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ORIGINAL ARTICLE

Lag Time of Pediatric Supra Tentorial Brain Tumors in Lower Middle Income Countries (LMIC)

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ABSTRACT

Background: The most common and frequent tumors in the children's are central nervous system tumors (CNS).
Objective: For evaluation of the lag time and clinical spectrum of pediatric supratentorial brain tumors from the time of appearance of symptoms in a patient to the time the patient presents to the hospital**.**
Study design: It is an observational and cohort study conducted in the radiology and oncology department of our institute teaching hospital.
Material and Methods: This prospective research was conducted at the oncology department of the children hospital ICH Lahore for one year. The study was approved by the IRB. The duration of the study was from March 2021 to March 2022. The sample size was calculated. The patients of age range between 0 months to 17 years were included in the study. SPSS version 24.0 was used for statistical analysis. Data will be stratified to see the effect modulators.
Results: This study included 60 patients 30 girls and 30 boys. The average age of the patients at the time they were diagnosed with pediatric supratentorial brain tumor was 7 years. The majority of the patients reported to have type I neurofibromatosis. Some of the most common symptoms that the patients reported were vomiting, oculo-visual issues, motor problems, headache and endocrine dysfunction.
Conclusion: The lag time and clinical spectrum of pediatric supratentorial brain tumors from the time of appearance of symptoms in a patient to the time the patient presents to the hospital was reported to be 2-6 months in majority almost 61% of the children. The 71% children visited the two regional area doctors before visiting the tertiary care hospital. The complex interplay of underdiagnoses, unavailability of the neuro-oncology treatments facilities and higher rates of abandonment in the LIMC are the basic reason behind survival gaps of the delayed presented patients.
Keywords: Pediatric supratentorial brain tumors, lag time, low/middle income countries (LMIC), Central nervous system (CNS) tumors and intraxial tumors.

INTRODUCTION

The most common and frequent tumors in the children's are central nervous system tumors (CNS). The tumors have varying epidemiology around the globe. The limited and insufficient data about these tumors epidemiology in in low/middle income countries (LMIC) is available. The supratentorial and infratentorial are the two types of central nervous system tumor. The unique group of cancers are observed in the pediatric and adolescent age groups. The highest mortality and morbidity are observed in the patients suffering from CNS tumors. The range of the neurological and physical morbidities are observed in the survivor's[1-2].

CNS tumors in children have different epidemiology than the tumor occur in adolescence and adulthood. These tumors are highly characterized by the age and site of origin. The wide range of different histopathological subtypes and topographical distribution require specific treatment regimens with variable outcomes and prognosis[1]. Different biological behavior of brain tumor are observed from the onset of symptoms till the patient presentation[3]. There is a highlighted difference in reported regional and global incidence of CNS tumors in the different countries around the globe. The CNS tumors shared 27% of the pediatric malignancies. It is highly known as the second most frequent neoplasm of childhood after leukemia. The annual incidence of CNS tumor are 5.26 per 100,000 population[2]. 30,000–40,000 new cases diagnosed per annum worldwide. According the cancer registry the prevalence of CNS tumors in 8% in Asia while 11% in the Africa. The literature have very scarce data about the incidence and prevalence patterns of CNS tumors in the LIMC countries[4-5].

The lack of cancer registries in the LMIC poses the oncologist with more difficult situation as such countries do not have the reported data on CNS tumors. There is a greater lag time from the symptomatic origin of the tumor to the medical attention because these tumors are less commonly associated with ventricular obstruction. The accurate diagnosis is the critical step in management of these tumors[6]. Visual deficits ranging from nystagmus to visual field defects and blindness, macrocephaly in infants are common for optic pathway tumors, and seizures and motor deficits for supratentorial tumors. Several factors contribute to delayed diagnosis in countries with limited resources. The factors that contribute to delayed diagnosis are the place of residence of patient from medical centers, lack of radiological facilities and financial barriers. The lack of the specialized treatment centers for brain tumors and unavailability of trained health professionals especially pediatric neurosurgeons. In the Higher income countries HIC the steady improvements for treatment of the children with central nervous system (CNS) tumors have been made in the past decades[7-8].

It was found that the delayed in accurate and timely diagnosis of pediatric supratentorial brain tumors is prevalent and the trend has not changed over the period of time. The complex interplay of underdiagnoses, unavailability of the neuro-oncology treatments facilities and higher rates of abandonment in the LIMC are the basic reason behind survival gaps of the delayed presented patients. The resources and facilities are limited in such countries. These result in increased lag time of these patients when they arrive tertiary hospitals for seeking treatment of pediatric brain tumors[9].

MATERIAL AND METHODS

This research was conducted at the radiology and oncology department of the children hospital ICH Lahore for one year. The IRB approved this study. The duration of the study was from March 2021 to March 2022. The sample size was calculated[10]. The confidence level was 95% while margin of error was 5%.

$$n = \frac{Z^2 p(1-p)}{e^2}$$

The non-probability and consecutive sampling technique were used. The patients of age range between 0 months to 17 years were included in this research. According to the inclusion criteria the patients presenting with supratentorial tumors both intra axial and extra axial including intraventricular tumors. These tumors will include all astrocytomas, oligodendrogliomas , DNET/DIA , pleomorphic xanthoastrocytoma , choroid plexus tumors, SEGA, ependyomas ,atypical teratoid rhabdoid tumors ,

pineal glad tumors , glioblastoma multiforme , primary neuroectodermal tumors,arachnoid cysts etc were selected for the study. According to the exclusion criteria the patients diagnosed with Infratentorial tumors were excluded.

The statistical analysis was performed by using SPSS version 24.0. The numerical variables mean and standard deviation were calculated. The categorical variables (such as MRI pattern of brain injury and gender) percentage, age and frequency was calculated. Data will be stratified to see the effect modulators and p value ≤ 0.05 of consider significant.

RESULTS

This study included 60 patients 30 girls and 30 boys, written consent was taken from the patients and they were fully aware of the study. The 7 years was the average age of the patients at time they were diagnosed with pediatric supratentorial brain tumor. Most of the patients belonged to urban areas where there were poor socioeconomic conditions prevalent.

As per our data the parents were not educated, and among all 60 patients there were more than half patients that had more than one siblings. Among 60 patients that contributed in this study there were some patients that were reported to have type I neurofibromatosis. Majority of the patients used to live away from the hospitals. They travelled a distance of 3 5 and 7 hours to reach the tertiary care hospital.

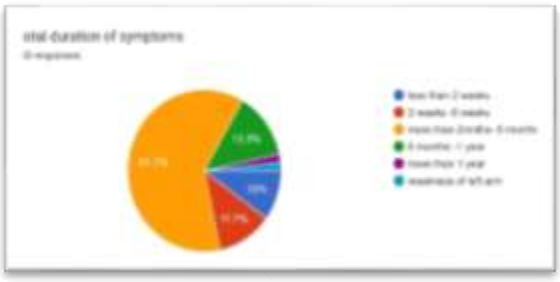

Fig 1: Lag time and total duration of symptoms

Table 1: the lag time after appearance of symptoms

Lag time	No of patients	Percentage
Less than 2 weeks	6	10%
2 weeks-6months	7	11%
More than 2 months- 6 months	36	61%
6 months-1 year	8	13%
More than 1 year	2	1.6%
Weakness of the left arm	1	1%

The 10% patients visited the hospital after 2 weeks of symptoms appearance while 60% visited the hospital after more than 2 months to 6 weeks.

Table 2: of doctors visited by patients before arriving tertiary care center

No. of doctors visited before approaching tertiary care center	No. of patients (%)
1 doctors	9 (15%)
2 doctors	43 (71.7%)
3 doctors	5 (8.3%)
4 doctors	1 (1.7%)

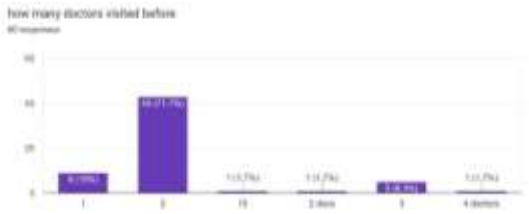

Fig 2: The bar graph showing the number of doctors visited

The table 1 showed that the 15% patients visited one doctor before attending the tertiary care hospital while 71% visited 2 doctors and 8% visited 3 doctors. The only 1% visited 4 doctors before attending the tertiary care hospital. The characteristics of the patients are described in table 3.

Some of the most common symptoms that the patients reported were vomiting, oculo-visual issues, motor problems, headache and endocrine dysfunction. All the patients had supratentorial brain tumors. There were some patients that underwent biopsies, and some patients were diagnosed simply after imaging.

Table 3: Characteristic features of patients

Features	No. of patients
Gender	
Male	30
Female	30
Age	
Less than 1 year	4
1-10years	15
10-17 years	11
Travel time to the hospital	
Less than 3 hours	16
5 hours	8
More than 6 hours	4
Urban	13
Rural	17
Parents level of education	
Low	30
High	8

The 16 patients travelled for 3 hours to reach the tertiary care hospital while 8 travelled for 5 hours. The level of education of the patient's parents was also low as majority of them belong to rural areas.

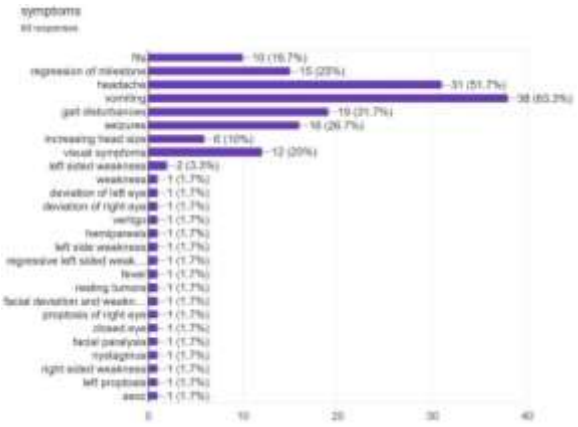

Fig 3: The reported symptoms and their percentage ratio

Table 4: symptoms reported by the patients

Signs	No. of patients	No. of times the signs and symptoms are reported
Neurological issues		
fits	9	16
Motor problems	10	7
Gait issues	19	8
Writing difficulty	5	5
Ataxia	1	3
Vertigo	5	6
General		
Headache	31	17
Vomiting	38	14
Abdominal pain	21	15
Endocrine		
Gain of weight	5	1
Early puberty	4	1
Acute dehydration	6	1

The fits were reported in the 16% patients, whilethe 25% reported the regression of milestone the headache was reported in 51% patients and vomiting in 63%. Other symptoms were gait disturbances 31%, seizures 26%, increasing head size 10% and visual symptoms in 20% patients.

DISCUSSION

One of the challenging aspects to treat brain tumors is that the diagnosis is delayed in majority of the cases. Although, now a day, computed tomography and magnetic resonance imaging has made it possible to diagnose supratentorial brain tumor at appropriate time[11]. As compared to PSIs of other tumors that occur in childhood, there is a prominent delay in the diagnosis of pediatric brain tumor over the decade. It was found that the average time of diagnosis was 2 months in case of most of the patients. However, it ranged from 1 week to 18 months in other cases as well. A study was carried out for 200 patients that had brain tumor diagnose time was an average of 2.5 months[12-13]. Another study showed that the average time of diagnosis was 60 days in cohort of 250 children that were diagnosed with brain tumor. It was found in a study that the longest PSIs were found in patients of age greater than 5 years and also it occurred in case of supratentorial brain tumors. The shortest PSIs were found to be present in case of medulloblastomas and in patients younger than 5 years. Excluding single child families, the length of PSIs was constant over the range of time in all demographic features that include sex, parental education levels, either the patients are living in urban areas or rural areas, and other socioeconomic status[14].

There is a lot of research going on, and there are a number of testing facilities available in developed countries now to get early diagnosis of the brain tumors, like MRI and other medical imaging scans but still long PSIs for children that are suffering from brain tumor are prominently found. There is a lot of study going on to find the reason behind the long lag stage of supratentorial brain tumor. The main reason why there is delay in the prognosis and treatment of this brain tumor is that there is lack of health facilities in the low middle income countries[15]. As per previous reports that worked to find the PSI length according to the histological type of the tumor, its localization and its grade showed similar sort of results. It was found that the long average PSIs are linked to supratentorial localization. The older age of the children also linked to PSIs. This duration is observed to be longer in patients suffering from convulsions as well[16-17].

As per another study, the average diagnosis time was approximately 5 months in case of low grade tumor and it was found to be 1 month in case of adverse form of tumor. The advanced form of medulloblastomas are majorly linked with shorter PSIs as compared to as compared to the localized form of medulloblastomas. The PSIs of the brain cancer in metastatic form is very much shorter, that suggest that the biology of the tumor is a significant factor that play role in determining the delayed prognosis and the probability of survival[18]. As per previous studies there was found marked differences in the clinical features that the patient showed that included general to specific signs. The common signs included the prominent appearance of vomiting, headache, then neurologic symptoms[19-20]. Longest PGIs are found in case of older children and in patients with supratentorial tumor and shorter PSIs are found in case of children with age shorter than 5 years. To deal with it, the physician should consider the chance of brain tumor if children are presented with non-specific signs and symptoms.

The variation and prominent occurrence of such symptoms like headache, vomiting plays an important role in delaying the early prognosis of the disease, as these are some of the signs that are commonly found in every disease. Although the issues like behavioral disorder, and certain school issues are not frequently found, such signs can also be the reason the delaying diagnosis is made. Some features like convulsions and other endocrine disturbances are also some of the distracting signs that cause delaying of the diagnosis[21]. As in the LMIC the majority of the people reside at a certain distance from tertiary care hospital and there is little advancement of medical facilities therefore the lag time and clinical spectrum of pediatric supratentorial brain tumors from the time of appearance of symptoms in a patient to the time the patient presents to the hospital is almost 6 months. And also the brain tumor of children spread quickly, therefore the time they reached the hospital the disease has progressed to the major extent and it is even more difficult to manage it at that time.[22-23].

CONCLUSION

The lag time and clinical spectrum of pediatric supratentorial brain tumors from the time of appearance of symptoms in a patient to the time the patient presents to the hospital was reported to be 2-6 months in majority almost 61% of the children. The 71% children visited the two regional area doctors before visiting the tertiary care hospital. The complex interplay of underdiagnoses, unavailability of the neuro-oncology treatments facilities and higher rates of abandonment in the LIMC are the basic reason behind survival gaps of the delayed presented patients.

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