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Research Paper

Histopathological Spectrum Analysis of Central Nervous System Tumours - A 5-Year Study

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ABSTRACT
Introduction: *Central Nervous System (CNS) tumours present a global challenge with consistent incidence patterns. This study delves into the histopathological spectrum of CNS tumours, exploring their prevalence, demographic variations, and diagnostic challenges.*
Methodology: *This retrospective and prospective study included 587 cases of all ages with clinical diagnoses of CNS tumours, supported by imaging and histopathological findings. Diagnoses adhered to the revised WHO classification. Standardized processing and grading using Hematoxylin and Eosin stain ensured methodological robustness. Data were recorded and analysed statistically.*
Results: *The study revealed a mean patient age of 33.00±18.00 years, with a predominant representation in the 21-40 years age group. Males constituted 54.51% of cases. Headache emerged as the dominant clinical feature (83.4%), while post fossa sol was the most commonly affected site (25.56%). Astrocytic tumours dominated (42.90%), with Glioblastoma Multiforme as the most frequent histopathological diagnosis (18.56%). Grading demonstrated 47.87% in Grade-I and 29.47% in Grade-IV. Correlation analyses revealed an intriguing correlation between grading and radiological/tumour features. Astrocytic tumours were more prevalent in males, while meningeal tumours favoured females. High-grade tumours were significantly associated with age and shorter durations.*
Conclusion: *These findings contribute valuable insights into the clinicopathological characteristics of CNS tumours, emphasizing the need for tailored approaches in their diagnosis and management.*
Keywords: *CNS tumours, histopathology, WHO grading, High-grade tumours, Astrocytic tumour.*

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I. INTRODUCTION

Central Nervous System (CNS) tumours, constituting 1%-2% of adult tumours worldwide (approximately 257,000 cases annually), exhibit consistent incidence across regions and populations [1]. Predominant types include glial neoplasms, meningiomas, and metastases, necessitating varied trends in incidence based on histology, gender, and age. Despite lower incidence in underdeveloped countries, CNS tumours encompass a diverse range affecting the brain and spinal cord, meninges, pituitary and pineal glands, and nerves. Around 100 histopathological variants represent less than 2% of all tumours [1, 2]. Incidence increases with age, with a bimodal onset, peaking in childhood and the 40–70-year-old range [3]. Supratentorial tumours, primarily in the frontal, temporal, and parietal lobes, prevail in adults, with a higher incidence in males, except in meningiomas where females predominate [1,4]. Diagnostic tools, including Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), aid neurosurgeons in surgical planning, supported by stereotactic biopsies and intraoperative squash smears [5]. Despite their rarity, CNS tumours exhibit poor survival compared to other cancers. In adults, common CNS tumours encompass metastasis, glial neoplasms, and meningiomas [6]. The worldwide incidence of brain tumours is estimated at approximately 3.9 per million males and 3.0 per million females annually, with variations in South Central Asia [5,7]. Current trends in industrialized countries indicate a drop in low-grade tumours and an increase in high-grade tumours, while factors like certain jobs, diet, and chemical exposure are associated with elevated CNS neoplasm incidence [7,8]. While primary CNS tumours are uncommon, they rank as the second most prevalent malignancy in children, constituting less than 2% of all malignant neoplasms [8]. WHO classifies these tumours histologically, emphasizing molecular diagnosis for future diagnostic frameworks [8]. The new WHO classification prioritizes

molecular genetics, but histomorphology remains crucial for initial diagnosis, emphasizing the preparatory nature of histological studies corroborated by immunohistochemistry [9]. Understanding CNS tumour epidemiology is crucial for early detection and treatment, given their characteristic clinical presentation involving headaches, vomiting, and seizures [10,11]. Despite initial perceptions of rarity in India, advances in neuroimaging have revealed the prevalence of brain tumours in line with global patterns [11,12]. The basic aim of our study was to analyze the histopathological spectrum and frequency of CNS tumours in the tertiary care centre.

II. MATERIAL AND METHODS

This study was conducted collaboratively by the Department of Pathology and the Department of Neurosurgery at King George's Medical University, Lucknow, and encompassed both retrospective (2017-2019) and prospective (2019-2021) evaluations. Ethical clearance and informed consent were diligently secured before collecting demographic and clinical variables via a personal information form. A total of 587 cases of CNS tumours were retrieved from the Department of Pathology archives, following inclusive criteria for patients of all ages with clinical diagnoses of CNS tumours, supported by imaging and histopathological examination findings indicative of malignancy. Exclusion criteria comprised autolyzed/poor morphology biopsy tissue and non-consented patient cases. Diagnoses were meticulously established through histological examination, aligning with the revised WHO classification. The study adopted a case-control design, where the cases of CNS tumours served as the case group, while autopsy specimens and histomorphologically normal brain tissues acted as controls. encompassing various CNS tumour types such as mesenchymal-non meningothelial tumours, metastatic tumours, astrocytic tumours, choroid plexus tumours, embryonal tumours, ependymal tumours, neuronal tumours, oligodendroglial tumours, tumours of cranial and paraspinal nerves, tumours of the sellar region, tumours of meninges, vascular tumours, and lymphomas. Controls were autopsy specimens and histomorphologically normal brain tissues. Brain tumour processing adhered to standard protocols, with specimens meticulously examined and graded using Hematoxylin and Eosin stain (H&E). The histological types of CNS tumours were categorized into grades I, II, III, and IV, following World Health Organization guidelines. Grade I and II were classified as low-grade gliomas, while Grade III and IV were categorized as high-grade gliomas. This rigorous methodology ensures the credibility of the study's findings, providing valuable insights into the diverse spectrum of CNS tumours.

Statistical Analysis*:*

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for the Windows program (26.0 version). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency and were analyzed using Chi-square or Fisher Extract test. Analysis by Student t-test with 95% confidence interval was used to compare the means between the two groups. A p-value of < 0.05 or 0.001 was regarded as significant.

III. RESULTS

The study encompassed 587 cases with a mean patient age of 33.00±18.00 years. The majority fell within the 21-40 years age group (33.22%), followed closely by those aged 41-60 years (31.35%). Males constituted 54.51% of the cohort. The mean duration of symptoms was 13.09±19.19 months, with 64.39% presenting within 0-6 months. (Tab-1) Headache was the predominant clinical feature (83.4%), followed by vomiting and nausea (39.52%). (Fig-1) Post fossa sol was the most commonly affected site (25.56%). Astrocytic tumours were predominant (42.90%), with Glioblastoma Multiforme being the most frequent histopathological diagnosis (18.56%). (Tab-2) WHO Grading revealed 47.87% in Grade-I and 29.47% in Grade-IV. (Fig-2) Among astrocytic tumours, Grade-IV comprised 42.02%, most prevalent in the 21-40 age group (n=50) and a duration of 0-6 months (n=78). (Fig-3 and 4) Astrocytic tumours were more common in males, while meningeal tumours were more prevalent in females. (Fig-5a and b) Tumour types associated with duration; cranial and paraspinal nerve tumours had longer durations (12+ months), while embryonal tumours had shorter durations (0-6 months). (Tab-3) High-grade tumours numbered 212 and 375 were low-grade, with a significant association between age and grade ($p=0.0013$*). Most high- and low-grade cases presented within 0-6 months ($p<0.0001$*). (Tab-4) Grade-IV tumours were prominent in post fossa and frontal sol. (Fig-6) Correlation analyses showed negative associations between grading and radiological/tumour features and a positive correlation with histopathological diagnosis ($p<0.0001$*). (Tab-5) These findings contribute valuable insights into the demographic, clinical, and histopathological characteristics of CNS tumours, facilitating a comprehensive understanding for improved diagnostic and therapeutic strategies.

IV. DISCUSSION

In our study, the mean age of patients was 33.00±18.00. Most patients were 21-40 years old, constituting 33.22% of the total, followed closely by those aged 41-60 years at 31.35%. This distribution aligns with findings from Thambi R et al. [13] and other relevant studies. [14] Regarding gender distribution, our study included a higher percentage of male patients (54.51%) than females (45.49%). This male predominance is consistent with observations in other studies [14-17]. The mean duration of illness in our study was 13.09±19.19. A significant portion of patients (64.39%) reported symptoms duration of 0-6 months, followed by those with a duration of 12 months onwards (22.14%). [18] Common presenting symptoms included headache (83.4%), vomiting/nausea (39.52%) and weakness/ataxia/gait abnormality (18.05%), in line with observations from other studies. [17,19] Concerning the anatomical location of lesions, the preponderance of patients in our study exhibited afflictions in the post fossa region (n=150, 25.56%), followed by the frontal region (n=87, 14.82%) and the CP angle (n=69, 11.75%). While these findings align with reports from Rasschou-Nelsen et al. [20], it is noteworthy that some studies, such as those conducted by Vimal S et al. (2020) [21], presented divergent results. [13,16,21] During histopathological diagnosis in our study, most patients were diagnosed with Glioblastoma Multiforme (18.56%), an Astrocytic Tumour. This was followed by Meningioma (14.31%), Schwannoma (11.93%), a Tumour of Cranial and Paraspinal Nerves, and Medulloblastoma (5.45%), an Embryonal Tumour. These findings align with several previous studies. [15,17,22-24] However, it is noteworthy that other studies have reported meningioma as the predominant tumour [21,25]. According to the WHO grading system, among the 587 brain tumours in our study, the majority of patients were diagnosed with Grade-I tumours (n=281, 47.87%), followed by Grade-IV (n=173, 29.47%) and Grade-II (n=96, 16.35%). Notably, Grade-I brain tumours were the most common in our study, which is consistent with findings from Chawla N et al. and other relevant studies. [25-27] In our study, according to the WHO grading system, out of a total of 587 brain tumours, the majority of patients were diagnosed with Grade-I tumours (n=281, 47.87%), followed by Grade-IV (n=173, 29.47%), and Grade-II (n=96, 16.35%), respectively. Notably, Grade-I brain tumours were the most prevalent in our study, consistent with findings from Almutrafi A et al. and other researchers. [14,25,26,27] Specifically focusing on Astrocytic tumours in our study, the majority of patients were diagnosed with Grade-IV tumours (n=100, 42.02%), followed by Grade-I (n=61, 25.63%) and Grade-II (n=52, 21.85%). The distribution across grades also revealed that Grade IV patients aged 21-40 years were most common, followed by Grade IV patients aged 11-20 years and Grade I patients aged 11-20 years. These findings agree with the study by Thambi R et al., where most Astrocytic tumour patients were of Grade IV with a mean age of 55.5 years. [13] Similarly, Almutrafi A et al. reported that most Astrocytic tumour patients were of Grade IV with a mean age of 45.6 years, aligning with our study. [27] However, Manoharan N et al. found a peak in Grade IV patients aged 55-64 years, deviating from our results. [29] Examining the duration of symptoms, the majority of Grade IV patients (n=78) in our study had symptoms for 0-6 months, while Grade I patients (n=43) and Grade II patients (n=30) had symptoms for 12 months onwards. [30] Regarding anatomical location, most Astrocytic tumours (n=101) in our study were found in the frontal site, followed by Tumours of Cranial and Paraspinal Nerves (n=69) located at the CP angle region. These findings are consistent with Rani V et al., who reported 33.3% of Astrocytic tumours in the frontal lobe. [16] Chawla N et al. and other studies also reported similar results. [14,26] Additionally, among female patients in our study, the majority with brain tumours had Astrocytic Tumours (n=107, 18.23%), followed by Tumours of Meninges (n=54, 9.20%) and Tumours of Cranial and Paraspinal Nerves (n=44, 7.50%), respectively. [26,29] On the male patient side, the majority were diagnosed with Astrocytic Tumours (n=138, 23.51%), followed by Tumour of Cranial and Paraspinal Nerves (n=35, 5.96%) and Tumours of Meninges (n=30, 5.11%). These findings are in concordance with previous studies. [13,29,31] For patients with Tumours of Cranial and Paraspinal Nerves (n=70), the majority had a duration of 12 months onward, followed by Tumours of Meninges (n=70) with a duration of 6-12 months, and Embryonal Tumour (n=20) with a duration of 0-6 months, respectively. Notably, no relevant study on the duration of CNS tumour types was found in English literature based on our knowledge. In terms of age distribution among patients with High-grade CNS tumours in our study, the majority (n=75) fell within the 41-60 years age group, followed by those aged 21-40 years (n=65) and 0-10 years (n=35). This aligns with findings from Manoharan N et al., where most high-grade tumours were in the 55-64 age group, approximating our study. [29] Rani V et al. reported a concentration of high-grade tumours in the 41-50 years age group, which is also consistent with our findings. [16] Additionally, Kanthikar S et al. found a similar pattern with high-grade tumours in the 41-50 years age group. [31] In our study, the majority of low-grade tumour patients were in the 21-40 years age group (n=130), followed by those aged 41-60 years (n=109), and 11-20 years (n=73), respectively. A statistically significant difference was found between these age groups (P=0.0013*), a pattern consistent with findings from Mondal S et al., where low-grade tumours were predominant in the 21-40 years age group. [17] Similarly, Kanthikar S et al. observed that most low-grade tumours were found in the 21-40 years age group. [31] Regarding the duration of symptoms, our study revealed that high-grade tumours had a majority of cases with a duration of 0-6 months (n=193), followed by 7-12 months (n=15) and 12 months

onward (n=4), respectively. In contrast, the majority of low-grade tumour patients had a duration of 0-6 months (n=185), followed by 12 months onward (n=126), and 7-12 months (n=64), with a statistically significant difference between them (P=0.0001*). This suggests that high-grade tumours tend to have a shorter duration, less than six months, while low-grade tumours are associated with a longer duration, exceeding 12 months. This finding aligns with the study by Rasmussen B et al., where shorter durations were indicative of high-grade gliomas, while longer durations correlated with low-grade gliomas. [32] In terms of tumour location, the majority in our study were found at the post fossa (n=101) and frontal (n=47) regions, with Grade-IV tumours, followed by the CP angle region (n=60) with Grade-I tumours. [16,17] Examining age correlation within specific tumour types, the majority of Astrocytic tumours were found in patients between 41-60 years (n=77), followed by 21-40 years (n=76) and 11-20 years (n=42), respectively. Similarly, most Meninges Tumours occurred in patients between 41-60 years (n=47), followed by 21-40 years (n=34), and above 60 years (n=3). Tumours of Cranial and Paraspinal Nerves were prevalent in patients between 21-40 years (n=38), followed by 41-60 years (n=25), and 11-20 years (n=12). These findings align with the age distribution trends discussed earlier. Furthermore, in our study, the majority of Astrocytic tumours (42.93%) were followed by Tumours of Meninges (14.65%), Tumour of Cranial and Paraspinal Nerves (13.29%), and Tumours of Sellar Region (8.51%). Chen L et al. conducted a study supporting our research, reporting different CNS tumour categories and their frequencies. [33] Similarly, Ghanghoria S et al. found that meningioma was the most common lesion followed by astrocytoma in their study, providing additional support to our findings. [14]

V. CONCLUSION

The findings revealed a statistically significant correlation between Grading vs Radiological, Tumour and Histo-pathological diagnosis. The current study's findings corroborate with earlier research and add to the available information about CNS tumours and their histopathological examinations. Furthermore, the limited patient flow to our tertiary care centre during the COVID-19 pandemic constrained our study's design due to a small sample size. A larger, multicentric study with increased precision is recommended to enhance reliability. Generalizing our findings is challenging since results are confined to a single centre. Additionally, the scarcity of literature on histopathological analysis of CNS tumours and our limited experience posed difficulties in selecting an effective and safe protocol. Further research and collaboration are essential to address these challenges and broaden our understanding.

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TABLES AND FIGURES

TABLE-1: Clinico-demographic parameters of enrolled patients.

Clinico-demographics		Number	Percentage
Age (Years)	0-10	88	14.99%
	11-20	94	16.01%
	21-40	195	33.22%
	41-60	184	31.35%
	>60	105	17.89%
Gender	Female	267	45.49%
	Male	320	54.51%
Duration (months)	0-6	378	64.39%
	7-12	79	13.45%
	12 onwards	130	22.15%
Site	CP angle sol	69	11.75%
	Frontal sol	87	14.82%
	Frontotemporal region	23	3.91%
	Fronto-perital sol	30	5.11%
	Parital lobe	42	7.15%
	Parito-occipital region	26	4.42%
	Parito-temporal region	30	5.11%
	Temporal region	22	3.74%
	Sellar/suprsellar sol	47	8.0%
	Post fossa sol	150	25.56%
	Others		

	Ventricular sol	26	4.42%
	Spinal/vertebral level region	16	2.72%
	Thalamic sol	19	3.23%

TABLE-2: Histopathological diagnosis of enrolled patients

Types of Tumours	Histopathological Diagnosis	
	Number	Percentage
ASTROCYTIC TUMOUR	**252**	**42.90%**
SUBEPENDYMAL GIANT CELL ASTROCYTOMA	3	0.17%
ANAPLASTIC ASTROCYTOMA	21	1.36%
DIFFUSE ASTROCYTOMA	44	3.92%
GEMISTIOCYTIC ASTROCYTOMA	2	0.34%
OLIGOASTROCYTOMA	10	0.68%
GLIOBLASTOMA MULTIFORME	109	18.56%
PILOCYTIC ASTROCYTOMA	52	0.34%
PILOMYXOID ASTROCYTOMA	3	0.51%
PLEOMORPHIC XANTHOASTROCYTOMA	2	0.34%
GLIOSARCOMA	6	1.02%
CHOROID PLEXUS TUMOURS	**4**	**0.51%**
CHOROID PLEXUS CARCINOMA	1	0.17%
CHOROID PLEXUS PAPILLOMA	3	0.34%
EMBRYONAL TUMOUR	**38**	**5.96%**
MEDULLOBLASTOMA	38	5.45%
EPENDYMAL TUMOUR	**22**	**3.92%**
ANAPLASTIC EPENDYMOMA	3	0.51%
EPENDYMOMA	19	3.07%
MESENCHYMAL-NON MENINGOTHELIAL TUMOUR	**13**	**2.39%**
HEMANGIOBLSTOMA	13	2.21%
METASTATIC TUMOURS	**16**	**2.56%**
CARCINOSARCOMA	1	0.17%
METASTATIC ADENOCARCINOMA	4	0.51%
METASTATIC EPITHELIAL MALIGNANCY	2	0.34%
METASTATIC UNDIFFERENTIATED CARCINOMA	1	0.17%
METASTATIC MELANOMA	1	0.17%
ROUND CELL TUMOUR	3	0.51%
CHONDRO-SARCOMA	1	0.17%
SQUAMOUS CELL CARCINOMA(M.D.)	1	0.17%
GERM CELL TUMOUR	1	0.17%
MIXED GERM CELL TUMOUR	1	0.17%
NEURONAL TUMOUR	**2**	**0.34%**
CENTRAL NEUROCYTOMA	1	0.17%
GANGLIOGLIOMA	1	0.17%
OLIGODENDROGLIAL TUMOUR	**20**	**3.24%**
ANAPLASTIC OLIGODENDROGLIOMA	9	1.02%
OLIGODENDROGLIOMA	11	1.53%
LYMPHOMAS	**3**	**1.19%**
DIFFUSE-LARGE B-CELL LYMPHOMA	1	0.17%

PRIMARY CNS LYMPHOMA	1	0.17%
LARGE B-CELL LYMPHOMA	1	0.17%
TUMOUR OF CRANIAL AND PARASPINAL NERVES	**78**	**13.29%**
NEUROFIBROMA	4	0.68%
SCHWANOMMA	74	11.93%
TUMOURS OF MENINGES	**86**	**14.31%**
ANAPLASTIC MENINGIOMA	2	0.34%
ATYPICAL MENINGIOMA	9	1.53%
FIBROUS MENINGIOMA	4	0.68%
MENINGIOMA	23	3.24%
MENINGIOTHELIAL MENINGIOMA	32	5.45%
PSOMOMMATOUS MENINGIOMA	7	1.19%
SECRETORY MENINGIOMA	1	0.17%
TRANSITIONAL MENINGIOMA	8	1.36%
TUMOURS OF SELLAR REGION	**50**	**0.85%**
CRANIOPHARYNGIOMA	26	0.85%
PITUITARY ADENOMA	23	0.85%
PINEOCYTOMA	1	0.17%
VASCULAR TUMOURS	**3**	**0.51%**
CAVERNOUS HEMANGIOMA	1	0.17%
HEMANGIOMA	2	0.34%
Grand Total	**587**	**100.00%**

TABLE-3: Association of histopathological diagnosis with age in patients.

Parameters		**Types of Tumours**												
		AT	**CPT**	**EmT**	**ET**	**MNMT**	**OT**	**MT**	**TCPN**	**TSR**	**TM**	**L**	**VT**	**NT**
Age	0-10	41	1	22	10	3	2	3	2	3	2	1		
	11-20	42	1	8	2	3	2	2	12	12	2			
	21-40	76	2	7	7	3	8	5	38	14	34		1	1
	41-60	77		1	3	4	8	5	25	17	37	2	2	
	>60	16		1			1	1	2	1	3			1
Duration	0-6		2	20	12	9	5	6	3	4	10	1	1	2
	6-12		2	18	5	4	5	10	5	16	70	2	1	
	12 onwards						10		70	30	6		1	
Site	**CP angle sol**	10							69		12		1	
	Frontal	101			2		5	4		5	26	1		1
	Temporal	28			2		6		2		14			

	Parital	20			2		2		4		16	1		
	Sellar/suprsellar	18			2	1	2	6	2	45	8			
	Post fossa sol	61		30	18	2	1				2			
	Others	14	4	8	20	10	4	6	1	10	2	1	2	1

Astrocytic Tumour (AT), Choroid Plexus Tumours (CPT), Embryonal Tumour (EmT), Ependymal Tumour (ET), Mesenchymal-Non Meningiothelial Tumour (MNMT), Oligodendroglial Tumour (OT), Metastatic Tumours (MT), Tumour of Cranial and Paraspinal Nerves (TCPN), Tumour of Sellar Region (TSR), Tumours of Meninges (TM), Lymphomas (L), Vascular Tumours (VT), Neuronal Tumour (NT).

TABLE-4: Association of age and duration with WHO Grade of enrolled patients

Parameters		**High**	**Low**	**Grand Total**	**P-value**
Age	0 to 10	35	53	88	X=17.9 **P=0.0013***
	11 to 20	21	73	94	
	21 to 40	65	130	195	
	41 to 60	75	109	184	
	> 60	16	10	26	
Duration	0 to 6	193	185	378	X=108.1 **P<0.0001***
	7 to 12	15	64	79	
	12 onward	4	126	130	

TABLE-5: Spearman correlation analysis of grade and other parameters.

	Grading Vs Radiological Diagnosis	**Grading Vs Tumour**	**Grading Vs Histopathological Diagnosis**
Spearman r	-0.1848	-0.4311	0.4854
95% confidence interval	-0.264 to -0.103	-0.4967 to -0.3606	0.419 to 0.5466
P value	<0.0001	<0.0001	<0.0001

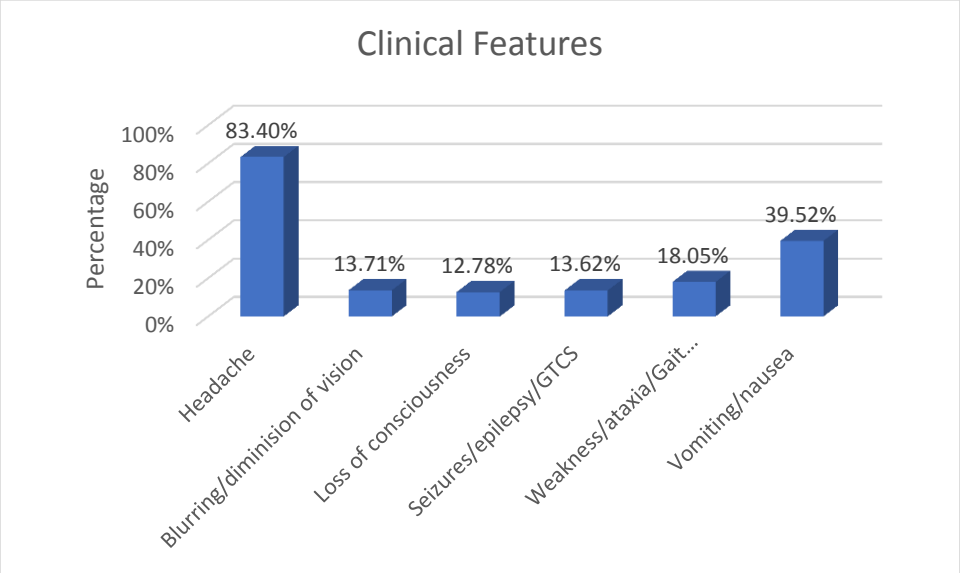

FIGURE-1: Clinical features of enrolled patients.

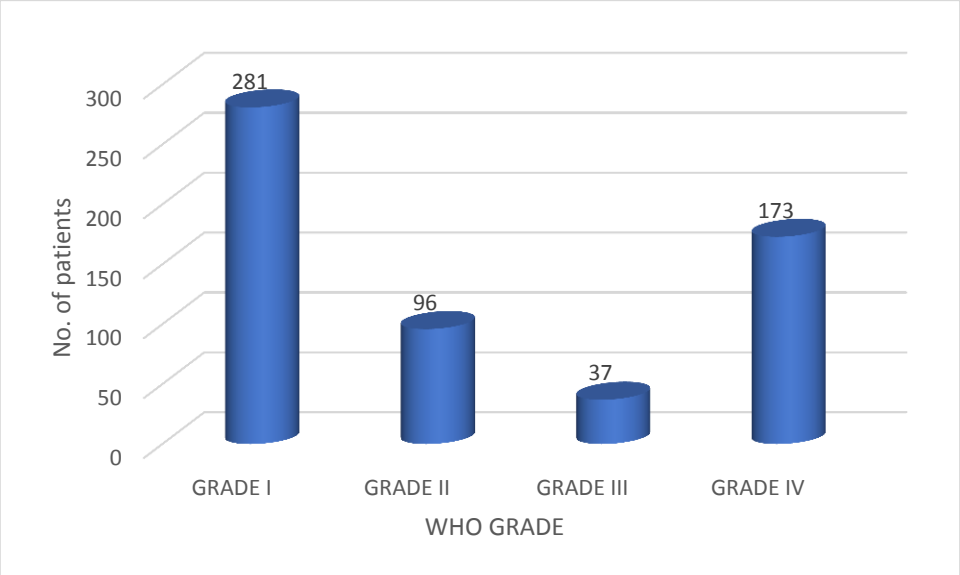

FIGURE-2: **Grade of patients as per WHO grading system.**

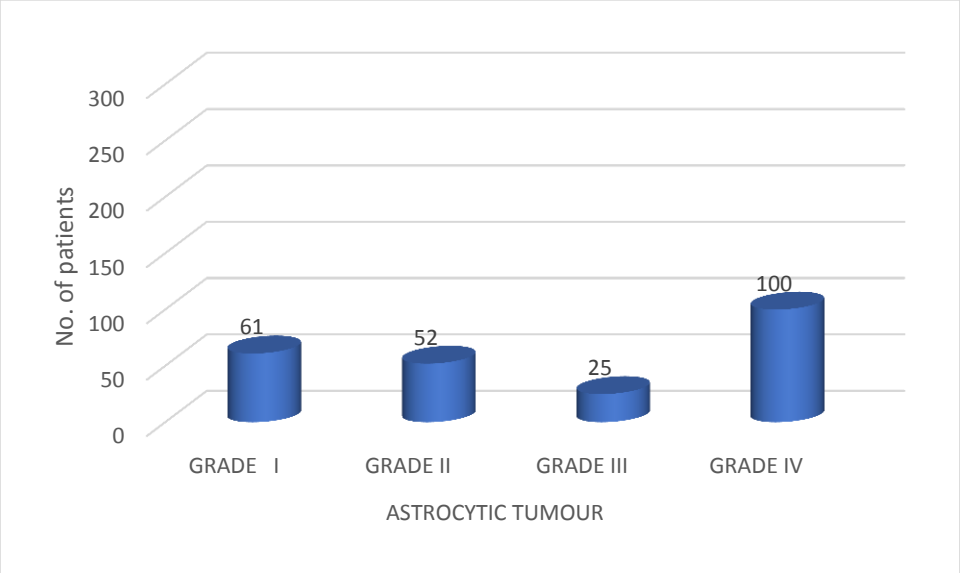

FIGURE-3: **Grade of astrocytic tumour in patients.**

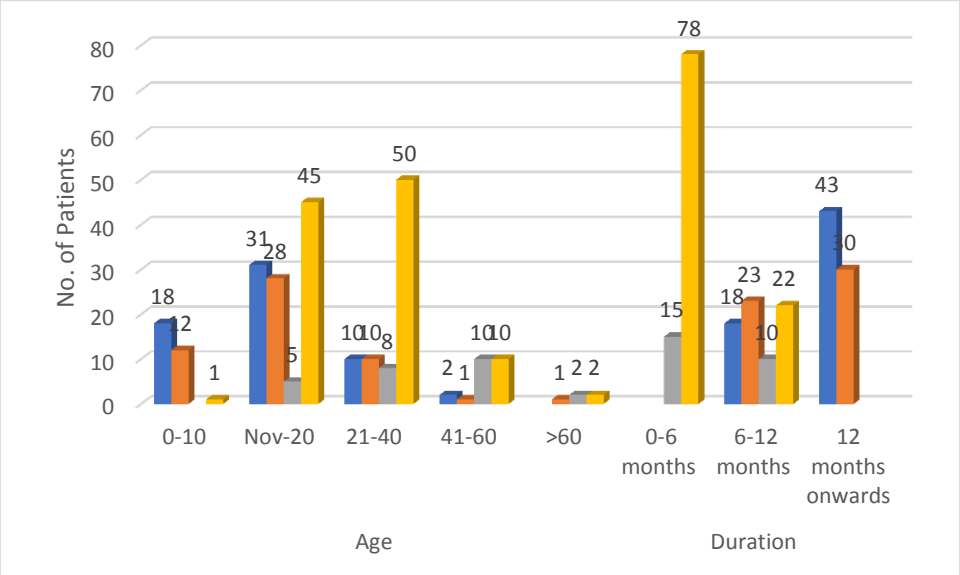

FIGURE-4: Association of astrocytic tumours with different parameters of enrolled patients.

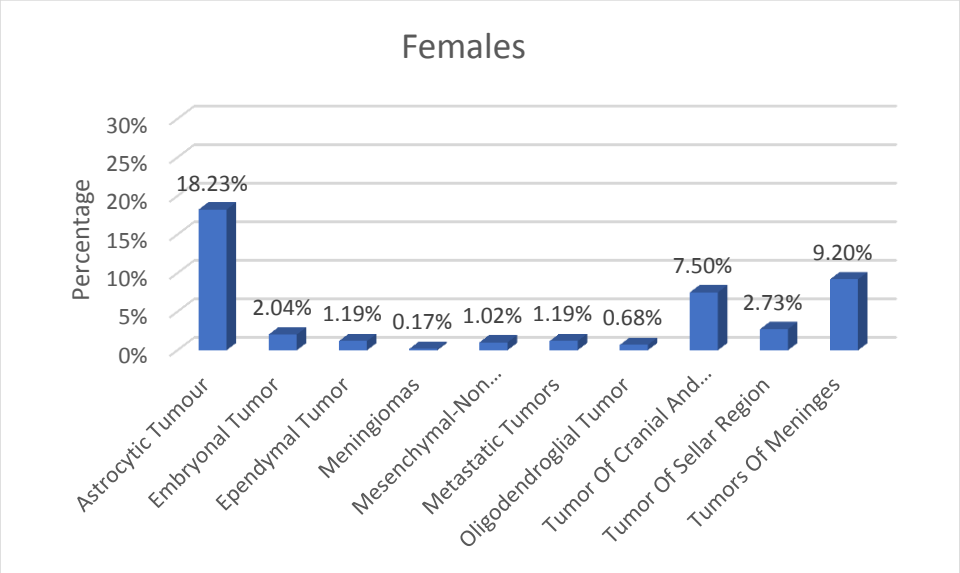

FIGURE-5a: Association of tumour types with gender (female).

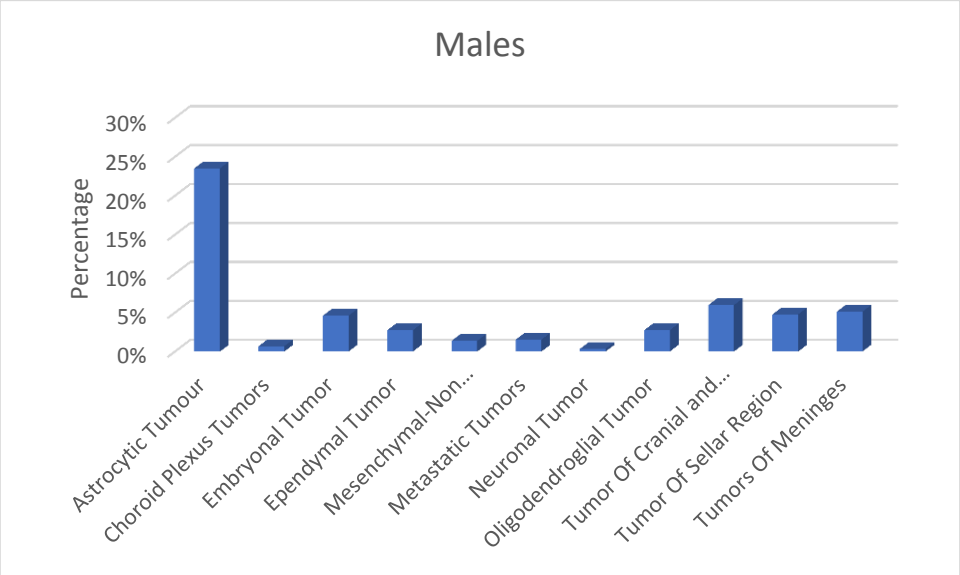

FIGURE-5b: **Association of tumour types with gender (male).**

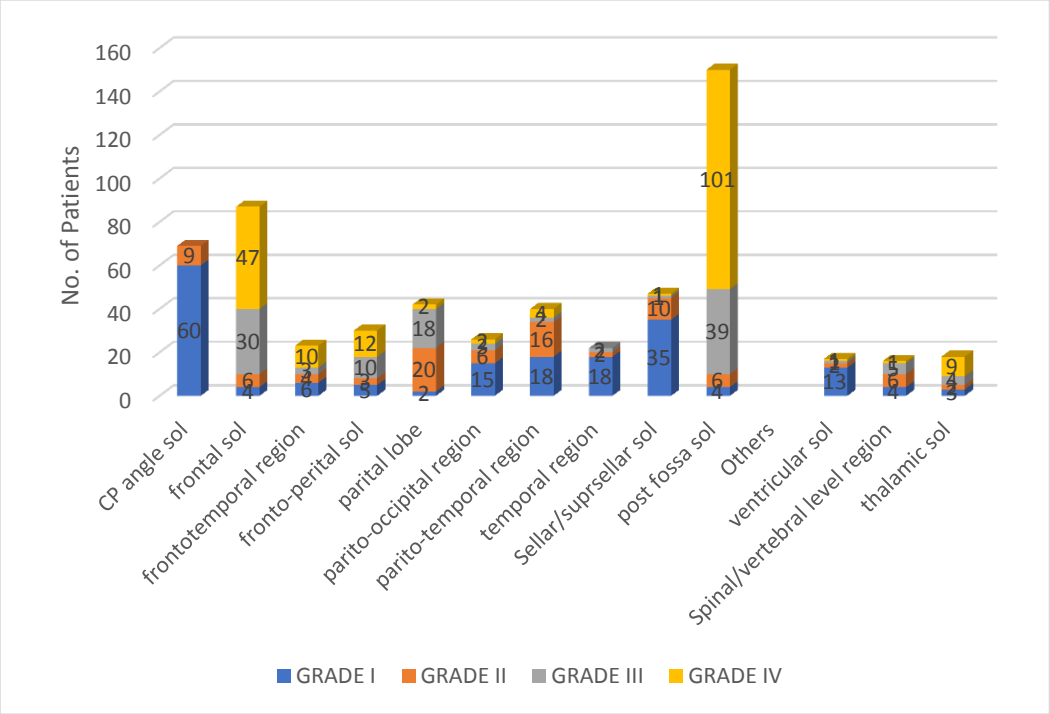

FIGURE-6: **Association of sites with the grades of enrolled patients.**