 15–19 year olds.[14] Our analysis showed similar results with respect to the age of patients. Most of the gliomas were of high grade and that too were seen in patients more than 40 years of age.

Various international studies have analyzed variations in the incidence of adult primary brain cancers with respect to various demographic parameters. While as white populations in the west have been shown to have highest incidence rates, the southeast Asian populace have been shown to have lowest incidence rates.[15] All our patients were of a single ethnic and racial background.

Our study did not show any familial aggregation of brain tumors or history of any brain tumors. Although, its deliberate that cancers other than glioma in family members also may be related to glioma risk our analysis did not take into account any heritability risk estimates (genetic analysis).

Table 1: Clinical parameters of all the thirty patients

S No	Clinical parameters	%
1.	Presentation	
	Headache=30	100
	Vomiting=26	86
	Seizures=24	80
2.	Tumor location by MRI	
	Fronto-parietal=14	46.6
	Temporal=08	26.6
	Frontal=06	20
	Parietal=02	06
	Occipital=0	0
3.	Surgical intervention	
	Decompression=24	80
	Biopsy=05	16
	No intervention=01	3
4.	Tumor grade	
	WHO Gr I=04	13.3
	WHO GrII=04	13.3
	WHO GrIII=06	20
	WHO GrIV=16	53.3
5.	Post op complication (s)	
	Yes=06	20
	No=24	80
6.	Adjuvant treatment	
	Radiotherapy=24	80
	Chemotherapy(oral)=24	80
	Chemo.+ RT=24	80
	None=06	20
7.	Outcome at 6 months	
	Improved=18	60
	Same=06	20
	Deteriorated=04	13.3
	Death=02	6

Table 2: Demographic parameters

S. No.	Demographic parameters	%
1	Gender	
	Males=20	66.6
	Females=10	33.3
2	Age	
	>40=18	60
	<40=12	40
3	Family history	
	Yes=03	10
	No=27	90
4	Tobacco	
	Yes=08	26.6
	No=22	73.3
5	Residence	
	Rural=24	80
	Urban=06	20
6	Radiation exposure	
	Yes=0	0
	No=30	100
7	Diet	
	Veg=05	16.6
	Non Veg=25	83.3
8	Occupation	
	House wife=08	26
	Farmer=06	20
	Private job=04	13
	School teacher=04	13
	Mechanic=04	13
	Mason=02	6
	Government servant=02	6

Risk of glioma has been seen to be elevated among adults who report a relative with a cancer of the brain/nervous system.[8] In an analysis carried out by SEER to assess the age standardized and relative risk variation by race/ethnic groups in HGGs, it was found that rates varied about three-to-four-fold, with the highest rates among non-Hispanic Caucasians, followed by Hispanic Caucasians, Africans, Asian/Pacific Islanders, and American Indians/Alaskan Natives. As with GBM, rates for non-GBM were highest among non-Hispanic Whites, followed by Hispanic Whites, with rates among Blacks, Asian/Pacific Islanders, and American Indians/Alaskan Natives each about 40% of the rates among non-Hispanic Whites.[15] All of our patients belonged to same ethnic background.

Males have been seen to have higher incidence rate than females for any race/ethnic group. Although this difference is limited to incidence and outcome, little is known about sex differences in GBM at the disease phenotype and genetical/molecular level.[16] Our study too revealed a male preponderance in the ratio of 2:1. However, another analysis by Birthe Krogh Rasmussen did not show any significant gender difference.[6]

Association of diet with gliomas is not well established. Data from three large prospective trials have not shown any significant association of pattern of diet with incidence of brain tumors.[17] Our analysis was primarily based on vegetarian or non-veg habits. Non-veg patients outnumbered as majority of the population is assumed to be non-vegetarian. Occupation and glioma risk have been reported in the literature. In a study conducted by Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas, increased incidence of gliomas was seen in populations associated with specific works such as painters, petroleum and gas workers, aircraft and motor vehicle operators, and textile workers. White collar jobs too have been seen to have association with various gliomas.[18]

Our study cohort was less in number so any significant association could not be inferred. Of the thirty patients occupation, glioma distribution was more or less equal and none had a high risk occupation except four mechanics involved in vehicle repair as shown in Table 2.

Retrospective data in pediatric populations have shown a clearly increased risk in glioma after therapeutic intracranial radiation incidence that is both patient age- and radiation dose/volume-dependent. Data in adults are more limited but show heightened risk in certain groups exposed to radiation.[13]

Moreover, there is no evidence linking increased risk associated with routine exposure to diagnostic radiation. None of the patients in our study had history of any radiation exposure, either accidental or therapeutic. The association between cigarette smoking or tobacco consumption and the risk of developing malignant glioma remains unclear. Various analyses have shown mixed results as far as tobacco as incriminating agent in glioma is concerned. The role of cigarette smoking and the risk of glioma studied in three large prospective studies of men and women with detailed and updated smoking information, with over 350 glioma cases, and 26 years of follow-up suggested no additional risk of association by any of the exposures evaluated.[19] However, in yet another analysis from the Korean National Health Insurance System cohort, 9,811,768 people over 20 years old without any cancer history in 2009 were followed until the end of 2017. They documented 6100 malignancy glioma cases during follow-up period of over 7 years. Current smokers were found to have a higher risk of developing malignant glioma (hazard ratio [HR] = 1.22, confidence interval [CI]: 1.13–1.32) compared with never-smokers, after adjusting for confounders. This association was stronger for those who smoked ≥20 cigarettes daily (HR = 1.50, CI: 1.36–1.64). Furthermore, having 30 or more pack-years of smoking over the course of one's lifetime was associated with an increased risk of developing MG in a dose-dependent manner. Paradoxically our study shows over 70% of patients being never smokers. This in part might be due to less powered study due to less number of patients.

In west the incidence of glioma has been seen to be high in societies with high socioeconomic status (SES) as compared with low SES. These differences are more pronounced among white non-Hispanic individuals and white Hispanic individuals residing in urban areas.[20]

Moreover, better survival was observed in high SES counties, even when adjusting for extent of surgical resection, and when restricted to those who received radiation and chemotherapy for GBM. Differences in incidence and survival were associated with SES and race, rather than rural versus urban status. Our study had more patients from rural population. To the best of our knowledge, no randomized analysis has been done in India comparing incidence of gliomas in rural versus urban population. They are indirect extrapolation of high socioeconomic status assumed to be prevalent in urban population.

CONCLUSION

Male gender and advancing age seem to be the only determinants affecting incidence of gliomas in our study.

Our analysis was limited by the small cohort of patients, indirectly affecting statistical inference for any demographic or clinical parameter.

AUTHORS DECLARATION

Genetic analysis of gliomas was not done due to financial constraints.

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