



## **Clinico Pathological Study of Central Nervous System Neoplasms**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

The central nervous system consists of brain and spinal cord invested with meninges. It is made up of two types of cells, Nerve cells or neurons which show numerous long processes and Glial cells which are the supporting cells of the nervous system, which occupy the space between neurons. Four principal types of neuroglial cells are recognized: Oligodendrocytes, Astrocytes, Microglial cells and Ependymal cells. Central Nervous System (CNS) tumors account for 85% of brain tumors and 15% of spinal cord tumors, however metastatic tumors are usually extradural. Brain tumors are the second most common solid tumors in children next to Leukemia. Medulloblastoma is the commonest tumor among the pediatrics age group. Risk factors affecting brain tumors still persist unclear. Neoplasms of central nervous system accounts for approximately 1% of tumors of the human body, and they can be primary or secondary (metastatic), benign or malignant, and intra-axial or extra-axial. Neoplasms of the CNS can occur in both adults and pediatrics populations. Although adult and children may experience similar tumors, their incidences vary greatly with age. To study the spectrum of central nervous system space occupying lesions and the grade of neoplasms according to the guidelines provided by the World Health Organization (WHO). To correlate the diagnosis of these lesions with radiological findings in certain tumors, special stains and Immunohistochemistry were applied wherever needed.

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## 1. INTRODUCTION

The central nervous system (CNS) is made up of the spinal cord, brain and meninges. The human nervous system is formed by the specialized network of cells called neurons. The neurons are responsible for the ability to receive, store and transmit information. Intracranial space occupying lesions are the important cause of neurological morbidity [1,2]. CNS tumors are well known for their life threatening behavior; hence the malignant potential is of two types, anatomic and biologic. Anatomic lesions are close to the vital centres and are deeply settled that could not be reached by physician, and it developed until it become fatal. Biologic lesions are violent tumors that rapidly growing with the resulting of neurophil attack and damage. CNS tumors do not fix in to the common meaning of malignancy as they rarely spread outside the chief locality [3].

Among the top ten causes of cancer deaths in the world, a brain tumor remains high. According to the Central Brain Tumor Registry of United States (CBTRUS), the whole frequency was found to be 21.97 per 100,000 persons. Brain tumors are the second most common solid tumors in children next to Leukemia. Medulloblastoma is the commonest tumor among the paediatric age group. Risk factors affecting brain tumors still persist unclear. Radiation contact, persons working in metal, rubber industries and family history of brain cancer are found to elevated the risk of brain tumor [4,5,6]. Increasingly sophisticated radiological investigations are available for diagnosing the brain tumor, but these modalities are harmonizing to the finding, not for assenting. These imaging techniques can tell us the probable diagnosis only [7,8,5,6,9,10]. The confirmation of diagnosis is done by histological examination of the tissue biopsy. Hence histopathology remains the gold standard for diagnosis.

The tumors are graded according to the modified 2007 WHO classification criteria. Grading is essential for the management plan and treatment strategy [11-15]. In this era of clinical research Immunohistochemistry play a vital tool to help in giving the confirmatory diagnosis as the cell of origin is found out. The diagnosis of certain CNS

tumors is very challenging; in such instances immunohistochemistry is used. It is found to be very useful in arriving at final diagnosis.[16-23]

## 2. MATERIALS AND METHODS

This study was conducted in the Department of Pathology, Sree Balaji Medical College and Hospital, Chennai during the study period of April 2015 to September 2016. All the specimens received from the department of Neurosurgery, Sree Balaji Medical College and Hospital, Chennai were studied and 95 cases were included in this study.

Biopsies were carried out for aggregate measuring 0.5cc to 4cc in the specimen. A thorough history with clinical symptoms and signs were noted. Site of the tumors were noted, and correlated with the imaging findings.

All the specimens were received in formalin and fixed in 10% neutral formalin. 4 micron thickness sections were made followed by routine haematoxylin and eosin staining.

During the study period between April 2015 and September 2016, all the cases received from the department of neurosurgery, Sree Balaji medical college and hospital were analysed and 95 cases were included in the study conducted at the department of Pathology, SBMCH. Out of 95 cases of CNS neoplasms, 49 cases were Astrocytomas which is found to be the most common neoplasm constituting about 52% of cases, followed by 19 cases of Meningiomas constituting 20%, 12 cases (13%) of Nerve sheath tumors were seen, 4 cases of Medulloblastoma followed by 4 cases of Pituitary adenoma (4%) and 3 cases of Ependymoma constituting 2%. We reported one case each in Oligodendroglioma, Craniopharyngioma, Primitive Neuro Ectodermal Tumor and Lymphoma constituting 1% each.

## 3. RESULTS

### 3.1 Gender Incidence in CNS Neoplasm

Among 95 cases, 50 (53%) were females and 45 (47%) were males, with slight female preponderance as in chart 2.

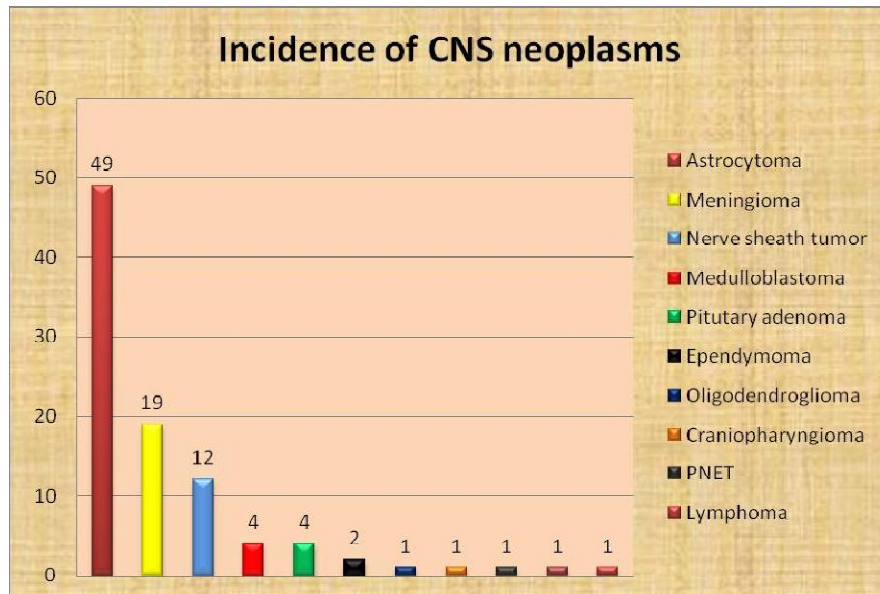


Chart 1. Incidence of CNS neoplasms in our study

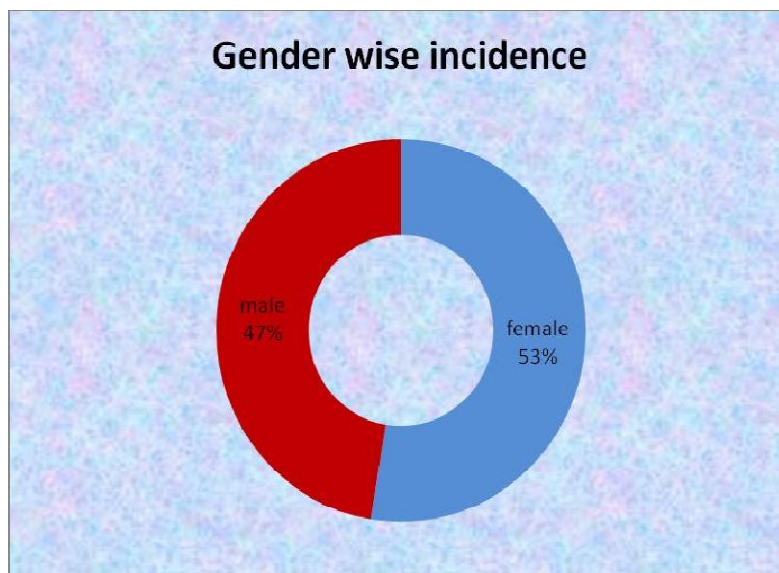


Chart 2. Gender wise incidence

### 3.2 Incidence of Age in CNS Neoplasms

In this study there were 3(3%) cases found in less than 10 yrs. 10 (10%) cases were between 11 -20. yrs, 10 cases (11%) between 21-30 yrs, 19 (20%) cases between 31 - 40yrs, 26 cases (27%) between 41 – 50yrs, 14(15%) cases between 51 -60 yrs, 10 (11%) cases between 61 -70 yrs and 3(3%) cases between 71-80 yrs as in.(Chart 3).

### 3.3 Presentation of Symptoms in CNS Tumors

In our study we observed that majority of patients 41 (43%) presented with Headache, followed by 19 cases (20%) presented with Seizures, 11 (12%) cases presented with hemiparesis, 11 cases (12%) with vomiting, 8 (8%) with diminution of vision and 5 (5%) with loss of consciousness as in (chart 4 ).

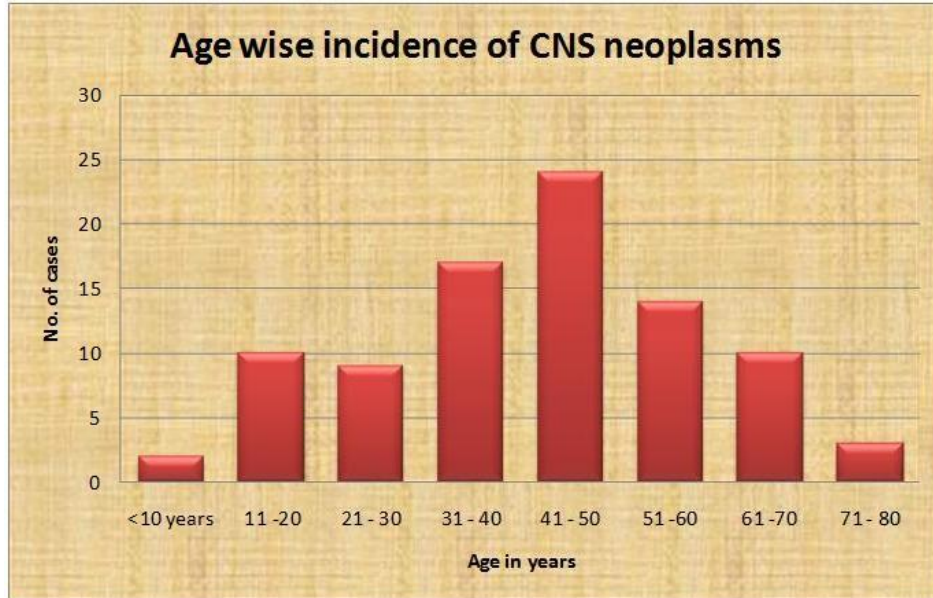


Chart 3. Age wise incidence of CNS neoplasms

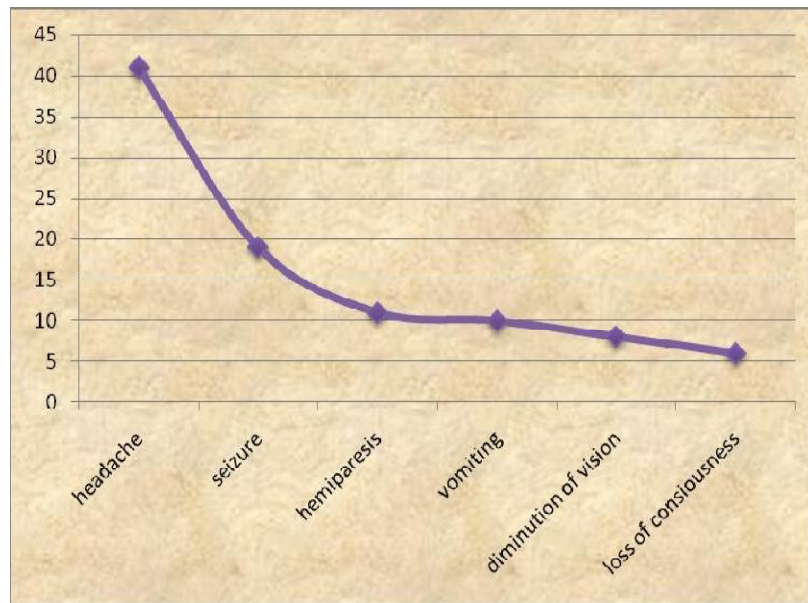


Chart 4. Presentation of symptoms in CNS tumors

### 3.4 Overall Site of Occurrence of CNS Tumors

In our study we found that most common site being the frontal lobe with 27 cases (29%) followed by 20 cases in parietal lobe (2%), 9 (10%) cases were seen in Temporal lobe. 8 cases (8%) were seen in CP angle and 8 (8%) in spine, 5 cases (5%) in supra sellar region, 4 (4%)

in Occipital lobe, 3 cases (3%) in posterior fossa, and 2 cases (2%) in sphenoid wing as in (chart – 5).

The tumors are graded according to the following features, it includes - crossing midline, edema, signal heterogeneity, necrosis, haemorrhage, borders and mass effect<sup>34</sup>.



Radiologically Low grade glioma appears hypo intense on T1WI, hyperintense on T2WI with mass effect and no enhancement. High grade glioma contains necrosis , haemorrhage, edema with mass effect. Glioblastoma shows irregular margins, haemorrhage and central areas of necrosis surrounded by extensive edema<sup>34</sup>.

Among the 7 cases, 3 were radiologically diagnosed as Metastasis as it has ring enhancement, in histo pathology it came out as GBM. Two cases were reported as tuberculoma in radiology, out of which one came out to be high grade glioma and the other came out to be low grade glioma in histopathology. Two cases were diagnosed as Meningioma in radiology as it is attached to the dura, came out to be Astrocytoma in histopathology. Hence radiology was found to be useful in giving the preoperative diagnosis in CNS neoplasms and histopathology was found to be the gold standard in diagnosing the CNS neoplasms.

### 3.5 Histopathological Features of Astrocytomas Seen in Our Study

#### GRADE I

Among 49 cases (52%) of astrocytomas 4 cases (8%) were Pilocytic astrocytoma which comes under Low grade or Grade I astrocytoma. Histopathology showed the presence of Rosenthal fibres and eosinophilic granular

bodies among a delicate network of hair like cytoplasmic processes with micro cysts. No microvascular proliferation and no necrosis (Fig .1)

#### GRADE II

Totally 13 cases (26%) were reported as grade II tumors or Diffuse astrocytoma.

#### Gemistocytic astrocytoma

We reported five cases of Gemistocytic astrocytoma, a variant of diffuse astrocytoma. Microscopy showed tumor cells with eosinophilic cytoplasm and nuclei pushed towards the periphery with prominent nucleoli in a coarse fibrillary background. Perivascular lymphocytic proliferation is seen (Fig. 2 ).

#### Grade III

#### Anaplastic astrocytoma

We reported 13 (26%) cases in grade III astrocytomas according to the histopathological features .Microscopy showed acellular neoplasm composed of hyperchromatic and pleomorphic nuclei arranged in sheets in a background of fibrillary stroma. Areas of proliferating capillaries, mitotic figures and microcystic degeneration are seen. No evidence of necrosis. (Fig. 3).

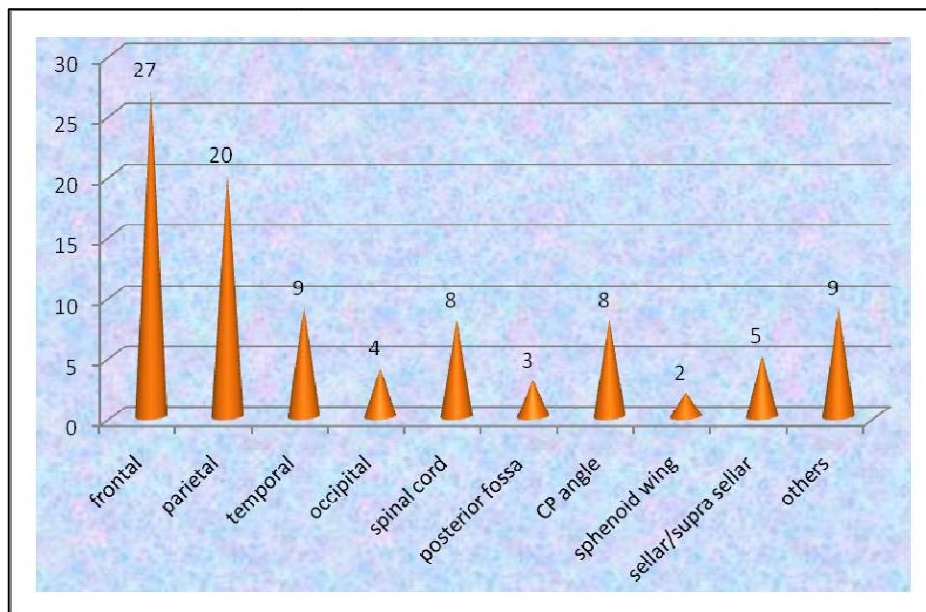


Chart 5. Site of occurrence of CNS tumors

#### Grade IV

Totally 19 cases were reported in grade IV with 15 cases of Glioblastoma multiforme and 4 cases of Gliosarcoma, a variant of GBM.

#### Glioblastoma multiforme (GBM)

Microscopy showed fragments of a cellular neoplasm composed of pleomorphic giant cells, anaplastic cells, epitheloid cells with hyperchromatic nuclei. There are areas of necrosis surrounded by tumor cells known as pseudo pallisading necrosis. Microvascular proliferation, tumor giant cells and atypical mitotic figures are seen (Fig. 4).

#### Gliosarcoma

Microscopy showed round to oval pleomorphic cells having open chromatin with prominent nucleoli arranged around blood vessels along with foci of spongiform cells. Excessive proliferation of blood vessels and extensive areas of necrosis were seen. Many foci showed spindle cells with hyperchromatic and elongated nuclei arranged in fascicles. Many mitotic figures are seen in both spindle cell component and glial component (Figs. 5, 6).

#### Immunohistochemistry

**GFAP** immuno staining was done in which only the glial components stains brown and the non glial component remains unstained (Fig. 7).

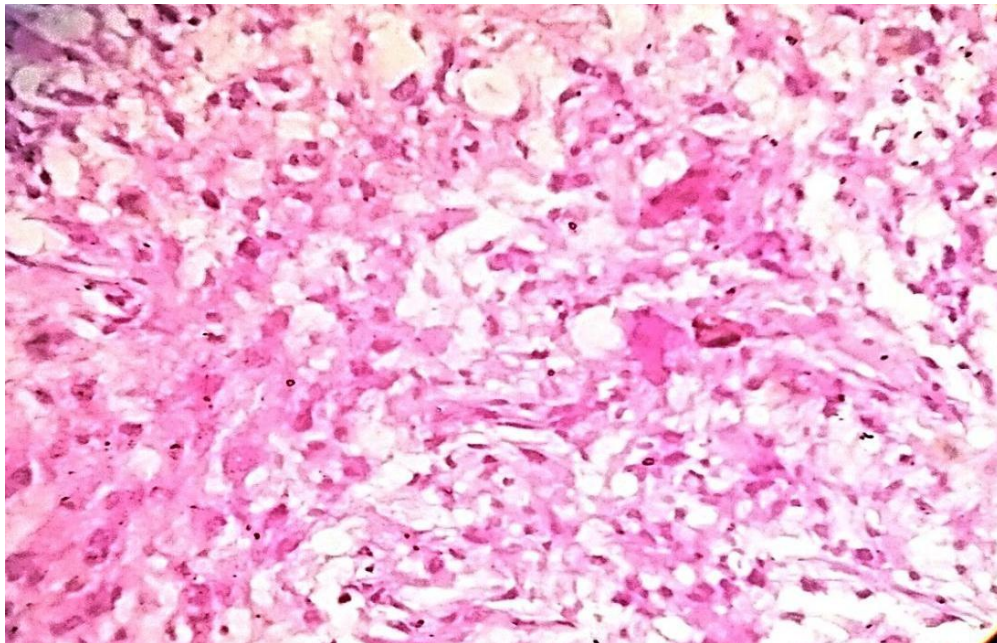
#### Special stain

Reticulin stain was applied to demonstrate the mesenchymal component, the staining was seen around individual tumor cells.

#### 4. DISCUSSION

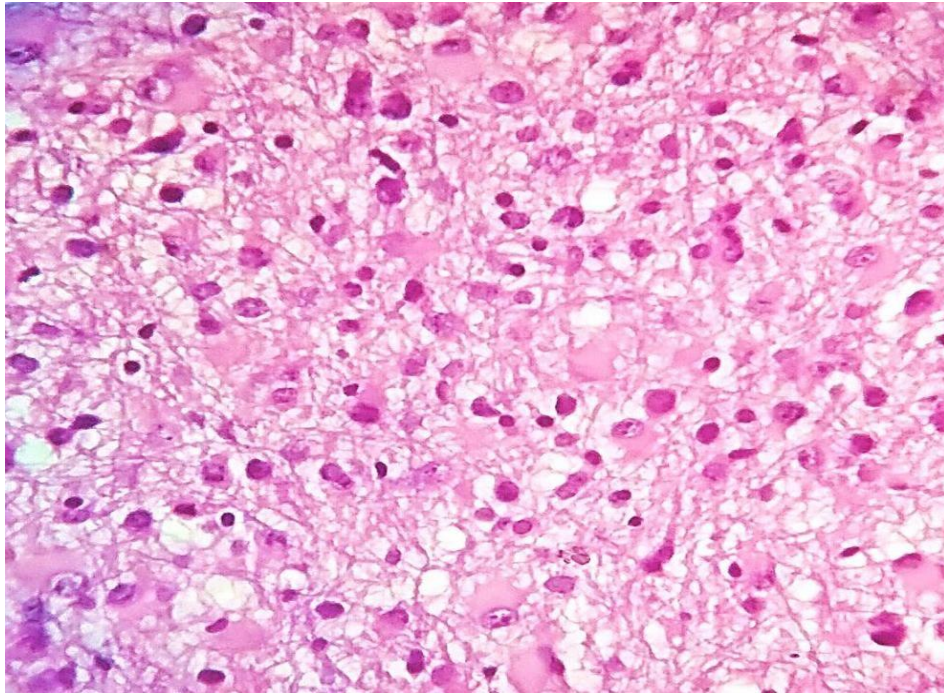
In the present study about 95 CNS neoplasms reported during April 2015 – September 2016 were included. In our study CNS tumors are most commonly seen in the age group of 41 -50 years with 24 cases (27 %), followed by 31 – 40 years with 19 cases ( 19%). Least number of cases were seen in the first decade.

In our study astrocytomas are found to be more common in males with 32 cases (65% ) than in females with 17 cases (35% ) which is similar to the studies done by Das et al [4] and Intisar et al [4] who also showed an increase incidence in males.

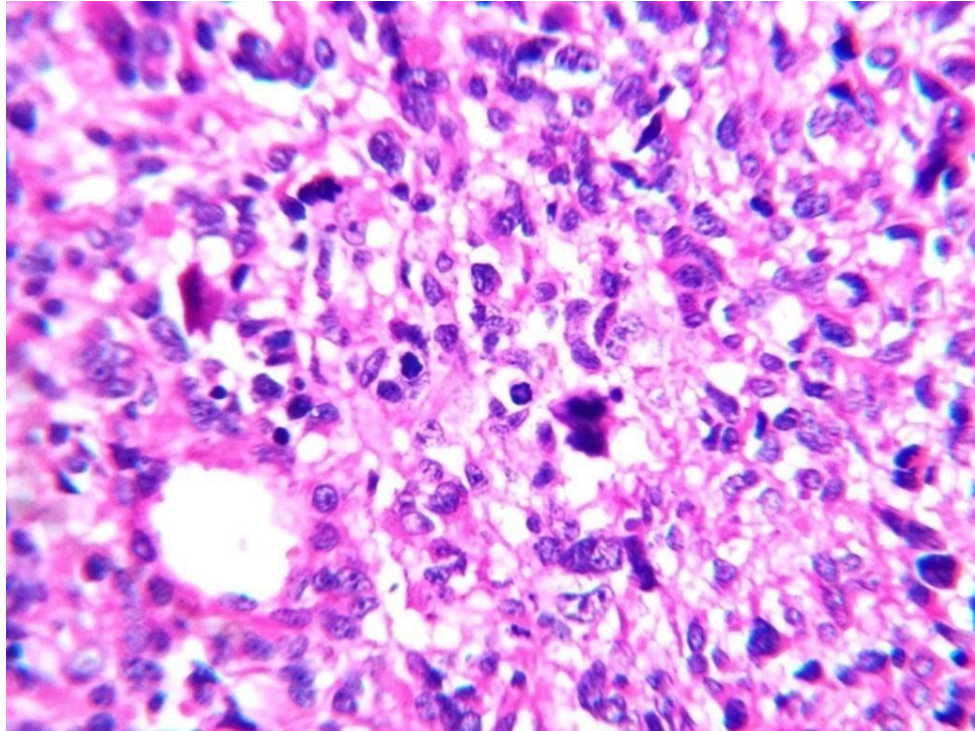


**Fig. 1. Pilocytic Astrocytoma -shows numerous rosenthal fibres lie among a delicate network of hair like cytoplasmic processes. H & E. 400X**



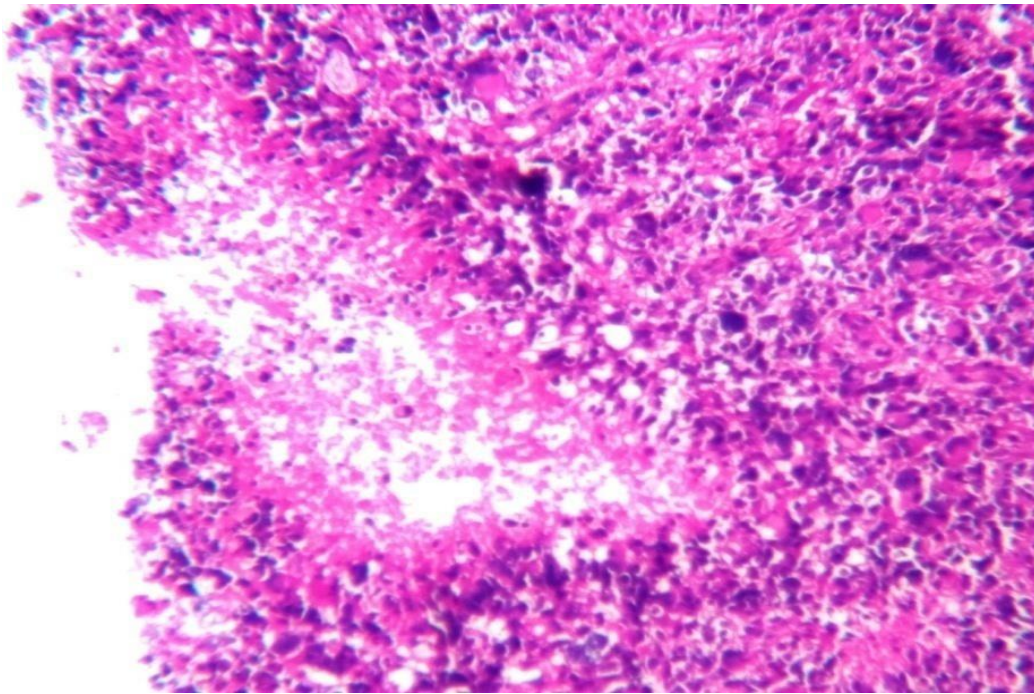


**Fig. 2. Grade II - gemistocytic astrocytoma - high power view shows gemistocytes with eosinophilic cytoplasm and eccentrically placed nucleus.H&E. 400X**

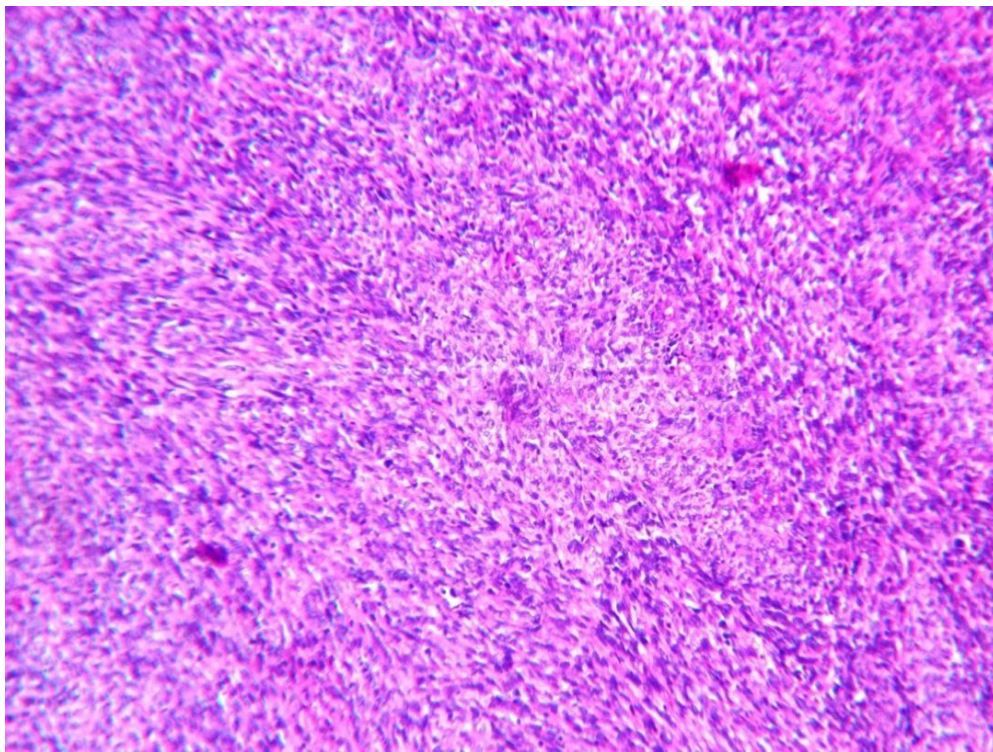


**Fig. 3. Astrocytoma Grade III – high power view shows a cellular neoplasm composed of pleomorphic nuclei and mitosis. H&E 400X**



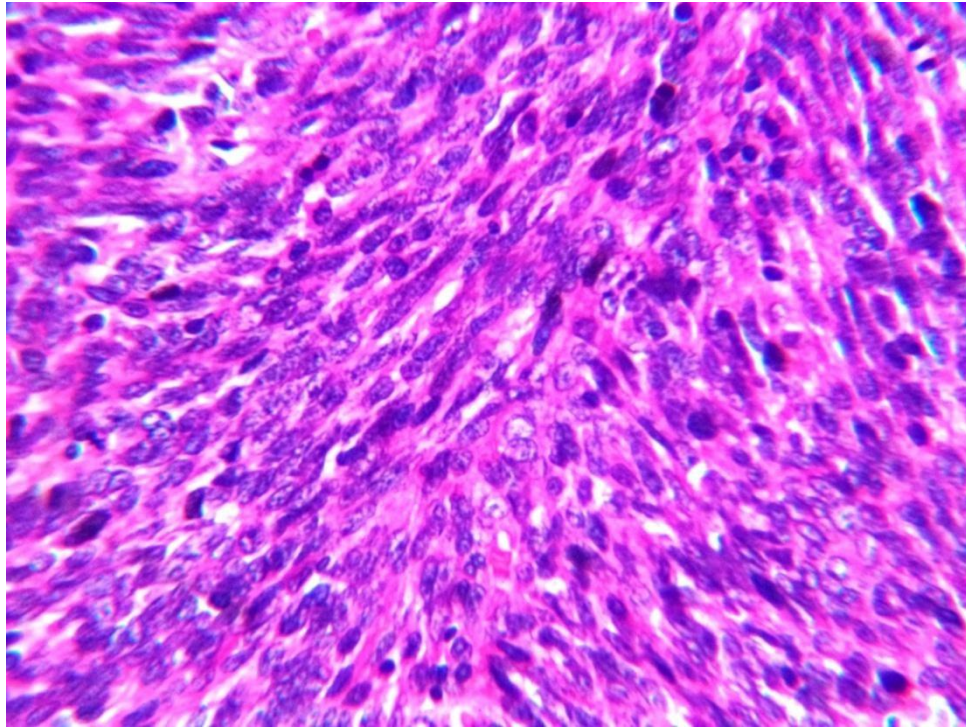


**Fig. 4. Astrocytoma grade IV- Glioblastoma multiforme – high power view shows central area of necrosis surrounded by tumor cells (pseudopalisading necrosis). H & E.100x**

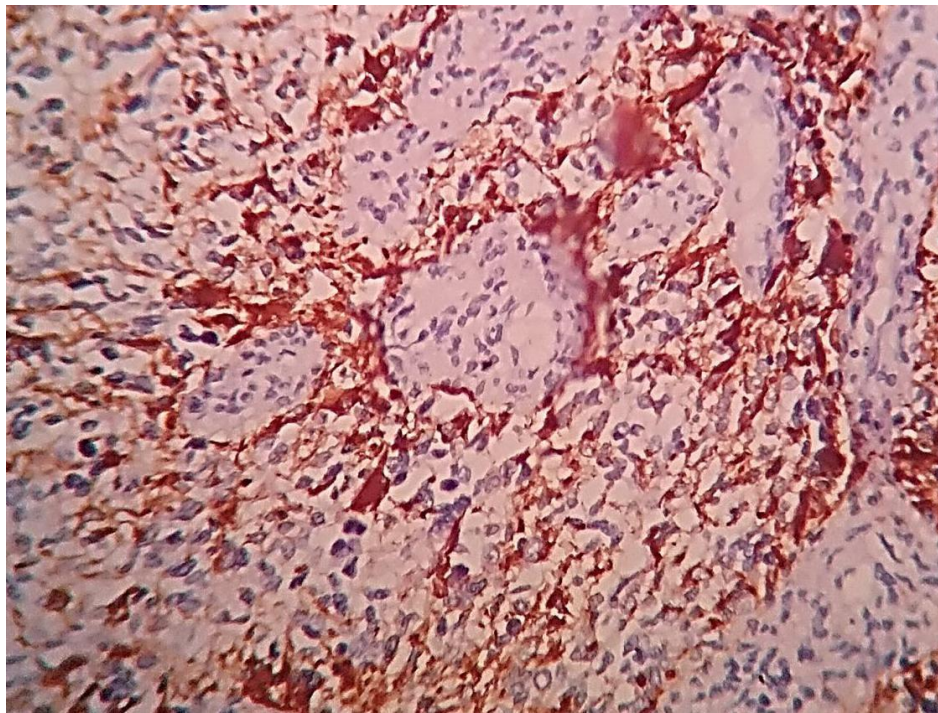


**Fig. 5. Gliosarcoma- Low power view shows both spindle cell component and glial component. H & E 100X**





**Fig. 6. High power view of the same showing pleomorphic spindle cells with hyperchromatic nuclei. Mitotic figures are seen. H & E-400 X**



**Fig. 7. Gliosarcoma – GFAP immunostaining – shows cytoplasmic positivity in the glial cells and negative in the nonglial areas. (400X)**

**Table 1. Comparison of Incidence of brain tumors in other studies with our study**

| Age (years) | Dogar et al (2015) (%) | Massodi et al (2012) (%) | Our study (%) |
|-------------|------------------------|--------------------------|---------------|
| 1 -10       | 4                      | -                        | 3             |
| 11-20       | 8                      | 10                       | 10            |
| 21-30       | 16                     | 8                        | 11            |
| 31-40       | 18                     | 25                       | 20            |
| 41-50       | 26                     | 23                       | 27            |
| 51-60       | 12                     | 17                       | 15            |
| 61-70       | 13                     | 14                       | 11            |
| 71-80       | 3                      | 3                        | 3             |

**Table 2. Comparison of incidence of glial tumors in other studies with our study**

| Tumor              | Cbtrus (%) | Ejas et al (%) | Bushra et al (%) | Kothari et al (%) | Ourstudy (%) |
|--------------------|------------|----------------|------------------|-------------------|--------------|
| Astrocytoma        | 23.7       | 41             | 48               | 53.2              | 49%          |
| Meningioma         | 36.4       | 23             | 18               | 23.4              | 19%          |
| Nerve sheath tumor | 8.6        | 11             | 1                | 6.4               | 12%          |
| Pituitary adenoma  | 13.1       | 2              | -                | 8.5               | 4%           |
| Medulloblastoma    | 1          | 2.4            | 4                | -                 | 4%           |
| Ependymoma         | 1.9        | 4.8            | 6                | -                 | 2%           |
| Oligodendroglioma  | 2          | 4.8            | 8                | -                 | 1%           |
| PNET               | -          | -              | -                | -                 | 1%           |
| Lymphoma           | 2          | -              | -                | 2.1               | 1%           |
| Others             | 11.3       | 11             | 11               | -                 | 1%           |

**Table 3. Comparison of incidence of glial tumors in our study with studies done in other institutions**

| Study                                 | Astrocytoma | GBM    | Medulloblastoma | Oligodendroglioma | Ependymoma |
|---------------------------------------|-------------|--------|-----------------|-------------------|------------|
| Tata memorial hospital, Mumbai        | 46.3%       | 21.5%  | 11.1%           | 6.3%              | 6.8%       |
| Cancer institute, Adyar               | 39%         | 29.05% | 5.9%            | 4.4%              | 3.4%       |
| Kidwai institute, Bangalore           | 41.1%       | 22.95% | 11.2%           | 9.6%              | 1.92%      |
| Regional cancer institute, Trivandrum | 41.35%      | 13.3%  | 12.7%           | 3.35%             | 2.1%       |
| Our study                             | 49%         | 21%    | 4%              | 1%                | 3%         |

**Table 4. Comparison of Incidence of pediatrics tumor in our study with other study**

| Tumor              | Cbtrus | Chang et al | Our study |
|--------------------|--------|-------------|-----------|
| Astrocytoma        | 29.1%  | 22%         | 17%       |
| Medulloblastoma    | 13%    | 13.5%       | 34%       |
| Ependymoma         | 1.9%   | 5.3%        | 8%        |
| Nerve sheath tumor | 4.7%   | 6.6%        | 17%       |
| Pituitary tumor    | 3%     | 11.5%       | 8%        |

Meningiomas are very common neoplasm of elderly age group in India. In our study Meningiomas are the second most common neoplasms seen in 19 cases (20%) rank next to

astrocytomas which is similar to the study of Ejas et al 26. Grade I tumors are the most common with 18 cases (95%) among all the grades which is similar to the study done by Sameh et al 74

and Sasidhar et al [6]. Incidence was found to high in females with 14 cases (74%) in our study which is well established in many studies.

The nerve sheath tumor falls next to Meningiomas in our study with 12 cases (13%). Schwannomas are found to be more common with 9 cases (75%) than Neurofibroma with 3 cases (25%) which is similar to the study done by Intisar et al[40]. In our study there is a male preponderance, which is similar to many studies.

Pituitary adenomas represents 10 - 20% of all CNS neoplasms [11]. We reported 4 cases (4%) of pituitary adenomas with one in the first decade one in second decades and the other two in third and seventh decade respectively. Male Female ratio was found to be equal in our study.

Three cases of Ependymoma were reported in our study one in paediatric age group, one in the third decade and the other in fifth decade. We reported a single case of Myxopapillary Ependymoma in a 35 year old male at the level of L1-L2 level. One case of lymphoma was reported in our study in 35 year old female in the frontal lobe.

Brain tumors in children represent the second most common solid tumors in the children. According to CBTRUS study 4350 children were diagnosed with brain tumor per year[14]. The etiology was not known clearly, but ionizing radiation is thought to induce both benign and malignant gliomas and occasionally primitive neuro - ectodermal tumor (PNET).

According to Ron Modan et al most of the tumors are multifactorial with both genes and environment playing a vital role. A total of 13 cases (14%) of paediatric brain tumors occurred in our study. According to the CBTRUS study about 7% of the brain tumors are seen in children [14]. Incidence of childhood brain tumors are compared with other studies.

In our study 50 cases (53%) were seen in females and 45 cases (47%) were seen in males. Das et al 4, Andrew et al and Anadure et al also showed that CNS neoplasms are more common in females than in males, which is similar to our study. In our study 27 cases (29%) were located in frontal lobe and 20 cases (21%) were seen in the parietal lobe. Frontal lobe is the most common site of occurrence for CNS neoplasms in our study followed by parietal lobe. Headache was the most common symptom encountered in

our study as it is seen in 41 cases (43%) followed by seizures in 19 patients (20%) 34 which is similar to the study done by Masoodi et al 24 and Intisar et al 26 .

In this study gliomas were the most common tumors hence we compared radiological diagnosis of astrocytomas with the histopathological diagnosis. Radiologically astrocytomas are reported as low grade and high grade gliomas. Low grade includes Grade I and Grade II tumors; high grade includes Grade III and Grade IV tumors.

Out of 49 cases studied, radiology diagnosed 19 low grade gliomas and 23 high grade gliomas. Histopathology diagnosed 22 low grade and 27 high grade gliomas. Hence discrepancies between clinical and histopathological diagnosis were noted in 7 cases. Among the 7 cases, 3 were radiological diagnosed as Metastasis as it has ring enhancement, in histopathology it came out as GBM.

Two cases were reported as Tuberculoma in radiology, in histopathology one came out to be high grade glioma and the other came out to be low grade glioma. 2 cases were diagnosed as Meningioma in radiology because of its attachment to the dura, it came out to be Astrocytoma in histopathology. Hence radiology was found to be useful in giving the preoperative diagnosis in CNS neoplasms and histopathology was found to be the gold standard in diagnosing the CNS neoplasms. This is in accordance with study done by Intisar et al 26.

Histopathological diagnosis and grading of brain tumors is the corner stone upon which the management plans and treatment depends. Despite of the great advancement in ancillary studies, histopathology remains an invaluable means in the grading and diagnosis of brain tumors. Out of 95 cases of CNS neoplasms, 49 cases were Astrocytomas which was found to be the most common neoplasm constituting about 52% of cases, followed by 19 cases of Meningiomas constituting 20%, 12 cases (13%) of Nerve sheath tumors were seen, 4 cases of Medulloblastoma followed by 4 cases of Pituitary adenoma (4%) and 3 cases of Ependymoma constituting 2%. We reported one case each in Oligodendroglioma, Craniopharyngioma, Primitive Neuro Ectodermal Tumor and Lymphoma constituting 1% each. Radiological findings along with special stains and Immunohistochemistry were found very helpful to



get an accurate diagnosis under Histopathology examination.

## 5. CONCLUSION

In our study Medulloblastoma was found to top among all other tumors. According to the CBTRUS study Medulloblastoma does the most common malignancy in children that constitutes about 20% of all malignant tumors. Histopathological diagnosis and grading of brain tumors is the corner stone upon which the management plans and treatment depends. Despite of the great advancement in ancillary studies, histopathology remains an invaluable means in the grading and diagnosis of brain tumors.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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