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Clinicopathological Analysis of Pediatric Brain Tumors: A Single-Center Study

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Abstract

Background: Pediatric brain tumors, comprising 20-25% of childhood cancers, are the second most common pediatric malignancy with a global incidence of 2-5 per 100,000 children, varying by region and healthcare access. In high-income countries, advanced MRI and molecular diagnostics based on the 2021 WHO classification have improved the survival rates to 70-80%. In low- and middle-income countries like Iran, limited neuroimaging, neurosurgery, and molecular profiling cause diagnostic delays of 4-6 months, disease advancement, and survival rates below 60%.

Materials and Methods: A cross-sectional descriptive study was conducted at Shahid Rahnamoun Hospital, Yazd analyzing 32 pediatric patients (aged ≤ 15 years) diagnosed with brain tumors from 2013 to 2023. The data on demographics, presenting symptoms, tumor types and locations, were extracted from pathology department records. The tumors were classified histologically according to the 2021 World Health Organization (WHO) central nervous system tumor classification, without routine molecular subtyping due to resource constraints. Statistical analysis was performed using Fisher's exact tests in SPSS version 22, with the level of significance set at $p < 0.05$.

Results: The patients had a mean age of 7.1 ± 3.5 years, and the male-to-female ratio was 1.3:1. Astrocytoma was the most common tumor (40.6%), followed by medulloblastoma and glioblastoma (12.5%, each). The frontal lobe (22.2%) and cerebellum (19.4%) were the most frequent tumor sites. Headache (56.3%) and seizures (37.5%) were the prevalent symptoms. The significant associations included cerebellar tumors with balance disorders ($p = 0.006$), fourth ventricle tumors with speech disorders ($p = 0.018$), and thalamic tumors with decreased consciousness ($p = 0.002$).

Conclusion: This study highlights the distinct clinicopathological patterns of pediatric brain tumors in Yazd, with elevated meningioma rates suggesting potential diagnostic biases or environmental influences. Improved imaging, molecular profiling, and multicenter investigation of regional risk factors are essential to enhance the outcomes in Iran.

Keywords: Brain neoplasms, Clinical presentation, Iran, Pathology, Pediatric

Introduction

Pediatric brain tumors are the second leading cause of cancer-related mortality in children under 15, surpassed only by hematologic malignancies (1). Globally, the incidence of primary central nervous system (CNS) tumors in children ranges from 2 to 5 per 100,000 annually, varying by geography, ethnicity, and diagnostic access (2).

In Iran, the incidence is lower at 1.43 per 100,000, with astrocytoma and medulloblastoma being the most common types (3, 4). A 360% increase in glioblastoma incidence in southern Iran from 2001 to 2017 suggests diagnostic delays or limited access to advanced imaging, which are prevalent issues in low- and middle-income countries (LMICs) like Iran (5, 6).

The 2021 World Health Organization (WHO) classification has categorized

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advanced tumors in terms of histological and molecular features (7). For example, medulloblastoma is now divided into four molecular subgroups, namely WNT-activated, SHH-activated, Group 3, and Group 4, with distinct prognostic implications (8). In Iran, gliomas and astrocytomas predominate, typically diagnosed around age 8.6 (9, 10). However, limited molecular profiling and histopathological challenges in LMICs often result in an advanced disease at presentation (11). In regions like Yazd, the data on tumor location-specific symptoms and histopathological patterns are scarce, hindering timely diagnosis.

Clinically, pediatric brain tumors often arise in the posterior fossa (50–60% of cases), with nonspecific symptoms like headache, vomiting, or ataxia (12). In Iran, headaches (60.8%) and seizures (15.7%) are common, with diagnostic delays of 4-6 months due to misdiagnosis or resource scarcity (13, 14). Linking symptoms to tumor pathology, such as ataxia with medulloblastoma, is critical for early detection (15). Prognosis depends on tumor type, location, and surgical outcomes, with Iran's 5-year survival rates (59–68.5%) lagging behind global benchmarks (e.g., 80% for standard-risk medulloblastoma) due to limited advanced care (16, 17, 18).

This study addresses the gaps in understanding the clinicopathological characteristics of pediatric brain tumors in Yazd, Iran, focusing on epidemiology, tumor patterns, symptom associations, and histopathological challenges to improve diagnosis and management.

Materials and Methods

Study design and setting

This research is a cross-sectional descriptive study conducted at Shahid Rahnamoun Hospital, a tertiary care center for pediatric oncology in Yazd, Iran, from 2013 to 2023. The study aimed to analyze the clinicopathological characteristics of brain tumors in children aged ≤ 15 years.

Study population

The research population consisted of all the pediatric patients (aged ≤ 15 years) with a confirmed histopathological diagnosis of brain tumors. They were identified through pathology department records. The inclusion criteria were complete medical records and the age of ≤15 years at diagnosis. The patients with incomplete records, concurrent malignancies, or non-brain-origin tumors were excluded. Only the cases with histopathological confirmation were included to ensure diagnostic accuracy, potentially limiting the sample size.

Data collection

The data were collected using a checklist capturing the following points:

- Demographic data: Age at diagnosis, gender
- Clinical data: Presenting symptoms (e.g., headache, seizures, vomiting), duration of symptoms
- Tumor characteristics: Anatomical location (e.g., frontal lobe, cerebellum), histopathological type (per 2021 WHO classification)
- Diagnostic and treatment data: Imaging findings (MRI/CT), surgical resection status, adjuvant therapies

The symptoms were extracted from medical records and supplemented by parental reports where necessary to ensure completeness.

Histopathological evaluation

The tumor specimens were reviewed by experienced pathologists and classified histologically based on the 2021 WHO CNS tumor classification (7). Due to resource constraints, routine molecular subtyping (e.g., PCR, NGS, or IHC for IDH1, BRAF, H3K27M) was not performed, limiting classification to histological features. Special attention was given to distinguishing the subtypes of common pediatric brain tumors, such as medulloblastoma and astrocytoma.

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Statistical analysis

The data were analyzed using SPSS version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics (frequencies, percentages, means, standard deviations) summarized the demographic and clinical characteristics. The normality of continuous variables (e.g., age) was assessed using the Shapiro-Wilk test. To make comparisons, Fisher's exact tests were used for the categorical variables (due to the small sample size) and independent two-sample t-tests or ANOVA for the continuous variables. A p-value of < 0.05 was considered significant. Multivariate analysis was not performed due to the small sample size, limiting the ability to control for confounding factors.

Results

Demographic characteristics

The study included 32 pediatric patients with a mean age of 7.1 ± 3.5 years (ranging from 1 to 15 years). Most of the patients (56.3%, n = 18) were aged ≤ 7 years, and 43.7% (n = 14) were 8-15 years old, based on epidemiological patterns in pediatric CNS tumors (1). The age groups were defined to reflect typical incidence peaks in pediatric brain tumors. The males comprised 62.5% (n = 20), yielding a male-to-female ratio of 1.3:1. No significant relationship was found between age or gender and tumor type (Fisher's exact test, $p > 0.05$). This male dominance aligns with global trends, possibly reflecting biological or referral differences, though the small sample limits conclusions.

Tumor types

Astrocytoma was the most common tumor (40.6%, n = 13), followed by medulloblastoma and glioblastoma (12.5%, n = 4 each) (Table I). The other types included ependymoma (9.5%, n = 3), meningioma (12.5%, n = 4), hemangioblastoma (6.2%, n = 2), ganglioglioma (3.1%, n = 1), and neuroepithelial tumor (3.1%, n = 1). No significant differences by age or gender were observed (Fisher's exact test, $p > 0.05$). The high meningioma prevalence may reflect regional diagnostic practices or environmental factors, although further investigation is needed.

Tumor location

Among 32 patients, 36 tumor locations were identified (three patients had tumors in two regions). The frontal lobe was the most common site (22.2%, n = 8/36), followed by the cerebellum and temporal lobe (19.4%, n = 7/36 each) (Table II). The locations were determined by MRI (n = 28) or CT (n = 4). The percentages reflect the proportion of the total locations (n = 36).

Presented symptoms

The most frequent presented symptom was headache, observed in 56.3% (n = 18/32) of the patients, followed by seizures in 37.5% (n = 12/32) and vomiting in 15.6% (n = 5/32). Less common symptoms included decreased level of consciousness (9.4%, n = 3/32), balance disorders (6.3%, n = 2/32), and speech disorders (3.1%, n = 1/32). One patient (3.1%, n = 1/32) was asymptomatic, identified incidentally during imaging for an unrelated head injury. The symptoms were extracted from medical records, supplemented by parental reports where necessary. Some patients presented multiple symptoms, resulting in a total of 42 symptoms across the 32 patients (Table III).

Associations between tumor location and symptoms

The significant associations included cerebellar tumors with balance disorders (2/7, Fisher's exact test, $p = 0.006$), fourth ventricle tumors with speech disorders (1/5, $p = 0.018$), and thalamic tumors with decreased consciousness (1/1, $p = 0.002$)

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(Table IV). To avoid Type I errors, these findings should be interpreted cautiously due to the small sample size, particularly for thalamic tumors. Tumor type-symptom associations (e.g., astrocytoma with headaches, 61.5%) were not significant (Fisher's exact test, $p > 0.05$) (Table V).

Radiological findings

The radiological data were limited to three patients due to incomplete archiving, a challenge in resource-limited settings. MRI confirmed tumors in the cerebellum (n = 2) and frontal lobe (n = 1). This limitation precludes comprehensive imaging analysis and underscores the need for improved record-keeping and access to diagnostic imaging.

Table I: Distribution of the tumor types based on histopathological diagnosis

Tumor type	Frequency (n)	Percentage (%)
Astrocytoma	13	40.6
Medulloblastoma	4	12.5
Glioblastoma	4	12.5
Ependymoma	3	9.5
Meningioma	4	12.5
Hemangioblastoma	2	6.2
Ganglioglioma	1	3.1
Neuroepithelial tumor	1	3.1

Table II: Distribution of the tumor locations

Tumor location	Frequency (n)	Percentage (%)
Frontal lobe	8	22.2
Cerebellum	7	19.4
Temporal lobe	7	19.4
Parietal lobe	5	13.9
Fourth ventricle	5	13.9
Occipital lobe	2	5.6
Brainstem	1	2.8
Thalamus	1	2.8

Note: The percentages are calculated based on the total number of the tumor locations (n = 36); three patients had tumors in two regions.

Table III: Distribution of the presented symptoms

Presented symptom	Frequency (n)	Percentage (%)
Headache	18	56.3
Seizures	12	37.5
Vomiting	5	15.6
Decreased level of consciousness	3	9.4
Balance disorders	2	6.3
Speech disorders	1	3.1
Asymptomatic	1	3.1

Note: The percentages are calculated based on the total number of the patients (n = 32). Some patients presented multiple symptoms, resulting in a total of 42 symptoms.

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Table IV: Significant associations between tumor location and symptoms

Tumor location	Symptom	Frequency (n)	p-value
Cerebellum	Balance disorders	2/7	0.006
Fourth ventricle	Speech disorders	1/5	0.018
Thalamus	Decreased level of consciousness	1/1	0.002

Note: The p-values were calculated using Fisher's exact test. The findings, particularly for thalamic tumors, should be interpreted cautiously due to the small sample size.

Table V: Relationship between tumor types and symptoms (exploratory)

Tumor type	Headache (n, %)	Seizures (n, %)	Vomiting (n, %)	p-value
Astrocytoma	8/13 (61.5%)	5/13 (38.5%)	2/13 (15.4%)	> 0.05
Medulloblastoma	3/4 (75.0%)	1/4 (25.0%)	1/4 (25.0%)	> 0.05
Glioblastoma	2/4 (50.0%)	2/4 (50.0%)	1/4 (25.0%)	> 0.05

Note: The p-values were calculated using Fisher's exact test.

Discussion

This study has performed a comprehensive clinicopathological analysis of 32 pediatric brain tumor patients in Yazd, Iran, addressing critical gaps in regional data. The mean age at diagnosis (7.1 ± 3.5 years) and male predominance (1.3:1) align closely with the global trends reported in the CBTRUS Statistical Report (1) and the national data from Shiraz (mean age 8.6 years) (9). The higher proportion of the patients aged ≤ 7 years (56.3%) may reflect delayed referrals, a common issue in low- and middle-income countries (LMICs) like Iran, where access to specialized care is limited (6). This delay often exacerbates the disease severity at presentation, complicating treatment and prognosis (14). A systematic review was conducted of the Iranian pediatric CNS tumor reports from 1980 to 2015, analyzing 3,484 cases. They have reported a similar mean age of 7.5 years and a male-to-female ratio of 1.4:1, reinforcing the consistency of demographic patterns across Iran (4). A population-based study in Europe also noted a comparable mean age of 7.2 years and male predominance (1.3:1) in pediatric CNS tumors, suggesting that the demographic patterns in Yazd are broadly consistent with the international data (19).

Astrocytoma (40.6%) was the most prevalent tumor type, consistent with the national studies that report astrocytoma as a leading pediatric brain tumor in Iran (3, 4). Similarly, the dominance of posterior fossa tumors (37.5%), particularly in the cerebellum (19.4%), aligns with global patterns; 50-60% of pediatric brain tumors arise in this region (12). For instance, a multicenter Iranian study of 3,484 cases found astrocytoma in 34.5% and medulloblastoma in 20.1%, closely mirroring our findings (4). In the broader Middle East, a population-based analysis in Lebanon reported astrocytoma at 28% and embryonal tumors (including medulloblastoma) at 22.8% among 2,309 CNS cases from 2005 to 2015 (20). However, the elevated meningioma rate (12.5%) in our cohort is notably higher than the national estimates (5-7%) and global rates (< 5%) (1, 9). This discrepancy may stem from regional diagnostic practices, such as reliance on histological features without molecular confirmation, potentially leading to misclassification of other tumors as meningiomas (7, 11). Environmental factors, such as exposure to ionizing radiation or regional genetic predispositions, could also contribute, as

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suggested in the studies of CNS tumor epidemiology in Iran (21). A recent meta-analysis of pediatric meningiomas highlighted their rarity (1–5% of all meningiomas) but noted higher incidence in certain populations, potentially linked to radiation exposure in Middle Eastern cohorts (22). A study on Iranian-born Jews in Israel reported elevated benign meningioma rates, possibly tied to hereditary and environmental factors, which may parallel observations in Iran (23). Further investigation into local environmental or genetic risk factors is neededto clarify this finding.

The high prevalence symptoms such as headaches (56.3%) and seizures (37.5%) mirrors the national data, where headaches (60.8%) and seizures (15.7%) are frequently reported (13). These symptoms often lead to diagnostic delays of 4–6 months in Iran, attributed to misdiagnosis or limited access to advanced imaging like MRI (14). Our study identified significant associations between tumor location and symptoms, such as the association of cerebellar tumors with balance disorders, fourth ventricle tumors with speech disorders, and thalamic tumors with decreased consciousness. These findings align with the functional anatomy of the brain, where cerebellar lesions disrupt coordination and ventricular tumors may compress speech-related pathways (12). However, the small sample size, particularly for thalamic tumors (n = 1), necessitates cautious interpretation to avoid Type I errors, as statistical significance may be inflated in small cohorts (14). The novel association of fourth ventricle tumors with speech disorders, though based on limited cases, suggests a need for further exploration in larger studies to confirm its clinical relevance. Comparatively, a recent Iranian study of 102 pediatric brain tumor cases from 2010 to 2020 reported headaches in 68% and seizures in 42%, with similar location-symptom links, such as posterior fossa tumors associated with ataxia in 35% (24). A historical cohort in Syria (1993–2002) found vomiting (45%) more prominent alongside headaches, differing slightly due to regional variations in presentation (25).

The absence of routine molecular profiling in our study, due to resource constraints, limited our ability to align fully with the 2021 WHO classification, which emphasizes molecular markers like IDH1, BRAF, and H3K27M for precise tumor subtyping (7). This reliance on histological features alone may contribute to diagnostic inaccuracies, particularly for complex tumors like gliomas or medulloblastomas, where molecular subgroups (e.g., WNT-activated or SHH-activated medulloblastoma) have distinct prognostic and therapeutic implications (8, 11). In LMICs, such limitations are common and exacerbate the challenges in achieving diagnostic precision, thus leading to suboptimal treatment planning (6). Similarly, the limited radiological data (n = 3) in our study, due to incomplete archiving, underscores systemic issues in resource-limited settings, where MRI access and record-keeping are often inadequate (6, 13). These constraints hindered comprehensive imaging-based analysis, highlighting the need for improved infrastructure.

Despite these limitations, this study has certain strengths including detailed clinicopathological insights into an understudied region and use of the 2021 WHO classification for histological diagnosis. The single-center design and small sample size (n = 32), however, restrict the generalizability of the results. The findings of this study lay a foundation for future research. Multi-center studies across Iran, incorporating molecular profiling and standardized imaging protocols, could enhance diagnostic accuracy and better agreement with international standards (7, 11). Investigating the regional factors

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contributing to elevated meningioma rates, such as potential environmental exposures and diagnostic biases, is a critical next step (21). Additionally, addressing diagnostic delays through improved access to MRI and training for primary care providers could reduce the diagnosis time, thus improving the outcomes (14, 15). Collaborative efforts with international research networks could also facilitate access to molecular testing, bridging the gap between LMICs and high-income countries in pediatric brain tumor management (6, 19).

Conclusion

This study highlights the prevalence of astrocytoma (40.6%) and posterior fossa tumors (37.5%) in Yazd, Iran. It also reports the significant symptom-location associations of those diseases (e.g., cerebellar tumors with balance disorders Elevated meningioma rates (12.5%) and diagnostic delays denote regional challenges. Thus, improved imaging, molecular profiling, and multicenter research are critical to enhance pediatric brain tumor management in Iran.

This study offers detailed clinicopathological insights into an understudied region. However, the single-center design, small sample (n = 32), limited radiological data (n = 3), and absence of molecular profiling have restricted the generalizability of the results and their alignment with modern classifications. As a recommendation for future research, enhanced MRI access, standardized histopathology, and multicenter studies could improve diagnostic accuracy. Investigating regional factors (e.g., meningioma prevalence) is also insightful.

Ethical Considerations

The study was approved by the Ethics Committee of Yazd University of Medical Sciences (IR.SSU.MEDICINE.REC.1402.092). Informed consent was obtained from the participants' parents or legal guardians, and the patient data were anonymized.

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Authors' Contributions

Mahlagha Zahedi, as the first author, was responsible for the study design, data collection, and drafting the manuscript. Shokouh Taghipour, as the corresponding author, supervised the study, provided critical revisions, and ensured the accuracy of the histopathological evaluations. Mohammad Peymani, a medical student, contributed to data analysis and manuscript preparation. All the authors collaborated in writing the manuscript and approved the final version.

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Conflict of Interest

The authors declare that they have no conflict of interests regarding this research.

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