World Neurosurgery: X 20 (2023) 100227

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x

"A tumour registry initiative"

Rajesh Nair [a], Bhavna Nayal [b], Saurabh Beedkar [a], Girish Menon [a,*]

[a] Department of Neurosurgery, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, India
[b] Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, India

ARTICLE INFO

Keywords:
Astrocytoma
Craniopharyngioma
Epidemiology
Medulloblastoma
Paediatric brain tumour
World Health Organization classification

ABSTRACT

Background: Published literature on epidemiological profile of paediatric brain tumours in India is limited. **Aim**: To present a retrospective analysis of the histological spectrum of 158 paediatric age group central nervous system tumours operated in a single tertiary care hospital in Coastal South India between January 2015 and December 2021.

Material and methods: Retrospective analysis of the data regarding frequencies of various primary brain tumours among 158 paediatric patients (<18 years of age). The tumours were categorised according to the revised 4th edition of World Health Organization (WHO) classification of tumours of the Central Nervous system.

Results: Paediatric CNS constituted 8.5% of total intracranial tumours (158/1860) operated in the study period. The mean age of the patients was 10.2 years and a definite male predominance was noted (1.54:1) Astrocytomas, glioneuronal tumours, and neuronal tumours constituted the majority (72/158; 45.6%) followed by embryonal tumours (31/158; 19.6%) and craniopharyngiomas(24/158; 15.4%).Of the glial neoplasms majority were pilocytic and other astrocytic tumours(41.6%), followed by mixed neuroglial tumours (19.4%), diffuse high grade astrocytomas (Grade III/IV) (11.1%), diffuse low -grade astrocytomas (Grade II) (9.7%) and ependymomas (13.8%). Our series also included six meningiomas (3.8%), five germ cell tumours (3.16%), four nerve sheath tumours (2.53%), two choroid plexus tumours (1.26%), two pineal parenchymal tumours (1.26%) and one metastasis from a soft tissue sarcoma from the thigh. Supratentorial tumours (58.2%) were more common than posterior fossa (34.6%) and spinal tumours (7.6%) and visual pathway gliomas accounted for 5.6% of all our tumours.

Conclusions: Paediatric central nervous system tumours are more common in boys and in the second decade of life. Astrocytomas are the most common paediatric brain tumours followed by medulloblastomas and craniopharyngiomas. Pediatric tumours affect the supratentorial compartment more often than the infratentorial compartment. The profile of paediatric brain tumours in our series is similar to that reported from other Indian centres as well as most western literature.

1. Introduction

Across the globe, the incidence of childhood cancers has increased over the last 25 years probably related to the increased availability of imaging facilities and early detection. India too has recorded an alarming 55–120% increase in childhood tumours seen in both sexes.[1] Globally, over 200,000 children develop cancer annually of which India accounts for nearly 60% of the numbers.[1,2,3] The prognosis for children with central nervous system (CNS) tumours is generally poor, with only 25% overall survival at 5 years.[1,4] Constituting approximately 35% of all childhood malignancies, paediatric central nervous system (CNS) tumours remains the leading cause of cancer-related deaths in children.[5,6] In the absence of well documented tumour registries in developing countries like India, data on paediatric brain tumour burden is often inaccurate and underestimated. Jain et al attempted to compile data on paediatric CNS tumours from seven major tertiary neurosurgical centres in India and later Asirvatham et al published their experience with nearly 1000 CNS tumours among children treated at a single tertiary care centre at Christian Medical College, Vellore.[7,8] Apart from these two major publications, data on paediatric CNS tumours from India is limited.[1,9] The present study attempts to profile the hospital-based prevalence of paediatric CNS tumours in a tertiary care

* Corresponding author. Department of Neurosurgery Kasturba Medical College Manipal Academy of Higher education Manipal, 576104, India.
E-mail addresses: rajeshnair39@yahoo.com (R. Nair), bhavnayal@yahoo.com (B. Nayal), Saurabh.beedkar@manipal.edu (S. Beedkar), girish.menon@manipal.edu (G. Menon).

https://doi.org/10.1016/j.wnsx.2023.100227
Received 17 January 2023; Received in revised form 2 June 2023; Accepted 12 June 2023
Available online 25 June 2023

centre in coastal South India. The data has been compared with other published national and international literature.

2. Material and Methods

Data on CNS tumours in the paediatric age group (<18 years of age) was collected from the neuropathology records of patients operated in the time period January 2015 to December 2021. All primary and secondary tumours were included and categorized according to the 4th edition of the WHO classification prevalent at the time of diagnosis. [10] With these criteria, a total of 158 paediatric brain tumours were collected and analysed to assess breakup of different histological types and grades and compared with available national and international data.[4,6,7, 11–28,11]

3. Results

Paediatric CNS tumours accounted on an average 8.5% of total intracranial tumours (158/1860). The age of the patients ranged from 3 months to 18 years, the mean being 10.2 years (Table 1). Our series had five infants (3.2%), 24 children between 2 and 5 years (15.8%), 48 between 6 years and 10 years (30.4%), 53 children between 11 and 15 years (33.5%) and 28 children above 16 years (17.7%). Our study cohort had 96 boys (60.8%) and 62 girls (39.2%) and boys exceeded girls in all age group divisions. The percentage breakup of various histological subtypes is provided in Table 2. Astrocytomas, glioneuronal tumours, and neuronal tumours constituted the majority (72/158; 45.6%). Embryonal tumours including medulloblastomas, supratentorial primitive neuroectodermal tumours (PNETs), Atypical teratoid rhabdoid tumours (ATRTs), comprised the second largest group after astrocytomas (31/158; 19.6%). Craniopharyngiomas was the third most common type (24/158; 15.4%) with all of them being of the adamantinomatous type and only one tumour of the papillary type. Of the 72 glial neoplasms majority were pilocytic astrocytomas and other astrocytic tumours (41.6%), followed by glioneuronal lesions (19.4%), diffuse high grade astrocytomas (11.1%), diffuse low -grade gliomas (9.7%) and ependymomas (13.8%). Neuronal and mixed neuroglial tumours (gangliogliomas and DNET) comprised 19.4% of our glial tumours. Pilocytic astrocytomas[12] was the single most common glial neoplasm. Of the pilocytic astrocytomas the most common location was the cerebellum[13] followed by chiasm (09) brain stem (02), tectum and thalamus (one each). Other low grade astrocytic tumours apart from pilocytic astrocytomas included one pleomorphic xanthoastrocytoma, one sub ependymal giant cell astrocytoma and two central neurocytomas. We had 10 ependymomas of which one was one was a spinal myxopapillary ependymoma. The frequency of glioblastoma and high grade astrocytomas in our study was 11.1% of all astrocytomas. This series included five germ cell tumours (3.16%). Of these two were mixed germ cell tumours, two teratomas and one germinomas. Our series also included six meningiomas (3.8%), five germ cell tumours (3.16%), four nerve sheath tumours (2.53%), two choroid plexus tumours (1.26%), two pineal parenchymal tumours (1.26%) and one metastasis from a soft tissue sarcoma from the thigh. The location of the tumours is summarised in Table 3. Supratentorial tumours (58.2%) were more common than posterior fossa (34.6%) and spinal tumours (7.6%). Our series had 34 sellar suprasellar tumours which included 24 craniopharyngiomas, 9 Visual pathway gliomas, one pituitary adenoma and two germ cell tumours. Of the 31 embryonal tumours 23 (74.19%) were medulloblastomas located in the posterior fossa and four were supratentorial embryonal tumours and four ATRTs. We also had one orbital tumour and two mesenchymal tumours involving the skull base. Table 4 compares the frequency of various CNS tumours reported in different countries, including developed countries such as Canada, Sweden, Japan and Germany as well as developing ones like Brazil, China and Morocco.[12–29] The profile of Pediatric CNS tumours in our series is similar to that reported from other Indian centres as well as most western literature (Table 4).

Table 1
Age and Sex distribution of paediatric CNS tumours in our series.

	Total	Male	Female
0 to 1	5 (3.2%)	3 (60%)	2 (40%)
2 to 5	24 (15.8%)	12 (55%)	10 (45%)
6 to 10	48 (30.4%)	34 (70.9%)	14 (28.1%)
11 to 15	53(33.5%)	32 (60.4%)	21(39.6%)
16 to 18	28 (17.7%)	16 (57.1%)	12 (42.9%)

Table 2
Breakup of various histological subtypes of paediatric CNS tumours in our series of 158 patients.

Gliomas, glioneuronal tumors, and neuronal tumors	72
Diffuse Astrocytoma	07
Anaplastic astrocytomas and glioblastomas	08
Other astrocytic tumours	
Pilocytic astrocytoma	27
Pleomorphic xanthoastrocytoma	02
Subependymal giant cell astrocytoma	01
•*Oligodendroglioma*	01
Neuronal and mixed neuro-glial tumours	
Ganglioglioma	11
Dysembryoplastic neuroepithelial tumor	03
Diffuse glioneuronal tumor	01
Central neurocytoma	02
Ependymal tumors	
Posterior fossa ependymoma	09
Spinal ependymoma	01
Choroid plexus tumors	**02**
Choroid plexus papilloma	02
Embryonal tumors	**31**
Medulloblastoma	23
Atypical teratoid/rhabdoid tumor	04
CNS embryonal tumor, NOS	04
Tumours of the pineal region	**02**
Pineocytoma	01
Pineal parenchymal tumor of intermediate differentiation	01
Tumours of the Cranial and paraspinal nerve	**04**
Schwannoma	04
Meningiomas	**06**
Mesenchymal, non-meningothelial tumors	**07**
Hemangiomas	02
Primary intracranial sarcoma	01
Ewing sarcoma	03
Chondrosarcoma	01
Histiocytic tumours	**03**
Germ cell tumors	**05**
Mature teratoma	02
Germinoma	01
Mixed germ cell tumor	02
Tumors of the sellar region	**25**
Craniopharyngioma	24
Pituitary adenoma/PitNET	01
Metastases to the CNS	**01**

Table 3
Location wise break up of our series 158 paediatric CNS tumours.

Supra tentorial92 (58.22%)	
Lobar	24
Sellar suprasellar	34 (chiasmal 9)
Pineal	07
Thalamic	02
Lateral ventricle	02
Infratentorial 54 (34.6%)	
Cerebellum	
Brain stem	03
Spine 12 (7.6%)	

Table 4
Frequency of various types of paediatric CNS tumours reported in different published series (in percentage).

	Brazil	Korea	Germany	Canada	China	Morocco	Japan	AIIMS	CMC	Ours
Astrocytomas	32.5	27.8	41.7	39.4	30.5	37.1	35.7	34.7	47.3	28.4
Oligo	0.9	2.6	1.1	1.7	6.2	1.7	0	1.1		0.63
Epednymomas	7.4	8.1	10.4	7	5.6	12	4.8	9.8	4.8	6.32
Chordoid plexus	03	2.2	Na	2.3	1.8	Na	0	1.8		1.26
Neuronal &Glioneuronal	7.6	6.2	3.2	<2	3.1	1.3	0	2.4		8.86
MB & PNET	13.9	19.8	25.7	15.4	14.6	28.9	10	22.4	11.4	19.6
Meningeal	3	2.6	1.2	<2	3.1	2.2	1.9	3.26		3.8
NERVE sheath	NA	0.4	Na	3.1	2.8	Na	0	3.6		2.53
Germ Cell	3.6	8.1	Na	3.1	7.9	0.9	14.3	2		3.16
Cranio	11	9.2	4.4	6.8	18.4	6.6	10.5	10.2	9.7	15.18
Pineal	NA	NA	1.3	0.5	0.6	0.7	0	1.3		2.53

4. Discussion

Tumours of the nervous system are the third most common childhood tumours after leukaemia and lymphomas, accounting for up to 20% of all tumours.[1,2,4,5,30] Paediatric CNS tumours constitute approximately 35% of all childhood malignancies and remain the leading cause of cancer-related deaths in children.[6] In the absence of large population based tumour registries, literature reports exclusively profiling paediatric CNS tumours from India is sparse and limited to few hospital based data.[7,8] Our study attempts to add to the available national data on Pediatric CNS tumours by collecting data categorized according to the most recent WHO classification. We have also attempted to compare our data with published national and international data. We believe that this information can assist the field of paediatric brain tumour research by planning treatment protocols and strategies.

The incidence of paediatric CNS tumours in India is not well documented whereas in the United States it is approximately 5.67 per 100,000 person-years.[13] The pathogenesis of most brain tumours in children is unclear but a genetic association and radiation exposure are probable risk factors[27,28] Neurofibromatosis type 1 (NF-1), tuberous sclerosis, Li-Fraumeni syndrome, Gorlin syndrome and Turcot syndromes are few of the genetic conditions associated with paediatric CNS tumours. The mean age in our series was 10.2 years which is similar to the one reported from other centres in India and comparable to the that reported from France (9 years) and China (12.6 years).[6,7,14,20,21] The most commonly affected age group was 11–15 years (34%), which is again similar to the that reported from Vellore, India but much higher than the European (1–4 years), Japanese (5–9 years), and French (5–9 years) series [6,12, 14, 15]. More than 50% of all tumours occurred after age 11 and more than 80% after age 5. Only five children (3.1%) were between the ages 0 and 1 year which is lower than the data from Taiwan (6.2%).[22]

Similar to what has been reported in other series, boys were affected more frequently than girls in our series (1.54:1). This ratio, however, is higher than that seen in Europe and most Asian countries (China, Korea, Iran) but lower than Brazil.[5,17–21,12] As observed in other series, supratentorial tumours (58.8%%) were more common than the infratentorial tumours (34.8%) in our series too. This preferential involvement for supratentorial compartment has been uniformly observed in almost all paediatric CNS tumour series.[4,13,14,31,16,18,20,21,24] However, studies from Pakistan and Iran, however have observed preferential involvement of Infratentorial compartment.[9,10,15–17,23,29] Another uniform observation confirmed in our series too is that supratentorial tumours are more common in infants and children up to 3 years of age and again after age 10, whereas between ages 4 and 10 Infratentorial tumours are more common.[4,14,16,18–21,24] Another interesting observation with regards to the age linked pathological profile of tumours is that younger children have a higher incidence of tumours of embryonal origin, such as medulloblastoma or atypical teratoid/rhabdoid tumour (ATRT), whereas older patients tend to have tumours of glial origin.[7,8]

Central nervous system tumours include a diverse spectrum of neoplasms and differ significantly from adult brain tumours with regards to their sites of origin, clinical presentation, histological features and their outcome. Metastasis, glial neoplasms and meningeal tumours constitute the predominant CNS tumour types in adults. In children besides gliomas, other major tumour types include embryonal neoplasms and craniopharyngiomas. In our study, the most common brain tumours in descending order are a) Astrocytomas, neuroglial tumours b) embryonal tumours c) craniopharyngiomas. This is similar to what was reported in other Indian centres. Jain et al's analyses of nearly 4000 paediatric CNS tumours complied from seven major tertiary neurosurgical centres in India and Asirvatham et al's study of 1000 tumours from one centre in South India revealed a similar profile.[7,8] However, in a large meta-analysis Rickert et al observed that internationally, ependymomas are the third most common tumours followed by craniopharyngioma.[24] This trend can be seen in the data from Canada, Germany, Sweden, and Morocco while figures from Korea and Brazil are similar to Indian data.[4,5,7,8,25–27,12,29] Report from a single institute in China, showed craniopharyngiomas to be the second commonest tumour.[20,28,32] Our study correlates with other Indian studies suggesting that the spectrum of brain tumours in Indian children seems to resemble Western studies.[7,8]

In our series majority of the tumours were glial neoplasms (45.5%). The overall frequency of astrocytomas is around 40% in Europe and varies between 25% and 35% in other Asian countries like Japan, China, Korea and Pakistan.[16,17,20,21,23–25,33] In our series too, among astrocytomas, Pilocytic astrocytoma was the most common (60%) which is similar to that reported in other studies.[17,24] Amongst pilocytic astrocytomas, visual pathway gliomas which involve the optic nerve, chiasm, tract, and optic radiations accounted for 5.6% of all our paediatric CNS tumours. In most reported series visual pathway gliomas account for 4%–8% of all brain tumours in children and are frequently associated with NF-1.[27,32,34] Children with High grade gliomas (HGGs) have an overall poor prognosis despite intensive therapy and approximately 20% of all childhood gliomas are HGGs which include anaplastic astrocytoma (AA), diffuse intrinsic pontine glioma (DIPG), and glioblastoma multiforme (GBM).[32,35,36] The frequency of GBM and high grade gliomas in our study was only 11.1% of all astrocytomas, lesser than that reported by Cho et al (17.2%).[18] Brain stem gliomas (BSGs), now classified as diffuse midline gliomas, H3 K27Mmutant, account for 10%–15% of all paediatric CNS tumours.[31,37] Our series, however, had only three biopsy proven case of brain stem gliomas. This is probably related to the fact that most brain stem gliomas undergo direct radiotherapy without biopsy confirmation. Ependymomas are the third most common brain tumour in children and account for approximately 8%–10% of all childhood CNS tumours.[38] Our series, however, had only ten ependymomas all of them except one located in the posterior fossa. The standard of care for most paediatric glial neoplasms except brain stem gliomas and visual pathway gliomas is maximal safe resection followed by adjuvant therapy. The use of irradiation in children younger than 3 years remains controversial, but chemotherapy is typically used to delay or avoid irradiation to avoid the long-term consequences.

An embryonal tumour of the posterior fossa, Medulloblastoma comprises up to 20% of all paediatric brain tumours.1 and have a male predominance.[27] Based on molecular subtyping medulloblastomas are now subdivided into four groups: wingless (WNT), Sonic hedgehog (SHH), group 3, and group 4.[10,31,39] Medulloblastoma was the second most common tumour in our study similar to other studies from India and those from Brazil, Iran, and Korea.[7,8,18,19] Though individual studies from different countries in Europe did find medulloblastomas to be the second most common tumour, analysis of 19,531 paediatric CNS tumours from the European Database Automated Childhood Cancer Information System found medulloblastomas to be a distant fourth (3%) after astrocytoma (40%), PNET (11%), and ependymoma (5%).[14,17,24] Earlier known as CNS-primitive neuroectodermal tumours (PNETs), supratentorital embryonal tumours represent a group of rare paediatric supratentorial tumours comprising fewer than 3% of paediatric brain tumours and carry a poor prognosis.[27] ATRTs are rare malignant intracranial neoplasms most commonly occurring in infants and young children. They account for only 1%–2% of all paediatric brain tumours but approximately 10%–20% of CNS tumours in patients younger than 3 years.[27] Our series had four cases (2.5%) each of embryonal tumours and ATRTs all of whom had a poor long term outcome.[24] The standard of care for all these tumours is gross total removal followed by radiation therapy, and chemotherapy, regardless of molecular subtype.

Craniopharyngiomas are slow-growing benign epithelial tumours that arise from embryonic remnants of the Rathke pouch in the suprasellar region adjacent to the optic chiasm and account for approximately 5%–10% of paediatric brain tumours.[40] In our series craniopharyngioma constituted 15.2% of our total tumours similar to that reported from Brazil and Korea but higher than that reported from other Indian series.[5,7,8,18] In China, craniopharyngioma is the second most common tumour after glial lesions.[20,21] Although considered histologically benign tumours, paediatric craniopharyngiomas remain a challenge with respect to treatment options due to the close proximity to many vital structures.[41] Surgery with adjuvant radiotherapy for residual/recurrent lesions remains the mainstay of treatment, with *a* >85% progression-free survival rate.[27]

Intracranial germ cell tumours (GCTs) represent approximately 3% of paediatric brain tumours and most commonly arise in midline locations, such as the pineal or suprasellar region.[27] The frequency of germ cell tumours varies markedly in different countries ranging from as low as 0.9% in Morocco to as high as 14.3% in Japan, China and oriental countries (7.8–11%).[16,20,21,29] The frequency of germ cell tumours in our series was 2.8% comparable to European literature [12]. Asian countries particularly Korea, China, and Japan, show higher frequency for germ cell tumours and craniopharyngiomas probably related to environmental and/or genetic differences.

Choroid plexus tumours are intraventricular papillary neoplasms derived from the choroid plexus epithelium and account for fewer than 1% of all brain tumours and 3%–4% of paediatric intracranial tumours. Approximately 50% of choroid plexus tumours are found in the lateral ventricles, 40% in the fourth ventricle and 5% in the third ventricle and multiple ventricles in the remaining 5%.[27,12] Our series had only two choroid plexus tumours accounting for 1.3% of total tumours. Gross total resection is typically curative for choroid plexus papillomas whereas the invasive nature of choroid plexus carcinomas makes it difficult to achieve complete resection, necessitating the use of adjuvant therapy.[27]

Primary spinal cord tumours are rare CNS tumours and accounted 7.5% of all childhood CNS tumours in our series. Spinal cord tumours can be intramedullary, intradural-extramedullary, and extradural, the most common in children being astrocytomas and ependymomas.[27] In our study, the frequency of nerve sheath tumours 2.5% was similar to that reported by Wong et al (1.4%) and Bauchetet al. (2%) but less compared to other Indian reports (4.1%) [6,7, 12, 20].

We also had few unique pathologies in our series. Pediatric meningiomas are known to be rare accounting for 2.5% of paediatric CNS tumours.[42] We had six (3.7%) cases of meningiomas most of them in skull base locations. We also had three cases each of histiocytosis and Ewing's sarcoma and one case of intracranial metastasis from a soft tissue sarcoma in the thigh. We had one case of paediatric pituitary adenoma another rare pathology in childhood.[43]

5. Conclusion

Pediatric CNS tumours are more common in boys and in the second decade of life. Astrocytomas are the most common paediatric CNS tumours followed by medulloblastomas and craniopharyngiomas. Paediatric tumours affect the supratentorial compartment more often than the Infratentorial compartment. The profile of Pediatric CNS tumours in our series is similar to that reported from other Indian centres as well as most western literature. The present survey revealed the spectrum of CNS tumours in children in tertiary centre from coastal south India.

Study approval statement

This study protocol was reviewed by *Kasturba Medical College Institutional Ethical Committee (KMCIEC)*. No ethics approval was required and was granted an exemption from requiring ethics approval. Reference No: IEC No: 267/2022.

Consent to participate statement

Written informed consent was not required and the study was granted exemption from requiring written informed consent as per KMCIEC, reference number IEC No: 276/2022.

Funding sources

All the authors involved in this submission have no vested interests or funding sources to declare.

CRediT authorship contribution statement

Rajesh Nair: Conceptualization, Data curation, Writing – review & editing. **Bhavna Nayal:** Data curation, Resources, Validation. **Saurabh Beedkar:** Investigation. **Girish Menon:** Conceptualization, Data curation, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Nil.

References

1 Arora RS, Eden TO, Kapoor G. Epidemiology of childhood cancer in India. *Indian J Cancer*. 2009;46:264–273.
2 Kusumakumary P, Jacob R, Jothirmayi R, Nair MK. Profile of pediatric malignancies: a ten year study. *Indian Pediatr*. 2000;37:1234–1238.
3 Louis DN, Perry A, Wesseling P, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. *Neuro Oncol*. 2021;23(8):1231–1251. https://doi.org/10.1093/neuonc/noab106.PMID:34185076. PMCID: PMC8328013.
4 Kaatsch P, Rickert CH, Kühl J, Schüz J, Michaelis J. Population-based epidemiologic data on brain tumors in German children. *Cancer*. 2001;92:3155–3164.
5 Rosemberg S, Fujiwara D. Epidemiology of pediatric tumors of the nervous system according to the WHO 2000 classification: a report of 1,195 cases from a single institution. *Childs Nerv Syst*. 2005;21:940.
6 Jemal A, Siegel R, Ward E, et al. Cancer statistics. *CA Cancer J Clin 2006*. 2006;56:106–130.

7 Jain A, Sharma MC, Suri V, et al. Spectrum of pediatric brain tumors in India: a multi-institutional study. *Neurol India*. 2011;59(2):208–211. https://doi.org/10.4103/0028-3886.79142.PMID:21483119. Mar-Apr.
8 Asirvatham JR, Deepti AN, Chyne R, et al. Pediatric tumors of the central nervous system: a retrospective study of 1,043 cases from a tertiary care center in South India. *Childs Nerv Syst*. 2011 Aug;27(8):1257–1263. https://doi.org/10.1007/s00381-011-1407-z. Epub 2011 Feb 23. PMID: 21344241.
9 Tyagi BB. Childhood cancer incidence in Delhi, 1996– 2000. *Indian J Med Paediatr Oncol*. 2006;27:13–18.
10 Louis DN, Perry A, Wesseling P, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. *Neuro Oncol*. 2021 Aug 2;23(8):1231–1251.
11 Wen PY, Packer RJ. The 2021 WHO classification of tumors of the central nervous system: clinical implications. *Neuro Oncol*. 2021 Aug 2;23(8):1215–1217. https://doi.org/10.1093/neuonc/noab120.PMID:34185090. PMCID: PMC8328017.
12 Hjalmars U, Kulldorff M, Wahlqvist Y, Lannering B. Increased incidence rates but no space-time clustering of childhood astrocytoma in Sweden, 1973-1992: a population-based study of pediatric brain tumors. *thCancer*. 1999;85:2077–2090.
13 Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011-2015. *Neuro Oncol*. 2018;20(suppl_4):iv1–iv86. https://doi.org/10.1093/neuonc/noy131. Erratum in: Neuro Oncol. 2018 Nov 17;:null. PMID: 30445539; PMCID: PMC6129949.
14 Bauchet L, Rigau V, Mathieu-Daude H, Fabbro-Peray P, Palenzuela G, Figarella-Branger D, Moritz J, Puget S, Bauchet F, Pallusseau L, Duffau H, Coubes P, Tretarre B, Labrousse F,.
15 Dhellemmes P. Clinical epidemiology for childhood primary central nervous system tumors. *J Neuro Oncol*. 2009;92:87–98.
16 Makino K, Nakamura H, Yano S, Kuratsu J. Population based epidemiological study of primary intracranial tumors in childhood. *Childs Nerv Syst*. 2010;26:1029–1034.
17 Peris-Bonet R, Martinez-Garcia C, Lacour B, et al. Childhood central nervous system tumours–incidence and survival in Europe (1978–1997): report from automated childhood cancer information system project. *Eur J Cancer*. 2006;42:2064–2080.
18 Cho KT, Wang KC, Kim SK, Shin SH, Chi JG, Cho BK. Pediatric brain tumors: statistics of SNUH, Korea (1959–2000). *Childs Nerv Syst*. 2002;18:30–37.
19 Mehrazin M, Rahmat H, Yavari P. Epidemiology of primary intracranial tumors in Iran, 1978–2003. *Asian Pac J Cancer Prev APJCP*. 2006;7:283–288.
20 Zhang R, Shen WQ, Zhou LF. Primary pediatric central nervous system tumors statistic: study of 763 cases in a single institution. *Zhonghua Yixue Zazhi*. 2007;87:442–447.
21 Zhou D, Zhang Y, Liu H, Luo S, Luo L, Dai K. Epidemiology of nervous system tumors in children: a survey of 1,485 cases in Beijing Tiantan Hospital from 2001 to 2005. *Pediatr Neurosurg*. 2008;44:97–103.
22 Wong TT, Ho DM, Chang KP, et al. Primary pediatric brain tumors: statistics of Taipei VGH, Taiwan (1975–2004). *Cancer*. 2005;104:2156–2167.
23 Ahmed N, Bhurgri Y, Sadiq S, Shakoor KA. Pediatric brain tumours at a tertiary care hospital in Karachi. *Asian Pac J Cancer Prev APJCP*. 2007;8:399–404.
24 Rickert CH, Paulus W. Epidemiology of central nervous system tumors in childhood and adolescence based on the new WHO classification. *Childs Nerv Syst*. 2001;17:503–511.
25 Suh YL, Koo H, Kim TS, et al. Tumors of the central nervous system in Korea: a multicenter study of 3221 cases. *J Neuro Oncol*. 2002;56:251–259.
26 Kaderali Z, Lamberti-Pasculli M, Rutka JT. The changing epidemiology of paediatric brain tumours: a review from the Hospital for sick children. *Childs Nerv Syst*. 2009;25:787–793.
27 Udaka YT, Packer RJ. Pediatric brain tumors. *Neurol Clin*. 2018;36(3):533–556. https://doi.org/10.1016/j.ncl.2018.04.009. PMID: 30072070.
28 Ron E, Modan B, Boice Jr JD, et al. Tumors of the brain and nervous system after radiotherapy in childhood. *N Engl J Med*. 1988 Oct 20;319(16):1033–1039. https://doi.org/10.1056/NEJM198810203191601.PMID:3173432.
29 Karkouri M, Zafad S, Khattab M, et al. Epidemiologic profile of pediatric brain tumors in Morocco. *Childs Nerv Syst*. 2010;26:1021–1027.
30 Malbari F. Pediatric neuro-oncology. *Neurol Clin*. 2021 Aug;39(3):829–845. https://doi.org/10.1016/j.ncl.2021.04.005. Epub 2021 Jun 10. PMID: 34215389.
31 Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol*. 2007;114(2):97–109. https://doi.org/10.1007/s00401-007-0243-4. Epub 2007 Jul 6. Erratum in: Acta Neuropathol. 2007 Nov;114(5):547. PMID: 17618441; PMCID: PMC1929165.
32 Pollack IF. Brain tumors in children. *N Engl J Med*. 1994;331(22):1500–1507.
33 Wilne S, Collier J, Kennedy C, Koller K, Grundy R, Walker D. Presentation of childhood CNS tumours: a systematic review and meta-analysis. *Lancet Oncol*. 2007 Aug;8(8):685–695. https://doi.org/10.1016/S1470-2045(07)70207-3. PMID: 17644483.
34 Silva MM, Goldman S, Keating G, Marymont MA, Kalapurakal J, Tomita T. Optic pathway hypothalamic gliomas in children under three years of age: the role of chemotherapy. *Pediatr Neurosurg*. 2000 Sep;33(3):151–158. https://doi.org/10.1159/000028996.PMID:11096362.
35 Braunstein S, Raleigh D, Bindra R, Mueller S, Haas-Kogan D. Pediatric high-grade glioma: current molecular landscape and therapeutic approaches. *J Neuro Oncol*. 2017 Sep;134(3):541–549. https://doi.org/10.1007/s11060-017-2393-0. Epub 2017 Mar 29. PMID: 28357536.
36 Wisoff JH, Boyett JM, Berger MS, et al. Current neurosurgical management and the impact of the extent of resection in the treatment of malignant gliomas of childhood: a report of the Children's Cancer Group trial no. CCG-945. *J Neurosurg*. 1998 Jul;89(1):52–59. https://doi.org/10.3171/jns.1998.89.1.0052. PMID: 9647172.
37 Freeman CR, Farmer JP. Pediatric brain stem gliomas: a review. *Int J Radiat Oncol Biol Phys*. 1998;40(2):265–271.
38 Allen JC, Siffert J, Hukin J. Clinical manifestations of childhood ependymoma: a multitude of syndromes. *Pediatr Neurosurg*. 1998;28(1):49–55.
39 Northcott PA, Buchhalter I, Morrissy AS, et al. The whole-genome landscape of medulloblastoma subtypes. *Nature*. 2017;547(7663):311–317. https://doi.org/10.1038/nature22973.PMID:28726821. PMCID: PMC5905700.
40 Garre ML, Cama A. Craniopharyngioma: modern concepts in pathogenesis and treatment. *Curr Opin Pediatr*. 2007;19(4):471–479.
41 Müller HL, Albanese A, Calaminus G, et al. Consensus and perspectives on treatment strategies in childhood craniopharyngioma: results of a meeting of the Craniopharyngioma Study Group (SIOP), Genova, 2004. *J Pediatr Endocrinol Metab*. 2006 Apr;19(Suppl 1):453–454. PMID: 16700324.
42 Menon G, Nair S, Sudhir J, Rao BR, Mathew A, Bahuleyan B. Childhood and adolescent meningiomas: a report of 38 cases and review of literature. *Acta Neurochir (Wien)*. 2009 Mar;151(3):239–244.
43 Walz PC, Drapeau A, Shaikhouni A, et al. Pediatric pituitary adenomas. *Childs Nerv Syst*. 2019 Nov;35(11):2107–2118.

Abbreviations

WHO: World Health Organization
CNS: Central nervous system
PNETs: Primitive neuroectodermal tumours
ATRTs: Atypical teratoid rhabdoid tumours
DNET: Dysembryoplastic neuroepithelial tumours
NF-1: Neurofibromatosis type 1
HGGs: High grade gliomas
AA: Anaplastic astrocytoma
DIPG: Diffuse intrinsic pontine glioma
GBM: Glioblastoma multiforme
BSGs: Brain stem gliomas
WNT: Wingless
SHH: Sonic hedgehog
GCTs: Intracranial germ cell tumours