Original Article

# The Histopathological and Epidemiological Study of Pediatric Brain Tumors in A Tertiary Care Hospital, Mumbai

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## ABSTRACT

**Background:** The primary pediatric brain tumors (PBT) are the second most common cause of death due to malignancies in children. This study was done to analyze the histological spectrum of primary brain tumors in children and also to find out the epidemiology of the common pediatric brain tumors.

**Methods:** Data regarding age, gender, topography, and histopathology of 239 pediatric patients (0–18 years) with brain tumors operated over a period of 15 years (January-2001 to December-2015) was collected and analyzed according to World Health Organization 2007 classification

**Result:** PBTs were more common in males (54.8%) as compared to females (45.2%) with male to female ratio of 1.21:1. Frequency of tumors was higher in childhood age group (>5-<15 years) i.e. (55.6%) when compared to adolescent age group (15.9%). The most common anatomical site was cerebellum (40.5%), followed by hemispheres (21.4%). Supratentorial tumors (51.9%) were predominant than infratentorial tumors (45.2%) and 2.9% at spinal location. Astrocytomas (46.8%) and embryonal tumors (18.4%) were the most common histological types followed by ependymal tumors (12.5%) and craniopharyngiomas (9.2%). Medulloblastoma was the most common histological type with pilocytic astrocytoma being most common astrocytic tumor. In comparison to adults, meningiomas and lymphomas were rare in children.

**Conclusion:** Astrocytomas and medulloblastomas are the most common tumors among children and adolescents in our region. Except for a slightly higher frequency of craniopharyngiomas, the histological profile of pediatric brain tumors in India is similar to that reported in the Western literature.

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## Introduction

Tumors of the nervous system are the second most common childhood tumor after leukemia, [1] constituting approximately 25-35% of all childhood malignancies and remain the leading cause of cancer-related deaths in children. [2] Childhood central nervous system (CNS) tumors differ significantly from adult brain tumors in reference to their sites of origin, clinical presentation, tendency to disseminate early, histological features and their biological behaviour [3]. Whereas in adults the predominant CNS tumor types are metastases, glial neoplasms and meningiomas, in children, besides gliomas, other major tumor types including primitive embryonal neoplasms are also common[4].

## Materials and Methods

Two hundred and thirty nine paediatric brain tumour (PBT) specimens of patients aged 0 to 18 years were included in this study. The data collected from Department of Pathology of the major tertiary care hospital in Mumbai, India. The case summaries, histopathological records and discharge reports of all the children up to 18 years of age, were reviewed who were operated for brain tumors during the period from January 2001 to December 2015. Only patients with the proven histopathological diagnosis were included in the study. In addition to the location and histological types of the tumor, patient demographics including age and sex were also recorded. Patients with tumor-like cystic lesion (arachnoid cysts, epidermoid cysts and colloid cysts), space occupying lesion of infectious etiology and vascular malformation were excluded from the study. The hemotoxylin and eosin (H and E) stained slides of all 239 cases were studied and grading was done according to the 2007 World Health Organization classification system[5] .

## Result

During the 15 year study period, 21% occurred in the pediatric age group [239 pediatric tumors vs. total 1140 brain tumours cases]. Among these 239 cases, 131 were males and 108 were females, with Male: female ratio being 1.21:1. Their ages varied from 5 months to 17 years. Children (5–15 years) accounted for 133 cases, on the other hand, adolescents (15–18 years) accounted for 46 cases. This clears that the frequency of paediatric brain tumours is higher in childhood age group when compared to adolescent age group.

In the present study, PBT were commonly located supratentorially (124 cases) as compared to infratentorial one (108 cases) and 7 cases at spinal level. Comparing location under 15 years of age, Infratentorial tumors (100 cases) were common than supratentorial one (84 cases). The most common anatomical site for PBT was cerebellum (40.5%) followed by cerebral hemispheres (21.4%). The distribution of PBTs according to anatomical location in the present series is shown in figure 1.

The most common histological entities encountered were medulloblastomas accounting for 16.3% of all PBTs, and then Grade-I astrocytomas (15.5%), ependymomas (12.5%), Grade-II astrocytomas (10.9%), oligodenrocytoma (10%), & craniopharyngiomas (9.2%). Grade-I astrocytomas included pilocytic astrocytomas (13%) and subependymal giant cell astrocytomas (2.5%). Grade-II astrocytomas included pleomorphic xanthoastrocytomas (1.7%) and diffuse fibrillary astrocytomas (9.2%). Less common entities included mixed gliomas (10 cases), Grade IV astrocytomas- Glioblastoma multiforme, schwanomas & meningiomas (7 cases each), anaplastic astrocytomas (5 cases), whereas, central neurocytomas, hemangioblastomas, germ cell tumor, primitive neuroectodermal tumor and atypical teratoid/rhabdoid tumors (AT/RT) constituted rare histological entities (1.3% each) with choroid plexus tumors (2 cases), and 1 case each of gangliogliomas, pineoblastoma, medulloepithelioma, neuroblastoma. One case each of Wilms' tumor and Non Hodgkin's lymphoma had metastasized. Thus, astrocytomas (46.8%) and embryonal tumors (18.4%) were the most common histological types almost contributing more than half of all PBTs as shown in [Figure 2].

## Discussion

The management of PBTs is important due to their high incidence, challenging aspects of surgery and high mortality. In developing countries like India, the exact tumor burden of such diseases goes unnoticed and is underestimated [6]. Jain et al (2011)[7] had assessed the hospital-based prevalence of such tumors by collecting data on CNS tumors in the pediatric age group (<18 years of age) from the neuropathology records of seven tertiary hospitals in India, which included GB Pant Hospital, New Delhi; Christian Medical College (CMC), Vellore; Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh; National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore; Tata Memorial Hospital (TMH), Mumbai; Chhatrapati Shahuji Maharaj Medical University (CSMMU), Lucknow, and All India Institute of Medical Sciences (AIIMS), New Delhi. We also compared our data with this study and other studies to know prevalence of PBT.

In the present study, we studied the data regarding demographics and histological profile of 239 pediatric patients operated for brain tumors at one of the major

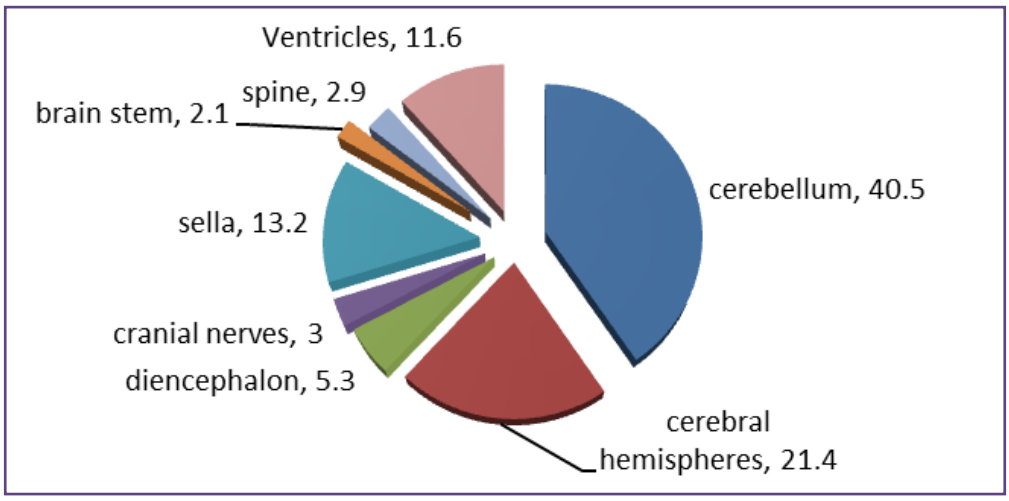


**Fig. 1: Distribution of pediatric brain tumors according to anatomical location**

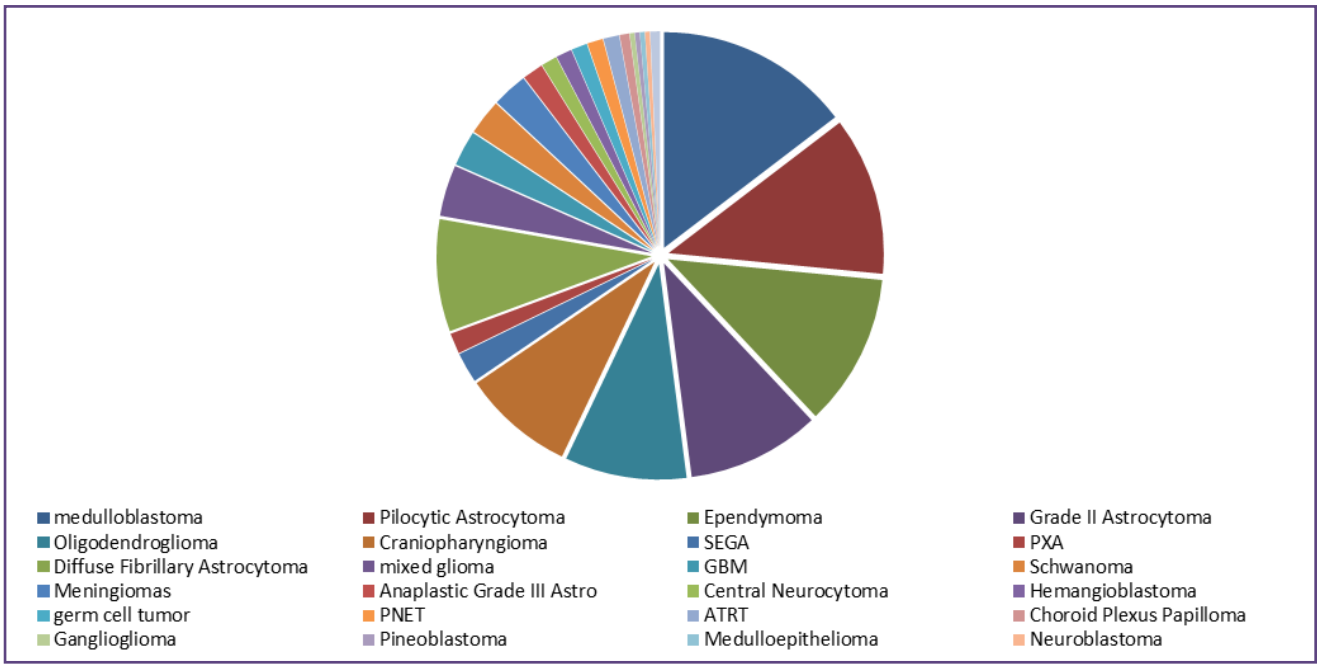


**Fig. 2: Distribution of different histological types of pediatric brain tumors.**

tertiary care hospital, Mumbai, India over a period of 15 years. Pediatric CNS tumors accounted on an average 21% of total intracranial tumors. [Table 1].

Thus the incidence of PBT in our study is comparable with GB Pant, TMH & Harshil Shah Study, while others show relatively lower incidence.

We found the slightly higher proportion of brain tumors in males as compared to in females with male to female ratio of 1.21:1 which was consistent with the findings of other studies on PBTs, in which male to female ratio in pediatric patients varied from as low as 1.03 to as high as 2.52[8,9,10,11,12,13,14]. In our study, males and females with PBT were evenly distributed among different age groups and observed differences which was in line with the findings of other studies [8,15,16] .

**Age-wise and Gender-wise Distribution:** The frequencies of PBTs in children (>5-15 yrs.) was 55.6% and adolescents (>15 yrs.) was 19.2%, which were comparable to the frequencies observed in Harshal Shah [8] & other studies, which states higher among childhood age group when compared to the adolescent age group[16],[17]

Pilocytic Astrocytoma and medulloblastomas were most common in posterior fossa. Patients with astrocytomas

**Table 1: Prevalence of paediatric tumours reported in India.**

| Institute /Study | Time Period | PBT % |
|---|---|---|
| AIIMS[7] | 2002-2007 | 17 |
| NIMHANS[7] | 2003-2007 | 11 |
| TMH[7] | 2006-2007 | 21 |
| CSMMU[7] | 2003-2007 | 10 |
| PGIMER[7] | 2003-2007 | 15 |
| CMC Vellore[7] | 1990-2007 | 10 |
| GB Pant[7] | 2003-2007 | 20.1 |
| Shah[8] | 2012-2013 | 10.2 |
| Present study | 2001-2015 | 21 |

presented at a higher age, probably because of greater number of glioblastoma cases. Similar was also reported by Rosenberg [1] who studied epidemiology of 1195 pediatric brain tumors in single institute. Childhood primitive neuroectodermal tumor (PNETs) presented at a mean age of 7.4 years, similar to the observations made by Grotzer et al. and Chan et al. [18,19]. There was equal distribution of boys and girls suffering from brain tumor when all tumors were taken together; however, girls outnumbered boys in case of Pilocytic Astrocytomas, while male predominance was found in medulloblastomas. Similar was observed by Sehgal et al [6].

**Location Wise Distribution**: A total of 47.7% tumors were located supratentorially, with even distribution among different age groups. In childhood age group (0-15yrs.), infratentorial tumors were bit predominant whereas, in adolescent age group, supratentorial tumors were more common, which was consistent with the findings of other studies [4,16,17]. Topographically, the cerebellum was found to be the most common site for PBTs followed by cerebral hemispheres. Medulloblastomas and most of the pilocytic astrocytomas, which comprise the major histological entities of PBTs, were frequently found involving the cerebellum. These findings were in line with the results of other studies [8,10,16].

**Histopathological Distribution:** In the present study, medulloblastoma was the single most common histological entity, followed by pilocytic astrocytomas (Grade-I). However, overall, astrocytomas were the most common tumors followed by embryonal tumors including medulloblastomas, supratentorial PNETs, and AT/RT. Kumar et al [20], GB Pant & TMH [7] institute had reported a higher incidence of medulloblastomas amongst Indian children. While other Indian studies like AIIMS, NIMHANS, CSMMU, CMC Vellore, PGIMER, Jain [7], Shah et al [8]and most of Western studies showed predominance of astrocytic tumors [21,22,23,24,25,26][Table 2].

There were one case each of pilocytic astrocytoma with extensive myxoid changes (Figure 3a ) and another with nuclear degeneration and multinucleation. The histology of PXA was confused with high grade gliomas, but CT findings helped for diagnosis (Figure 3b ).

Ependymoma formed third most common entity, followed by Oligodendrogliomas and Craniopharyngiomas in our series. Similar was also observed by TMH study. In a large meta-analysis by Rickert and Paulius, [17] it was seen that internationally, ependymomas are the third most common tumors followed by craniopharyngioma occupying the fourth place. This trend can be seen in [Table 4] in the data from Canada, [15] Germany, [10,22] Sweden, [23] and Morocco [9] but contradicted with the multi-institutional study carried out in India and studies from Korea [21] and Brazil [1] which showed craniopharyngiomas as third most common PBT. Data from a single institute in Beijing, China, however, showed craniopharyngiomas to be the second commonest tumor[12,24] [Table 3]. There were one case each of clear cell ependymoma (Figure 3c), with subependymoma and oligodendroglioma like features. In case of Clear cell Ependymoma, the histology was confused with Oligodendroglioma. But CT, MRI findings confirmed the Ependymal origin. While there were oligodendrogliomas with marked microcalcification and prominent microcystic change (Figure 3 d).

Four and half year old child presented with vomiting and headache with convulsions. The resected tumor is composed predominantly of elongated cells with eosinophilic cytoplasm, some showing discernible cross striations (indicating myoblastic differentiation) and focally of round cells with scant cytoplasm (indicating neuroectodermal differentiation) (Figure 4). The differential diagnosis thought of were Medullomyoblastoma, Atypical teratoid rhabdoid tumor, and Metastatic rhabdomyosarcoma. Immunohistochemistry staining revealed positive expression of desmin and myogenin

in the elongated eosinophilic cells while the round cells were negative for the same. The round cells were weakly positive for synaptophysin and retained INI-1 protein expression (Figure 5). The diagnosis offered as a rare tumour "medullomyoblastoma" which is more aggressive in nature. Primary tumors of the CNS containing muscle elements are exceptional hence awareness and knowledge of this entity is necessary to make correct diagnosis.

In the present study, we had 3 cases of germ cell tumor. Rickert and Paulius found germ cell tumors to be the fifth most common type, [17] as seen from [Table 3]. The frequency of germ cell tumors varies markedly in different countries ranging from just 0.9% in Morocco [9] to 14.3% in Japan [11]. In particular, all the three oriental Asian countries included i.e. Korea, China, & Japan, show higher frequency for germ cell tumors and craniopharyngiomas, suggesting environmental and/or genetic differences. For germ cell tumour (GCT), the treatment approach depends on the histological subtypes. In general, with the exception of malignant teratoma, GCT is chemo- and RT sensitive [25]. Thus it is important to recognize it on histomorphology.

We could find few cases (2.9%) of intracranial nerve sheath tumors and meningiomas, which form the predominant entities in adulthood.

The incidence of various CNS tumors in the current study falls well within the range seen in the international studies for every tumor category. This can have important connotations in the field of pediatric brain tumor research in India, particularly when analyzing differences in their molecular and genetic pathways, which could aid in the development of targeted, individualized therapies and planning treatment protocols and strategies.

**Table 2: Percentage breakup of various histological subtypes of pediatric CNS tumors in Indian studies.**

| Tumor | AIIMS [7] | NIMHANS[7] | GB PANT[7] | TMH[7] | CSMMU[7] | CMC[7] | PGIMER[7] | SHAH[8] | PRESENT |
|---|---|---|---|---|---|---|---|---|---|
| Astrocytoma | 33.7 | 44.1 | 22.3 | 28.6 | 30.6 | 46.7 | 37 | 40.8 | 46.8 |
| Mb & PNETs | 16.8 | 19.7 | 32 | 29 | 27.7 | 10.3 | 21.6 | 29.0 | 18.4 |
| Ependymoma | 8.5 | 8.5 | 12.2 | 19.1 | 9.4 | 4.8 | 6.3 | 6.6 | 12.5 |
| Oligodendroglioma | 0.7 | 0.9 | 2.9 | 1.4 | 1.5 | 0 | 0 | 2.6 | 10 |
| Craniopharyngioma | 12.7 | 7.7 | 13.5 | 4.5 | 13.1 | 8.5 | 11.5 | 11.8 | 9.2 |
| Schwanomma | 7 | 4.3 | 1.3 | 2.4 | 2.2 | 4.6 | NA | 2.6 | 2.9 |
| Meningioma | 5.6 | 4.3 | 0.3 | 3.4 | 2.2 | 3.5 | NA | 1.3 | 2.9 |
| Neuronal & Mixed neuronal glial | 4.1 | 2.8 | 5.2 | 2.1 | 0 | NA | NA | 1.3 | 1.7 |
| Germ cell tumor | 2.2 | 2.2 | 3.3 | 1.7 | 2.2 | NA | NA | 0 | 1.3 |
| Chroid plexus tumor | 1.5 | 2.6 | 1.6 | 1.7 | 1.5 | NA | 3.5 | 2.6 | 0.8 |
| Pineal tumors | 0.7 | 1.4 | 1.3 | 1 | 3 | NA | NA | 1.3 | 0.8 |
| Lymphoma | 1 | 0.5 | 0.3 | 0 | 0 | 1.1 | NA | NA | 0.8 |

**Table 3: Frequency of various types of pediatric CNS tumors reported in different countries (in percentage).**

| Tumor | Brazil [1] | Korea [21] | Germany [23] | Canada [15] | Bejing [12] | Sweden [23] | Morocco [9] | Japan [11] | Hongkong [26] | PRESENT |
|---|---|---|---|---|---|---|---|---|---|---|
| Astrocytoma | 32.5 | 27.8 | 41.7 | 39.4 | 30.5 | 51 | 37.1 | 35.7 | 57.0 | 46.8 |
| Mb & PNETs | 13.9 | 19. | 25.7 | 15.4 | 14.6 | 17 | 28.9 | 10 | 23.0 | 18.4 |
| Ependymoma | 7.4 | 8.1 | 10.4 | 7 | 5.6 | 8 | 12 | 4.8 | 8.0 | 12.5 |
| Oligodendroglioma | 0.9 | 2.6 | 1.1 | 1.7 | 6.2 | 0 | 1.7 | 0 | NA | 10 |
| Craniopharyngioma | 11 | 9.2 | 4.4 | 6.8 | 18.4 | 4.6 | 6.6 | 10.5 | 6.0 | 9.2 |
| Chroid plexus tumor | 3 | 2.2 | Na | 2.3 | 1.8 | 1.9 | NA | 0 | NA | 0.8 |
| Neuronal & Mixed neuronal glial | 7.6 | 6.2 | 3.2 | <2 | 3.1 | 0 | 1.3 | 0 | NA | 1.7 |
| Meningioma | 3 | 2.6 | 1.2 | <2 | 3.1 | 1.6 | 2.2 | 1.9 | NA | 2.9 |
| Schwanomma | NA | 0.4 | NA | 3.1 | 2.8 | 1.1 | NA | 0 | NA | 2.9 |
| Germ cell tumor | 3.6 | 8.1 | NA | 3.1 | 7.9 | 1.5 | 0.9 | 14.3 | 2.0 | 1.3 |
| Pineal tumors | NA | NA | 1.3 | 0.5 | 0.6 | 2.7 | 0.7 | 0 | NA | 0.8 |

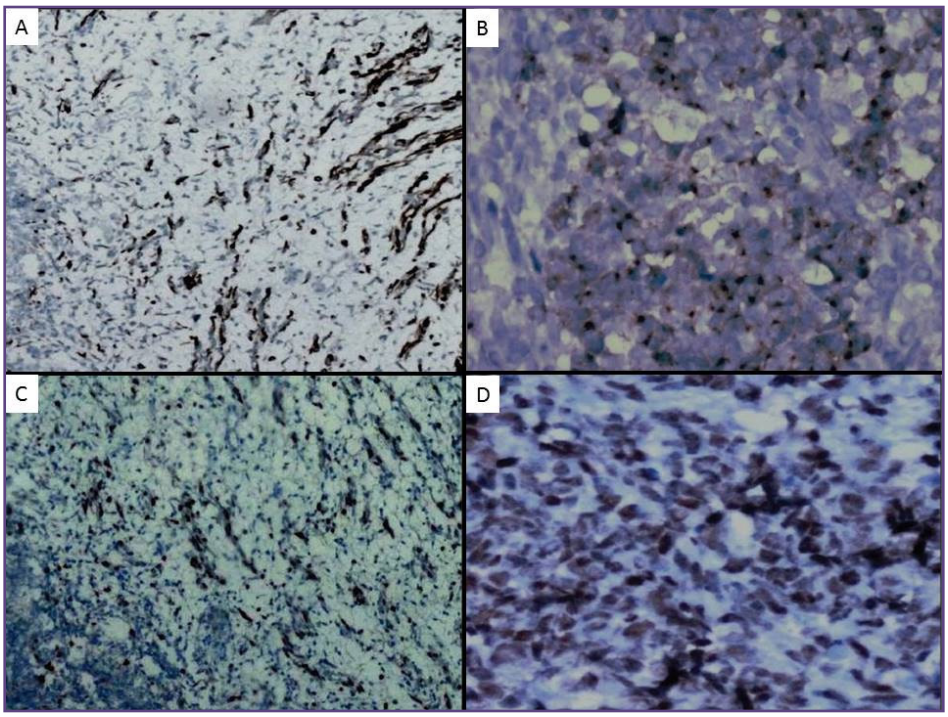


**Fig. 3: Different Histological variation of pediatric brain tumor viz. (A) Pilocytic astrocytoma with marked myxoid change with cystic degeneration, (B) pleomorphic xanthoastrocytoma showing multinucleated giant cells and mitotic figures, clear cell ependymoma (C) was confused with oligodendroglioma and microcystic pattern of oligodendroglioma (D).**

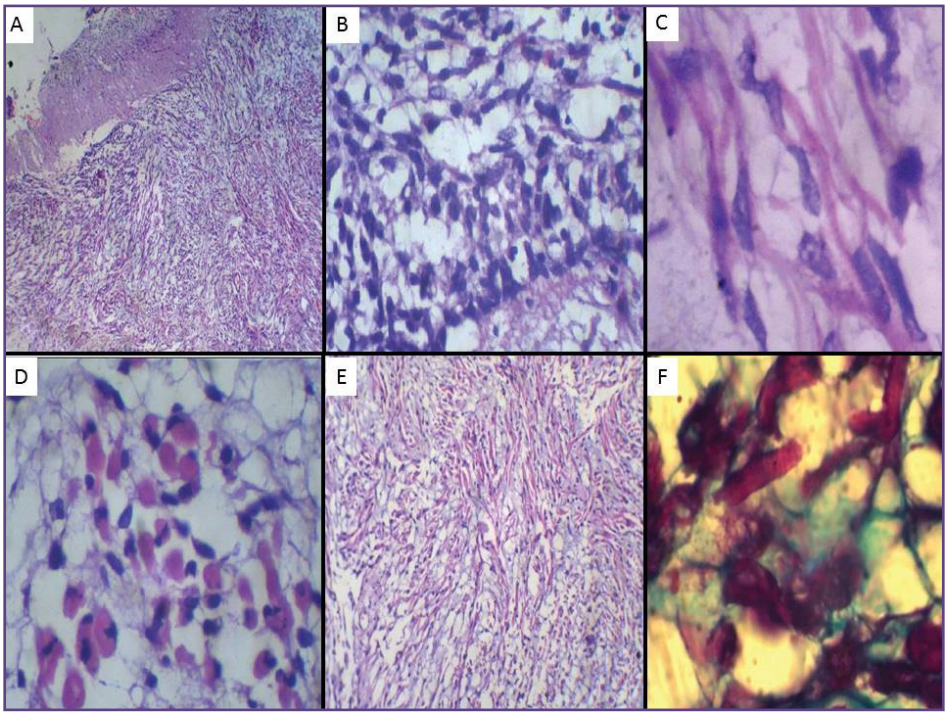


**Fig. 4: H & E sections from tumour showing two populations of cells (A) - H & E 100 X, predominantly of spindle shaped elongated strap-like cells with elongated nuclei and eosinophilic cytoplasm showing discernible cross striations(C & D) - H & E 400 X and foci of small round cells with hyperchromatic nuclei with scant cytoplasm.(B) - H & E 400 X Rhabdomyoblastic spindle shaped elongated strap-like cells (E) - H & E 100 X which highlighted on (F) Masson's Trichome stain- 1000 X.**

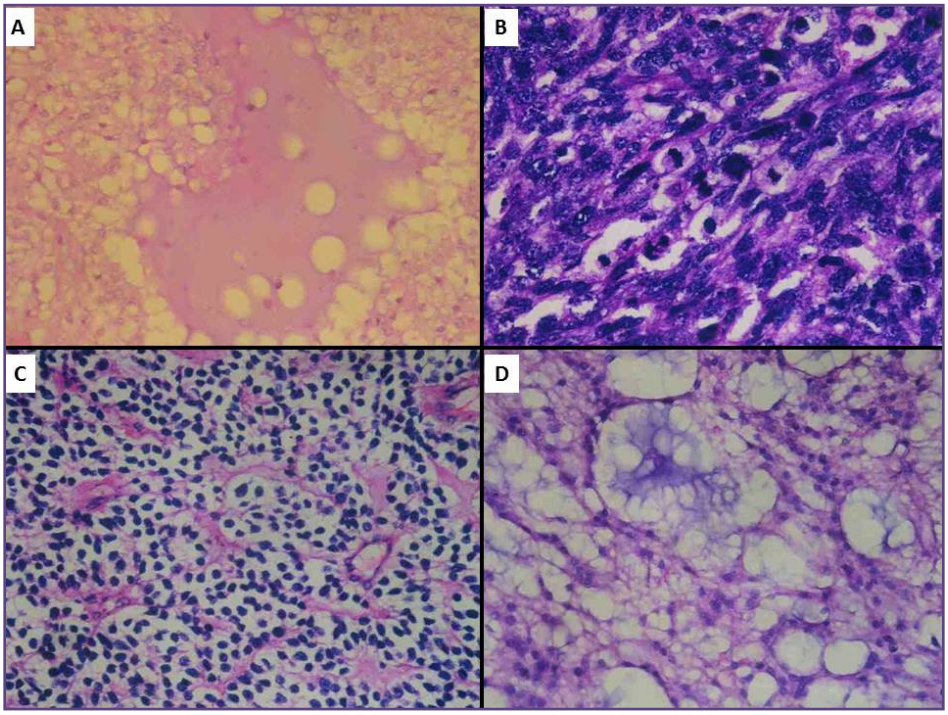


**Fig 5: Immunohistochemistry revealed positive staining for desmin and myogenin in the elongated eosinophilic cells while the round cells were negative for the same ( A & C) 100 X. The round cells were weakly positive for synaptophysin (B) 100 X. The tumor showed retained INI-1 protein expression. (D) 100 X.**

## Conclusion

From the present series, we conclude that, there is a rising global trend in the incidence of pediatric CNS tumors. The frequencies of major histologic types of PBTs found in the study do not differ substantially from that found in other developed and developing countries. Medulloblastomas and astrocytomas, are the major histologic types in pediatric patients. Epidemiological surveillance of various histological types of PBTs is of great importance which helps in planning the disease management and preventive programs.

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## Competing Interests

None Declared

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