# Retrospective Epidemiological Study of Pediatric Primary Central Nervous System Tumors in Mansoura University Hospital

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## Abstract:

**Background:** Central nervous system (CNS) tumors are the second most common malignancy in children after leukemia and lymphoma combined. They account for 26% of all pediatric tumors and are the leading cause of cancer-related death in children. Advances in management have led to better survival.

**Methods:** A total of 62 patients with primary CNS tumors who attended the Clinical Oncology and Nuclear Medicine Department, Mansoura University, from the first of January 2012 to 31 March 2020 were evaluated retrospectively. To assess their prognostic significance, all factors were correlated with overall survival (OS) and progression-free survival (PFS).

**Results:** The median OS was 105 months. The 1,2, 5, and 7-year OS were 80.7%, 63.7%, 59.9%, and 55.1% respectively. Univariate analysis revealed that metastatic disease at diagnosis (p = 0.029) and radiotherapy site (p = 0.02) were statistically significant factors influencing OS. However, in multivariate analysis, metastatic disease at diagnosis remained the only significant predictor of OS (p = 0.042). The median PFS was 86.08 months. The 1,2, 5, and 7-year PFS were 72.7%, 65.3%, 60.3%, and 52.8% respectively. The univariate analysis of PFS revealed statistically significant associations with gender (P=0.047), chemotherapy (0.041), and radiotherapy site (0.02), while in multivariate analysis, the radiotherapy site remained the only significant predictor for PFS.

**Conclusion**: Our study provides epidemiological insights into pediatric CNS tumors. Further prospective studies focusing on various pathological CNS tumor subtypes with larger sample sizes are encouraged.

**Keywords**: Pediatric CNS tumors, epidemiology, progression-free survival, overall survival

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## Introduction:

Central nervous system (CNS) tumors are the most typical solid tumors in pediatrics and represent the most significant cause of childhood cancer–related mortality [1]. The incidence in developing countries is much lower, usually below 20 per million, than in developed countries [2]. The lower incidence of pediatric CNS tumors in developing countries may be related to underestimation and underreporting because of relatively poor access to neuroimaging and neurosurgical facilities, resulting in missed diagnoses in children with non-specific initial manifestations such as headaches, seizures, and altered levels of consciousness [3].

Prior exposure to ionizing radiation and genetic predisposition syndromes, such as neurofibromatosis (NF), tuberous sclerosis (TSC), Li-Fraumeni syndrome (LFS), Gorlin syndrome, familial adenomatous polyposis (FAP) syndrome, and constitutional mismatch repair deficiency (CMMRD) are the most known risk factors for developing pediatric CNS tumors [4].

Pediatric CNS tumors are heterogeneous in histopathology and molecular characteristics. They are broadly categorized into glial and neuronal tumors. The most common types of gliomas in children include astrocytomas, oligodendrogliomas, ependymomas, brainstem gliomas, optic nerve gliomas, and diffuse intrinsic pontine gliomas. Most neuronal tumors are

embryonal, with the most common types being medulloblastoma, atypical teratoid/rhabdoid tumors, and central nervous system primitive neuro-ectodermal tumors [5]. The tumor's location, pathology, potential resection extent, and molecular characterization are critical prognostic variables for pediatric CNS cancers [6, 7].

Several important factors influence the multimodality treatment plan for children with CNS tumors, including tumor histology, patient age, performance status, tumor location, resectability of the cancer, and previous management. Multimodal treatment includes surgical management, treatment with radiation therapy, and systemic therapy according to international guidelines [8]. Survival and cure rates for childhood CNS tumors in high-income countries have greatly improved over the past decades but remain poor in many low- and middle-income countries [9].

In our retrospective study, we aimed to analyze the demographic data of pediatric CNS tumors attended to the Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospital, to define the prognostic factors and assess the patients' survival.

## Patients and Methods:

The current study is a retrospective study of children who were 18 years old or less with primary CNS tumors who attended the Clinical Oncology and Nuclear Medicine Department from the first of January 2012 to the end of March 2020. Our study was submitted for approval by the Institutional Research Board, Faculty of Medicine, Mansoura University.

The recorded patient history included age, sex, associated comorbidities, and presenting symptoms. Clinical examination was also collected, including general, neurological, visual, and hearing examinations. Eastern Cooperative Oncology Group Performance Status (ECOG PS) and growth development in young patients were assessed [10]. Regarding the diagnosis and tumor characteristics, diagnostic radiological study, tumor location, pathological type, tumor grade, and disseminated tumor from the start were recorded. The classification of CNS tumors was initially based on the 4th edition of the World Health Organization (WHO) which was published in 2007, then the updated 4th edition in 2016 after its release [11, 12]. Treatment modalities applied by the different disciplines and documented in the sheet were determined.

Patients who underwent surgery were referred from the Neurosurgical Department at Mansoura University Hospital or private hospitals. Chemotherapy protocols were administered in pediatric unit based on pathology, either as adjuvant therapy or concomitantly with radiotherapy. The most commonly used chemotherapy protocol was carboplatin and vincristine. External beam 3D conformal radiotherapy was delivered using a linear accelerator machine, either as a full dose to the primary tumor, ranging from 45 to 60 Gy over 5–6 weeks (5 sessions per week) with daily fractions of 1.8–2 Gy, or as craniospinal irradiation (CSI) with doses ranging from 23.4 to 36 Gy, followed by boosts up to 54 Gy to the primary tumor. Multiple beams were used aiming at more sparing of organs at risk (OAR) and increase the tumor dose homogeneity.

The end point of our work is to asses demographic, clinical, anatomical, and histological prognostic factors affecting OS and PFS. The OS was calculated from the date of diagnosis to the date of death from any cause, last follow-up, or the end of the study. The PFS was calculated from the date of diagnosis to the date of first progression, or if no progression occurred, until death, last follow-up, or the end of the study.

*Statistical Analysis:*

Statistical Package for Social Sciences (SPSS) software, version 26, performed data analysis. Qualitative data were described using numbers and percentages. Quantitative data were described using median or mean± standard deviation for normally distributed data after testing normality using the Kolmogrov-Smirnov test. The significance of the obtained results was judged at the (0.05) level. Chi-Square and Fisher's exact tests were used to compare qualitative data between groups appropriately. The Kaplan-Meier test was used to calculate overall survival and progression-free survival using log-rank $\chi 2$ to detect the effect of risk factors on survival. Cox regression was used to assess survival predictors with the hazard ratio calculation.

## Results:

Table (1) summarizes the characteristics of 62 patients. The median age was 11 years, ranging from 1.8 to 18 years old. Thirty-eight patients (61.3%) were between 10 and 18 years old. There was male predominance in (74.2%) of the whole study patients. The most common presenting complaint was headache associated with ocular signs (25.8%). Two patients (3.2%) had pre-existing comorbidities; one had epilepsy for two years before diagnosis, while the other had had motor affection since birth. These conditions did not impact their treatment plan.

We summarized the diagnosis and tumor characteristics in Table (2). The cerebellum was the predominant site of the primary tumor, observed in 23 patients (37.1%); the cerebral lobes were the following presenting site of tumors in 21 children (33.9%). Brain stem tumors were identified in 6 patients (9.7%), and pineal body tumors were present in 4 patients (6.5%). Three children (4.8%) had a tumor in the corpus callosum that was the same as the thalamic tumors. Finally, 2 patients (3.2%) had their primary tumor in the spinal cord. In this study, gliomas were the most common pathological type of primary pediatric CNS tumors found in 25 patients (40.3%); these included astrocytomas (pilocytic, diffuse, and anaplastic subtypes) in 11 patients (17.7%). Medulloblastomas were pathologically proved in 19 patients (30.6%), and ependymomas were in 7 patients (11.3%). By classifying the tumor grades, grade I was found in 5 patients (8.1%), grade II in 10 patients (16.1%), grade III in four patients (6.5%), and grade IV in 33 patients

(53.2 %). Four patients (6.5%) presented with disseminated meningeal disease at the time of diagnosis, while the remaining patients (93.5%) showed no evidence of metastases.

The treatment lines are explained in table (3). The majority of children received radiotherapy as postoperative radiotherapy alone in 10 patients (16.1%) or as adjuvant with either concurrent chemoradiotherapy in 29 patients (46.8%) or sequentially postoperative radiotherapy followed by chemotherapy in 9 patients (14.5%). On the other hand, 6 patients did not undergo surgery; of these, 2 patients (3.2%) were treated with radiotherapy alone, and the remaining 4 (6.5%) received sequential radiotherapy followed by chemotherapy. Fifty-six (90.3%) of the patients underwent surgery. The most frequent surgical procedures were subtotal excision and biopsy, each performed in 21 patients (33.9%), while total excision was completed in 14 patients (22.6%). Shunt procedures were done in 15 patients (24.2%). Our study showed that 45 children (72.6%) received chemotherapy, either as adjuvant therapy or concurrently with radiotherapy. We also found that 54 children (87.1%) received radiotherapy, either as adjuvant therapy or definitive treatment, when no surgery was done. Twenty-seven children (50%) received localized radiotherapy to the primary brain tumor, and two patients (3.7%) received localized radiotherapy to the primary spinal tumor. Twenty-five patients (46.3%) received craniospinal irradiation (CSI). Regarding the radiotherapy dose, 16 children (29.6%) received radiotherapy doses below 54 Gy, while 38 children (70.4%) were treated with 54 Gy or more doses. Regarding surgical complications, 45 patients (80.4%) who underwent surgery showed no postoperative complications. Some children experienced complications from chemoradiation, including early toxicities such as vomiting in 4 cases (7.4%) and headache or blurred vision in 2 cases (3.7%), which could also be attributed to the disease itself. Additionally, bone marrow suppression was observed in 1 child (1.9%), wet desquamation in another (1.9%), and 1 case (1.9%) reported an arrest on the radiotherapy machine. While short stature was observed in 1 patient (1.9%), a brain abscess in 1 patient (1.9%), and 1 case (1.9%) developed a secondary malignancy, which was skull osteosarcoma as late toxicities, and those were discovered with RT dose ≥ 54Gy.

During a median follow-up time of 40 months (ranging from 1-142 months), 24 patients (38.7%) died. Twenty patients (32.3%) died from the disease itself, while 4 patients died from unrelated causes (two patients died from secondary malignancies, while the others died from febrile neutropenia). Twenty-two patients failed treatment. Local recurrence occurred in 16 patients (72.7%), and disseminated meningeal disease occurred in 3 cases (13.6%). Three children (13.6%) had both local recurrence and disseminated disease.

Regarding the OS, the median OS for patients was 105 months with 95% CI (73.44 to 136.52). The OS rates were 80.7% at one year, 63.7% at two years, 61.4% at three years, 59.9% at five years, and 55.1% at seven years (Figure 1). The prognostic factors affecting OS are mentioned in Table (4). Starting with univariate analysis, Patients with metastatic disease at diagnosis showed a lower median survival than those without metastasis (P=0.029). Additionally, Patients who received radiotherapy targeted only to the brain showed a lower median survival time compared to those who received radiotherapy to both the brain and spine or to the spine alone (p=0.02). In the multivariate analysis, metastatic disease at diagnosis emerged as a significant independent prognostic factor for OS, with a hazard ratio of 3.58 (95% CI, 1.04–12.23; p = 0.042).

The median PFS time was 86.08 months with a 95% CI (67.96-104.20). The PFS rates were 72.7% at one year, 65.3% at two years, 60.3% at three years, 60.3% at five years, and 52.8% at seven years (Figure 2). The prognostic factors affecting PFS are mentioned in table (5). Starting with univariate analysis, female gender is associated with a statistically significant decrease in PFS (p=0.047). Similarly, chemotherapy cases demonstrated a statistically significant lower median PFS (p=0.041). Furthermore, patients who received radiotherapy on the brain showed a statistically significant reduction in PFS compared to those who received radiotherapy to the spine alone or craniospinal irradiation (0.002). In the multivariate analysis, the radiotherapy site was a statistically significant predictor of progression-free survival among studied cases (HR= 4.36; (95% CI, 1.55-12.32; p=0.005).

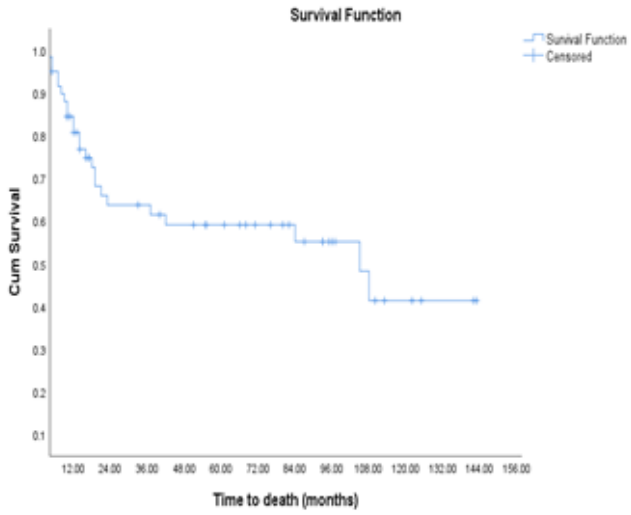


Figure (1): Kaplan -Meier curve showing OS of 62 pediatric patients with CNS tumors

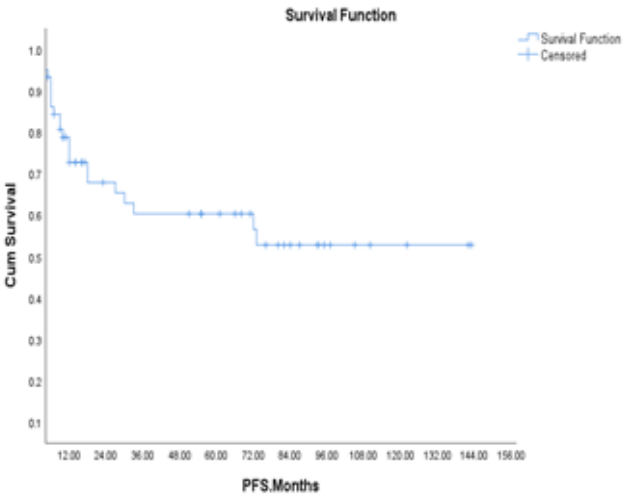


Figure (2): Kaplan -Meier curve showing PFS of 62 pediatric patients with CNS tumors

Table (1): Baseline characteristics of the 62 patients with CNS tumors.

| Characteristic | Number of patients N=62 | % |
|---|---|---|
| Age (years) | | |
| Median (Range) | 11(1.8-18) | |
| Mean± SD | 10.73±4.22 | |
| ≤3 | 2 | 3.2 |
| >3-<10 | 22 | 35.5 |
| ≥10 | 38 | 61.3 |
| Sex | | |
| Male | 46 | 74.2 |
| Female | 16 | 25.8 |
| ECOG PS | | |
| 0 | 11 | ١٧.7 |
| 1 | 15 | 24.2 |
| 2 | 1 | 1.6 |
| 3 | 5 | 8.1 |
| Not mentioned | 30 | 48.4 |
| Comorbidity | | |
| Yes | 2 | 3.2 |
| No | 60 | 96.8 |
| Presenting symptoms | | |
| Headache+ ocular | 16 | 25.8 |
| Headache+ vomiting | 15 | 24.2 |
| Motor | 14 | 22.6 |
| Motor + ocular | 7 | 11.3 |
| Fits | 6 | 9.7 |
| Vomiting | 4 | 6.5 |

SD; Standard deviation, ECOG PS; Eastern Cooperative Oncology Group Performance Status. Ocular signs include squint, decreased visual acuity, or diplopia; Motor signs include paresis, paralysis, or ataxia

Table (2): Diagnosis and baseline tumor characteristics of the 62 patients with CNS tumors.

| Characteristic | N=62 | % |
|---|---|---|
| Site | | |
| Cerebellum | 23 | 37.1 |
| Cerebral lobes | 21 | 33.9 |
| Brain stem | 6 | 9.7 |
| Pineal body | 4 | 6.5 |
| Corpus callosum | 3 | 4.8 |
| Thalamus | 3 | 4.8 |
| Spinal cord | 2 | 3.2 |
| Pathological type | | |
| Gliomas | 25 | 40.3 |
| • *Astrocytoma* | 11 | 17.7 |
| • *GBM* | 8 | 12.9 |
| • *Brain stem glioma* | 6 | 9.7 |
| Ependymoma | 7 | 11.3 |
| Medulloblastoma | 19 | 30.6 |
| PNET | 4 | 6.5 |
| Pineoblastoma | 2 | 3.2 |
| Germ cell tumors | 5 | 8.1 |
| Grade | | |
| Grade I | 5 | 8.1 |
| Grade II | 10 | 16.1 |
| Grade III | 4 | 6.5 |
| Grade IV | 33 | 53.2 |
| Unknown | 10 | 16.1 |
| Disseminated disease from the start | | |
| Yes | 4 | 6.5 |
| No | 58 | 93.5 |

Table (3): Treatment received by 62 patients with CNS tumors.

| Treatment modalities | N=62 | % |
|---|---|---|
| Surgery + follow up | 5 | 8.1 |
| Surgery + RT | 10 | 16.1 |
| Surgery+ CCRT | 29 | 46.8 |
| Surgery+ sequential RT, then CHT | 9 | 14.5 |
| Surgery + CHT | 3 | 4.8 |
| Radiotherapy only | 2 | 3.2 |
| Chemoradiotherapy only | 4 | 6.5 |
| Surgery | 56 | 90.3 |
| No surgery | 6 | 9.7 |
| Received chemotherapy | 45 | 72.6 |
| No chemotherapy | 17 | 27.4 |
| Received radiotherapy | 54 | 87.1 |
| No radiotherapy | 8 | 12.9 |
| Radiotherapy site | N=54 | |
| Brain | 27 | 50 |
| Craniospinal irradiation | 25 | 46.3 |
| Spine | 2 | 3.7 |
| Radiotherapy dose | N=54 | |
| <54 Gy | 16 | 29.6 |
| ≥54 Gy | 38 | 70.4 |

RT; radiotherapy, CCRT; concurrent chemoradiotherapy, CHT; chemotherapy, Gy; Gray

Table (4): Prognostic factors affecting OS of 62 patients with CNS tumors.

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | Median OS in months (95% CI) | P value | HR (95% CI) | P value |
| Age/years | | | | |
| ≤3 | 71.5(37.8-145.65) | | | |
| >3-<10 | 82.6(59.03-106.20) | | | |
| ≥10 | 76.6(55.38-97.82) | 0.702 | | |
| Sex | | | | |
| Female | 105(35-238.82) | 0.620 | | |
| Male | 108(3.32-212.67) | | | |
| ECOG PS | | | | |
| 0 | No statistics computed | 0.327 | | |
| 1 | | | | |
| 2 | | | | |
| 3 | | | | |
| Comorbidities | | | | |
| No | 105(73.58-136.43) | 0.368 | | |
| Yes | 14(14-14) | | | |
| Presenting symptoms | | | | |
| Headache + ocular | 108.0(39.81-200) | | | |
| Headache + vomiting | 103.68(71.31-136.04). | | | |
| Motor | 105.0(38.99-16.56) | 0.214 | | |
| Motor + ocular | 84(69.19-219.62) | | | |
| Fits | 92.4(56.28-128.51) | | | |
| Vomiting | 8.0(1.0-16.82) | | | |
| Site | | | | |
| Cerebral lobes | 58.29(33.09-83.49) | 0.659 | | |
| Cerebellum | 104.41(78.73-130.09) | | | |
| Corpus callosum | 30(17.68-64.65) | | | |
| Brain stem | 47.3(4.92-89.75) | | | |
| Pineal body | 84(26.38-141.61) | | | |
| Thalamus | 48.0(31-109.62) | | | |
| Spinal cord | 105.0(105-105) | | | |
| Pathological type | | | | |
| Gliomas | No statistics computed | 0.280 | | |
| Ependymoma | | | | |
| Medulloblastoma | | | | |
| PNET | | | | |
| Pineoblastoma | | | | |
| Germ cell tumors | | | | |
| Grade | | | | |
| Grade I- III | 87.76(64.48-111.05) | 0.404 | | |
| Grade IV | 85.23(60.56-109.91) | | | |
| Metastasis from the start | | | | |
| No | 108(73.36-142.63) | | | |
| Yes | 7(5-17.78) | 0.029* | 3.58(1.04-12.23) | 0.042* |
| Surgery | | | | |
| No | 105(63.63-229.72) | 0.406 | | |
| Yes | 108(65.46-150.54) | | | |
| Chemotherapy | | | | |
| No | 80.66(57.15-104.16) | 0.606 | | |
| Yes | 81.02(60.76-101.27) | | | |
| Radiotherapy site | | | | |
| Brain | 45.73(25.60-65.86) | 0.02* | 2.62(0.267-25.79) | 0.409 |
| Craniospinal | 105.43(80.24-130.62) | | 1.02(0.087-12.02) | 0.988 |
| irradiation | 105(105-105) | | | |
| Spine | | | | |
| Radiotherapy dose | | | | |
| <54 Gy | 57.62(39.16-96.08) | 0.650 | | |
| ≥54 Gy | 79.62(57.34-101.89) | | | |

*statistically significant.

HR; Hazard ratio, CI Confidence interval, ECOG PS; Eastern Cooperative Oncology Group Performance Status, PNET; Primitive neuroectodermal tumors, Gy; Gray.

Table (5): Prognostic factors affecting PFS of 62 patients with CNS tumors.

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | Median OS in months (95% CI) | P value | HR (95% CI) | P value |
| Age/years | | | | |
| <10 | 74.78(49.92-99.66) | 0.749 | | |
| ≥10 | 86.91(64.53-109.28) | | | |
| Sex | | | | |
| Female | 46.9(20.77-73.03) | 0.047* | 2.26(0.861-5.93) | 0.098 |
| Male | 94.56(74.40-114.72) | | | |
| ECOG PS | | | | |
| 0 | 79.72(45.71-113.73) | 0.052 | | |
| 1 | 66.41(42.66-90.15) | | | |
| 2 | 7(7-7) | | | |
| 3 | 30.4(7.0-63.28) | | | |
| Comorbidities | | | | |
| No | No statistics computed | 0.446 | | |
| Yes | | | | |
| Presenting symptoms | | | | |
| Headache + ocular | 51.35(29.53-73.17) | | | |
| Headache + vomiting | 94.26(59.83-128.69) | | | |
| Motor | 102.25(77.33-127.17) | 0.498 | | |
| Motor + ocular | 48.06(11.59-84.52) | | | |
| Fits | 52.83(20.15-85.52) | | | |
| Vomiting | 42.67(13.32-72.01) | | | |
| Site | | | | |
| Cerebral lobes | No statistics computed | | | |
| Cerebellum | | 0.054 | | |
| Corpus callosum | | | | |
| Brain stem | | | | |
| Pineal body | | | | |
| Thalamus | | | | |
| Spinal cord | | | | |
| Pathological type | | | | |
| Gliomas | 71.76(46.86-96.67) | 0.170 | | |
| Ependymoma | 59.96(21.92-98.01) | | | |
| Medulloblastoma | 109.4(81.89-137.04) | | | |
| PNET | 8.75(4.08-13.42) | | | |
| Pineoblastoma | 52.0(7.0-114.37) | | | |
| Germ cell tumors | 40.0(0.310-79.69) | | | |
| Grade | | | | |
| Grade I- III | 61(38.74-83.28) | 0.611 | | |
| Grade IV | 92.81(67.88-117.74) | | | |
| Metastasis from the start | | 0.288 | | |
| No | No statistics computed | | | |
| Yes | | | | |
| Surgery | | | | |
| No | 75.8(26.20-125.39) | 0.929 | | |
| Yes | 85.64(66.59-104.68) | | | |
| Chemotherapy | | | | |
| No | 91.29(73.59-109.0) | 0.041* | | |
| Yes | 73.56(52.44-94.68) | | 2.34(0.536-10.22) | 0.258 |
| Radiotherapy | | | | |
| No | 54.6(31.49-77.71) | 0.611 | | |
| Yes | 85.6(66.48-104.72) | | | |
| Radiotherapy site | | | | |
| Brain | 51.89(29.42-74.36) | 0.002* | 4.36(1.55-12.32) | 0.005* |
| CSI +spine | 113.62(91.23-136.02) | | | |
| Radiotherapy dose | | | | |
| <54 Gy | 80(50.61-109.54) | 0.796 | | |
| ≥54 Gy | 84.04(61.38-106.71) | | | |

*statistically significant

HR; Hazard ratio, CI Confidence interval, ECOG PS; Eastern Cooperative Oncology Group Performance Status, PNET; Primitive neuroectodermal tumors, CSI; Craniospinal irradiation, Gy; Gray.

## Discussion:

Regarding the prevalence of pediatric CNS tumors in Egypt, Ezzat et al. documented that these cases accounted for 14.3% of all pediatric cancer patients; 96 % of the patients had primary brain tumors, while only 4 % of the primary lesion was in the spinal cord [13]. In our department, the brain was the most frequent site for cancer in children below the age of 15 years. It was diagnosed in 18 children (26.1%) out of the patients presented in this age group in 2015 [14]. Our study was a clinico-epidemiological analysis of 62 pediatric patients with primary CNS tumors, registered in the Clinical Oncology & Nuclear Medicine Department at Mansoura University Hospital from 1 January 2012 to the end of March 2020.

The mean patient age was 10.73±4.22 years, with 2 patients (3.2%) aged 3 years or younger, 35.5% between 3 and 10 years, and 61.3% aged 10 years or older, indicating a predominance of pediatric CNS tumors in young adolescents. This aligns with Stanić et al. who reported a slightly lower mean age of 8.96 years [15]. In contrast, Maaz et al. reported that 82.3% of pediatric CNS tumor cases were under 10 years, while only 17.6% were older; this is difference likely due to the referral of younger patients under 3 years old to pediatric units rather than our department for receiving chemotherapy and delay radiotherapy [16].

Males were more affected than females, with a male-to-female ratio of 2.8:1. This result was consistent with Stocco et al. who reported that male to female ratio was 3: 2, as well as Suresh et al. who also noted a male to female ratio 2.5:1 [17, 18]. In contrast, Ostrom et al. found a higher incidence of primary CNS tumors in females than in males, likely due to the inclusion of meningioma cases and most of these cases were treated in the neurosurgery department rather than being referred to our department [19].

In our study, 32 patients (51.6%) had documented performance status, with 81.3% of the evaluated patients displaying an ECOG performance status of 0 or 1. Almost all of our patients had no comorbidities. This finding is similar to the results reported by Madrigal-Avila et al. where among 56 treated patients, 35 were assessed using the ECOG scale, with 74.2% of the assessed children showing fully active performance status, able to engage in all pre-disease activities without restriction [20].

The most common presenting symptom was headache, which occurred in nearly 50% of our cases. It was accompanied by vomiting in 15 patients and by ocular symptoms (such as squint, decreased visual acuity, or diplopia) in 16 patients. These findings are consistent with Wilne et al. where headache was observed in 41% of cases, and with Maaz et al. who reported headache and vomiting as presenting symptoms in 36.2% of patients [16, 21].

In our study, supratentorial tumors were identified in 31 patients (50%), infratentorial tumors in 29 patients (46.8%), and spinal cord tumors in 2 patients (3.2%). These findings are consistent with those reported by Stocco et al. where 51% of CNS tumors in their cases were located in the supratentorial region [17]. Maaz et al. found that 58.8% of CNS tumors in their patients were supratentorial, 33.3% were infratentorial, and 7.8% were spinal, which is nearly similar to our results [16]. Gliomas were the most common histopathological type of primary CNS tumors in our cases, representing 40.3% of cases, followed by medulloblastoma (30.6%), ependymoma (11.3%), and germ cell tumors (8.1%). These findings align with Ezzat et al. who documented gliomas in 40% of their patients, medulloblastoma in 18.7%, ependymal tumors in 7.9%, and germ cell tumors in 3.1% [13]. Our results also correspond with Adel Fahmideh and Scheurer's study, which found that gliomas accounted for 53% of all primary CNS tumors in children [5]. Our study observed that most pediatric CNS tumors were high-grade (Grade III/IV), accounting for 59.7% of cases, followed by low-grade tumors (Grade I/II) in 24.2% of cases, while the grades of 10 cases were not registered. This finding aligns with Ostrom et al. who found a significant increase in the incidence of high-grade gliomas from 2004 to 2016 [22]. However, it contrasts with El-Gaidi who documented that 62.5% of cases were low-grade tumors, while only 37.5% were high-grade; this may be attributed to the fact that most cases of pilocytic astrocytoma were managed at the department of neurosurgery without referral to our oncology department [23].

In our study, 58 patients (93.5%) had localized tumors at Presentation. These findings are slightly consistent with those of Maaz et al. who reported that 82.4% of their patients had no evidence of disseminated disease at presentation [16].

In our study, surgery followed by radiotherapy and chemotherapy constituted the primary treatment strategy in most cases (61.2%), while surgery followed by adjuvant radiotherapy was in 16% of the patients. This aligns with findings by Mai et al. who analyzed 177 pediatric cases and reported that the primary treatment strategy involved surgery followed by chemotherapy and radiotherapy in 31.1% of cases and surgery followed by radiotherapy in 7.3% of cases [24]. Similarly, Stanić et al. found that the majority of their pediatric cases received the same multimodal treatment approach [15].

Regarding late complications following chemoradiation, our study documented one case (1.9%) with short stature; this may be due to endocrine deficiency or bone hypoplasia. Gurney et al. reported endocrine problems in 18% of their cases, likely due to their more extensive cohort study of 1,818 cases [25]. Dörr et al. studied the relation between bone effects and radiation dose in 146 cases and found clinically relevant growth defects at doses >35 Gy in children aged 6 years or older.

Twenty-four patients (38.7%) died during the study period. The causes of death were categorized as follows: 32.3% died directly from the disease, and 6.4% died from unrelated causes. These findings nearly align with those reported by Pogorzala et al. where 33.6% of patients (110 cases) died due to disease progression, and 8.2% died from other causes [26].

The median follow-up time in our study was 40 months for all cases. During this period, 22 patients (35.4%) experienced disease progression. These results are relatively consistent with findings from Mai et al. where the median follow-up time was 34.6 months, and disease progression was observed in 28% of patients [24].

Our study's median overall survival (OS), including patients with disseminated disease at diagnosis, was 105 months (95% CI: 73.44–136.52 months). The 2-year and 5-year OS rates were 63.7% and 59.9%, respectively, aligning with findings by Stanić et al. who reported 2-year and 5-year OS rates of 68.8% and 59.4% among 173 patients [15]. Similarly, Pogorzala et al. documented a 5-year OS rate of 60.9% ± 4.7% in their cohort of 110 pediatric patients [26]. In Egypt, Maher et al. reported a slightly higher 5-year OS rate of 64.6% in their study, which included 5051 children with CNS tumors [27]. Researchers who studied pediatric brain tumors from Australia and Sweden reported higher 5-year survival rates of 80% and 76%, as documented by Ramanan and Chaseling and Lannering et al. respectively [28, 29]. In contrast, researchers from Nigeria, Tunisia, and Sudan observed significantly lower rates of 47%, 45%, and 13%, respectively, as highlighted by Uche et al., Bellil et al., and Elhassan et al. [3, 30, 31]. This is primarily due to poor access to neuroimaging, neurosurgical, and other treatment facilities in many low- and middle-income developing countries, resulting in decreased survival in these countries.

To enhance therapeutic strategies, it is essential to identify the factors influencing the prognosis of pediatric CNS tumors. This includes determining whether patients are at higher or lower risk for local recurrence and death. In the current study, age, sex, ECOG, comorbidities, presenting symptoms, tumor size, pathological type, grade, the extent of surgery, receiving radiotherapy, radiotherapy dose, and using chemotherapy were not found to affect the overall survival. However, disseminated disease at Presentation (p=0.029) and radiotherapy site (p=0.02) affected the OS in univariate analysis. In multivariate analysis, disseminated disease at Presentation was the only statistically significant predictor of OS (p=0.042). Patients with disseminated disease at diagnosis demonstrated poorer OS compared to those with localized disease. This finding aligns with Stanić et al. who similarly reported a high statistical significance of the extent of disease at Presentation on OS in both univariate and multivariate analyses (p<0.001) [15]. Also, Hansford et al. documented that disseminated disease at diagnosis was significantly associated with an inferior 5-year OS rate (P = .0016). Their study involved 178 pediatric patients from the Children's Oncology Group [32].

Our study showed that patients who received spinal RT had better OS than those who received localized brain RT. However, the number of patients was too small to be considered, which complies with the results of Oh et al. who studied 58 pediatric patients and found that patients who received radiotherapy for upper spinal tumors had better OS (p=0.048) [33].

Regarding the median PFS in our study, it was 86.08 months (95% CI; 67.96-104.20), with a 5-year PFS of 60.3% for all cases. This result is relatively near to Mai et al. who reported a PFS of 53.1 % ±4.2 for their cases [24]. Additionally, our results are similar to those of Fukuoka et al. who studied 127 children and documented a 5-year PFS of 61.8% [34]. In contradiction, Youland et al. demonstrated a higher 5-year PFS of 75.8% for all their cases [35]. This discrepancy may be attributed to their study involving 188 patients, primarily diagnosed with low-grade gliomas, over an extended period from 1990 to 2009.

Our study indicated that the PFS of pediatric CNS tumors was influenced by gender (p = 0.047), radiotherapy site (p=0.002), and chemotherapy (p = 0.041). We found that females had poorer PFS than males. This aligns with Ostrom et al. who documented that females had lower progression survival outcomes in glioblastoma, embryonal tumors, and germ cell tumors [36]. Additionally, our results are consistent with those of Oh et al. who found that patients receiving radiotherapy for upper spinal tumors had improved PFS (p = 0.031) [33]. In contrast, Hansford et al. observed no significant association between chemotherapy and PFS [32]. This discrepancy may be because, in our study, patients receiving chemotherapy were more likely to have high-risk diseases, which contributed to their poorer survival outcomes compared to those who did not receive chemotherapy.

Regarding treatment modalities, the study was designed to outline the treatment approaches for the entire studied patient rather than for each histological subtype individually. This analysis was made because some subtypes had very small absolute numbers and could be treated with different therapeutic approaches, making statistical analysis less meaningful. This was considered a limitation of our study, along with the disadvantages of a retrospective design, including incomplete data on chemotherapy details and treatment complications for many patients. Additionally, the small sample size derived from a single-center database was a limitation in our case series. Future prospective studies focusing on various pathological CNS tumor subtypes, with larger sample sizes and the involvement of a dedicated multidisciplinary team, are strongly encouraged.

## Conclusion:

Pediatric CNS tumors comprise a heterogeneous group of pathologies. The results of our study provide epidemiological insights into children with CNS tumors. Various factors, including age at diagnosis, sex, presenting symptoms, metastatic disease at diagnosis, tumor pathology, tumor location, and treatment lines, were correlated with the prognosis of pediatric CNS tumors.

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