DOI: https://dx.doi.org/10.4314/ejpch.v17i1.4

Ethiopian Journal of Pediatrics and Child Health, 2022, 17(1)
Open access articles distributed in terms of Creative Commons Attribution Licence [CC by 4.0]
ISSN 2413-2640 *eISSN* 2519-0334

ORIGINAL ARTICLE

A-5-YEAR ANALYSIS OF PEDIATRIC BRAIN TUMORS IN A TERTIARY CARE CENTER IN A SUB-SAHARAN AFRICAN COUNTRY

Chalew Alemayehu Balcha[1], Damte Shimelis Awoke[1*], Daniel Hailu Kefene[1]

[1]Addis Ababa University, College of Health Sciences, Department of Pediatrics and Child Health

*Corresponding author: Damte Shimelis, email: dshimelis2017@gmail.com

ABSTRACT

Background: *Tumors of the central nervous system (CNS) are the second most common group of cancers in childhood, exceeded by the leukemias. It is the most common pediatric solid tumor accounting for 20% of all childhood malignancies. The pattern and outcome of these tumors in children has not been studied in Ethiopia. This study aimed to assess the epidemiology and outcome of pediatric brain tumors in a tertiary care center in Addis Ababa, Ethiopia.*

Methods: *A retrospective review of medical records of children less than 15 years of age diagnosed with primary brain tumor in Tikur Anbessa Specialized Hospital Department of pediatrics from January 1, 2014 to January 1, 2019 was done. Treatment outcome was assessed clinically based on resolution of symptoms and absence of neurologic disability*

Results: *There were 86 children with the diagnosis of brain tumor in the study period and 49/86 (57%) were males and the male to female ratio was 1.5:1. The age at presentation ranges from 2.4 -14 years (mean 7.1 years). Headache was the commonest presentation among 65/86 (75.5%) children while early morning vomiting accounted for 57/86 (66.2%). Ataxia and gait abnormality contributed to 42/86 (48.8%). Among the 41 children whose pathologic result was available, the commonest tumor was medulloblastoma 13/41 (31.7%), followed by astrocytoma 8/41 (19.5 %) and craniopharyngioma 5/41 (12.1%). Six months and 5 years survival was 40% (35/86) and 2.3% (2/86) respectively.*

Conclusion: *Medulloblastoma and astrocytoma were common brain tumors in children, we had the longest PSI and as a result, very low survival which calls for early diagnosis and treatment.*

Keywords: brain tumor, children, survival, Sub-saharan Africa

Citation : Balcha C. A., Awoke D. S, Kefene D. H. A-5-year analysis of pediatric brain tumors in a tertiary care center, in a Sub-saharan African country. *Ethiop J Pediatr Child Health*. 2022;17 (1):31-42
Submission date: *18 July 2022* ***Accepted****: 26 July 2022* ***Published****: 11 September 2022*

INTRODUCTION

The brain tumor is the most common pediatric solid tumor accounting for 20% of all childhood malignancies, and affecting 35 per million children globally (1,2). Unlike leukemia, management of CNS tumors requires a good multidisciplinary team. Higher rate of treatment abandonment is documented in view of complexity of the treatment. Treatment is of long duration, involving neurosurgery, radiation, chemotherapy, and high cost of treatment (3-5).

CNS tumors are the leading cause of cancer related deaths in childhood and adolescents. Furthermore, they may cause short- and long-term consequences due to the disease itself or its treatment. The overall mortality among this group approaches 30% (6). The incidence of CNS tumors is highest in infants and children 5 years of age or younger (6,7). However, only scarce data is available about pediatric brain tumors in low/ mid income countries (LMIC) (3).

For all histologic types, pediatric and young adult populations have a better survival than do older adults. As an example, for all primary malignant brain tumors combined, the five-year survival rate among children under age 14 is 62 percent, compared to 5 percent in adults 65 years of age and older (8).

Only a few risk factors have been proven: predisposing genetic syndromes (such as neurofibromatosis, tuberous sclerosis), ionizing radiation (therapeutic or accidental exposure), parental age, birth defects, particularly for nervous system anomalies. Strong protective dose-response relations observed for maternal consumption of fruit, vegetables, vitamin C, nitrate, and folate (2,9,10)

The aim of this study is to identify the magnitude and outcome of children with brain tumor in a tertiary care center.

Patients and Methods

Study area

The study was conducted in Tikur Anbessa Specialized Hospital Department of Pediatrics and Child Health, Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia which is located at an altitude of 2355 meters above sea level, the hospital started giving service in 1952. It has many departments among which pediatrics and child health is the one that is launched in 1964. Pediatrics neurosurgical and the oncologic unit has been functional for the last 5 years. It is the only tertiary hospital in the country where ppediatric brain tumors are being treated with proper neurosurgical intervention, chemotherapy as well as radiotherapy. Patients are usually referred from different centers across the country.

Study design

A retrospective review of medical records of children below 15 years of age with the diagnosis of primary brain tumor from January 1, 2014 to January 1, 2019 was done.

Data were collected regarding age, sex, location of the tumor, clinical features, imaging modality, histologic features, treatment modality, and outcome of treatment was

analyzed. Treatment outcome was assessed clinically based on the resolution of symptoms and absence of neurologic disability. We adopted the WHO (world health organization) classification of brain tumors (9). Data were analyzed using SPSS version 21 and the findings were analyzed and compared with available literature.

Ethical clearance

This study was cleared ethically by the Department of Pediatrics and Child Health Research and Publication Committee.

Definition of terms

Primary brain tumors are defined as tumors of the brain parenchyma, cranial nerves, meninges, and the pituitary gland and immediate surrounding structures.

Operational definitions

- Infratentorial: below the tentorium cerebelli: including fourth ventricle, brain stem, cerebellum and spinal cord (NB. Spinal cord tumors are not included in the study).
- Supra-tentorial : above the tentorium cerebelli: including, 3rd ventricle, lateral ventricle and cerebral hemispheres.
- Diffuse: tumors having disseminated feature involving both supratentorial and infratentorial regions;
- Survival: was defined according to D.H Fiser (10).
- Disability was defined accordD.H.Fiser's recommendation of 'assessing the outcome of pediatric intensive care (10). According to the D.H.Fiser pediatrics cerebral performance category scale in children less than 16 years of age: scale 1 is normal at age-appropriate level of functioning, stage 2 is mild disability (may have minor developmental delay and mild neurologic deficit), scale 3 is moderate disability (child will have below aage-appropriate functioning, could attend special education because of cognitive difficulties), scale 4 is severe disability (child is conscious but unable to attend school and the child will be dependent on others), in scale 5 the child will be in coma at various degrees with no evidence of cortical function.

Results

Among the study participants 52/86 (60.5%) were males with male to female ratio of 1.5:1. Mean age at presentation was 7.1 years (ranging from 2 months to 14 years). The majority of the cases 43/86 (50%) were between 5-9 years and 6/86 (6.9%) below one year. Family income was less than 1000 birr (equivalent to $23.14) per month in 26/86 (30.2%) and 30/86 (34.9%) were from Oromia region (central and eastern part of Ethiopia). Demographic characteristics of these children is shown in table 1.

Table 1: Demographic characteristics of children with primary brain tumor attending a tertiary care center, Addis Ababa, Ethiopia.

Variable	Number	Percent (%)
Age (years)		
< 1	6	6.9
1-4	15	17.4
5-9	43	50
10-14	22	25.5
Gender		
Male	52	60.4
Female	34	39.6
Family income (Birr/month)		
< 1000	26	30.2
1000-4999	31	36.0
5000-10,000	6	6.9
>10,0009	7	8.1
Unknown	16	18.6
Address (region)		
Oromia	30	34.9
Amhara	19	22.4
Addis Ababa	20	23.3
Others	17	19.8

Headache was the commonest presenting symptoms in 65/86 (75.5%) of all children who could express themselves. While early morning vomiting accounted for 57/86 (66.2%) of the patients. Ataxia and gait abnormality was present in 42/86 (48.8%) of children who could ambulate. Clinical presentation of children is shown in table 2.

Table 2: presenting symptoms of patients with primary brain tumor who were on follow up in a tertiary care center , Addis Ababa, Ethiopia.

Presenting symptoms	Frequency	Percent
Headache	65	75.5
Early morning vomiting	57	66.2
Weight loss	52	60.0
Ataxia and gait abnormality	42	48.8
Impaired vision	42	48.8
Motor deficit	39	45.3
Seizure	36	41.8
Increased head size	30	34.8
Change in behavior	28	32.5
Growth impairment	26	30.8
Cognitive impairment	22	25.5
Incontinence	16	19.2
Facial nerve palsy	13	15.1
Aphasia	12	13.9
Neck stiffness	10	12.3
Squinting	8	9.3
Cushing triad	1	1.1

Increased head size and seizure is highest in children less than 5 years of age 15/21 (71.4%) and 13/21 (61.9%) respectively then decreasing with increasing age. Motor weakness was high in age groups > 5 years.

The median pre-diagnostic symptomatic interval (PSI) was 90 days (range 1-2555 days) with parental delay of 60 days (range 2-730 days). The Health professional's delay was 49.5 days (range 1-1975 days). The median duration before intervention after reaching the treatment center was 19.5 days (range 1-150 days).

Out of the 71 children for whom the reasons for delay was known, the majority, 28/71 (39.4%) were delay in diagnosis and intervention (physician related), 20/71 (28.2%) were because of financial constraint and another 20/71 (28.2%) were because of religious reasons or traditional medicine.

Most of the children 50/86 (58.1%) had CT and the remaining had MRI but few had both. MRI result was taken as final imaging diagnosis when patients had both investigations. The most likely imaging diagnosis in all ages was astrocytoma 27/86 (31.4%) followed by medulloblastoma 23/86 (26.7%), . Ependymoma and craniopharyngioma each accounting for (12.7%) of the diagnosis. Table 3 shows the imaging diagnosis of brain tumors.

Table 3: imaging based diagnosis of brain tumors in children who were on follow-up in a tertiary care center in Addis Ababa, Ethiopia

Type of tumor	Number	Percent
Astrocytoma	27	31.4
Medulloblastoma	23	26.7
Craniopharyngioma	11	12.8
Ependymoma	11	12.8
Tuberculoma	4	4.7
Germ cell tumor	1	1.2
PNET*	4	4.7
Choroid plexus Carcinoma	2	2.3
Papilloma	3	3.5
Total	86	100

*PNET:primitive neuro-ectodermal tumor

Medulloblastoma was the imaging diagnosis in 6/21 (28.5%) children <5 years of age, but astrocytoma was the commonest in 34/65 (52.4%) of children 5 years and above.

Most of the tumors were shown to be su-pratentorial in all age groups 50/86 (58.1%)

Among the 41/86 (47.7%) children for whom biopsy was taken, the commonest tumor was found to be medulloblastoma 13/41(31.7%), followed by astrocytoma 8/41 (19.5%) and craniopharyngioma 5/41 (12.1%). Table 4 shows the histologic diagnosis of brain tumors.

Table 4: age based histologic diagnosis of brain tumors in children who were on follow up in care center, Addis Ababa, Ethiopia

Type of tumor	0-<1 year	1-4 years	5-9 years	10-14 years	Total
	N (%)	n (%)	n (%)	n (%)	
Medulloblastoma	0	2/8(25)	7/19(36.8)	4/14(28.6)	13
Astrocytoma	0	1/8(12.5)	6/19(31.6)	2/14(14.2)	9
Craniopharyngioma	0	1/8(12.5)	2/19(10.5)	2/14(14.3)	5
Ependymoma	0	1/8(12.5)	2/19(10.5)	0	3
Tuberculoma	0	0	0	2/14(14.3)	2
Papilloma	2/8(25)	0	0	0	2
Oligodendroglioma		0	1/19(5.3)	1/14(7.1)	2
Gliosarcoma		0	1/19(5.3)	0	1
Meningioma		1/8 (12.5)	0	0	1
Neuroepithelial tumor		0	0	1//14(7.1)	1
Dysmoplastic NE*		0	0	1/14/14(7.1)	1
Pituitary macroadenoma		0	0	1/14(71)	1
Total	2	6	19	14	41

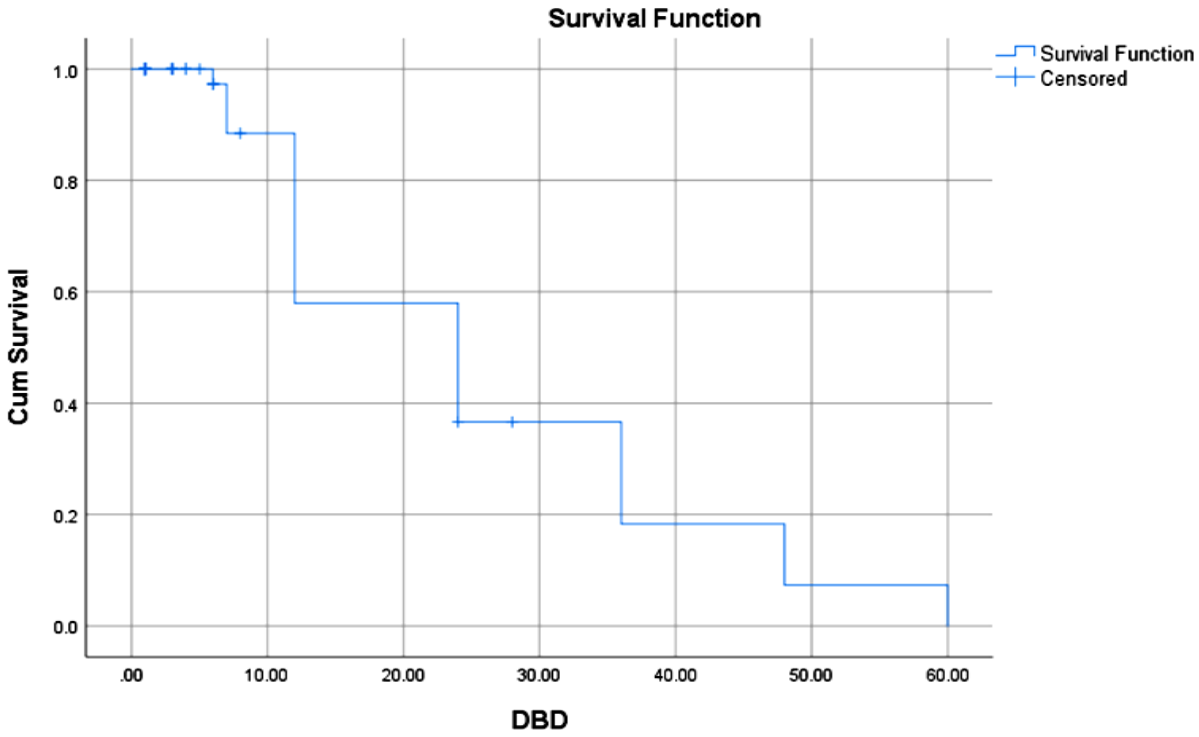
*NE: neuroepithelioma;

The WHO grading of the tumors was done for 26 of the histopathologic types of tumor, most 14/26 (53.8%) were grade I, followed by grade IV 9/26 (34.6%).

Among the most common three histologic types the highest mortality was observed in craniopharyngioma, medulloblastoma and astrocytoma, (2/5, 5/13, 1/8 respectively). When risk stratification was done using the modified Chang's Staging for medulloblastoma 5/13 were high risk and 8/13 were low risk.

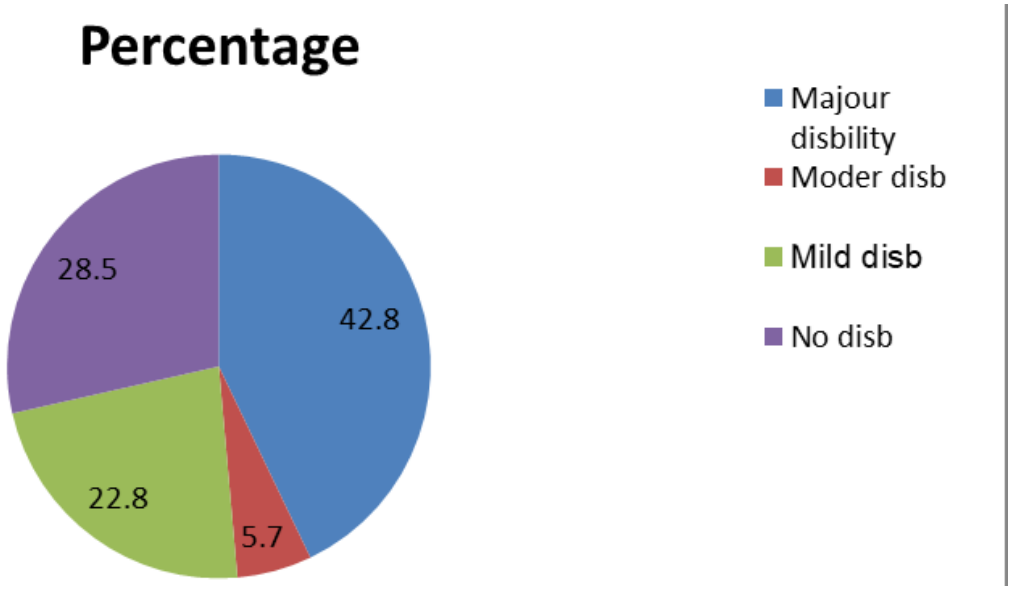
Different neurosurgical interventions was done in 64/86 (74.4%) of the patients. Surgery was the main stay of treatment. In 26/86 children, emergency external ventricular drainage (EVD) or endoscopic third ventriculostomy (ETV) was done to decrease intra cranial pressure. In 48/86 children, GTR or STR of the tumor with or without EVD or ETV was done. Out of 22/86 (25.6%) children for whom intervention was not done, 15/22 (68.2%) children died before intervention. Radiotherapy was given for 10/86 and chemotherapy was given for 27/86 children..

Overall, 6 months, 2 years and 5 years survival as 35/86 (40%), 20/86 (23.2%) and 2/86 (2.3%) respectively but 14/86 were lost to follow-up. The Kaplan -Meier survival curve is as shown in figure 1. Out of the survivors 10/35 sur,vived with no disability while 15/35 survived with major disability. Graph 2 shows the quality of life of survivors.



DBD- duration before death in months

Figure 1. Kaplan-Meier survival curve of children with brain tumor who were on follow up at a tertiary care center, Addis Ababa, Ethiopia



Graph 2: the quality of life of children with brain tumor who attended the follow-up clinic of a tertiary hospital, Addis Ababa, Ethiopia

Discussion

In our study the mean age at presentation was 7.1 ± 3.7 years and this is comparable with the Egyptian study which was 7.1 ± 4.2 years (3), but slightly lower than a Nigerian study which was 9.8 ± 1.5 years (15) and a Moroccan study which was 9.3 years but they included adolescents up to the age of 19 years (4), A study done in Tehran which included children less than 15 years showed a mean age of 6.1 ± 3.65 years was slightly lower but comparable with our study (16).

In our study males were predominantly affected with a male to female ratio of 1.5:1 and this was consistent with many studies. A South Indian study showed a male to female ratio of 1.9:1 (17). Another study which was conducted in morocco showed male to female ratio of 1.2:1 and a similar study in Tehran showed male to female ratio of 1.9:1 (16).

In our study headache, early morning vomiting, visual disturbance, ataxic gait and motor deficit were the most common complaints in that order. This finding is comparable with a Nigerian, Canadian and South Indian studies (13, 15, 17).

The PSI in our study with a median of 90 days and a range of 1-2555 days was significantly higher when compared with other studies. An Israeli study of 300 children average total PSI was 7.7 days (±16.7 days), Denmark study showed median PSI duration of 7 days (range 0-365 days), Japanese study showed median duration of 20.5 days. But the PSI of a Nigerian study mean duration of PSI was 13.4 months which was worse than ours (8-12, 15). Among the causes of delay in our children were parental (religious issues and financial constraints), and delay in diagnosis and intervention. This is similar with the Nigerian study (15).

The imaging diagnosis for the overall children in our study, was medulloblastoma, astrocytoma, ependymoma and craniopharyngioma in that order. This was consistent with pathology result. This result was comparable with the north Indian and Moroccan studies (4, 20, 21).

The age based histologic diagnosis in our study showed medulloblastoma, papilloma, craniopharyngioma, astrocytoma and ependymoma were the commonest in this order in under 5 years of age. This was consistent with a Moroccan study (4).

The histologic diagnosis of the commonest brain tumor for age 5-9 years was medulloblastoma followed by astrocytoma, craniopharyngioma and ependymoma in this order. But, comparatively the imaging diagnosis in this age group rather shows astrocytoma followed by medulloblastoma and Craniopharyngioma. The difference in the two results could be most of the children with the imaging diagnosis of astrocytoma were not operated and histologic diagnosis was not possible. The histologic result shows still medulloblastoma to be the commonest tumor in this age group among children with histologic results. The Egyptian and Moroccan studies showed astrocytoma to be common in this age group (3, 4).

The histologic diagnosis for those ≥10 years

of age showed still medulloblastoma to be the commonest followed by PNET but the imaging diagnosis was astrocytoma followed by medulloblastoma. This variation could be due to lack of surgical intervention for primary imaging diagnosis of astrocytoma tumors in our study.

The fact that most of the tumors were located in the supratentorial region followed by posterior fossa was comparable with the Indian study that showed the majority of the tumors were supratentorial followed by posterior fossa (17).

The main modality of treatment in our children was surgery followed by chemotherapy and radiotherapy. The proportion of children who received radiotherapy was significantly lower when compared with South Indian study (17). Many factors were attributed to this low percentage in our set up; one of which was long waiting list for radiotherapy. Chemotherapy was given mainly for Medulloblastoma, 6/86 (7%). The proportion who got chemotherapy was also lower compared with the same South Indian study, where 50% of their children received chemotherapy (17).

Survival was 40.6% (35/86), death accounted for 41.8% (36/86) while 15/86 (17.4%) were lost from follow up. Among the survivors 19/86 (21.6%) had major disabilities but 10/35 (28.5%) survived without disability. This clinical outcome is very low compared with various studies including developing countries. In South India the death rate was 15.3% (17). The death rate in our study was comparable with Tehran (16) where 41.4% died, yet the five-year survival in that study was 36% which was significantly higher when compared with ours, where 5 years overall survival was 2.3%. This could be because of long PSI and delay in intervention.

The majory of our patients are from Oromia and Amhara regions this might be because of geographical proximity to the treatment center and also these are the largest tribes in the country.

Conclusion: medulloblastoma and astrocytoma were common brain tumors in children, we had the longest PSI and as a result very low survival that calls for early diagnosis and treatment

Limitations: Some of the medical records had incomplete information.

Acknowledgement

We would like to thank the Department of Pediatrics and Child Health for giving us approval to complete this study.

Contributions of authors

CA inception of idea, data collection, DS: data analysis and writeup, DA: review of the manuscript

Declarations

Funding: this project has no funding source

Conflict of interest: we declare no conflict of interest

Availability of data: Data is available on request

References

1. A Lacayo, P.M Farmer. Brain Tumors in Children: A Review. Ann Clin Lab Sci. 1991;21(1):26-35
2. Johnson K.J, Cullen J, Barnholtz-Sloan J.S, Ostrom Q.T, Langer C.E., Turner M.C. et.al., Childhood Brain Tumor Epidemiology: A Brain Tumor Epidemiology Consortium Review. Cancer Epidemiol Biomarkers Prev; 2014 Dec;23(12):2716-36..
3. Ezzat S, Kamal M, El-Khateeb N, El-Beltagy M, Awad M, Abouelenaga S. Pediatric brain tumors in a low/middle income country: Does it differ from that in the developed world? *J Neurooncol* 2016 **126,** 371–76
4. Karkouri M, Zafad S, Khattab M, Benjaafar N, El Kacemi H, Sefiani S. et.al., Epidemiologic profile of pediatric brain tumors in Morocco, Childs Nerv Syst. 2010; 26(8): 1021–27
5. Derek R. Hanson, Mak P. Atlas. Central nervous system malignancy, Lanzkowsky's manual of pediatric hematology and oncology. ed. Philip Lanzkowsky, JeffreyM, Lipton, Sixth edition, Elsevier printing press, London, 2016, Page 454-62
6. Joann L. Ater, John F. Kuttesch Jr., Brain tumor in childhood, Nelson text Book of pediatrics, 20th edition, Kliegman et al eds, Elsevier, printing press, Philadelphia Copyright © 2016. Page 2453-55.
7. Merchant T.E., Pollack I.F., Loeffler J.S. Brain tumors across the age spectrum: biology, therapy, and late effects. Semin Radiat Oncol. 2010; 20(1): 58–66.
8. Shay V, Fattal-Valevski A, Beni-Adani L, Constantini S. Diagnostic delay of pediatric brain tumors in Israel: a retrospective risk factor analysis. Childs Nerv Syst 2012;28: 93-100
9. Louis D.N., Perry A, Reifenberger G., Von Deimling A., Figarella-Branger D., Cavenee W. K. et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016
10. D H Fiser. Assessing the outcome of pediatric intensive care. J Pediatr 1992; 121 (1):68-74
11. Armstrong GT. Long-term survivors of childhood central nervous system malignancies: the experience of the Childhood Cancer Survivor Study. Eur J Paediatr Neurol 2010; 14:298-303
12. Hayashi N, Kidokoro H, Miyajima Y. How do the clinical features of brain tumors in childhood progress before diagnosis? Brain Dev 2010; 32:636-41
13. Nicholson C L., Hilden J M., Cohen B.H., Brain tumor, American Academy of Pediatrics, et al ed. Thomas K. McInerny MD, FAAP, and Henry M. Adam MD, FAAP, Textbook of Pediatric Care, New York, 2009:1860-64
14. Subramanian S, Ahmad T. Childhood Brain Tumors. Stat Pearls [Internet]. Last Update: June 30, 2020.

15. Uche E.O, Shokunbi M. T, Malomo A.O, Akang E.E.U, Lagunju I, Amanor-Boadu S.D. Pediatric brain tumors in Nigeria: Clinical profile, management strategies, and outcome, *Child*s Nerv Sys 2013, Pub med.
16. Mehrvar A, Faranoush M, Abbas A Hedayati A, Tashvighi M, Fazeli M.A, et.al. Childhood central nervous system tumors at MAHAK's Pediatric Cancer Treatment and Research Center (MPCTRC), Tehran, Iran. Childs Nerv Sys 2014; 30 (3):491-6
17. Suresh S.G., Srinivasan A, , Scott J.X, Rao S.M, Chidambaram B, Chandrasekar S. Profile and Outcome of Pediatric Brain Tumors – Experience from a Tertiary Care Pediatric Oncology Unit in South India, J Pediatr Neurosci 2017; 12(3): 237–44.
18. Reulecke B.C, Erker C.G, Fiedler B.J, Niederstadt T.U, Kurlemann G. Brain Tumors in Children: Initial Symptoms and Their Influence on the Time Span Between Symptom Onset and Diagnosis. J Child Neurol. 2008 23(2):178-83
19. Klitbo DM, Nielsen R, Illum N.O, Wehner P.S, Carlsen N. Symptoms and time to diagnosis in children with brain tumours. Dan Med Bull 2011;58 (7): A4285.
20. Goldman R.D., Cheng S.D, Cochrane D. Improving diagnosis of pediatric central nervous system tumours: aiming for early detection. CMAJ 2016; 1-6
21. Shirazi N. Gupta M., Bhat N.K, Kalra B.P, Profile of Primary Pediatric Brain and Spinal Cord Tumors from North India, Indian journal of medical and pediatric oncology, 2017;38 (1):10-14.