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# Clinicopathologic and Survival Characteristics of Childhood and Adolescent Brain and Spinal Cord Tumors in Center of Iran

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**Abstract**

**Background:** The brain and spinal cord tumors account for 15% to 20% of all childhood malignancies. It is important to know the epidemiologic characteristics and survival of these patients to better understand the disease and the factors affecting its prognosis. The aim pf this study was to characterize the clinicopathology and survival rate of childhood and adolescent brain and spinal cord tumors in center of Iran.

**Materials and methods:** This descriptive-analytic study was carried out using a retrospective cohort design. Thirty patients with brain and spinal cord tumors who referred to Shahid Sadoughi and Rahnemoon hospitals in Yazd from 2006 to 2016 and aged 1 to 18 years were evaluated. . The epidemiologic characteristics, survival, and the factors affecting the survival of brain and spinal cord tumors were investigated.

**Results:** The findings showed that between 30 studied patients, brain and spinal cord tumors were more common in males (19 males and 11 females). The average age of the patients was 8.60 ± 5.70 years. Fifteen (50%) patients survived. Seventeen (57%) patients were resident in Yazd province and 13 (43%) were from southern Iran. Twenty two patients (73.3%) had recurrence after recovery. The average of survival was 36 months, with an average of 27 months in females and 37 months in males. However, this difference was not significant. The most common tumor was gliomas. There was no significant relationship between the mean of survival with age, gender, geographical status, or type of treatment (P value> 0.05); however, there was a significant relationship between the year of tumor diagnosis and survival (P value=0.0134).

**Conclusion:** It seems that survival of the brain and spinal cord tumors in children and adolescence is a multifactor event and it is affected by various factors.

**Key words:** Adolescent, Brain, Children, Spinal cord, Survival, Tumor

## Introduction

Although cancer is rare in childhood, brain and spinal cord tumors are the third most common tumors in childhood after leukemia and lymphoma (1). The central nervous system tumors affect about 35 cases per million in children under the age of 15 years (2). These tumors account for 15% to 20% of all childhood malignancies. The highest incidence of brain tumors occurs in the age group of 9-5 years and then in the age group of 10-14 years. There are many types of brain and spinal cord tumors diagnosed in different regions of the brain or spinal cord. The cause of many childhood brain and spinal cord tumors is still unknown (3). In most cases, childhood cancers originate from non-hereditary mutation in the growing cells and because of their unpredictability, there is no effective way to prevent them (4). Known risk factors for pediatric brain tumors include ionizing radiation, genetic disorders (such as Down syndrome), family history, nutritional habits during pregnancy, etc. (5).Tumors may be benign or malignant. Historically, brain tumors have been classified by their location and histological characteristics. Infratentorial tumors are the most common tumors (66.7%), among which there are

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medulloblastoma (70.4%), astrocytoma (20.4%) and ependymoma (5.6%); respectively. Among the supratentorial tumors (33.3%), astrocytomas (63%), ependymoma (18.5%), and mixed gliomas (7.4%) are the most common (6). Brain and spinal cord tumors in children can appear with many different signs and symptoms, largely dependent on the location of the tumor. The symptoms of brain and spinal cord tumors are not the same in all patients (7). Brain and spinal cord tumors may cause short and long term consequences due to the disease itself or its treatment. These sequelae cause a wide range of serious physical and neurological morbidities. So far, few studies have been conducted on the prevalence of brain and spinal cord tumors in children and adolescents in Yazd, Iran. This study aimed to define distinctive clinicopathologic features and treatment results of these tumors in a major tertiary care hospital located in central Iran.

## Materials and Methods

This descriptive-analytic study was done using historical cohort method. This study was approved by the Ethics Committee of Azad University of Medical Sciences (IR.Iau.Yazd.Rec1397.22). In this retrospective study, the medical records of cancer patients were reviewed from 2006 to 2016 and the medical charts of all children and adolescents diagnosed with brain and spinal cord tumors, treated in Shahid Sadoughi and Shahid Rahnemmon hospitals, were retrieved. The recorded variables included patient's registration number at the hospital, date, name, age, sex, address, the type of birth, family history of cancer, the type of the parents' marriage, presence of underlying illness, topography, morphology, treatment protocol, relapse, and survival. The patients were followed up via phone. The patients whose demographic or medical information was not complete were excluded from the study. In addition, histopathological diagnosis was based on Hematoxylin and Eosin-stained slides. Overall survival was calculated from the date of diagnosis until death or the date of last follow up. Statistical analysis included frequency table (for descriptive analysis) and Fischer exact and Chi-Square tests (for analytical analysis). Survival analysis was conducted using Kaplan- Meier estimates, and multivariate analysis was performed using Cox regression method. The p value $<0.05$ was considered statistically significant. Statistical analyses were performed using SPSS (version17).

## Results

According to the findings of this study, tumors of the brain and spinal cord were more common in males (19 males and 11 females). The average age of the patients was 8.60 ± 5.79 years. Fifteen (50%) patients survived and 15 (50%) died. Seventeen (57%) patients were resident in Yazd province and 13 (43%) were from southern Iran. Twenty patients (73.3%) had recurrence after recovery. None of the patients had underlying illness. In 8 cases (26.7%), the marriage of their parents was inter-family marriage. Two (6.7%) patients had a history of cancer in their family. Twenty four (80%) patients were born by normal vaginal delivery. Nausea, vomiting, headache, and dizziness were common symptoms. In this study, 4 (13%) patients suffered from benign tumors and 26 patients (87%) had malignant tumors. Four (13%) patients had spinal tumor and 26 (87%) had brain tumor. The most common tumors were gliomas which themselves include astrocytoma, oligodendroglioma, and ependymoma. Among them, astrocytoma was the most common type of tumor (Table I). The average of survival was 36 months, with an average of 27 months in females and 37 months in males (Figure 1); however, this difference was not significant (P value = 0.7326)( Figure 2). According to the results of the current study, there was no significant relationship between survival and age, gender, geographical status, or

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type of treatment, but there was a significant relationship between the year of tumor diagnosis and survival (P value=0.0134) (Figure 3). Therefore, those patients diagnosed with tumors during the years 2013 to 2016 had higher survivals.

No significant relationship was observed between the type of tumor and family history of cancer, type of delivery, type of parents' marriage, and relapse of the disease. There was no significant correlation between type of treatment and relapse of the disease either. Table II shows the frequency of brain and spinal cord tumors during the years studied in the present investigation. Moreover, a significant relationship was found between the type of tumor and the year of diagnosis of the tumor in this study. Therefore, the frequency of glial tumors and germ cell tumors have decreased from 2013 to 2016 but the frequency of embryonal neuroepithelial tumors and other types of tumors have increased(P value =0.044).

*Table-I: Frequency distribution of CNS tumor types*

| **Tumor type** | **Number** | **Percent** |
|---|---|---|
| Gliomas | 18 | **60** |
| Germ cell tumors | 2 | **6** |
| Emberyonal neuroepithelial tumors | 5 | **17** |
| Others | 5 | **17** |
| Sum | 30 | **100** |

Glioma tumors include the subgroups of astrocytoma, oligodendroglioma and ependymoma. Germ cell tumors include the subgroups of embryonal carcinoma and teratoma. Emberyonal neuroepithelial tumors include the subgroups of Ewing sarcoma,medulloblastoa and malignant round cell tumors. Other tumors include the subgroups pituitary adenomas, vascular tumors, and metastatic tumors.

*Table-II: Frequency distribution of brain and spinal cord tumors according to studied years*

| **Year** | **Number** | **Percent** |
|---|---|---|
| 2006 | 1 | **3.3** |
| 2007 | 2 | **6.7** |
| 2008 | 2 | **6.7** |
| 2009 | 3 | **10** |
| 2010 | 1 | **3.3** |
| 2011 | 4 | **13.13** |
| 2012 | 2 | **6.7** |
| 2013 | 3 | **10** |
| 2014 | 3 | **10** |
| 2015 | 3 | **10** |
| 2016 | 6 | **20** |
| Sum | 30 | **100** |

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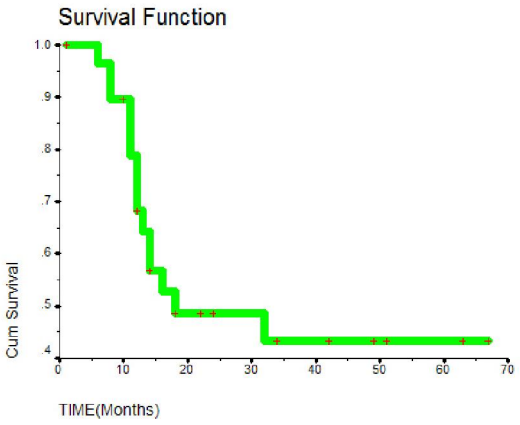



Figure 1. Overall Survival in children and adolescents with brain and spinal cord tumors

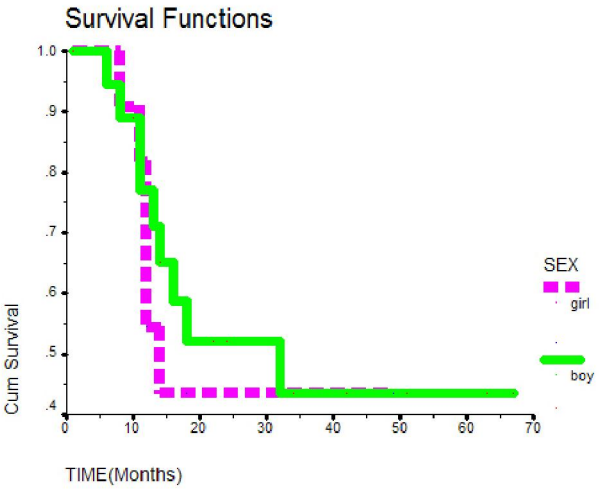



Figure2-Overall Survival in Children and Adolescents with brain and spinal cord tumors according to sex

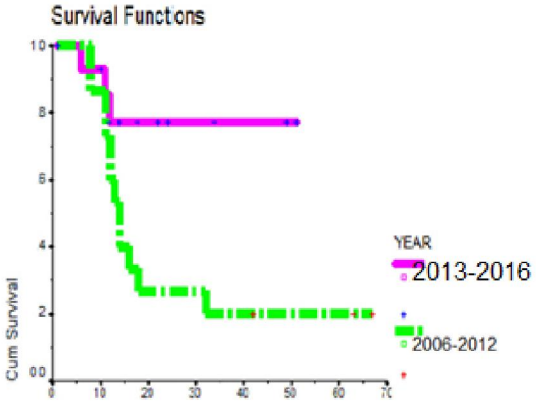



Figure3-Overall Survival in children and adolescents with brain and spinal cord tumors according to studied years

## Discussion

This study was conducted to determine the survival and profile of patients with brain and spinal cord tumors who referred to Shahid Sadoughi and Shahid Rahnemmon hospitals from 2006 to 2016. According to the findings of this study, tumors of the brain and spinal cord were more common in males (19 males and 11 females) that is in line with findings of Ezzat's et al., study (8) .The average age of our patients was 8.6 ± 5.7 years. The mean age at the time of diagnosis in the study conducted by Ezzat et al., was 7.1 ± 4.2 years (8) .The median age of the patients was 6.11 ± 3.65 years in another study which was done in Iran (9). Four (13%) patients had spinal tumor and 26 (87%) had brain tumor in this study that is consistent with Ezzat's et al., findings (8). They showed that 96 % of the patients had brain tumor, while only 4 % of the patients had lesions in the spinal cord. In the current study, the average of survival was 36 months, with an average of 27 months in females and 37 months in males. However, this difference was not significant. Zareifar et al., showed that overall 5-year survival rate was 59% in their study (10). Survival rate for brain tumor during 10 years follow-up was 72% in Lannering 's study (11).

Seventeen (57%) of our patients were resident in Yazd province and 13 (43%) were from Southern Iran. It is in consistent with Ezzat et al. that revealed most of their cases were resident in Cairo Metropolitan (38.4 %) or Delta (31.6 %) areas. Twenty two patients (73.3%) had recurrence after recovery. However, Zareifar et al., showed that 41 patients (26.5%) experienced at least one episode of recurrence (10). In this study, 4 (13%) patients suffered from benign tumors and 26 patients (87%) had malignant tumors, that is similar to findings of Ezzat et al. The most common tumors were glioma tumors, which themselves include astrocytoma, oligodendroglioma, and ependymoma. Among them, astrocytoma

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was the most common type of tumor. Ezzat et al., revealed that although astrocytic tumors were the most common subtype in both males and females yet, it represented 29.9 % of all subtypes among male while it accounted for 30.1 % among females(8). However, Zareifar et al., showed that the most common type of tumor was medulloblastoma followed by low grade glioma and ependymoma (10). Approximately, 57% of CNS tumors were gliomas in Desandes's study (12). In Duffner's study, low-grade supratentorial astrocytomas were 25%, medulloblastomas 23%, cerebellar astrocytomas 12%, high-grade supratentorial astrocytomas 11%, brainstem gliomas 9%, and ependymomas 8% (13). Another study in Iran showed that the majority of the tumors were infratentorial and the rest were supratentorial and spinal cases (9). Rafsengani et al., revealed that the frequency of medulloblastoma was significantly more than other kind of tumors (14). In the current study, nausea, vomiting, headache, and dizziness were common symptoms which is similar to Zareifar's findings (10). According to our results, there was no significant relationship between the mean of survival and age, gender, geographical status, or type of treatment; however, there was a significant relationship with the year of tumor diagnosis and survival. Nevertheless, Zareifar showed that girls had longer survival compared with boys in her study, and concluded that gender is an independent factor influencing survival (10). Duffner et al., showed that the lowest survivals were in children less than 2 years but the highest were in those aged 10 to 14 years (13). Farinotti et al., found that tumor histology is the most important prognostic factor regarding survival in children with a CNS tumors (15). The histological type of the tumor was the most powerful independent predictor of survival in children with a CNS tumor in a study conducted by Farinotti et al., and age at diagnosis and sex had no significant effect on survival in their study (15).

Zareifar revealed thar all evaluated variables (recurrence, neurological deficient, tumor site, tumor resection, and treatment) and showed significant association between those variables and survival of the patients but not for age at diagnosis, gender, and tumor grade (10). Purdy showed that patients treated with surgery and chemotherapy alone had a lower rate of survival than older patients who were treated with radiation therapy containing regimens (16).

## Conclusion

With respect to findings of the current investigation, it seems that survival in the brain and spinal cord tumors in children and adolescence is a multifactor event and it is affected by various factors. To explain this discrepancy, it should be noted that, regional and geographical differences as well as incidence variation affect response to treatment, prognosis, and survival for various types of tumors, including CNS tumors. Overall, factors known to contribute to racial disparities in mortality include differences in access to high-quality and timely diagnosis and treatment. In developing countries, such as Iran, the limited availability of resources is an obstacle for using advanced and more effective methods. In addition, childhood CNS tumor is an inharmonious disease and different treatment modality is needed according to different subtypes. In addition, childhood CNS tumor is a heterogeneous disease and different biological subtypes require specifically adapted treatment strategies. Children and adolescents with CNS tumor should be admitted to centers that have a multidisciplinary team of cancer specialists with experience in treating the pediatric cancers. Further studies are needed in order to enable an oncologist to make important decisions on patients' management and treatment.

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## Conflicts of interest

The authors declare no conflict of interest.

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