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ORIGINAL ARTICLE

Clinical Characteristics and Epidemiological Profile of Children Diagnosed with Central Nervous System Tumors - A 5-year retrospective Study

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ABSTRACT

Tumors of the central nervous system in children are significant health problem worldwide, these tumors disrupt the quality of life, growth, and neurodevelopment of this population, as they are usually silent rapidly progressing diseases. Their frequency is a source of concern in the medical field due to the sequelae and negative outcomes they generate. In Iraq, particularly our province, Karbala, studies concerned with this type of tumors in respect to their clinical and epidemiological profile are scarce, therefore, in this study we aimed to study the clinical and epidemiological profile of these tumors in pediatric population, hence, we carried out an observational, descriptive retrospective study during a period of 6 months (July-December, 2024) to analyze the available data for the years 2020-2024 of the registered child patients with primary CNS tumors during this period at Karbala city, diagnosis was made according to the classification of the World Health Organization for CNS tumors in pediatric population. We included medical files of 62 child patients with CNS tumors aged less than 18 years of both genders with different types of CNS tumors and management regimen. Our findings revealed that most cases (82.3%) at the age of 10 years or younger and predominance of males, (58.1%), with a male to female ratio of almost 1.4 to one. The most frequent primary site of tumors was cerebellum (53.2%), and the least frequent site, (1.6%), was each of optic nerve and pineal gland. Medulloblastoma and Pilocytic astrocytoma types were the more frequent histopathological types; 37.1% and 32.3%, respectively, while the least frequent type was Ependymoma in only 1.6%. The treatment modalities included surgery, chemotherapy and radiation as a single or combined treatment accordingly. The mortality rate among the studied group was 25.8%. In conclusion, the clinical and epidemiological profile of CNS tumors among Iraqi children is almost similar to that reported in other countries. We suggest conducting further studies on national level for further assessment.

Keywords: *Tumors of the Central Nervous System, Children, Clinical profile, Epidemiology*

1. INTRODUCTION

In the pediatric population, tumors of the central nervous system (CNS) are the leading cause of death from cancer in childhood, and are also the second most common malignant neoplasm after leukemia. The incidence varies between 1 to 3 per 100,000 children under 19 years of age for malignant neoplasms and 5.4 per 100,000 when benign tumors are included) [1–4].

In relation to anatomy, the CNS is divided into three main components that are useful for locating neoplasia: the supratentorial region, the infratentorial region, and the spinal cord Depending on the neoplasia, the signs and symptoms will be related to various factors such as the location of the tumor, age, and intrinsic characteristics of the tumor [5–7].

According to the clinical findings, the symptoms and signs that may be present are predominantly irritability, lethargy, vomiting, anorexia, headache, and very frequently behavioral changes other signs and symptoms include epilepsy, focal neurological deficit, endocrine disorders, and nausea. Symptoms are usually associated with an abnormal physical examination, and their evolution should be carefully analyzed [3,8,9].

Regarding location, between 40 and 60% of CNS tumors in the pediatric population are located in the posterior fossa. The most common location is supratentorial in children under 3 and over 10 years of age; while infratentorial tumors are more common in children between 3 and 10 years of age. Regarding histological characteristics, tumors of embryonal origin occur more frequently in younger children [2,10,11].

According to the types of CNS tumors, there is a greater presence of pilocytic astrocytoma in 15.5%, followed by embryonal tumors in 11.4%, mainly medulloblastoma and finally ependymal tumors in 5.2%, where the familial predisposition has been associated with a greater tendency to develop CNS tumors, with neurofibromatosis types 1 and 2 and tuberous sclerosis being the most related. Previous studies referred that the median age at diagnosis was almost 5 years, with a male to female ratio of 1.33. Additionally, it was identified that the most frequent location was the cerebellum Furthermore, most cases come from urban areas[12–16]

Regarding mortality, CNS tumors constitute high rates of morbidity and mortality in the pediatric population, the survival rates increased in the last decade from 55% in 1975 to reach

76% in 2017 in children under 15 years of age. Furthermore, in developed countries only 14% of patients diagnosed with CNS tumors have a survival rate of more than 10 years. From other point of view, different factors can contribute to the prognosis of these tumors; studies have shown that older age at diagnosis associated with better prognosis and survival compared to younger age at diagnosis. The main determinant of prognosis and survival of children with CNS tumors include sex, anatomical site of tumor, grade of tumor and histological types [17]. However, published epidemiological research on pediatric brain tumors are scarce, rather outdated, and primarily concentrated on the incidence rates. Studies examining survival rates and prognostic factors in pediatric brain cancer predominantly rely on very small datasets of specific histological types with constrained comparative analyses [17].

Brain tumors are the most prevalent solid tumors in children; they are one of the main causes of morbidity and mortality among this population [5]. There are different kinds of tumors, and they are varied in their types, site of primary lesion and clinical presentation. However, some tumors are more common than others. The most prevalent types are Medulloblastoma, Pilocytic astrocytoma (PA) and Ependymoma. Other types include high grade gliomas (HGG), germ cell tumors (GCTs), craniopharyngiomas and choroid plexus carcinomas (CPTs). We will outline below a brief overview of each type:

Medulloblastoma is a very aggressive embryonal tumor of the cerebellum mainly affect the children at the age of 3-8 years. It originates from primitive neuroectodermal cells and commonly causes headaches, vomiting, and ataxia due to obstructive hydrocephalus. Molecular subgroups, like WNT, SHH, Group 3, and Group 4, have an effect on treatment and prognosis [18,19].

Pilocytic astrocytoma (PA) is the primary tumor that commonly found in children and adolescents, they occur with an incidence rate of almost one per 100,000 children it constitutes about 30% of all primary tumors in children; they are well known as benign, circumscribed, grade I (WHO) with a 5-year survival of 85-100% after complete resection. They are slow-growing, highly vascularized and well-circumscribed tumors that displace surrounding tissues, have low cellularity and mitotic activity, and rarely metastasize. Exceptionally, they can undergo malignant transformation [20].

Ependymomas are the third most common type of central nervous system tumor in children (after astrocytomas and medulloblastomas) and account for 5.2% of all brain tumors, the annual incidence rate is up to 0.6 per 100,000 children . The median age at diagnosis is 6 years, however, about 30% of ependymomas are diagnosed in children under 3 years of age. Ependymomas are slow-growing tumors originated from the ependymal (inner) lining of the ventricular system and about 70% of ependymomas arise in the posterior fossa. Diagnosis is based on MRI and biopsy results. Treatment is usually a combination of surgery, radiation therapy, and chemotherapy [21].

High grade gliomas (HGG), contributed for 3-7% of newly detected primary brain tumors in pediatric population [22]. These tumors are primarily comprised of anaplastic astrocytoma and glioblastoma. In comparison to adult population, HGG are relatively less frequent in children and they have distinct molecular genetics [23]

Germ cell tumors (GCTs): These are heterogeneous group of tumors accounting for 2–4% of brain tumors among children, their incidence varies widely by geographic region. GCTs are derived from primordial germ cells. Most CNS GCTs are found in the pineal and suprasellar areas of the brain. They can be divided into two main groups: germinomas and non-germinomas GCTs [24].

Craniopharyngiomas: These are benign intracranial tumors represent almost 5-11% of intracranial tumors in children, these tumors can recur and usually associated with complications despite the advancement in the management protocols, leading to severe morbidity and negatively affect the quality of life due to visual, endocrinological and neuropsychological complications [25]

Choroid plexus carcinomas (CPTs) constitute 2%–4% of cerebral tumors in pediatric patients. The majority are low-grade tumors ((WHO) grade I and II)) that present in the early years of life. In the last few years, low-grade CPPs showed great survival rates after surgery alone, but the results for higher-grade choroid plexus carcinomas (CPCs) have not been as good as that for low grade CPC [26,27] .

In Iraq, particularly our province, Karbala, studies concerned with this type of tumors in respect to their clinical and epidemiological profile are scarce, therefore, in this study we aimed to study the clinical and epidemiological profile of these tumors in pediatric population.

Aims of Study:

General Objective:

To determine the clinical and epidemiological profile of the pediatric population diagnosed with central nervous system tumors at Karbala city, between 2021-2024

Specific objectives

1. Determine the sociodemographic characteristics of the child population CNS tumors
2. Identify the clinical characteristics of children with CNS tumors.
3. Find the prevalence of different types of central nervous system tumors.
4. Describe the main types of treatment and outcomes of the studied population.

2. METHODOLOGY

This was an observational, descriptive retrospective study conducted at Karbal city and included and analyzed the available registered data of pediatric patients with CNS tumors for the years 2020-2024 of the registered child patients with primary CNS tumors during this period at Karbala city, diagnosis was made according to the classification of the World Health Organization for CNS tumors in pediatric population. Data of CNS tumors in the pediatric age group (<18 years of age) was collected from the medical records of Imam Hussein Cancer Center at Kerbalaa governorate in the middle of Iraq. The data collection and analysis time was 6 months. Registered child Patients with primary CNS (brain and spinal cord) tumors who were younger than 18 years at the time of diagnosis were icluded. Data were retrieved from medical records and pathology databases. Patients included in this study were diagnosed depending on the characteristic site of the primary tumor, histological appearance, and necessary immunohistochemistry categorized according to the WHO classification prevalent at the time of diagnosis (3, 16). We reviewed patients' characteristics [demographics, tumor location, pathology, living site], treatment plan (chemotherapy, surgery, and radiotherapy), and outcome. The collected data were analyzed and compared with available published data in tumor registries and hospital-based studies. Data analysis was performed using the SPSS software for windows. Qualitative variables presented as frequencies and percentages.

3. RESULTS

We analyzed the medical files of 62 pediatric patients with CNS tumors who were registwered during the selected period (2021-2024). Demographic characteristics of the studied group are shown in (Table 1) where most the cases at the age of 10 years or younger who contributted for 82.3%. Males were dominant and represented 58.1% compared to 41.9% for female cases with a male to female ratio of almost 1.4 to one. Almost two-third of the cases, (61.3%) of urban areas and majority of them, (71%) from Karbala and Baghdad while 29% from other provinces including Babel, Diwaniya, Najaf, Wasit and Diyala

As shown in (**Table 2**), Cerebellum was involved as primary site in more than half of the cases, (53.2%) which is the most common affected site followed by cerebrum, Suprasellar, Spinal cord and brain stem in a rate of 19.4%, 9.7%, 8.1% and 6.5%, respectively, while tumors in the optic nerve and pineal gland were the least reported, each contributed for only 1.6%.

The distribution of pediatric CNS tumors according to Histopathology typing is summarized in (**Table 3**); Medulloblastoma and Pilocytic astrocytoma types were the more frequent; 37.1% and 32.3%, respectively, while the least frequent type was Ependymoma in only 1.6%.

Furthermore, the commonest histopathological types in the cerebellum was Medulloblastoma (69.7%), Pilocytic astrocytoma (21.2%), High grade glioma (6.1%) and Ependymoma (3%) out of 33 CNS tumors in the cerebellum. In Cerebrum Pilocytic astrocytoma, High grade glioma Supratentorial PNET and other types reported in 41.7%, 25%, 16.7% and 16.7%, respectively out of 12 CNS tumors in this site. All 6 suprasellar tumors of germinoma type. All the 5 spinal cord tumors were Pilocytic astrocytoma, Brain stem tumors were equally distributed; two cases for each of Pilocytic astrocytoma and high-grade glioma types. The only case with optic nerve involvement was pilocytic astrocytoma type and the one case with pineal gland involvement was pineoblastoma type, (**Table 4**).

The treatment modalities administered for management of CNS tumors among the studied group are shown in (**Table 5**) where 51.6% of the cases received combined surgery, radiotherapy, and chemotherapy, 22.6% treated with surgery and chemotherapy, 4.8% surgery and radiotherapy. Single mode of treatment used in the remaining cases; surgery only in 4.8%, chemotherapy only in 9.7% and radiotherapy alone used in only two cases, (3.2%).

The final outcome reported in the medical files of the studied group showed that 74.2% survived until the time of data collection while 16 cases were died giving a mortality rate of 25.8% among the registered cases, (**Figure 1**). However, among the survived cases, 11 abandoned treatment and 6 cases still receiving treatment.

Table 1. Demographic characteristics of the studied group

Variable	Category	No. of cases	%
Age (year)	≤ 5	27	43.5
	6-10	24	38.7
	> 10	11	17.7
Gender	Male	36	58.1
	Female	26	41.9
Residence	Urban	38	61.3
	Rural	24	38.7
Province	Karbala	23	37.1
	Baghdad	21	33.9
	Other*	18	29.0
Other*: Babel, Diwaniya, Najaf, Wasit, Diyala			

Table 2. Frequency distribution of pediatric CNS tumors according to the primary involved site

Involved site	No. of cases	%
Cerebellum	33	53.2
Cerebrum	12	19.4
Suprasellar	6	9.7
Spinal cord	5	8.1
Brain stem	4	6.5
Optic nerve	1	1.6
Pineal gland	1	1.6

Table 3. Frequency distribution of pediatric CNS tumors according to Histopathology typing

Histopathology	No. of cases	%
Medulloblastoma	23	37.1
Pilocytic astrocytoma	20	32.3
High grade glioma (HGG)	7	11.3
Germinoma	6	9.7
Ependymoma	3	4.8
Supratentorial PNET	2	3.2
Other types	3	4.8

Other types (Pineoblastoma, Oligodendro glioma, Choroid plexus carcinoma)
PNET: primitive neuroectodermal tumors

Table 4. Distribution of histopathological types across the primary site of CNS tumors among the studied group

Site	**Histopathology**	**Number of cases**	**%**
Cerebellum	Medulloblastoma	23	
	Pilocytic astrocytoma	7	21.2
	High grade glioma	2	6.1
	Ependymoma	1	3.0
	Total	**33**	**100.0**
Cerebrum	Pilocytic astrocytoma	5	41.7
	High grade glioma	3	25.0
	Supratentorial PNET	2	16.7
	Others	2	16.7
	Total	**12**	**100.0**
Suprasellar	Germinoma	6	100.0
	Total	**6**	**100.0**
Spinal cord	Pilocytic astrocytoma	5	100.0
	Total	**5**	**100.0**
Brain stem	Pilocytic astrocytoma	2	50.0
	High grade glioma	2	50.0
	Total	**4**	**100.0**
Optic nerve	Pilocytic astrocytoma	1	100.0
	Total	**1**	**100.0**
Pineal gland	Pineoblastoma	1	100.0
	Total	**1**	**100.0**

Table 5. Treatment modalities administered for management of CNS tumors among the studied group

Treatment	No. of cases	%
Surgery, Radiotherapy, Chemotherapy	32	51.6
Surgery, Chemotherapy	14	22.6
Surgery, Radiotherapy	3	4.8
Radiotherapy, Chemotherapy	2	3.2
Surgery only	3	4.8
Chemotherapy only	6	9.7
Radiotherapy only	2	3.2
Total	62	100.0

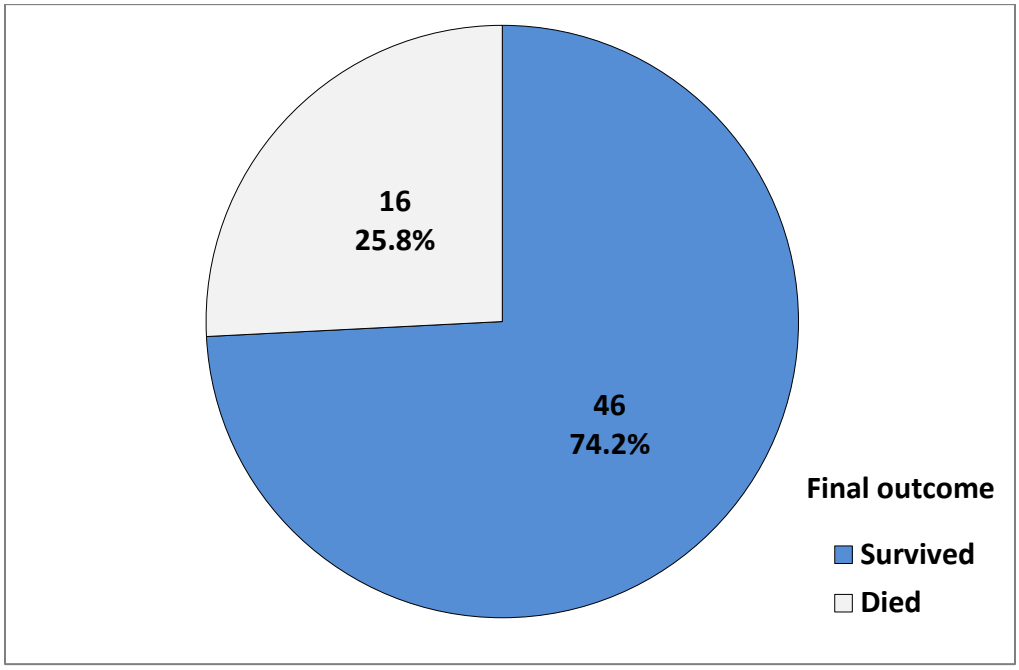

Figure 1. Final outcome and mortality rate among 62 pediatric patients with CNS tumors during the period 2021-2024 at Karbala city

4. DISCUSSION

In general, pediatric CNS tumors contributed for 14.8% of all intracranial tumors, with a range of 10% to 21%. In our study we found relatively higher frequency of males than females, with a male-to-female ratio of almost 1.34. However, this ratio is different in other studies from other countries [28–33]. We found that almost two-thirds of the children who had CNS tumors resided in urban areas. This suggests that CNS tumors are more common in urban than rural regions, this variation between urban and rural areas could be attributed to the environmental factors that cause tumors [34,35] In the present study, the most prevalent brain tumors reported among our studied group of children were the embryonal tumors (Medulloblastoma, supratentorial PNET, and pineoblastoma), Low-grade gliomas (LGG) such as pilocytic astrocytoma and oligodendroglioma, High-grade gliomas (HGG), CNS germinomas , Ependymomas , Choroid plexus cancers, the highest rate reported for medulloblastoma which accounted for 37.1% followed by Pilocytic astrocytoma (32.3%), High grade glioma (HGG) (11.3%) and Germinoma (9.7%) while the least reported rate for Ependymoma, Pineoblastoma, Oligodendro glioma and Choroid plexus carcinoma, with 1.6% for each.

Our results showed that embryonal tumors were more common than in other national studies[28–33,36]. LGG was the second most common tumor, whereas in earlier research, LGG was commonly rated as the most common pediatric CNS tumor [30–33,37]. In our series, HGG came in third order, however the number of cases reported in the literature varies substantially [28,36]. Germ cell tumors (GCT) were the fourth most prevalent form, making up 9.7% of all cases. They were much more common in Southeast Asia (Korea, China, Japan), which could be due to genetic or environmental factors [28,38].

International data generally stated that ependymomas are the third most prevalent CNS tumour in children, however in our study they only accounting for 4.8% of the cases, which put them in the fifth rank [30,33,36,37]. The rate of craniopharyngioma varies a lot among studies where its frequency ranged between (4.4% to 18.4%), in Korea, Brazil, and India having the third highest rates and Canada, Germany, Sweden, and Morocco having the fourth highest rates [28,33,37,39–42]. According to data from Beijing and Japan, it is the second and third most common tumor, respectively [43,44]. However, our investigation didn't find any cases, perhaps because they weren't reported. A lot of patients may skip seeing pediatric oncologists and go

to neurosurgeons or radiotherapy oncologists instead. Also, this may be attributed to the fact that not every case was completely registered in the local cancer registries. In the current study we found similar results to that reported in other developing countries, however the rates of survival and treatment abandonment were lower than those of developed countries[43–46].

Some of the main problems were Late referrals to pediatric cancer doctors, not working together across disciplines, people often though that cancer is always fata and financial problems that make it hard to get specialized care. In our study, we underscore how important to have hospital-based prevalence statistics for figuring out how often diseases happen, planning healthcare, and looking at how molecular and genetic profiles differ from one to another location. Because pediatric CNS tumors are becoming more common and deadly in developing nations than other childhood malignancies, it is very important to obtain accurate national data. Our study may not fully show how patients are distributed in Iraq because it was the country's first tertiary center for pediatric CNS tumors. Another problem is that not all patients were managed by pediatric oncologists, some cases might be managed by adult oncologists, neurosurgeons, or radiotherapy oncologists. Therefore, we highly recommend that all pediatric cases with CNS tumors have to be referred to specialized tertiary centers to assure the optimal management, care and follow up. That can be a crucial to improve the quality of reporting cases and get sufficient data about these tumors which can help to provide good epidemiological view about these tumors. However, despite, the aforementioned problems, our study highlighted and focus the light on the pediatric CNS tumor in our country, particularly, the cases registered in our center were from different Iraqi provinces which may partially reflect the profile of these tumors for the whole country.

5. CONCLUSIONS

According to the finding of our study we concluded that most of the CNS tumors occurred in pediatric patients aged 10 years or younger with a male to female ratio of 1.34 to one. Almost two-thirds of the studied group were from urban areas and from different Iraqi provinces. The most prevalent reported brain tumor was medulloblastoma followed by Pilocytic astrocytoma, High grade glioma (HGG) and Germinoma while the least reported rate for Ependymoma, Pineoblastoma, Oligodendro glioma and Choroid plexus carcinoma. We highly suggested that

all pediatric cases with CNS tumors have to be referred to specialized tertiary centers to assure the optimal management, care and follow up and it will be crucial to improve the quality of reporting cases and get sufficient data about these tumors, moreover, further studies, particularly, multi-center studies on national level are still required for better and further assessment and evaluation

Ethical Approval:

All ethical issues were approved by the author. Data collection and patient's enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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