MOSUL JOURNAL OF NURSING
Online ISSN: 2663-0311 - Print ISSN: 2311-8784
Website: https://mjn.mosuljournals.com

RESEARCH ARTICLE

Pediatric Central nervous system tumors, single institutional experience

Hanan Asaad Rasul[1], Zhyan Salah Ramzi[2], Karzan Marif Murad[3]

1- Zhianawa Cancer Center
2- College of Nursing-University of Sulaimani
3- Zhianawa Cancer Center

Corresponding author: Saman Muhammed Amin Saeed

Email: zean.ramzi@univsul.edu.iq

ORCID

Abstract

Objectives: The characteristics of 144 Iraqi children with primary CNS tumors were reviewed to identify median age at presentation, the disease distribution in terms of gender, main presenting symptoms, most common grade and histological subtypes, with predominant subsites in which central nervous system malignancies arise from, according to WHO 2016 classification.

Patients and methods: Medical records were used to collect data on primary CNS malignancies in children under the age of 18 years, in a single tertiary center in Kurdistan/Iraq, Zhianawa cancer center, the study time period was from March 2009 to December 2021 (12 years period study). We classified age into 5 sub-groups: (Infancy) less than 1, 1-4 years old, 5-9 years old, 10-14 years old and above 15.

Results: The study showed that, males were more frequently affected than females, median age at diagnosis was 8.7 years old, predominate age group was (5-9) %38, followed by (10-14) 24.3%. Medulloblastoma which is grade IV tumor was the most common histopathology subtype in 30% of the cases, followed by Astrocytoma and Brain stem glioma as the 2nd and 3rd histopathology. Infratentorial location was the most common involved location in central nervous system (57.6%), followed by supratentorial (40.3%), spinal cord (%2.08) only.

Conclusion: Pediatric CNS tumors in this study have specific characteristics when compared to those seen elsewhere in the world. Grade IV and infratentorial location for example, are the most common in our children.

Keywords: pediatrics, CNS, medulloblastoma, astrocytoma, zhianawa

Received: 13 May 2022, Accepted: 21 August 2022, Available online: 28 August 2022.

INTRODUCTION

Pediatric central nervous system tumors (CNS), are a group of heterogeneous diseases, the second most common cancer in children and the main cause of cancer-related deaths in both developed and developing countries, accounting for more than 15% of all cancer cases in children in the United States (1,2).

Intracranial tumors in children is different from intracranial tumors in adolescents and adults in regards to topographical distribution, clinical types, treatment modalities, prognosis and outcome. They are even variable between different developmental stages (3).

Although it affects all ages, the incidence peaks among children between the ages of 3 years to 7 years old.

In most of the literatures, boys are affected more than girls. Astrocytoma followed by Medulloblastoma were most common histologic subtypes. In adults and older children, most tumors are supratentorial in location while in young children they are more commonly infratentorial in location, predominate subsites was cerebellum and cerebrum.(3–7).

The mortality risk was shown to be very variable depending on the primary tumor location, grade, and histology. The risk of death was higher in the tumors arising from the brainstem and cerebrum. Similarly Grade II, Grade III, and Grade IV had a higher mortality risk than Grade I. High-grade glioma, Primitive neuroectodermal tumors, Medulloblastoma, and Ependymal tumors all had a higher death rate compared to low-grade glioma.(2).

The widespread use of neuroimaging and multimodal therapy have improved the prognosis of pediatric CNS tumors, but they are still the main cause of death and significant functional impairment in children because of the delay in diagnosis owing to the inadequate expression of symptoms in children and newborns. Furthermore, the symptoms of pediatric brain tumors are typically ambiguous and can be confused with those of other common childhood disorders (8,9).

While epidemiological data on CNS malignancies in Western countries is extensively established, similar research in underdeveloped and developing countries are scarce and inconclusive. Specifically, there is little recorded data on the profile of pediatric CNS malignancies in Iraq to date.(10) The goal of this study is to highlight the characteristics of primary childhood CNS tumors from a single tertiary center in Iraq in terms of age-related distribution, clinical presentations, location, and pathological types, using 2016 World Health Organization (WHO) Classification of Tumors of the Central Nervous System.

The current study will allow us to spot any unique trends in the epidemiology of primary CNS tumors and compare our findings to local and regional data. Because most developing countries, including Iraq, lack a central registry dedicated to reporting specific patient populations with malignancies, the unique and methodical approach described here could be valuable in guiding future reports in Iraq and other developing countries.

Materials and Methods

This retrospective Study, conducted in Zhianawa Cancer Center (ZCC), in Sulaymaniyah (Kurdistan – Iraq). This center is the only place in Kurdistan for treating pediatric cancer cases in whom anesthesia is used during radiotherapy, radiation therapy is one of the main modalities of treatment used for pediatric CNS tumors.

Data of 144 patients collected from medical records on primary CNS malignancies (brain and spinal cord) in children under the age of 18 years (patients' age was recorded at the time of diagnosis), excluding cases of secondary metastases from other primary sites to the CNS. Patients' characteristics (demographics, presenting symptoms, histopathology, grade and anatomical location of tumor) reviewed. Their age classified into 5 sub-groups of less than 1 year old (infancy period), 1 to 4 years old, 5 to 9 years old, 10 to 14 years old,15 and more (adolescents).(2,11–13)

The study period (March 2009 to December 2021), covering 12 years. The collected data were analyzed, using SPSS version (27), reference citation done using Vancouver method.

Results

Zhianawa cancer center in Sulaymaniyah is one of the few radiation oncology facilities in the whole Iraq which children in whom anesthesia is mandatory can be managed. There are many referrals to this center from all the different provinces. In this particular study one hundred forty-four cases of children with primary CNS tumors from 2009 to 2021 were reviewed. Only half the patients reviewed here were from our locality in Sulaymaniyah more than one third of the patients are referred to this treatment facility from mid and southern provinces of Iraq (35.4%), and the rest were referred from Erbil and Duhok provinces (8.3%) and (7.6%) respectively.

Regarding gender distribution of primary CNS tumors, male slightly more affected than female. seventy-Six patients (52.78%) were male and 68 (47.22%) were female.

Table 1. Distribution of different histologic subtypes according to gender and different age groups.

Histological type	≤ 1 year No. (%)	1-4 years No. (%)	5-9 years No. (%)	10-14 years No. (%)	15+ years No. (%)	M: F	Total No. (%)
Medulloblastoma	0 (0.00)	10 (38.50)	16 (29.10)	9 (25.70)	7 (30.40)	2.23: 1	42 (30)
Astrocytoma	0 (0.00)	2 (7.70)	17 (30.90)	9 (25.80)	7 (30.40)	0.79: 1	34 (24.3)
Brain stem glioma	0 (0.00)	4 (15.40)	11 (20.00)	5 (14.30)	1 (4.30)	0.61: 1	21 (15)
Atypical teratoid rhabdoid tumors	1(100.00)	3 (11.50)	0 (0.00)	0 (0.00)	0 (0.00)	3:1	4 (2.9)
Ependymoma	0 (0.00)	3 (11.50)	5 (9.10)	5 (14.30)	0 (0.00)	2.25: 1	13 (9.3)
Germinoma	0 (0.00)	0 (0.00)	1 (1.80)	1 (2.90)	0 (0.00)	2:0	2 (1.4)
Primitive neuroectodermal tumors	0 (0.00)	0 (0.00)	2 (3.60)	1 (2.90)	0 (0.00)	2:0	3 (2.1)
Adenoma	0 (0.00)	0 (0.00)	1 (1.80)	1 (2.90)	2 (8.70)	1:1	4 (2.9)
Craniopharyngioma	0 (0.00)	1 (3.80)	0 (0.00)	3 (8.60)	3 (13.00)	0.4:1	7 (5)
Schwannoma	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.30)	0:1	1 (0.7)
Pineoblastoma	0 (0.00)	2 (7.70)	0 (0.00)	1 (2.90)	1 (4.30)	0.33: 1	4 (2.9)
Pineocytoma	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.30)	0:1	1 (0.7)
Ganglioglioma	0 (0.00)	1 (3.80)	2 (3.60)	0 (0.00)	0 (90.00)	0.5:1	3 (2.1)
Total	1(100.00)	26 (100.00)	55 (100.00)	35 (100.00)	23 (100.00)	1.15: 1	140 (100)

In this study the most common age group diagnosed with CNS tumors was 5-9 years, median age was 8.7 years old. There was only one infant patient diagnosed with CNS tumor, which had embryonal tumor (atypical teratoid rhabdoid tumor). Medulloblastoma was the most common histologic subtype in 1–4-year-old age group, however in the 5-9-year-old age group Astrocytoma was higher by a very small margin, i.e. there was only 16 cases of medulloblastoma versus 17 cases of astrocytoma. There was an equal distribution in age group of above 10 years old. Brain Stem Glioma was mostly seen in the 5-9-year-old age group . More details showed above in Table 1.

Regarding different histopathological subtypes of CNS tumors in pediatrics, Medulloblastoma was the most common histology with 42 cases (30%), Astrocytoma (all grades) 35 cases (24.3%), Brain stem glioma 21 cases (15%), Ependymoma 13 cases (9.3 %), Craniopharyngioma 7 cases (5%), less common histologic subtypes were Atypical teratoid rhabdoid tumor, Pineoblastoma, Pituitary adenoma, Ganglioglioma, Germinoma, Schwannoma, Pineocytoma.

Medulloblastoma which was predominate histologic subtype frequently affected boys, ratio of male to female was 2.23:1. We had 2 cases of primitive neuroectodermal tumor & 2 cases of germinoma both of them were male gender, ependymoma and atypical teratoid rhabdoid tumor had the same gender distribution ratio, male mostly affected, male to female was 2.25:1, 3:1 respectively. All other subtypes slightly more common in female with the exception of pituitary adenoma which has an equal gender distribution.

Concerning anatomical locations Medulloblastoma exclusively raised in infratentorial region, Brain stem glioma mainly limited to infratentorial region in 18 cases, but 2 patients had diffuse brain stem glioma & involving both supra and infratentorial region of the cranial fossa. Astrocytoma was frequently arising from supratentorial location, adenoma & craniopharyngioma only seen in supratentorial area, detail of other histologic subtypes and their involved compartments are showed in Table 2.

Table 2. Different histologic subtypes and their involved compartments

Histology subtype	Site of the tumors	
	Infratentorial	Supratentorial
	No. (%)	N0. (%)
Medulloblastoma	42 (53.80)	0 (0.00)
Brain stem glioma	18 (23.10)	2 (3.60)
Ependymoma	6 (7.70)	5 (9.10)
Pilocytic astrocytoma	3 (3.80)	6 (10.90)
Diffuse astrocytoma	3 (3.9)	0 (0.00)
Glioblastoma multiforme	2 (2.60)	5 (9.10)
Atypical teratoid rhabdoid tumors	1(1.30)	3 (5.50)
Schwannoma	1 (1.30)	0 (0.00)
Anaplastic astrocytoma	1 (1.30)	1 (1.80)
Ganglioglioma	1 (1.30)	1 (1.80)
AnaplasticXanthoastrocytoma	0 (0.00)	10 (18.20)
Germinoma	0 (0.00)	2 (3.60)
Primitive neuroectodermal tumors	0 (0.00)	2 (3.60)
Adenoma	0 (0.00)	4 (7.30)
Craniopharyngioma	0 (0.00)	7 (12.70)
Pineoblastoma	0 (0.00)	4 (7.30)
Oligodendroglioma	0 (0.00)	1 (1.80)
Pineocytoma	0 (0.00)	1 (1.80)
Xanthoastrocytoma	0 (0.00)	1 (1.80)
Total	78 (100.00)	55 (100.00)

Astrocytoma was the second prevalent histologic subtypes of primary CNS tumor in this study, the most prevalent astrocytoma subtypes were pilocytic astrocytoma (a low-grade, slow-growing tumor) and anaplastic astrocytoma (a high-grade tumor) in 9 cases (28 percent) each, Pilocytic astrocytoma more common in female 0.5 :1. Glioblastoma multiforme which is the most aggressive brain tumor (grade IV astrocytoma), in the current study, 7 cases of glioblastoma multiforme were reported, 5 of which originated in the supratentorial region and 2 in the infratentorial region, 5 of which were in the (5-9) age group and 2 of which were in the (10-15) age group. There were four female cases and three male cases, with a small female predominance of 0.75:1.

Table 3. Different subtypes of astrocytoma and their grade.

Astrocytoma cases	Grade	No. (%)
Pilocytic astrocytoma	I	9 (28.13)
Oligodendroglioma	I	1 (3.13)
Diffuse astrocytoma	II	4 (12.50)
Xanthoastrocytoma	II	1 (3.13)
Anaplastic astrocytoma	III	9 (28.13)
Anapastic Xanthoastrocytoma	III	1 (3.13)
Glioblastoma multiforme	IV	7 (21.88)
Total		32 (100.00)

Concerning grading of primary central nervous system tumors, Grade IV histopathological type was the most common grade (50.9%), followed by Grade I (22.4%). In female Grade I was more common than male, with a ratio of 1:0.53, whereas grades II, III, and IV, were most common in male. In 28 cases grade was unknown, 18 cases of unknown grades were from brain stem lesions because role of surgical excision and pathological confirmation usually limited due to morbidity and mortality associated with surgical intervention of that critical part of brain, histopathological confirmation done only 2 cases of brain stem tumors, one of them grade II the other was grade III glioma.

CNS tumors resulted in a wide spectrum of symptoms, which were primarily determined by the tumor's location. Raised intracranial pressure (headache with or without nausea and vomiting) was the most common presenting sign or symptom of CNS malignancies, in both supratentorial and infratentorial tumors, as documented in 65 cases (45.12%), made their parents to seek for medical help, both supra and infratentorial lesions exhibited ocular complaints, Convulsion were presenting symptom of supratentorial lesions, while neurological symptoms and ataxia are more common with infratentorial lesions. The frequency of other presenting sign or symptoms with location of tumor showed in Table 4.

Table 4. Presenting sign or symptoms & location of tumors.

	Site of The Tumor		Total
	Infratentorial	Supratentorial	
	N0. (%)	No. (%)	No. (%)
Headache	36 (47.37)	27 (52.94)	63 (49.61)
Ocular symptoms	19 (25.00)	13 (25.49)	32 (25.20)
Neurological symptoms	15 (19.73)	3 (5.88)	18 (14.17)
Convulsion	1 (1.32)	5 (9.80)	6 (4.72)
Ataxia	4 (5.26)	2 (3.92)	6 (4.72)
Short stature	0 (0.00)	1 (1.96)	1 (0.79)
Total	76 (100.00)	51 (100.00)	127 (100.00)

Regarding topographical distribution of CNS tumors, location of each tumors verified by CT scan or MRI in all cases. Infratentorial location was the most common involved location in central nervous system 80 cases (57.6%), followed by supratentorial 56 cases (40.3%), spinal cord 3 cases 2.2%, 5 cases unknown. Predominant involved subsite in infratentorial region was cerebellum in 54 cases

(37.5 %), brain stem 23 cases 16%. For supratentorial tumors cerebral lobes were the most the frequent subsite in 26 cases (18.1%), then suprasellar 10 cases 6.9 %.

Discussion

Due to a lack of thorough recording of newly diagnosed cases with local cancer registries in underdeveloped countries like Iraq, the true tumor burden of such diseases stays unreported and underestimated. As a result, hospital-based prevalence data is used to estimate disease load, this data is essential for the management of these diseases, and assessing geographical differences.

In the present study median age of diagnosis of primary pediatric CNS tumors was 8.7 years old, (nearly same median age according to other studies done in Iraq, Egypt, Britain) predominate age group was (5-9) years old in 55 cases %38, (10-14) years in 35 cases 24.3% (8,10–14). Other Population-Based Epidemiologic Data on Brain Tumors in German Children showed (1-4) years old was the most common age group (3).

There was slight male predominance over all in our study 52.78% vs 47.22%, similar to other studies done in Iraq, most of the developing countries and developed countries (2,6,8,10–14). That male predominance difference is more pronounce in embryonal tumors and high-grade tumors in the present study, a study done in Bagdad showed more female had been affected than male (15).

Medulloblastoma which is grade IV embryonal tumor was the predominant histology in the current study, just like other studies done in Morocco, Baghdad, Karbala/Iraq and Syria, (10,15–17). This was not following the common histopathology subtypes of primary CNS tumors in most of the reported literature worldwide like, UK, US, Canada, Germany, and other arabic countries like Egypt, Tunisia, Saudi Arabia, in which astrocytoma was the predominant HP subtype,
(3,4,7,12–15,18).

HGG was slightly more than half of astrocytoma cases in our study, so it was the 2nd most common histology just like a study done in Canada, the incidence of HGG is variable in other studies (10,13).

The third most prevalent histology of CNS tumors in this study was Brain stem glioma, which is associated with a poor overall outcome, decreased performance of the patient, poor quality of life, and short-term survival mainly due to its location.(2,7).

Ependymomas were the third most prevalent tumors according to international data; they were ranked fourth in this study, accounting for 9% of all histological kinds, and fifth in other studies conducted in Iraq (3,5,10,19,20).

Craniopharyngioma is a low histological grade (WHO I) tumor that develops from the epithelial remnants of Rathke's pouch. Variable results have been reported from numerous published researches, ranging from 4.4% to 18.4%. It was the 2nd most common histology just after astrocytoma in Beijing and japan, and the 3rd most common CNS tumor from data reported from Korea and India, while figures from Canada, Germany, and Morocco showed that it was the 4th most common pediatric CNS tumor, (5,6,17,18,20–22) (in the current study it was the 5th most common type accounting for 4.9%).

Regarding the presenting signs or symptoms of CNS tumors, Signs of raised intracranial pressure (headache with or without vomiting) was the most common presenting symptom in our study, 45.13% which is similar to main presenting symptom of pediatrics tumor in most of the studies (9,10,14,16).

WHO grade I and grad II tumor of CNS was 33.6% in our study, markedly lower than Grade III & grade IV which was 66.3%, large cohort done in US also showed higher incidence of high-grade tumors, but different data from reported literature in Egypt, Tunisia, Germany, and Syrian, showed that low grade tumors are more common in children. (2,12,13,16,18). In most of the studies done in Arabic countries like Iraq, Egypt, Syria, Saudi Arabia just like our study infratentorial location was the predominate location, mainly in the cerebellum followed by supratentorial location mainly cerebral lobes (10,13–16). One possible explanation for that is geographical variances, because difference seen in literature on most frequent histology and location of pediatrics CNS tumors, more data from other Middle Eastern nations must be examined in order to validate or deny the applicability of our findings to the entire Middle East. Another explanation for the high prevalence of high-grade tumors in our center, despite geographical disparities, could be referral bias; because our facility is a tertiary center, many neurosurgeons may not see the need to refer some tumors for adjuvant radiotherapy, such as low-grade gliomas .

Conclusion

According to our results, median age of diagnosis was 8.7 years old, male slightly more affected than female, medulloblastoma and grade IV tumors were most common histological subtypes, infratentorial location was the most common location in which primary CNS tumors arise from, Pediatrics CNS tumors in this study have specific characteristics when compared to those seen elsewhere in the world. Grade IV and infratentorial location for example, are the most common in our children. As there is rising global trend in the incidence of pediatrics CNS tumors. The aim of this research is to shed light on the epidemiology of pediatric CNS tumors in Kurdistan/Iraq and motivate upcoming prospective

population-based studies to track incidence trends, risk factors, survival rates and quality of life in children with CNS malignancies. Limitation of this study is that its single-center retrospective design.

REFERENCES

Abbas AA, Shitran R, Dagash HT, Ali Khalil M, Abdulrazzaq R. Prevalence of Pediatric brain tumor in children from a tertiary neurosurgical center, during a period from 2010 to 2018 in Baghdad, Iraq. Annals of Tropical Medicine and Public Health. 2021;24(04).

Al-Jumaily U, Al-Safi R, Al-Mosawi S, Al-Obaidy H, Fawzi M. Clinico-pathological spectrum of Childhood Central Nervous System Tumors in Iraq: A Single-Institutional Study. Vol. 5, J Contemp Med Sci |.

Almutrafi A, Bashawry Y, Alshakweer W, Al-Harbi M, Altwairgi A, Al-Dandan S. The Epidemiology of Primary Central Nervous System Tumors at the National Neurologic Institute in Saudi Arabia: A Ten-Year Single-Institution Study. Journal of Cancer Epidemiology. 2020;2020.

Bellil S, Limaiem F, Mahfoudhi H, Bellil K, Chelly I, Mekni A, et al. Descriptive epidemiology of childhood central nervous system tumours in Tunisia: Experience of a single institution over a 15-year period (1990-2004). Pediatric Neurosurgery. 2008;44(5):382–7.

El-Gaidi MA. Descriptive epidemiology of pediatric intracranial neoplasms in egypt. Pediatric Neurosurgery. 2012 Jul;47(6):385–95.

Hirata K, Muroi A, Tsurubuchi T, Fukushima H, Suzuki R, Yamaki Y, et al. Time to diagnosis and clinical characteristics in pediatric brain tumor patients. Child's Nervous System. 2020 Sep 1;36(9):2047–54.

Hossain MJ, Xiao W, Tayeb M, Khan S. Epidemiology and prognostic factors of pediatric brain tumor survival in the US: Evidence from four decades of population data. Cancer Epidemiology. 2021 Jun 1;72.

Jain A, Sharma MC, Suri V, Kale SS, Mahapatra AK, Tatke M, et al. Spectrum of pediatric brain tumors in India: A multi-institutional study. Neurol India. 2011;59(2):208–11.

Kaatsch P, Rickert CH, Kuandhl J, Schuandz J, Michaelis J. Population-based epidemiologic data on brain tumors in German children. Cancer. 2001;92(12):3155–64.

Kadri H, Mawla AA, Murad L. Incidence of childhood brain tumors in Syria (1993-2002). Pediatric Neurosurgery. 2005 Jul;41(4):173–7.

Karkouri M, Zafad S, Khattab M, Benjaafar N, el Kacemi H, Sefiani S, et al. Epidemiologic profile of pediatric brain tumors in Morocco. Child's Nervous System. 2010;26(8):1021–7.

Lacour B, Guyot-Goubin A, Guissou S, Bellec S, Désandes E, Clavel J. Incidence of childhood cancer in France: National Children Cancer Registries, 2000-2004. European Journal of Cancer Prevention. 2010;19(3):173–81.

Larouche V, Toupin A-K, Lalonde B, Simonyan D, Jabado N, Perreault S. Incidence trends in pediatric central nervous system tumors in Canada: a 15 years report from Cancer and Young People in Canada (CYP-C) registry. Neuro-Oncology Advances. 2020;2(1):1–10.

Makino K, Nakamura H, Yano S, Kuratsu JI. Population-based epidemiological study of primary intracranial tumors in childhood. Child's Nervous System. 2010;26(8):1029–34.

Pongtanakul B, Sirachainan N, Surapolchai P, Charoenkwan P, Choeyprasert W, Komwilaisak P, et al. Pediatric primary central nervous system tumors registry in Thailand under National Health Security Office schemes. Journal of Neuro-Oncology [Internet]. 2020;149(1):141–51. Available from: https://doi.org/10.1007/s11060-020-03582-w

Rickert CH, Paulus W. Epidemiology of central nervous system tumors in childhood and adolescence based on the new WHO classification. Child's Nervous System. 2001;17(9):503–11.

Sharma N, Sharma D. An Overview of Pediatric CNS Malignancies. Current Cancer Treatment. 2020;1–25.

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA: A Cancer Journal for Clinicians. 2018;68(1):7–30.

Stiller CA, Bayne AM, Chakrabarty A, Kenny T, Chumas P. Incidence of childhood CNS tumours in Britain and variation in rates by definition of malignant behaviour: Population-based study. BMC Cancer. 2019;19(1):1–15.

Suh YL, Koo H, Kim TS, Chi JG, Park SH, Khang SK, et al. Tumors of the central nervous system in Korea: A multicenter study of 3221 cases. Journal of Neuro-Oncology. 2002;56(3):251–9.

Wilne SH, Ferris RC, Nathwani A, Kennedy CR. The presenting features of brain tumours: A review of 200 cases. Vol. 91, Archives of Disease in Childhood. 2006. p. 502–6.

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. Pediatric Neurosurgery. 2008;44(2):97–103.