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Original Article

Demographic and Histopathologic Profile of Pediatric Patients with Primary Brain Tumors Attending a Regional Cancer Center

Abstract

Background: Primary brain tumors (PBTs) are the most common solid childhood malignancies. However, epidemiologic profile of these tumors is scarce in developing nation like India. **Objective of Study:** The objective of this study was to study the demographic and histopathologic profile of pediatric patients with PBTs residing in Gujarat, and attending the Gujarat Cancer and Research Institute, Ahmedabad. **Materials and Methods:** Data regarding age, gender, anatomical site, and histopathology (according to the World Health Organization classification) of 242 patients with brain tumors (0–18 years) operated over 10 years (January 2006 to December 2015) were collected retrospectively, and analyzed. **Results:** Of total 242 patients with PBTs, 78.1% were from 5 to 14 years age group with the mean age being 9.38 ± 3.82 years (95% confidence interval). Brain tumors were more common in males (64.1%) as compared to females (35.9%) with a male-to-female ratio of 1.78:1. The most common anatomical site was cerebellum (46.3%), followed by cerebral hemispheres (14.1%). Infratentorial tumors (60.9%) were predominant than supratentorial tumors (39.1%) in 0–14 years age group while supratentorial tumors (58.3%) were predominant than infratentorial tumors (41.7%) in 15–18 years age group. Astrocytic tumors (38.9%) and embryonal tumors including medulloblastomas, supratentorial primitive neuroectodermal tumors, and atypical teratoid/rhabdoid teratomas (34.7%) were the most common histological subtypes comprising three-quarters of all tumors. Ependymomas (16.1%) and craniopharyngiomas (5%) were third and fourth most common tumors, respectively. Among astrocytic tumors, 71.3% were of lower grade histology (Grade I and II). **Conclusions:** Astrocytomas and medulloblastomas, which form the major histologic subtypes in children residing in Gujarat, needs special attention with respect to the distribution of infrastructure and resources. Histopathological profiles of cohort in this study do not differ substantially from other hospital-based and population-based studies.

Keywords: *Astrocytoma, cerebellum, craniopharyngioma, ependymoma, medulloblastoma, supratentorial*

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Introduction

After hematological malignancies as a group, primary brain tumors (PBTs) are the second most common malignancy among children. However, among all solid tumors in children, they are the most common form and also the leading cause of cancer-related deaths. They constitute approximately 15%–25% of all pediatric malignancies.[1-3] Childhood brain tumors are biologically distinct entity as compared to those that present in later life about their sites of origin, clinical presentation, histological features, biological behavior, and prognosis. In adults, the most common tumor site is the meninges and the most common primary histology being the meningioma. However, in children, the most common tumor site is the cerebellum with astrocytoma being the most common primary histology isolated.[4] A lot of development has happened in the field of pediatric brain tumors with regard to characterization of various molecular and genetic pathways, with change in classification dependent only on histogenesis (the World Health Organization [WHO] 2007 classification) to incorporation of both, genotypic and phenotypic parameters, as in the latest WHO 2016 classification.[5,6] There is no dearth of epidemiologic information on pediatric brain tumors in the Western literature; however, such knowledge is scarce in developing nation like India. Hence, this hospital-based study was conducted to characterize the demographic profile and histopathological subtypes of PBTs among the pediatric patients who presented to us.

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Materials and Methods

Data regarding age, gender, anatomical site, and histopathology (according to the WHO classification prevalent at the time of the diagnosis) of 242 patients with brain tumors (0–18 years) operated over 10 years (January 1, 2006 to December 31, 2015) were collected retrospectively, and analyzed using GraphPad. Patients with metastatic brain tumor, benign cystic lesion (arachnoid cysts, epidermoid cysts, and colloid cysts), space occupying lesion of infectious etiology, and vascular malformations were excluded from the study. Only patients residing in Gujarat and attending Gujarat Cancer and Research Institute, Ahmedabad, were enrolled in the study.

Results

Age- wise and gender-wise distribution

Of total 242 patients presenting with PBTs, 189 (78.1%) were from 5 to 14 years age group, with an almost equal number of patients in 5–9 (n = 94/189) and 10–14 (n = 95/189) years age group. Children (0–14 years) accounted for 95% of the cohort (n = 230/242) while adolescents (15–18 years) accounted for only 5% of the cohort (n = 12/242) [Table 1]. The mean age of presentation was 9.38 ± 3.82 years (95% confidence interval). PBTs were more common in males (64.1%) (n = 155/242) as compared to females (35.9%) (n = 87/242) with a male-to-female (M: F) ratio of 1.78:1. However, M: F ratio varied according to the histopathological diagnosis with M:F ratio being 3.33:1, 3:1, and 2.81:1 in patients with ependymal tumors, meningiomas, and medulloblastomas, respectively. Equal sex distribution was seen in patients with craniopharyngiomas and pineal gland tumors. Only female representation was seen in patients with oligodendroglial tumors (n = 2), choroid plexus tumors and ganglioglioma (n = 1 each). Among children, males accounted for 64.8% (n = 149/230) while females accounted for 35.2% (n = 81/230) of the cohort. Among adolescents, there was equal representation of the sexes.

Location wise distribution

The most common anatomical site, as shown in Figure 1, was cerebellum (46.3%) (n = 112/242), followed by cerebral hemispheres (14.1%) (n = 34/242), brainstem (13.6%) (n = 33/242) ventricles (9.9%) (n = 24/242), and sellar region (7.9%) (n = 19/242). Involvement of optic apparatus, hypothalamus, and thalamus (grouped as a diencephalic region) was seen in 7.4% of the patients. Infratentorial tumors (60.9%) were predominant than supratentorial tumors (39.1%) in 0–14 years age group while supratentorial tumors (58.3%) were predominant than infratentorial tumors (41.7%) in 15–18 years age group.

Table 1: Age-wise and gender-wise distribution of the patients in this study

Age group (years)	Gender	
	Male	Female
<1	7	1
1-4	22	11
5-9	62	32
10-14	58	37
15-18	6	6
Total	155	87

Histopathological distribution

The most common histological subtype isolated were medulloblastomas accounting for 33.1% (n = 80/242) of all PBTs, followed by ependymomas (16.1%) (n = 39/242), Grade I astrocytomas (14.9%) (n = 36/242), Grade II astrocytomas (12.8%) (n = 31/242), and Grade IV astrocytomas (9.5%) (n = 23/242). The distribution of other histological subtypes in this study and other national and international studies is shown in Tables 2 and 3. Among astrocytic tumors, lower grade histology (Grade I and II) was seen in 71.3% of the patients. However, the histopathological distribution also varied according to age groups. Table 4 shows the most common and second most common brain tumor histologies by age at the occurrence.

Discussion

The incidence and mortality of PBTs among pediatric population is high; however, its tumor burden is underestimated in developing countries like ours due to the lack of complete registration of newly diagnosed cases with local cancer registries. In such scenario, hospital- based prevalence data becomes the primary source for estimating the disease load. This data are essential for assessing geographical differences in phenotypic and genotypic profiles of PBTs and also ascertaining the required neuro-oncological health-care infrastructure for their management. Demographic and histopathological profiles of Indian pediatric PBTs are available from nine

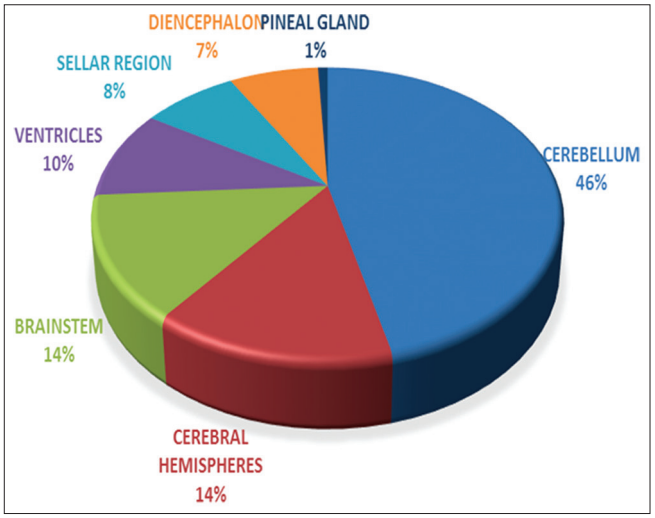

Figure 1: Distribution of primary brain tumors by the anatomical site in our study

Table 2: Frequency of various histological subtypes of pediatric primary brain tumors in Indian studies (%)

Tumour	AIIMS[3]	NIMHANS[3]	GB pant[3]	TMH[3]	CSMMU[3]	CMC[3]	PGIMER[3]	BJMC[2]	LTMMC[7]	Our study
Medulloblastoma	NA	NA	NA	NA	NA	NA	NA	NA	NA	33.1
Ependymoma	8.5	8.5	12.2	19.1	9.4	4.8	6.3	6.6	12.5	16.1
Grade I astrocytoma	23	29	19.4	17.4	14.6	34.9	NA	NA	NA	14.9
Grade II astrocytoma	2.7	1.1	1.1	7.7	12.4	5.3	NA	NA	NA	12.8
Grade III astrocytoma	2.4	4.8	0	1.4	0	2.9	NA	NA	NA	1.7
Grade IV astrocytoma	5.6	9.2	1.8	2.1	3.6	3.6	NA	NA	NA	9.5
Total astrocytic tumours	33.7	44.1	22.3	28.6	30.6	46.7	37	29	46.8	38.9
Craniopharyngioma	12.7	7.7	13.5	4.5	13.1	8.5	11.5	11.8	9.2	5
Meningioma	5.6	4.3	0.3	3.4	2.2	3.5	NA	1.3	2.9	1.7
Schwannoma	7	4.3	1.3	2.4	2.2	4.6	NA	2.6	2.9	1.2
PNET	NA	NA	NA	NA	NA	NA	NA	NA	NA	1.2
Oligodendroglioma	0.7	0.9	2.9	1.4	1.5	0	0	2.6	10	0.8
Pineal gland tumours	0.7	1.4	1.3	1	3	NA	NA	1.3	0.8	0.8
Choroid plexus tumours	1.5	2.6	1.6	1.7	1.5	NA	3.5	2.6	0.8	0.4
Neuronal and mixed neuronal glial	4.1	2.8	5.2	2.1	0	NA	NA	1.3	1.7	0.4
AT/RT	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.4
Total embryonal tumours	16.8	19.7	32	29	27.7	10.3	21.6	29	18.4	34.7
Germ cell tumors	2.2	2.2	3.3	1.7	2.2	NA	NA	0	1.3	NA
Lymphoma	1	0.5	0.3	0	0	1.1	NA	NA	0.8	NA
Total number of paediatric tumors	819	648	378	288	137	1297	369	76	239	242

AIIMS – All India Institute of Medical Sciences; NIMHANS – National Institute of Mental Health and Neurosciences; TMH: Tata Memorial Hospital; CSMMU – Chhatrapati Shahuji Maharaj Medical University; CMC – Christian Medical College; PGIMER – Post Graduate Institute of Medical Education and Research; BJMC – B. J. Medical College and Civil Hospital; LTMMC – Lokmanya Tilak Memorial Medical College; PNET – Primitive neuroectodermal tumor; AT/RT – Atypical teratoid/rhabdoid teratomas; NA – Not available

Table 3: Frequency of various histological subtypes of pediatric primary brain tumors in international studies (%)

Tumour	Brazil[8]	Korea[9]	Germany[10]	Canada[11]	Beijing[12]	Morocco[13]	Japan[14]	Hong Kong[15]	Our study
Astrocytoma	32.5	27.8	41.7	39.4	30.5	37.1	35.7	57	38.9
Medulloblastomas and PNETs	13.9	19	25.7	15.4	14.6	28.9	10	23	34.3
Ependymoma	7.4	8.1	10.4	7	5.6	12	4.8	8	16.1
Oligodendroglioma	0.9	2.6	1.1	1.7	6.2	1.7	0	NA	0.8
Craniopharyngioma	11	9.2	4.4	6.8	18.4	6.6	10.5	6	5
Choroid plexus tumour	3	2.2	NA	2.3	1.8	NA	0	NA	0.4
Neuronal and mixed neuronal glial	7.6	6.2	3.2	<2	3.1	1.3	0	NA	0.4
Meningioma	3	2.6	1.2	<2	3.1	2.2	1.9	NA	1.7
Schwanomma	NA	0.4	NA	3.1	2.8	NA	0	NA	1.2
Germ cell tumor	3.6	8.1	NA	3.1	7.9	0.9	14.3	2	NA
Pineal tumors	NA	NA	1.3	0.5	0.6	0.7	0	NA	0.8

PNETs – Primitive neuroectodermal tumors; NA – Not available

tertiary healthcare centers-GB Pant Hospital, New Delhi; Christian Medical College, Vellore; Post Graduate Institute of Medical Education and Research, Chandigarh; National Institute of Mental Health and Neurosciences, Bangalore; Tata Memorial Hospital, Mumbai; Chhatrapati Shahuji Maharaj Medical University, Lucknow; All India Institute of Medical Sciences, New Delhi; and B. J. Medical College and Civil Hospital (BJMC), Ahmedabad and Lokmanya Tilak Memorial Medical College, Mumbai, via studies conducted by Jain *et al*.,[3] Shah *et al*.,[2] and Sangita *et al*.[7] This study has analyzed similar data of patients residing only in Gujarat. The results were compared to other national and international studies.

The frequency of pediatric patients with PBTs was highest in 5–14 years age group (78.1%) which is in line with other studies.[2,7,16,17] The frequencies of PBTs were higher among children (0–14 years) as compared to the adolescents (15–18 years). The mean age at diagnosis in this study was 9.38 years while it was 10.69 years in BJMC study.[2] However, the difference was statistically

Table 4: First and second most common histopathological distribution by age group at the occurrence

Age group (years)	Most common histology	Second most common histology
<1	Ependymal tumors	Medulloblastomas
1-4	Medulloblastomas	Ependymal tumors
5-9	Astrocytic tumors	Medulloblastomas
10-14	Astrocytic tumors	Medulloblastomas
15-18	Astrocytic tumors	Craniopharyngiomas and schwannoma (equal frequencies)

insignificant (P = 0.0625, Unpaired t-test with Welch correction). Mean ages reported from Morocco,[13] Pakistan,[18] and China[19] were 9.3, 8.8, and 12.68 years, respectively. A higher proportion of brain tumors were found in males as compared to in females in this study, with a male-to-female ratio of 1.78:1, consistent with findings of other studies,[12-14,19,20] with Pakistan reporting the highest ratio of 2.52:1.[18] The ratio also varied according to the histological subtype with male predominance seen in subtypes ependymal tumors, meningiomas, and medulloblastomas. As observed in other studies,[2,7,11,16] males and females with PBT were evenly distributed among different age groups in our study and observed differences were not statistically significant (P = 0.3586, Fischer's exact test).

The most common anatomical site in this study was cerebellum followed by cerebral hemispheres, brainstem, and ventricles. The topographical predominance of cerebellum and cerebral hemispheres was due to the maximum isolation of medulloblastomas and astrocytomas at those sites. These findings were in line with the results of other published data.[2,7,8,10,16] In this study, infratentorial tumors were bit predominant in childhood age group whereas, in adolescent age group, supratentorial tumors were more common, which was consistent with the findings of other studies.[2,7,16,17] However, there was no statistically significant difference in the distribution of supratentorial and infratentorial tumors among children and adolescents (P = 0.2309, Fischer's exact test).

In the present study, medulloblastoma was the most common histological subtype (33.1%), followed by ependymomas (16.1%) and Grade I astrocytomas (14.9%). However, overall, astrocytomas (38.9%) were the most common tumors followed by embryonal tumors including medulloblastomas, supratentorial primitive neuroectodermal tumors, and atypical teratoid/rhabdoid teratomas (34.7%), together constituting almost three-quarters of all PBTs in the study population. Ependymoma appeared to be the third most common tumor in this study which contradicted the results of two Indian[2,3] and two international studies[8,9] (which showed craniopharyngioma as the third most common tumor) but was in line with major international studies.[10,11,13,16,17] Craniopharyngioma was the fourth most common tumor in this study which is in line with other studies[10,11,13] which contradicted with two Indian studies.[2,3] The frequency of various histological subtypes of pediatric PBTs in this study as compared to other national and international studies is shown in Tables 2 and 3. Histopathological distribution also varied according to age groups as shown in Table 4; however, it was different to that of Central Brain Tumor Registry of the United States report.[4] The primary limitation of our study was that it was restricted to only patients residing in Gujarat, and treated at a single institution. Hence, caution is required when extrapolating the results of this data to different geographic regions of our country.

Conclusions

Histopathological profiles of cohort in this study do not differ substantially from other hospital-based and population-based studies. Astrocytomas and medulloblastomas, which form the major histologic subtypes in children residing in Gujarat, needs special attention with respect to the distribution of infrastructure and resources. Hospital- based studies like ours play a major role in planning the distribution of neurosurgical infrastructure and radiation and medical oncological resources toward the disease management and preventive programs.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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