

**DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD  
BRAIN TUMORS AT KENYATTA NATIONAL HOSPITAL**

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**BY**

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## **DECLARATIONS**

### **Student's declaration**

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## **DEDICATION**

I would like to dedicate this work to my parents who have always supported my endeavours.

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## **LIST OF ABBREVIATIONS**

CBT.....Childhood Brain Tumors

CT .....Computed Tomography

CTA.....Computed Tomography Angiography

KNH.....Kenyatta National Hospital

MRA .....Magnetic Resonance Angiography

MRI.....Magnetic Resonance Imaging

PSI.....Pre-diagnostic Symptomatic Interval

UON.....University of Nairobi

NFM.....Neurofibromatosis

PNET.....Primitive Neuroectodermal Tumor

DNET .....Dysembryoplastic Neuroepithelial Tumor

ATT.....Atypical Teratoid/Rhamdoid Tumor

## **OPERATIONAL DEFINITIONS**

**Childhood brain tumor:** primary intracranial neoplasms occurring between 0-12 years of age.

**Pre-symptomatic interval:** time period between symptom onset and diagnosis of disease.

**Clinical guidelines:** systematically developed statements which support health practitioners and patients in making decisions concerning the appropriate management of specific conditions with the aim of improving the quality of health care

**Delphi process:** a structured method used as a means of developing a consensus amongst individuals. The process involves a series of sequential questionnaires interspersed by controlled feedback that assesses the degree of agreement and resolves disagreement amongst a group of experts

## **ABSTRACT**

**Background**-Brain tumors are the second commonest tumors after leukemia and the commonest solid tumors in children. Childhood brain tumors (CBT) are the commonest cause of cancer related deaths in children and adolescents.

Delayed diagnosis is a common occurrence which is associated with increased morbidity and mortality.

The development of guidelines will help in the early diagnosis and management of childhood brain tumors in Kenya and Sub-Saharan Africa and provide better outcomes.

### **Objective**

To develop clinical guidelines for early diagnosis of childhood brain tumors at Kenyatta National Hospital.

### **Methodology**

First, a cross-sectional study on childhood brain tumors at KNH was done to review the pattern of presentation, PSI and establish reasons for late diagnosis.

Sample included all patients between 0-12 years presenting with childhood brain tumors in KNH during the study period of seven months who meet the inclusion criteria. An informed consent was taken from the caregiver and an assent for the patients between the age of 7-12 years.

A questionnaire was used to collect the required data through an interview (symptoms of CBT, PSI and reasons for late diagnosis) and physical examination of the patient (neurological signs of CBT). Medical records (file, imaging and laboratory results) were also reviewed and findings recorded (type and location of tumor).

Secondly, the Delphi survey. The results of the cross sectional study were used to formulate statements for the Delphi Questionnaire. The questionnaire was presented to Neurosurgeons and Paediatricians from UoN and KNH. The members ranked their agreement to each statement using the Likert scale.

The feedback was analysed and the rankings for each statement was collated. The statements that reached the level of consensus (equal to or more than 80% of the respondents' score of 7-9) were

accepted. The statements that reached consensus were outlined into the final guideline document. The statements that did not achieve consensus were eliminated.

### **Data management and results**

Questionnaires were coded and data entered into a password protected database. The data was analysed using the Statistical Package for Social Sciences (SPSS) by use of descriptive statistics (mean, median). Bar graphs, tables and pie charts were used for presentation of results

### **Results**

Sixty-one children with brain tumor between the ages of 0-12 years who met the inclusion criteria for the cross-sectional study. A total of 25 signs and symptoms were recorded. The most common signs and symptoms were; headache (75.4%), nausea/vomiting (70.5%), lethargy & school difficulties (39.3%) and focal motor weakness (32.8%). The PSI ranged from one week to 3 years with a median PSI of 3 months and a mean PSI of 7.7 +/- 9.6 months.

The predominant reason for delayed diagnosis was lack of health worker expertise (59%) followed by lack of awareness by the parent/guardian (8.2%)

Delphi results: 18 (72%) of the statements achieved consensus while 7 (28%) did not meet the consensus threshold and were eliminated. The 18 statements formed the final guideline

### **Conclusion**

The findings have outlined the varied presentation of CBT with headache as the most common (75.4%) at KNH.

The study has clearly demonstrated delayed diagnosis of brain tumors in children at KNH. (Median PSI of 3 months and a mean of 7.7 +/- 9.6 months.)

The main reason for the delayed diagnosis (prolonged PSI) was lack of expertise by the health worker (59%).

Therefore, the guideline will assist the health worker primarily by providing the varied presentation pattern of CBT as well as imaging recommendations for children with brain tumors.

## CHAPTER 1: INTRODUCTION

Childhood brain tumor (CBT) is used to describe all primary intracranial neoplasms occurring between 0 and 12 years of age. CBT comprise 15-20% of all brain tumors. Brain tumors are the 2<sup>nd</sup> most common tumors in children, after leukemia and are the most common solid tumors in children. Approximately 1500-2000 children develop brain tumor annually in the USA(1). The management of CBT remains a great challenge to clinicians(2). The overall survival rate of children with brain tumor is 60-70%.CBT are more likely to cause death compared to leukemia-45% versus 42%(3).

Despite advances in neuroimaging, the timely diagnosis of CBT remains difficult. This is due to the varied presentation and perceived rarity of CBT.CBT initially present like other common but less serious illnesses. This leads to delayed diagnosis which is associated with increased morbidity, increased cognitive impairment and psychological distress. Delayed diagnosis has also been associated with less trust in the health care system by the healthcare seekers(4). The recognition that certain combinations of symptoms and signs indicate a focal brain lesion is crucial to the diagnosis of many CBT.

The pre-diagnostic symptom interval (PSI) of an illness is defined as the time period between symptom onset and diagnosis. The mean symptom interval in children with Central nervous system (CNS) tumors reported in studies published over 15years' ranges from 1.8 to 9.8 months and a median of 1to3months(4-17). A prolonged symptom interval in CBT is associated with an increased risk of life-threatening and disabling neurological complications at presentation and a worse cognitive outcome in survivors(18).

Early diagnosis of CBT is a fundamental goal to allow for timely treatment when the disease is still at its early stages.

The causes of delayed diagnosis can be grouped into three categories that include; patient and or caregiver related factors, health professional related causes, and factors related to the health care system.

Increasing awareness of the variable and complex symptomatology that occurs with CBT could help tumor diagnosis and reduce the prolonged symptom interval. This can be achieved through

development of clinical guidelines for the identification and referral of children who have a brain tumor.

Kenyatta National Hospital is the largest hospital in Kenya with a bed capacity of approximately 2000 beds. KNH hosts the largest Neurosurgery unit in Kenya. The hospital receives patients from all parts of the country.

## CHAPTER 2: LITERATURE REVIEW

### 2.1 Epidemiology

CBT are the second most frequent malignancy in children (after leukemia) and the commonest cancer cause of death. 60% of survivors are left with significant disability(19).

The overall incidence rate of CBT(0-19years) is 3.2 per 100,000 person years, with males at 3.4 and females at 3.0 per 100000 person years(11).

The incidence for CBT is highest in 0-4 years-3.9/100000 and lowest in 15-19 years-2.1/100000(20).Brain tumors rank 13 out of 15 malignancies in the Nairobi Cancer Registry, with glioma the commonest followed by meningioma. In Kenya the higher male incidence is well recorded. Brain tumors constitute several distinct histopathological subtypes whose incidence varies with patient age and anatomical location.The pathological classification and grading of brain tumors has been standardised since 1979(21).This standardization allows national and international collaboration in epidemiological studies and clinical trials. There are six broad histological categories of CBT according to the World Health Organization (WHO) depending on the cell of origin; tumors of the neuroepithelial origin, meningeal tumors, germ cell tumors, tumors of the sellar region, peripheral nerve sheath tumors and primary lymphomas & hematopoietic tumors. The six categories are further sub-classified into about forty different tumor types. The WHO classification also grades the tumors into grade 1 through to 4 in order of increasing aggressiveness, grade 3 and 4 form the malignant types. The most recent WHO classification(21) lists ten central nervous system tumor types that commonly occur in children (table 1).Glioma is the most common CBT with an incidence of 1.16 per 100000 person-years(22).The most common histological type of glioma is astrocytoma (52%).Juvenile pilocytic astrocytoma is the most common astrocytoma with an incidence of 0.8 per 100000 person-years. Juvenile pilocytic astrocytoma and diffuse fibrillary astrocytoma constitute the majority of low grade gliomas; grade 1 and 2 while anaplastic astrocytoma and glioblastoma are the malignant astrocytoma; grade 3 and 4 constituting about 15% of PBT although tumor location is as important in determining morbidity and mortality as histopathological grade(23). Astrocytoma is equally split between the supra and infratentorial brain(24) and occur with an equal incidence throughout childhood.



The second most common subgroup are the embryonal tumours (medulloblastoma, primitive neuroectodermal tumor (PNET), atypical teratoid rhabdoid tumors (ATT) 21%). These are the most common high grade tumors. Approximately 70% of embryonal tumours are medulloblastoma(24). The highest incidence occurs at the age of 1-4 years and is slightly lower in infants and children aged 5-9 years. The incidence decreases to approximately 50% by age of 10-14. Ependymoma rank third in frequency(9%);two thirds are infratentorial(24). Ependymoma is twice as common in children aged 0-4 as it is in older children. The other histological types contribute 18% and include germ cell tumors, ganglioglioma, craniopharyngioma, choroid plexus tumors and dysembryoblastic neuroepithelial tumor(DNET)(25). Information on the incidence of brain tumors in adolescence is less available since their care is divided between paediatric and adult services. The total incidence is lower than for children but similar to that of age 10-14 years. Astrocytoma are again the most frequent histological subtype however embryonal tumors are relatively rare in this age group.

## **2.2 Histological grading**

Histological grading predicts the biological behaviour of a tumor and is a key factor clinically in determining the choice of treatment, especially use of adjuvant radiation and specific chemotherapy protocols (21). Grade I refers to lesions with low proliferative ability. Surgical resection alone has a possibility of cure for grade one lesions. Grade 2 neoplasms are generally infiltrative and therefore have a high tendency to recur despite low proliferative activity. Some type 2 tumors progress to higher grades for example, low-grade diffuse astrocytoma transform to anaplastic astrocytoma and glioblastoma. Grade 3 lesions are characterized by histological evidence of malignancy that include nuclear atypia and brisk mitotic activity. The treatment of most of grade 3 tumors require adjuvant radiation and/or chemotherapy. The WHO grade 4 consists of cytologically malignant, mitotically active, necrosis-prone neoplasms; which are typically associated with rapid disease progression and a fatal outcome. Some of the grade 4 tumors have a widespread infiltration of surrounding tissue and a tendency for craniospinal dissemination.

**Table 1: World Health Organisation classification and grading of CNS malignancies**

<b>TUMOUR FAMILY</b>	<b>TUMOUR</b>	<b>GRADE 1</b>	<b>GRADE 2</b>	<b>GRADE 3</b>	<b>GRADE 4</b>
Astrocytic tumours	Pilocytic astrocytoma	*			
	Pilomyxoid astrocytoma		*		
	Diffuse astrocytoma		*		
	Anaplastic astrocytoma			*	
	Glioblastoma				*
Oligodendroglial tumours	Oligodendroglioma		*		
	Anaplastic oligodendroglioma			*	
Oligoastrocytic tumours	Oligoastrocytoma		*		
	Anaplastic oligoastrocytoma			**	
Ependymal tumours	Myxopapillary ependymoma	*			
	Subependymoma	*			
	Ependymoma		*		
	Anaplastic ependymoma			*	
Choroid plexus tumours	Choroid plexus papilloma	*			
	Choroid plexus carcinoma			*	
Neuronal and mixed neuronal-glial tumours	Ganglioglioma	*			
	DNET	*			
	Central neurocytoma		*		

	Cerebellar liponeurocytoma		*		
	Rosette-forming glioneuronal tumour of the fourth ventricle	*			
Pineal tumours	Pineocytoma	*			
	Pineoblastoma				*
	Pineal parenchymal tumour of indeterminate differentiation		*	*	
Embryonal tumours	Medulloblastoma				*
	AT/RT				*
	CNS PNET				*
Meningeal tumours	Meningioma	*			
	Atypical meningioma		*		
	Anaplastic/malignant meningioma			*	
Tumours of the sellar region	Craniopharyngioma	*			

DNET= Dysembryoplastic neuroepithelial tumour

AT/RT= atypical teratoid/rhabdoid tumour

PNET= primitive neuroectodermal tumour

## 2.3 Clinical Presentation

The signs and symptoms of CBT usually arise from the disruption of the neuroanatomic pathways by the tumor. The presentation is very diverse; headache is the most common symptom occurring in approximately 30% of all pediatric patient newly diagnosed with brain tumors. However headache alone without other neurological findings does not have a positive predictive value in the diagnosis of a brain tumor(29).The presentation depends on the location of the tumor, age of the patient and histological type of tumor. Seventy percent of CBT arise from the posterior fossa between 1-12 years, but in infants less than 1 year tumors in the supratentorial region are more than in the infratentorial location. In the older children and adolescents (13-19 years)the occurrence of tumors in the supratentorial equals that of the infratentorial region. The common endocrine abnormalities are associated with tumors of the hypothalamus-pituitary axis and include precocious or delayed puberty, anorexia and excessive urination. New onset seizures occur in 40% of cortical based tumors. However, only about 4% of all new onset seizures are due to CBT(29).

*Supratentorial hemispheric tumors.* These are generally gliomas; more commonly low grade astrocytoma,ependymoma or mixed gliomas. They are usually diffuse with generalized and localized manifestations. The generalized symptoms include a diffuse headache and nausea. Headache is less common than in infratentorial tumors (3). The localized manifestations depend on the anatomical location of the tumor. These include seizures and focal neurological deficits. Occipital lobe tumors cause visual field defects, temporal lobe tumors manifest with sensory aphasia or partial complex seizures, parietal lobe tumors cause contralateral extremity sensory impairment and reading difficulties. Frontal lobe tumors cause personality changes and disruption of motor function.

*Supratentorial midline tumors.* These include craniopharyngioma, pineal region tumors and optic chiasm gliomas. The pineal region tumors manifests with upward gaze palsy, hydrocephalus and impaired accommodation (parinaud's phenomenon). Craniopharyngioma usually present with visual field defects, hydrocephalus and short stature. The optic chiasm gliomas cause visual field defects and hydrocephalus when large.

*Infratentorial tumors.* These include medulloblastoma, ependymoma and cerebellar or brainstem astrocytoma. A triad of headache, nausea/vomiting and gait imbalance is the most common manifestation of posterior fossa tumors; usually early morning vomiting. Ependymoma frequently present with early morning vomiting due to the involvement of the vomiting centre close to the fourth ventricle. Brainstem tumors manifest with facial and extraocular muscle palsies, ataxia and hemiparesis. Twenty-five percent of brainstem gliomas present with hydrocephalus(3). Cerebellar astrocytoma and fourth ventricle tumors present with signs and symptoms of hydrocephalus; progressive morning headache,vomiting, double vision, unsteady gait, papilledema. The symptoms and signs worsen over several months due to the slow growth of the tumor compared to medulloblastoma which grow rapidly.

*Children less than two years.* They usually present with nonspecific signs and symptoms which include irritability,vomiting,unsteadiness,lethargy,macrocephaly,ataxia,hypereflexia,and cranial nerve palsies. They tend to have large tumors at the time of diagnosis.

## **2.4 Imaging Studies**

Radiological imaging is useful as a tool for early detection of CBT, tumor staging (e.g. MRI spine), monitoring the results of tumor resection, assessing therapeutic results of adjuvant therapies as well as detection of post-operative complications. Computed tomography (CT scan) is useful as a screening tool. It provides the bony anatomy and calcified lesions more adequately than MRI scan. Magnetic resonance imaging (MRI scan) provides details on soft tissues and anatomical evaluation better than CT scan. RI scan is more specific and sensitive for tumor diagnosis and is used in children with suspicious CT scan findings or those with focal symptoms and signs highly suggestive of intracranial pathology. The international standard procedures entail MRI scan with plain and contrast enhanced T1-weighted(T1W),T2-weighted(T2W),FLAIR-fluid attenuated inverse recovery and DWI-diffusion weighted imaging(30). Sonography is utilized in infants with open fontanelles. Angiographic studies (CTA/MRA) are used to evaluate the involvement of major arteries and dural venous sinuses. Positron emission tomography (PET) and other functional modalities are utilized in the assessment of treatment outcome and the biological activity of the residual tumor, selection of biopsy site and delineation of the tumor margins from the normal brain.

## 2.5 Pre-diagnostic Symptom interval (PSI)

The Prediagnostic symptom interval (PSI) of an illness is defined as the time period between symptom onset and time of diagnosis. The time to diagnosis for brain tumors is one of the longest of all childhood cancers, with a median ranging from 2 to 5 months(31) , only 33% of CBT are diagnosed within one month after the onset of symptoms(10). A prolonged symptom interval in childhood brain tumors is associated with an increased risk of life-threatening and disabling neurological complications at presentation and a worse cognitive outcome in survivors(18). It also has a negative effect on health professional relationships with patients and their families(32).

A prolonged symptom interval is associated with a lower possibility of complete tumor resection with choroid plexus carcinoma, ependymoma, medulloblastoma and high grade gliomas but with longer survival with medulloblastoma and brainstem gliomas(33)(34)(35)(36)(37);a highly malignant with a longer symptom interval is likely to be less aggressive. The association between symptom interval and mortality is less clear and is related to tumor biology.

The mean and median symptom interval for cohorts and case series of children with central nervous system(CNS)tumors published over a duration of 15 years' ranges from 1.8 to 9.8 and 1 to 3 months respectively (4-17)[table3]. In comparison, the mean and median symptom interval for children with Wilms' tumor has been reported as 3.3 and 3.6 months respectively and for children with leukemia as 1.0 and 1.7 months(9).

In a study of 247 children with cancer(79 with a brain tumor,45 with Wilms' tumor and 123 with acute leukemia),84% of the children with Wilms' tumor and 80% of those with leukemia were diagnosed within a month of symptom onset in comparison to 38% of those with a brain tumor(38).

The prolonged SI in CBT is attributed to multiple factors. Childhood brain tumors are relatively rare and have a very varied presentation. The symptoms and signs are diverse, fluctuate in severity and differ according to location of the tumor and the development stage of the child(39). Most of the initial signs and symptoms of CBT are non-specific and resemble other more common and less serious diseases. The health professionals may be reluctant to consider a brain tumor diagnosis and therefore not order for the necessary imaging studies. Brain imaging of

young children usually requires sedation or general anaesthesia which may also contribute to diagnosis delay.

In a study by Thulesius et al (11) on diagnostic delay in pediatric malignancies, he found the median parent's delay in visiting a health facility from the onset of symptoms and signs, and median doctor's delay in making a diagnosis from the time the patient was seen at the health facility were 5 and 3 weeks respectively .

**Table 2: Published symptom intervals for childhood brain tumors.**

<b>Authors</b>	<b>Data collection period; publication year</b>	<b>Number of patients</b>	<b>Mean SI/Months</b>	<b>Median SI/months</b>	<b>SI range/months</b>
All ages					
Pollock et al(5)	1982-1988; 1991	380	2.2	1	NR
Perek et al(6)	1997-2000; 2005	172	4.9	1	0.2-120
Saha et al(7)	1982-1990; 1993	28	3.1	1.6	0.2-16.6
Klein-Geltink et al(8)	1995-2000; 2005	418	NR	1.7	NR
Haimi et al(9)	1993-2001; 2004	72	4.8	1.7	0.2-48
Dobrovoljac et al(10)	NR; 2002	252	NR	1.8	0-99
Thulesius et al(11)	1984-1995; 2000	22	4.6	2.1	0.2-45.9
Wilne et al(40)	1988-2001; 2006	175	9.8	2.5	0-120
Mehta et al(12)	1995-2000;	103	7.3	3	NR

	2002				
Edgeworth et al(13)	1990-1994; 1996	74	4.6	NR	<0.2-30
<b>Children aged less than 3 years</b>					
Young and Johnston(14)	1988-1999; 2004	16	NR	0.2	0-6
Wilne et al(40)	1988-2001; 2006	31	1.8	1	0.3-8
Trujillo-Maldonado et al(15)	1981-1989; 1991	16	2.5	1	0.5-9
Jovani Casano et al(16)	1985-1995; 1998	21	2.4	1	0-18
Sala et al(41)	1987-1997; 1999	39	5.2	NR	0.2-19
Rivera – Luna et al(17)	1975-2002; 2003	61	1.9	NR	0.1-8.9

Klitbo et al (42) reviewed 55 cases and found astrocytoma were the commonest (34%) followed by medulloblastoma (25%), ependymoma (16%), choroid plexus papilloma (4%), ATT (4.6%) and others (2%). Supratentorial tumors constituted 41% while infratentorial made up 59%. The median age at diagnosis was 8.4 years (2 months-17.4 years) and the male-to-female ratio was 1:1.2 (21 males and 25 females). The main reason for delayed diagnosis was due to the insidious onset of symptoms. The most common symptoms were headache, vomiting and ataxia. The total PSI median time for supratentorial tumors was 113 days (range 0-412) and 36 days (range 3-730) for infratentorial tumors. The estimated mean time for the diagnosis of a brain tumour in children was 20-28 weeks. Symptoms such as headache, unstable gait and seizures were associated with long PSIs. The median duration of PSI-1 was seven days (range 0-365); PSI-2, was nine days (range 0-730), and PSI-3, i.e. time from received referral letter to a confirmed diagnosis, was six days (range 0-231). The total PSI was 66 days (range 0-730).



Wilne et al (39) did a Systematic review and meta-analysis on presentation of childhood tumors. This systematic review and meta-analysis of symptoms and signs patterns of childhood CNS tumors that reviewed studies done between 1962-2003. Seventy-four papers describing 4,171 children were reviewed and 56 symptoms and signs identified.

The most common symptoms and signs were headache (33%), nausea and vomiting (32%), abnormalities of gait and coordination (27%), and papilloedema (13%).

In children below 4 years, the most frequent symptoms and signs were macrocephaly (41%), nausea and vomiting (30%), irritability (24%), and lethargy (21%).

In children with an intracranial tumor and neurofibromatosis the common manifestations were reduced visual acuity (41%), exophthalmia (16%), and optic atrophy (15%).

Posterior fossa tumors presented with nausea and vomiting (75%), headache (67%), abnormal gait and coordination (60%), and papilloedema (34%).

The most common features of supratentorial tumors were unspecified symptoms and signs of raised intracranial pressure (47%), seizures (38%), and papilloedema (21%).

Tumors located centrally presented with headache (49%), abnormal eye movements (21%), squint (21%), and nausea and vomiting (19%).

Symptoms and signs of brainstem tumors included abnormal gait and coordination (78%), cranial nerve palsies (52%), pyramidal signs (33%), headache (23%), and squint (19%).

Thirteen studies were included in the analysis of children with intracranial tumours aged under 4 years. The symptoms and signs at diagnosis were macrocephaly (41%), nausea and vomiting (30%), irritability (24%), lethargy (21%), abnormal gait and coordination difficulties (19%), weight loss (14%), clinically apparent hydrocephalus (bulging fontanelle, splayed sutures; 13%), seizures (10%), papilloedema (10%), headache (10%), unspecified focal neurological signs (10%), unspecified symptoms of raised intracranial pressure (9%), focal motor weakness (7%), head tilt (7%), altered level of consciousness (7%), squint (6%), abnormal eye movements (6%), developmental delay (5%), and hemiplegia (5%).

Eight studies were included in the analysis of children with neurofibromatosis and an intracranial tumour. The most common symptom and signs at diagnosis were visual (optic glioma). The symptoms and signs were reduced visual acuity (41%), exophthalmia (16%), optic atrophy (15%), squint (13%), headache (9%), unspecified symptoms of raised intracranial pressure (8%), precocious puberty (8%), abnormal gait or coordination difficulties (7%), voice abnormalities (6%), developmental delay (5%), papilloedema (5%), and reduced visual fields (5%)

Other features noted in the review were weight loss, growth failure, and precocious puberty. Symptoms of raised intracranial pressure were absent in more than half of children with brain tumors. In another study by Wilne et al(4), a review of 200 cases in the UK to determine the presentation of CBT was done. The cases were managed between 1988-2001. The commonest presenting symptoms were headache (56%), vomiting (51%), behavioural or education problems (44%), unsteadiness (40%) and visual difficulties at (38%). The neurological signs detected were cranial nerve deficits (49%), cerebellar signs (48%), papilloedema (38%), long tract signs (27%) reduced level of consciousness (12%) and (11%) had somatosensory signs. The median symptom interval was 2.5 months (range 1-120). High grade tumors and children below three years were associated with a short PSI.

A study done by Wanyoike(43) on children of age 2-16 years with infratentorial tumours at KNH seen between 1996-2003 reported 37 patients with a male to female ratio of 1:1.8. Fifty percent of the children were less than five years and 30% were three years and below, and 15% were ages 1-15 years. Astocytoma and medulloblastoma were the commonest at 37.9% each followed by ependymoma and tuberculoma at equal frequency of 10.3%. The least common was meningioma at 3.4% and out of 11 medulloblastoma; only one was male. Cerebellar symptoms were the most common mode of clinical presentation (30%) followed by headaches then vomiting. Twenty percent of the patients were blind at presentation. Neck stiffness was the least frequent followed by speech disturbance. The mean duration of symptoms was 3.7 months and the symptom median interval was 3.7 months. The reasons for late diagnosis included lack of knowledge and awareness by the parents/caregivers and inadequate diagnostic tools especially in the rural areas necessitating referral to KNH.

Opala et al(44) conducted a study on the time intervals from symptom onset to diagnosis and treatment in childhood cancer at KNH. The symptom interval in KNH was found to be comparable to other developing countries but longer compared to more developed countries. The median symptom interval was 14.9 weeks. The prolonged symptom interval was attributed to delayed presentation to health facility, age at presentation and gender; males had a longer interval than females.

## **2.6 Clinical Guidelines**

Clinical guidelines are systematically developed statements which support health practitioners and patients in making decisions concerning the appropriate management of specific conditions with the aim of improving the quality of health care(45).

Clinical guidelines are a crucial component of appropriate, efficient and cost effective health care that improve patient management when effectively developed and implemented. The major purposes for guidelines are (1) assisting clinical decision making by patients and practitioners; (2) educating individuals or groups (3) assessing and assuring the quality of care; (4) guiding allocation of resources for health care; and (5) reducing the risk of legal liability for negligent care(46).

Guidelines development should be based on high quality evidence. Systematic reviews and meta-analysis provide the best quality evidence(47). In a situation where high quality evidence is not available, it is necessary to use other sources of information, which may include cohort and case-control studies and case reports.

In the absence of any evidence it is appropriate to use expert opinion and formal consensus techniques, such as the Delphi process, as a means of collating and summarising professional expertise(48). Professional expertise is especially important for recommendations that are not based on a clinical question or treatment intervention such as, recommendations on symptom specificity, referral systems, imaging indications and acceptable waiting times. The attributes of a high quality guideline (49)are listed in table 4.

**Table 3: Attributes of high quality guidelines**

Validity	Correctly interpreting the evidence in order that, when followed, guidelines lead to improvements in health
Reproducible	Given the same evidence, another guideline group would produce similar recommendations
Reliable	Given the same clinical circumstances, another health professional would apply them similarly
Representative of key disciplines and interests	All key disciplines and interests (including patients) have contributed to the development of the guideline
Clinically applicable	The target population (those whose health the guideline aims to improve) is defined in accordance with scientific evidence
Clinically flexible	The guidelines identify where exceptions to the recommendations lie, and indicate how patient preferences are to be incorporated indecision making
Clarity	The guidelines use precise definitions, unambiguous language and a user-friendly format
Well documented	The guidelines ‘methodology records all participants, any assumptions and methods and clearly links recommendations to the available evidence
Scheduled for review	The guidelines state when, how and by whom they are to be reviewed.

CBT have a heterogeneous presentation dependent upon the tumor location, tumor biology and age of the child. This commonly leads to a prolonged symptom interval, which is associated with increased morbidity, increased cognitive impairment and significant psychological distress for the patient, their family and the healthcare professionals.

Rapid diagnosis relies on clinicians considering the diagnosis with many different, common presenting symptoms and signs, searching for corroborative evidence and recommending imaging where appropriate(10). This can be achieved through the use of clinical guidelines (50).

Guidelines have recently been established on management of brain tumors in Kenya for use by Health Care Professionals. There are no guidelines for early diagnosis of CBT in Kenya.

## **2.7 The Delphi Survey**

The Delphi process is a structured method used as a means of developing a consensus amongst individuals. The process involves a series of sequential questionnaires interspersed by controlled feedback that assesses the degree of agreement and resolves disagreement amongst a group of experts(51). It is a practical and validated method for guideline development(48). The process maximizes the effectiveness of consulting a large number of experts over a short period of time while minimizing the weaknesses(like vested interests) of more traditional collective decision making processes like committee meetings or steering groups(52).

## **CHAPTER 3: STUDY JUSTIFICATION**

Identification of the relatively few and serious cases of childhood brain tumors from the many self-limiting conditions and changes in developmental processes and behaviour is a major diagnostic challenge for both primary and secondary health care (14)(50). Most of the initial symptoms and signs of CBT also occur with other much more common and less serious childhood disorders such as gastroenteritis, migraine and behavioural problems.

The period of diagnostic uncertainty that often precedes the diagnosis of a CBT is very distressing to patients and their families, many parents and caregivers report that pressure on their part had been necessary to make the diagnosis as the severity of symptoms remain unnoticed by the health professionals. This parental and caregiver perception that the medical response has been inadequate, incompetent or delayed may be associated with legal dispute(32).

The development of clinical guidelines will provide improved guidance for health professionals on the assessment and investigation of children who present with symptoms and signs that could result from a brain tumor. The guidance aims to reduce the symptom interval experienced by children with brain tumors.

### **3.1 Objectives**

#### **Main objective**

The study developed guidelines to assist in early diagnosis of childhood brain tumors.

#### **Specific objectives**

1. The pattern of signs and symptoms of CBT was described.
2. The prediagnostic symptomatic interval of CBT was established.
3. The reasons for delayed diagnosis of CBT were described.
4. The specificity of symptoms and signs of CBT was ascertained.

## **CHAPTER 4: METHODOLOGY**

### **4.1 MATERIALS AND METHODS**

#### **Study design**

The design was a cross-sectional study.

#### **Study setting**

The study was conducted at the Kenyatta National Hospital at the following units which host patients with childhood brain tumors; Neurosurgical clinics, Neurosurgical ward 4c, Pediatric wards and Accident and emergency neurosurgical areas.

#### **Study population**

The study population comprised all patients between 0-12 years who presented with childhood brain tumors in KNH and met the inclusion criteria.

#### **Inclusion criteria**

1. Patients between the age 0-12 years with a brain tumor confirmed either radiologically with CT scan and or MRI of the brain and or histologically.
2. Patients who met criteria (1) above between the age 7-12 years who assented to participate in the study
3. Patients who met criteria (1) above and whose caregivers who gave an informed consent to participate in the study.

#### **Exclusion criteria**

Patients/caregivers who declined to give consent/assent or opted out during the study

Patients with brain tumor whose radiological and or histological diagnosis record were unavailable.

## **Sample size determination**

Selection method was non-randomized consecutive sampling until the desired sample size of 61 was achieved. CBT constitute 15-20% of all brain tumors. (11)

Fisher's formula:

$$n = \frac{Z^2 x P(1 - P)}{E^2}$$

Where,

$n$  = Desired sample size

$Z$  = value from standard normal distribution corresponding to desired confidence level ( $Z=1.96$  for 95% CI)

$P$  = prevalence/proportion (0.2) (11)

$E$  =margin of error (+/- 10%)

Minimum number of patients 61

## **Methods**

### **Cross sectional study method**

This was done to provide information on childhood brain tumor presentation, establish the PSI and to determine factors associated with a prolonged symptom interval.

The study period was 2016/2017 (duration of 7 months).

### **Data collection**

This was done by the principle investigator.

The caregivers of patients and those patients between the ages of 7-12 years who meet the inclusion criteria were taken through the purpose of the study.



The patients' caregivers were asked to make an informed choice to participate in the study by signing the consent form

Those patients between the ages of 7-12 years were asked to assent by signing the assent form.

A questionnaire was used to collect the required data through an interview and physical examination of the patient. Medical records were reviewed and information recorded in the questionnaire. The data collected included; General information; the patient's age and gender

Clinical data; the patient and or caregiver was interviewed about symptomatology, the duration of symptoms and signs of the illness before diagnosis and reasons for delayed diagnosis where applicable. A neurological examination was carried out to elicit signs of the illness. Radiological images, patients file and or histological results were reviewed and the type and location of the tumor recorded in the questionnaire. The completed questionnaires were submitted to the statistician for analysis.

### **Data analysis**

Questionnaires were coded and data entered into a password protected database. The data was analysed using the statistical package for social scientists (SPSS). Analysis was done using descriptive statistics (mean, median) and summarized using frequencies and percentages. Bar graphs, tables and pie charts were used for presentation of results.

### **Professional consensus method-Delphi survey**

This was done to provide professional expertise through professional consensus hence for final stage of guideline development. The expertise helped to determine the specificity of symptoms and signs associated with childhood brain tumors and to advise on appropriate indications for imaging.

The results of the cross sectional study were used to formulate a Delphi Questionnaire. The presentation pattern of CBT obtained informed a series of statements. The questionnaire was presented to Neurosurgeons and Paeditricians from UoN and KNH. The purpose of the study was explained by the principle investigator. Those who agreed to participate filled and returned the questionnaire. The members ranked their agreement to each statement using the Likert scale.

The feedback was analysed by the statistician. The rankings for each statement was collated. The statements that reached the level of consensus (equal to or more than 80% score of 7-9) were accepted. The statements that reached consensus were outlined into the final guideline document. The statements that did not achieve consensus were eliminated.

### **Study limitations**

The information provided during interview was dependent on the patient and caregivers perception of the illness.

### **Ethical consideration**

The Institutional Research Ethics Committee (IREC) of KNH/UON gave approval before commencement of the study.

The aim of the study was fully explained to the participants/parents/guardians before signing an informed written consent and assent forms (7-12 years).

Data obtained was protected using a password while the hard copy was stored in a secured locker. The data was accessible to the principle investigator and statistician.

## CHAPTER 5: RESEARCH FINDINGS

### 5.1 Introduction

The findings of the study are presented in this chapter. The broad objective of the study was to develop clinical guidelines for early diagnosis of childhood brain tumors at Kenyatta National Hospital. A total of 61 patients between 0 - 12 years presenting with childhood brain tumors in KNH between September 2016 and June 2017 and who met the inclusion criteria were selected for the study. An informed consent was taken from the caregiver as well as assent from the patients between the ages of 7-12 years.

### 5.2 Demographic Information

The demographic distribution of the patients is as shown by Table 4.

**Table 4: Demographic Information of the Patients**

	Frequency n (%)
<b>Age</b>	
≤2 years	7 (11.5)
>2 years	54 (88.5)
<b>Gender</b>	
Male	38 (62.3)
Female	23 (37.7)

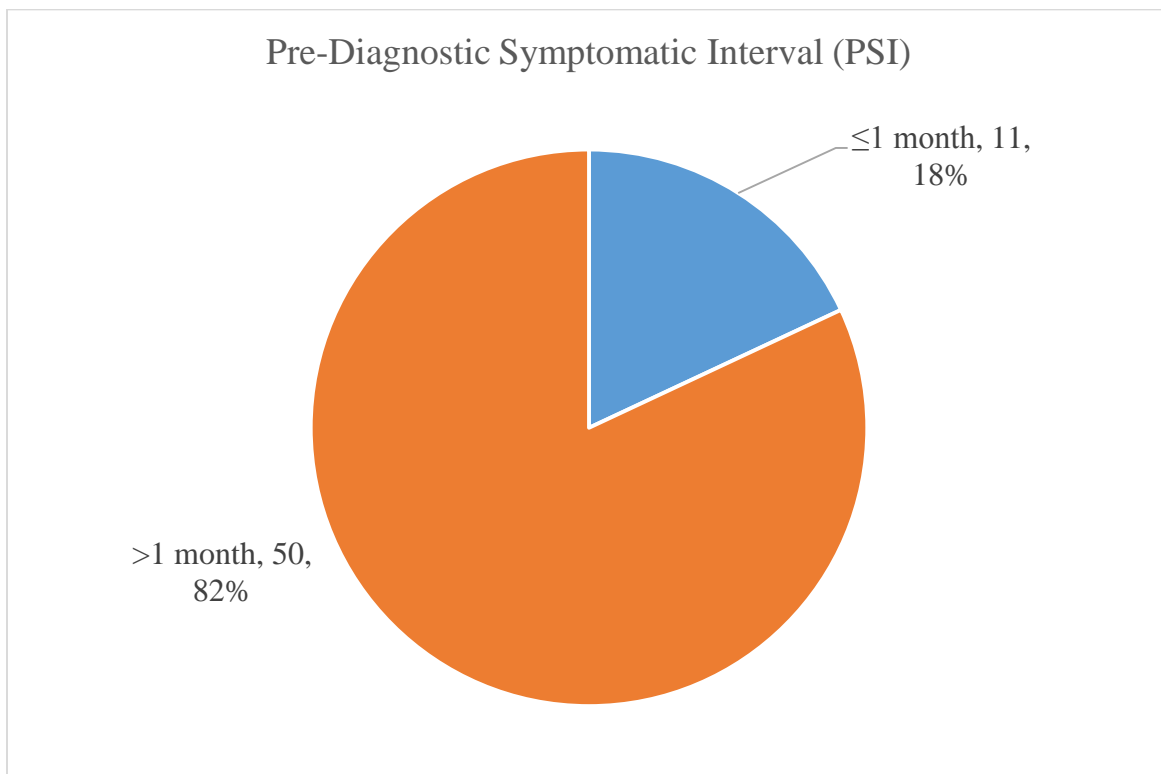
During the study period, a total of 61 patients presented with childhood brain tumors at the Kenyatta National Hospital, of which 38 (62.3%) were male while 23 (37.7%) were female, with a male to female ratio of 1.7:1. Patient ages ranged from as low as 1 month to 12 years with a median age of 8.2 years. The mean age was  $7.3 \pm 3.6$  years.

### 5.3 Clinical Data of the Patients

The clinical data of the patients is as shown by Table 5.

**Table 5: Clinical Data of the Patients**

	Frequency n (%)
<b>Pre-Diagnostic Symptomatic Interval (PSI)</b>	
≤1 month	11 (18.0)
>1 month	50 (82.0)
<b>Total</b>	<b>61 (100.0)</b>



**Figure 1: Pre-Diagnostic Symptomatic Interval**

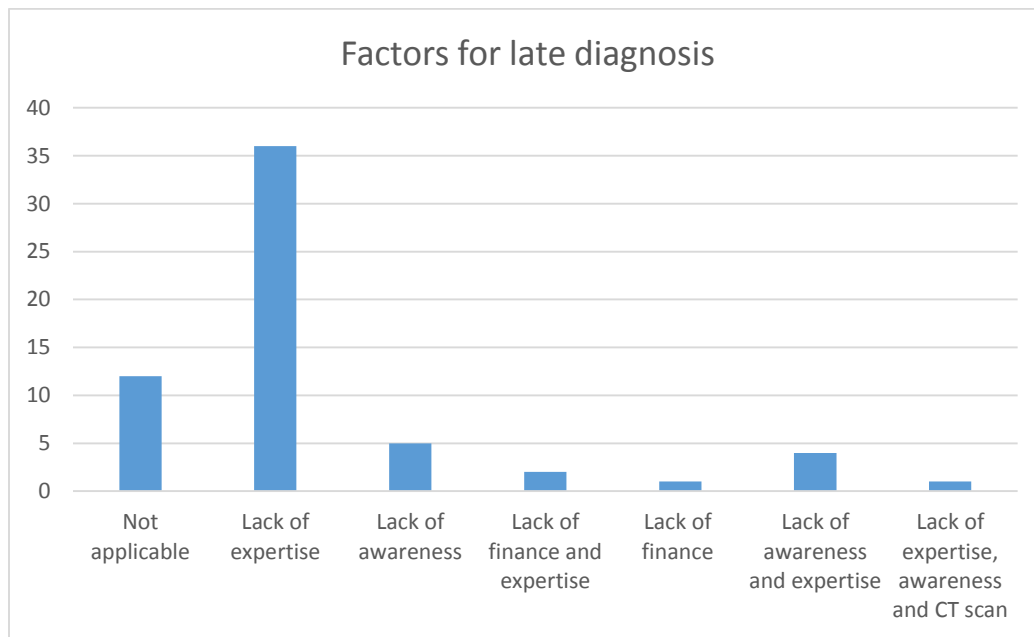
Pre-Diagnostic Symptomatic Interval (PSI) ranged from as low as 1 week to 3 years with a median PSI of 3 months. The mean PSI was  $7.7 \pm 9.6$  months. Eleven (18%) of the patients had a PSI of less than a month while 50(82%) had a PSI longer than one month.

**Table 6: Pre-Diagnostic Symptomatic Interval**

<b>Months</b>	<b>Frequency n (%)</b>
.2	2 (3.3)
.5	8 (13.1)
.7	1 (1.6)
1.0	9 (14.8)
1.5	1 (1.6)
2.0	9 (14.8)
3.0	5 (8.2)
4.0	3 (4.9)
5.0	1 (1.6)
6.0	1 (1.6)
7.0	1 (1.6)
8.0	2 (3.3)
11.0	1 (1.6)
12.0	4 (6.6)
16.0	1 (1.6)
18.0	2 (3.3)
19.0	1 (1.6)
24.0	6 (9.8)
28.0	1 (1.6)
36.0	2 (3.3)
<b>Total</b>	<b>61 (100.0)</b>

**Table 7: Factors for Late Diagnosis**

	<b>Frequency n (%)</b>
Not applicable	12 (19.7)
Lack of expertise(health Professional factor)	36 (59.0)
Lack of awareness(patient/Guardian factors)	5 (8.2)
Lack of finance and expertise	2 (3.3)
Lack of finance (patient/Guardian factors)	1 (1.6)
Lack of awareness and expertise	4 (6.6)
Lack of expertise, awareness and CT scan(health system factor)	1 (1.6)
<b>Total</b>	<b>61 (100.0)</b>

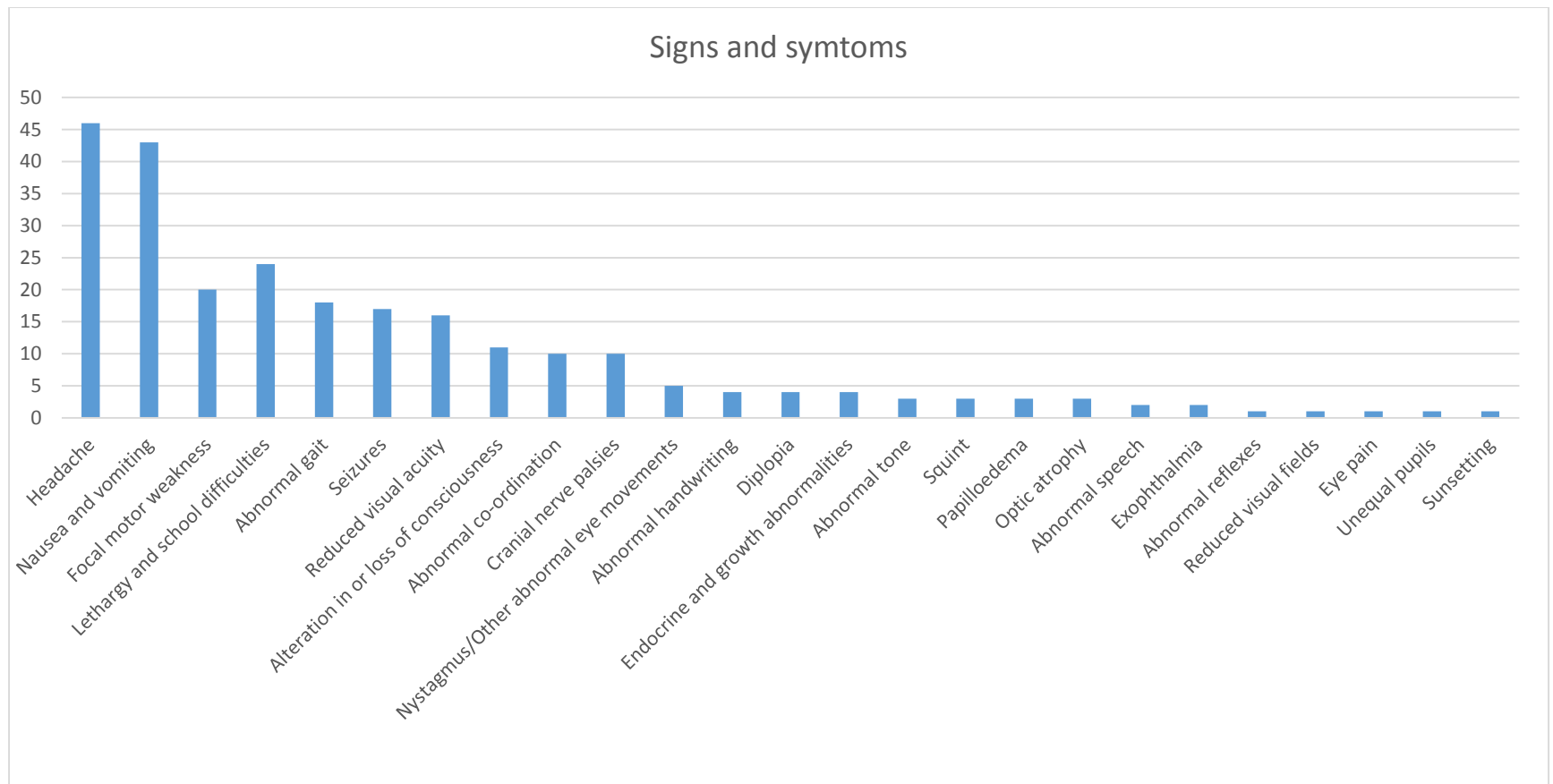


**Figure 2: Factors for late diagnosis**

On the factors for late diagnosis, the study found out that 36(59%) patients' late diagnosis was due to lack of expertise by the health worker, 12(19.7%) patients did not provide a reason since they felt the diagnosis was timely, 5 (8.2%) respondents lacked awareness on the illness, 4(6.6%) patients lacked awareness and professional expertise,2(3.3%)patients lack of finance and professional expertise. One (1.6%) patient lacked finance and another 1(1.6%) patient lacked awareness, professional expertise and availability of CT scan.

**Table 8: List of Signs and Symptoms**

<b>List of signs and symptoms</b>	<b>Frequency n (%)</b>
Headache	46 (75.4)
Nausea and vomiting	43 (70.5)
Focal motor weakness	20 (32.8)
Lethargy and school difficulties	24 (39.3)
Abnormal gait	18 (29.5)
Seizures	17 (27.9)
Reduced visual acuity	16 (26.2)
Alteration in or loss of consciousness	11 (18.0)
Abnormal co-ordination	10 (16.4)
Cranial nerve palsies	10 (16.4)
Nystagmus/Other abnormal eye movements	5 (8.2)
Abnormal handwriting	4 (6.6)
Diplopia	4 (6.6)
Endocrine and growth abnormalities	4 (6.6)
Abnormal tone	3 (4.9)
Squint	3 (4.9)
Papilloedema	3 (4.9)
Optic atrophy	3 (4.9)
Abnormal speech	2 (3.3)
Exophthalmia	2 (3.3)
Abnormal reflexes	1 (1.6)
Reduced visual fields	1 (1.6)
Eye pain	1 (1.6)
Unequal pupils	1 (1.6)
Sunsetting	1 (1.6)



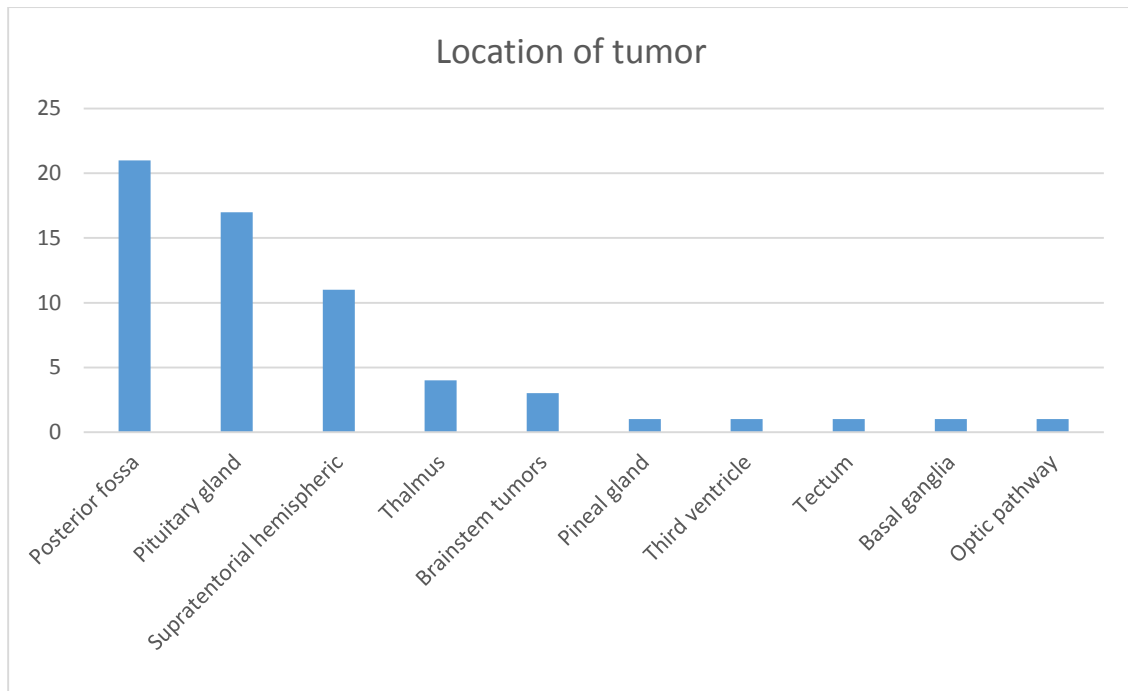
**Figure 3: Signs and symptoms**



The study identified 25 signs and symptoms. The top two signs and symptoms were headache from 46 (75.4%) patients, followed by nausea and vomiting 43 (70.5%) patients. The other prevalent signs and symptoms exhibited were lethargy and school difficulties from 24 (39.3%) patients, focal motor weakness from 20 (32.8%) patients, abnormal gait from 18 (29.5%) patients, seizures from 17 (27.9) of the patients and reduced visual acuity from 16 (26.2%) patients. Others signs and symptoms were alteration in or loss of consciousness 11(18%), abnormal co-ordination and cranial nerve palsies 10(16.4%) patients each, nystagmus 5(8.2%) patients, abnormal handwriting ,diplopia, endocrine and growth anomalies 4(6.6%) patients each, abnormal tone, squint, papilledema, and optic atrophy 3(4.9%) patients each, abnormal speech and exophthalmia 2(3.3%) patients each while abnormal reflexes, reduced visual fields, eye pain, unequal pupils and sunset eyes had 1(1.6%) patients each.

**Table 9: Location of Tumor**

<b>Location of tumor</b>	<b>Frequency n (%)</b>
Posterior fossa	21 (34.4)
Pituitary fossa	17 (27.9)
Supratentorial hemispheric	11 (18.0)
Thalamus	4 (6.6)
Brainstem tumors	3 (4.9)
Pineal gland	1 (1.6)
Third ventricle	1 (1.6)
Tectum	1 (1.6)
Basal ganglia	1 (1.6)
Optic pathway	1 (1.6)
<b>Total</b>	<b>61 (100.0)</b>

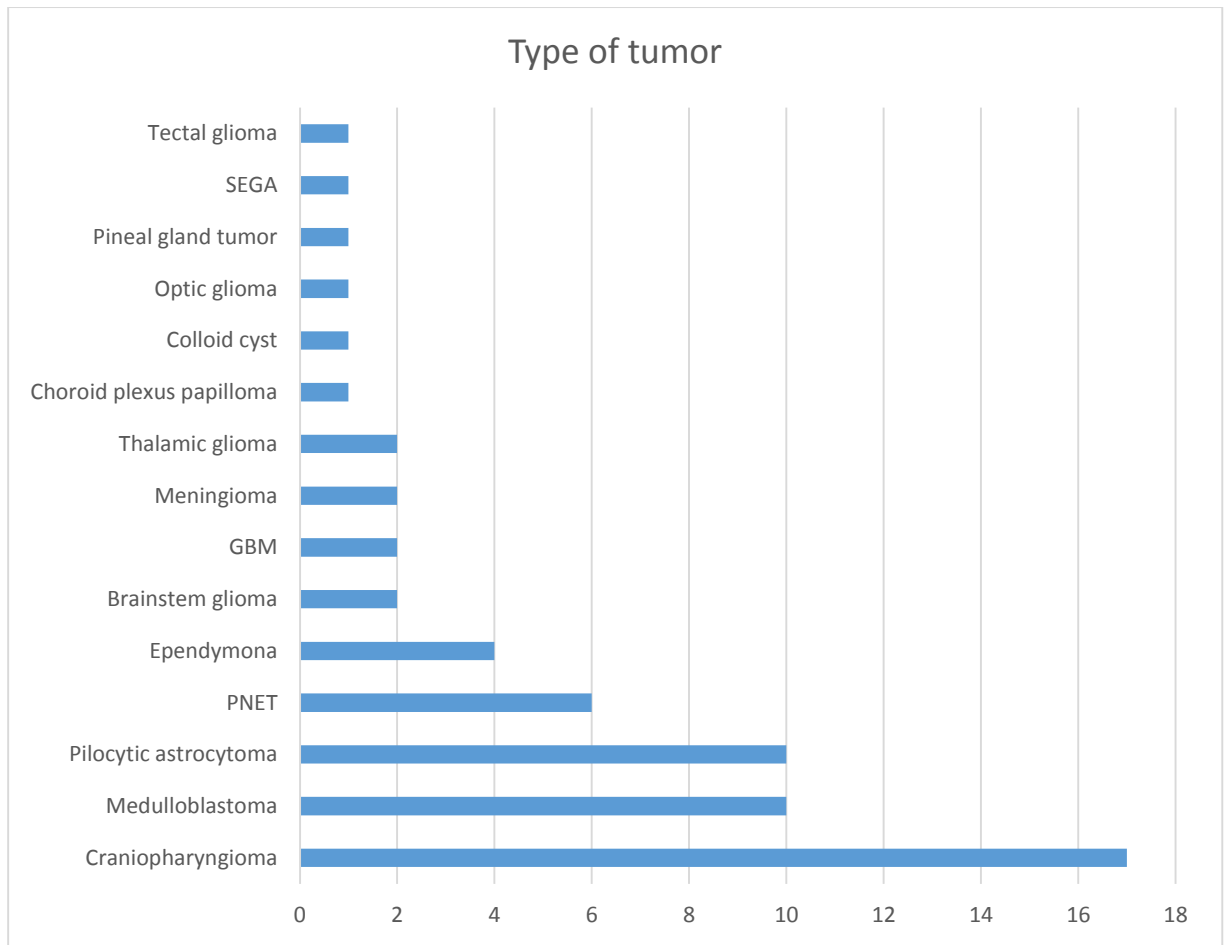


**Figure 4: Location of Tumor**

On the distribution of location of tumor, the study found that 21 (34.4%) of the tumors were of the posterior fossa, 17 (27.9%) were of the pituitary fossa, 11 (18.0%) were supratentorial hemispheric, 4 (6.6%) were of the thalamus, 3 (4.9%) were brainstem tumors while the pineal gland, third ventricle, tectum, basal ganglia and the optic pathway tumors were each 1 (1.6%).

**Table 10: Type of Tumor**

<b>Type of Tumor</b>	<b>Frequency n (%)</b>
Craniopharyngioma	17 (27.9)
Medulloblastoma	10 (16.4)
Pilocytic astrocytoma	10 (16.4)
PNET	6 (9.8)
Ependymoma	4 (6.6)
Brainstem glioma	2 (3.3)
GBM	2 (3.3)
Meningioma	2 (3.3)
Thalamic glioma	2 (3.3)
Choroid plexus papilloma	1 (1.6)
Colloid cyst	1 (1.6)
Optic glioma	1 (1.6)
Pineal gland tumor	1 (1.6)
SEGA	1 (1.6)
Tectal glioma	1 (1.6)
<b>Total</b>	<b>61 (100.0)</b>



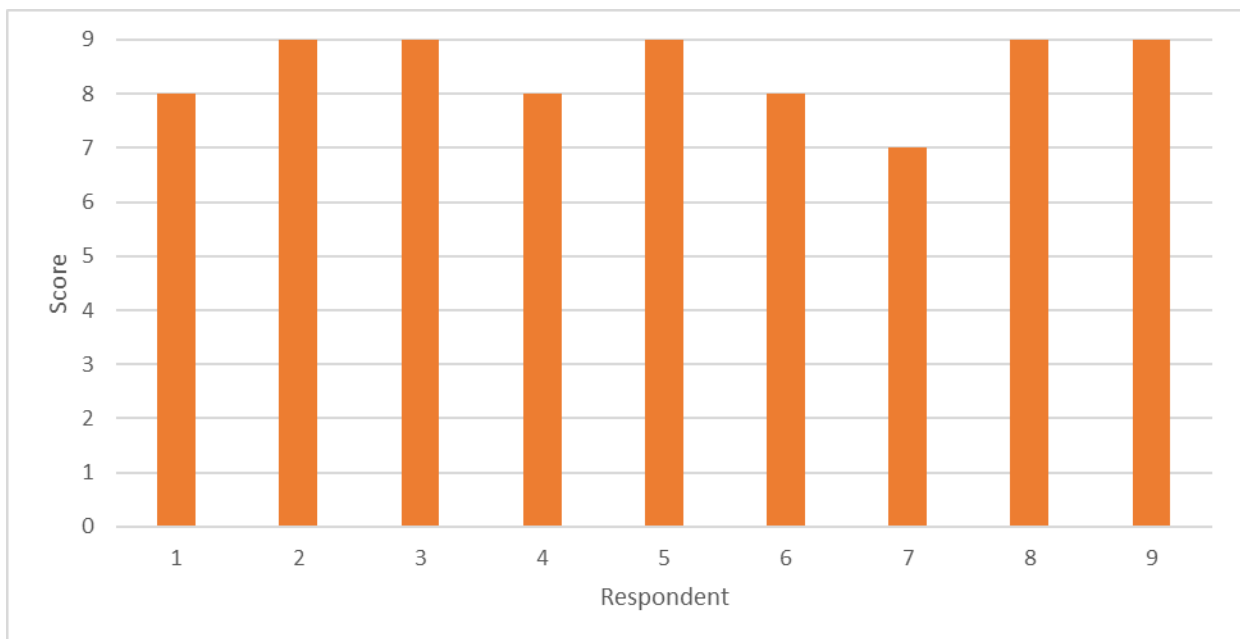
**Figure 5: Type of Tumor**

The type of tumor that was most prevalent was craniopharyngioma from 17 (27.9%) of the patients, this was followed by medulloblastoma and pilocytic astrocytoma which had 10 (16.4%) patients each, PNET from 6 (9.8%) patients, ependymoma from 4 (6.6%) patients. Brainstem glioma, GBM, meningioma and thalamic glioma each had 2 (3.3%) patients while choroid plexus papilloma, colloidcyst, opticglioma, pineal gland, SEGA and tectal glioma had 1 (1.6%) patient each.

## 5.4 Delphi Results

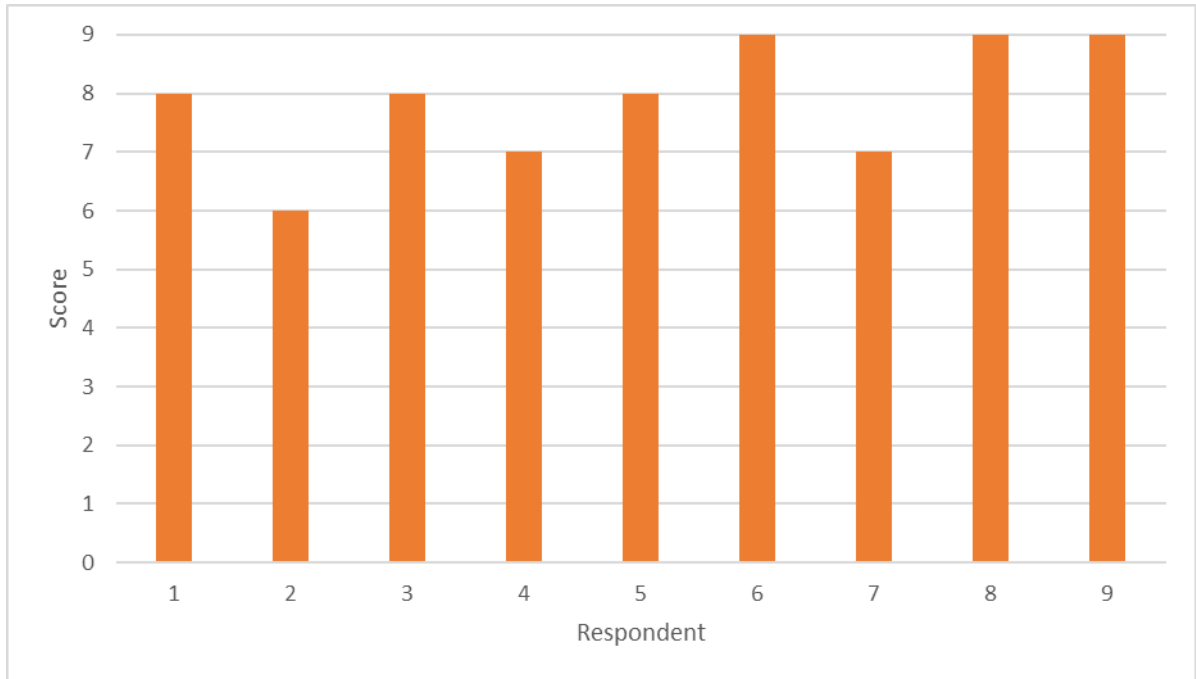
A total of 25 statements derived from the results of the cross-sectional part of the study were formulated into the Delphi questionnaire. The questionnaire was issued to 11 Consultants (Neurosurgeons and Pediatricians). Nine (81.8%) Consultants filled and returned the questionnaire. The level of agreement to the statements was rated using Likert's Scale with the least score as 0 and highest score of agreement at 10.

1. The initial symptoms of a brain tumor may resemble symptoms that occur with other more common and less serious childhood conditions. All the 9(100%) respondents scored between 7-9. Consensus was achieved.



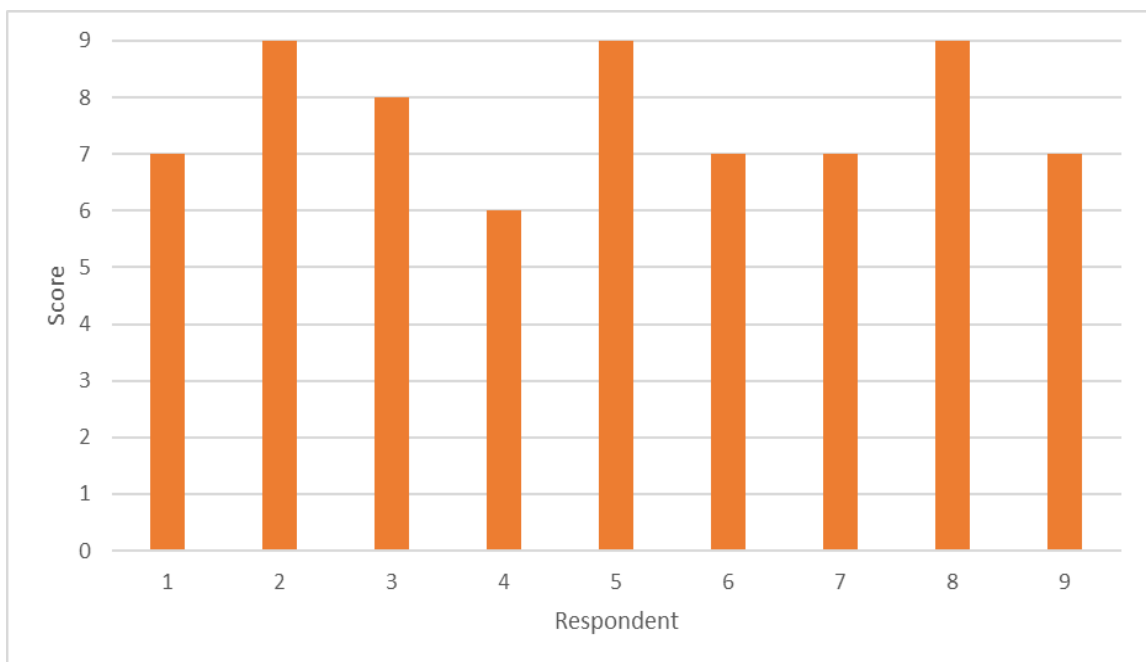
**Figure 6: Symptoms Resemblance**

2. Symptoms occurring with brain tumors may fluctuate in severity. Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.



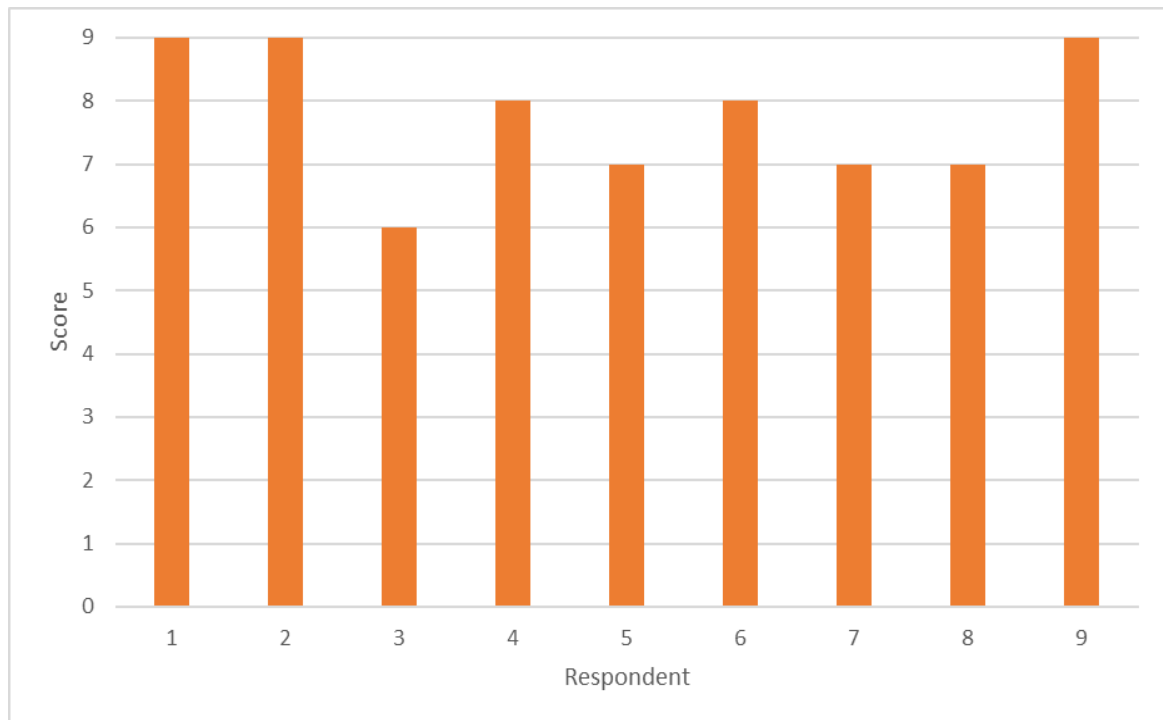
**Figure 7: Fluctuation of Symptoms**

- The absence of neurological abnormalities does not exclude a brain tumor. 8(88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.



**Figure 8: Absence of Neurological Abnormalities**

4. Children aged 3 years and under with a brain tumor may present differently from older children. 8(88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.

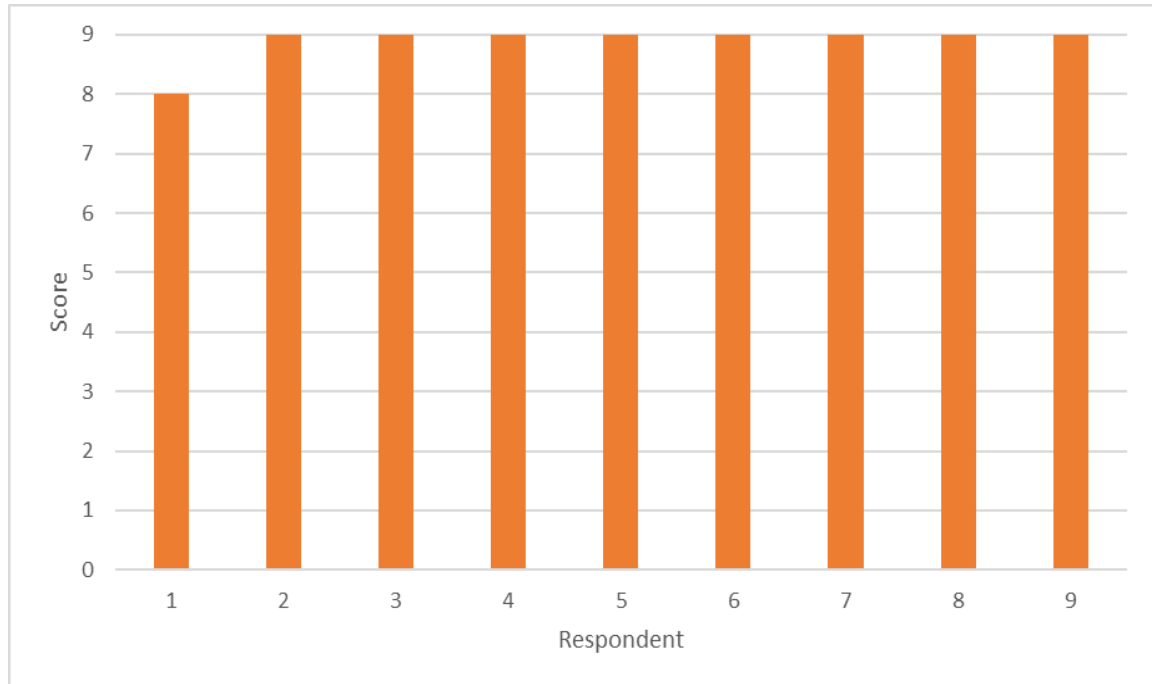


**Figure 9: Symptoms in different age groups**

5. A symptomatic child with a brain tumor will have one or more of the following symptoms and/or signs
- Headache
  - Nausea and vomiting
  - Focal motor abnormalities
  - Abnormal vision, eye movements and funduscopy findings
  - Altered consciousness
  - Abnormal gait and co-ordination
  - Seizures
  - Abnormal behavior including lethargy

- Abnormal growth

All the 9(100%) respondents scored between 7-9. Consensus was achieved.

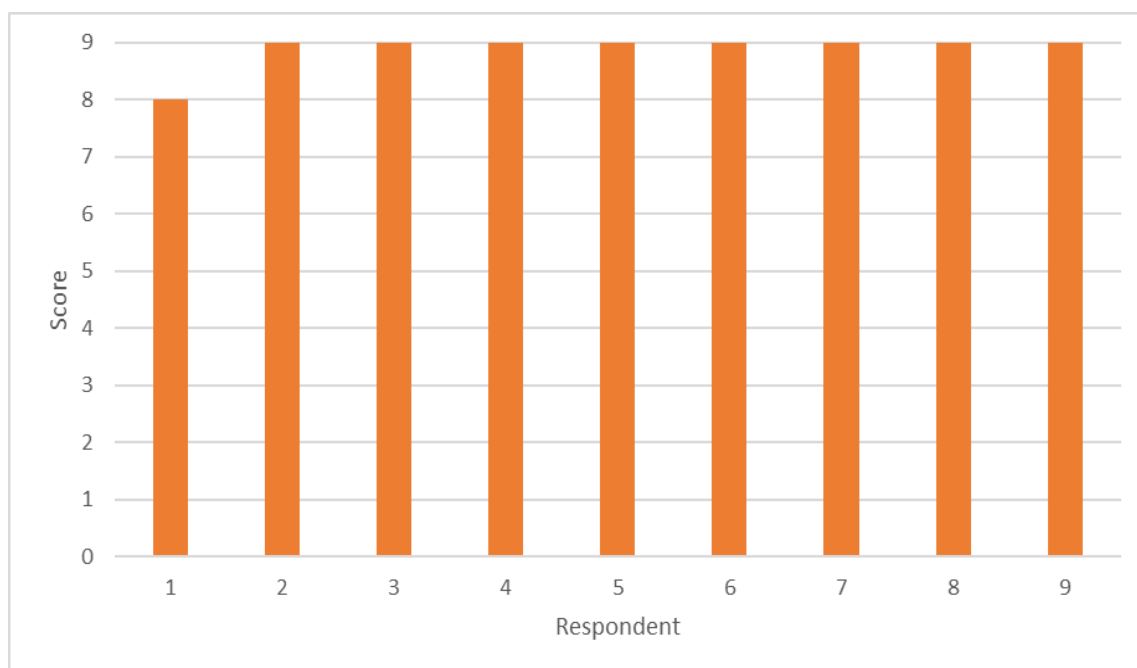


**Figure 10: Symptomatology of a brain tumor**

6. A child presenting with any of the symptoms and signs listed in 5 above requires the following
  - A detailed history including specific enquiry for associated symptoms
  - A complete neurological assessment
  - Assessment of height, weight & head circumference in a child aged < 2 year
  - Assessment of developmental stage in a child < 5 years

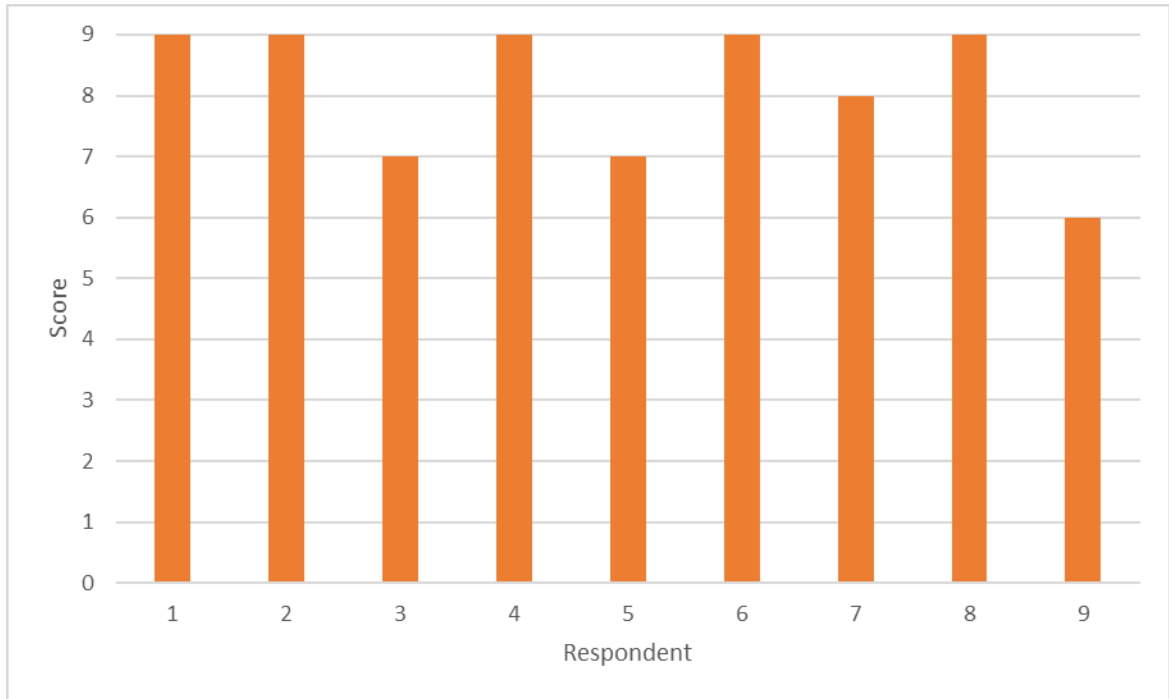
All the 9(100%) respondents scored between 7-9. Consensus was achieved.





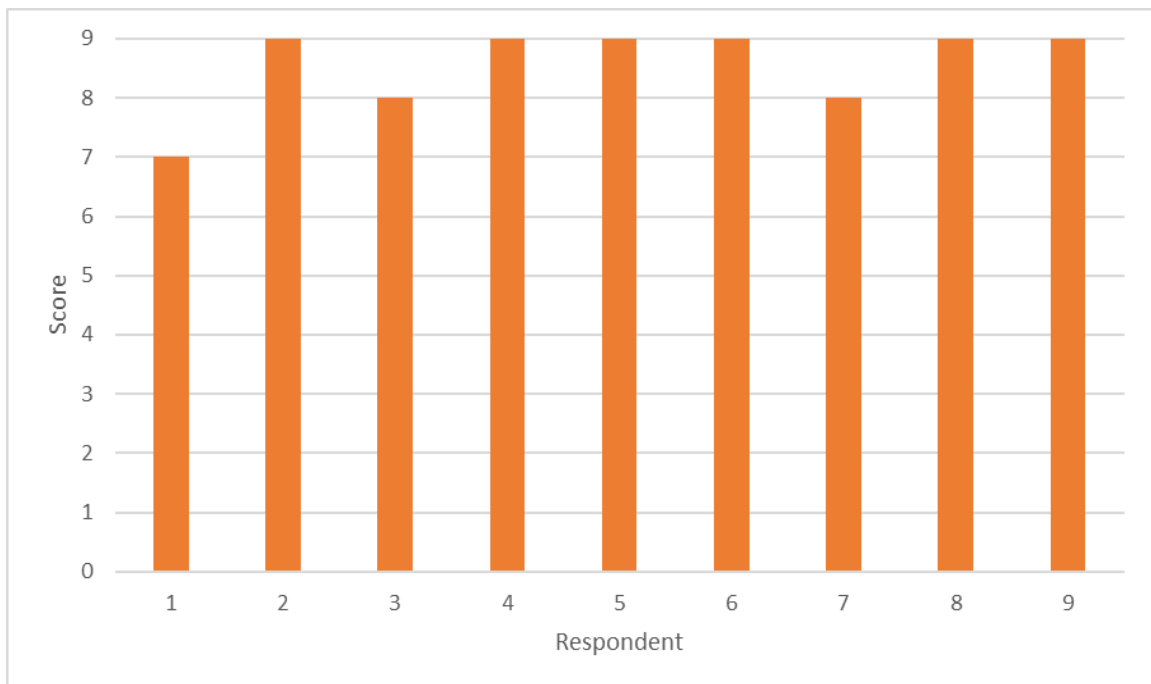
**Figure 11: History and assessment**

7. A continuous or recurrent headache lasting more than 4 weeks should be regarded as persistent. Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.



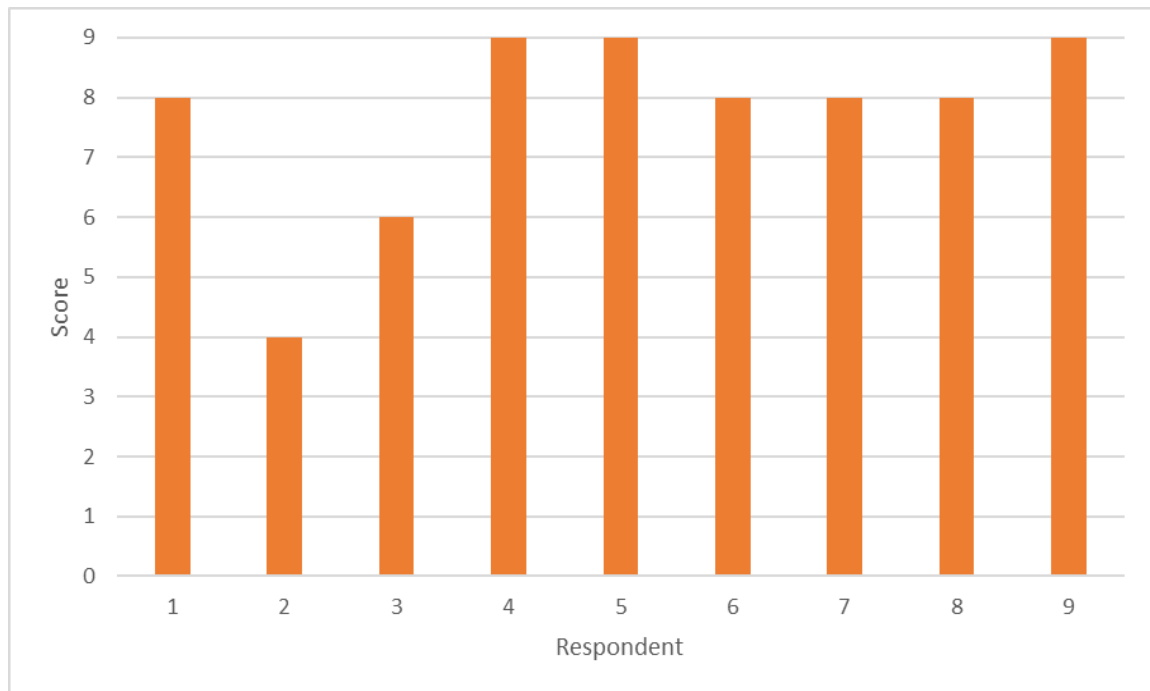
**Figure 12: Persistent headache**

8. Persistent headache requires Brain imaging. All the 9(100%) respondents scored between 7-9. Consensus was achieved.



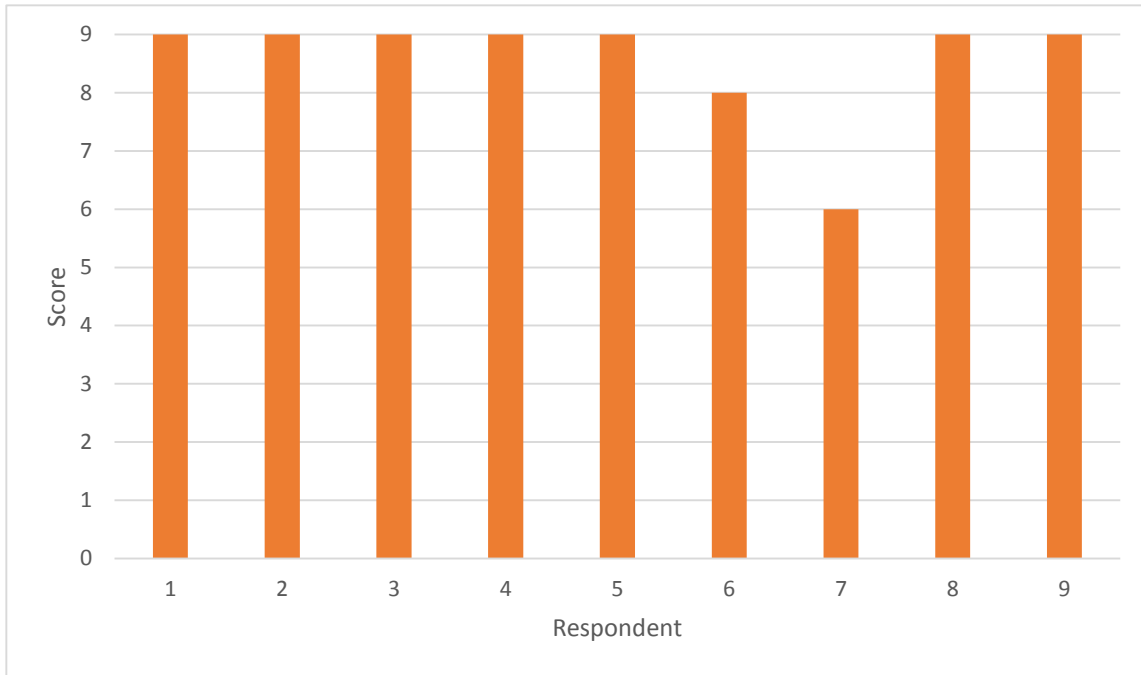
**Figure 13: Brain imaging in persistent headache**

9. A young child who is unable to complain of headache may demonstrate head pain by holding their head, lethargy or withdrawal. Seven (77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was not achieved.



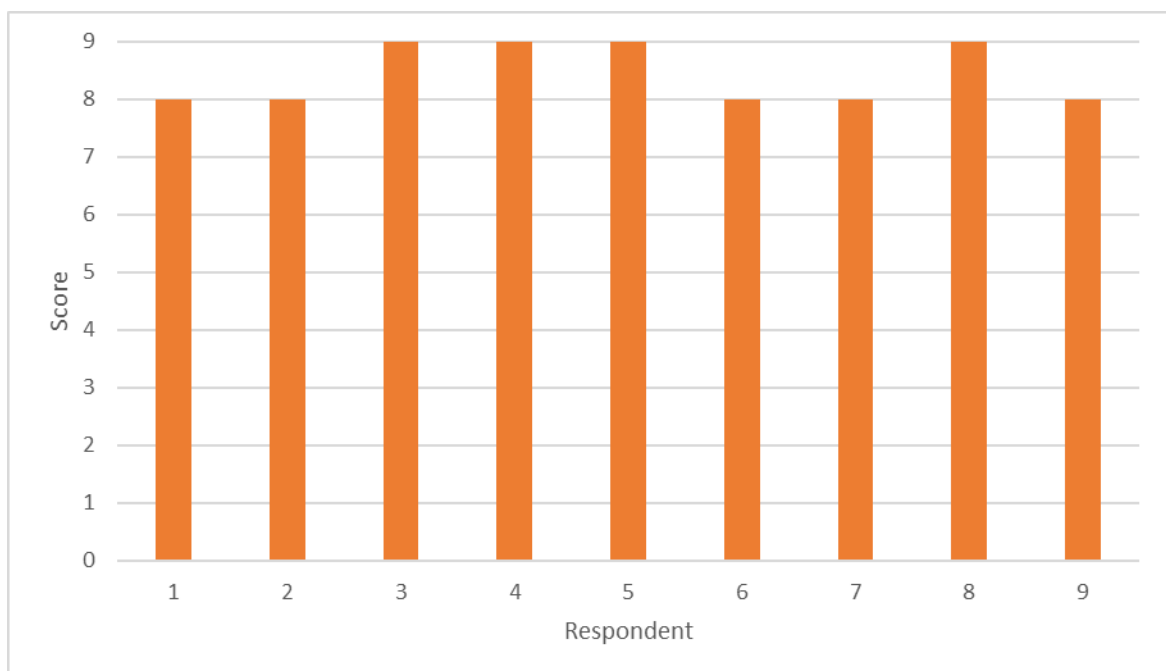
**Figure 14: Demonstration of headache**

10. A child with headache and episodes of confusion requires Brain imaging. Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.



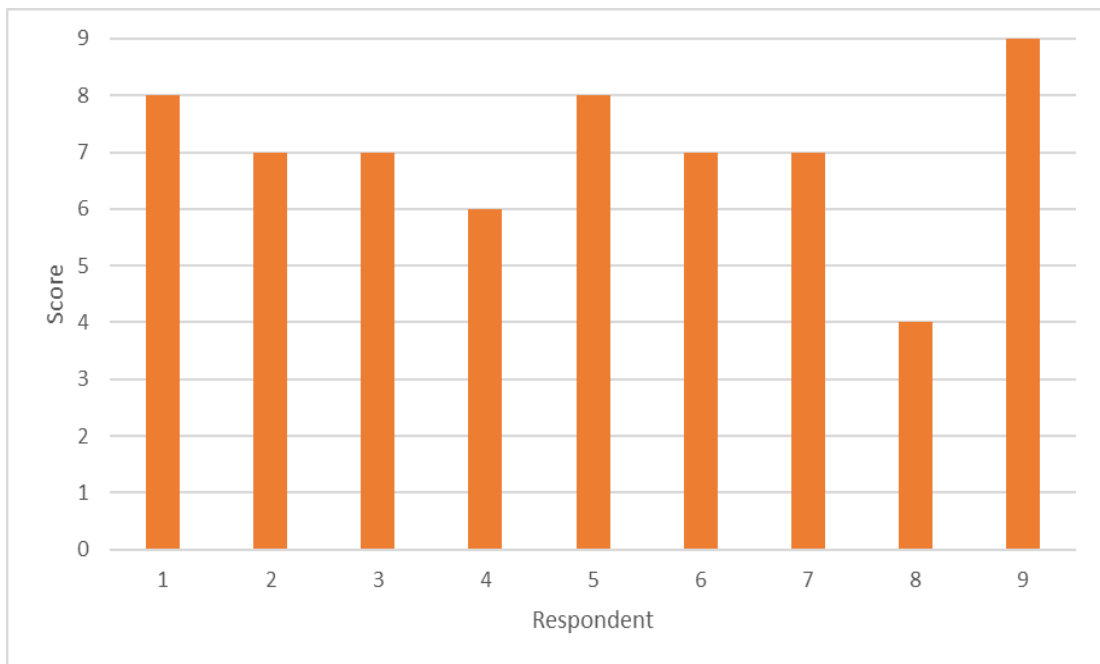
**Figure 15: Imaging in headache and confusion**

11. Nausea and/or vomiting for longer than 2 weeks should be regarded as persistent and possibility of a brain tumor considered. All the 9(100%) respondents scored between 7-9. Consensus was achieved.



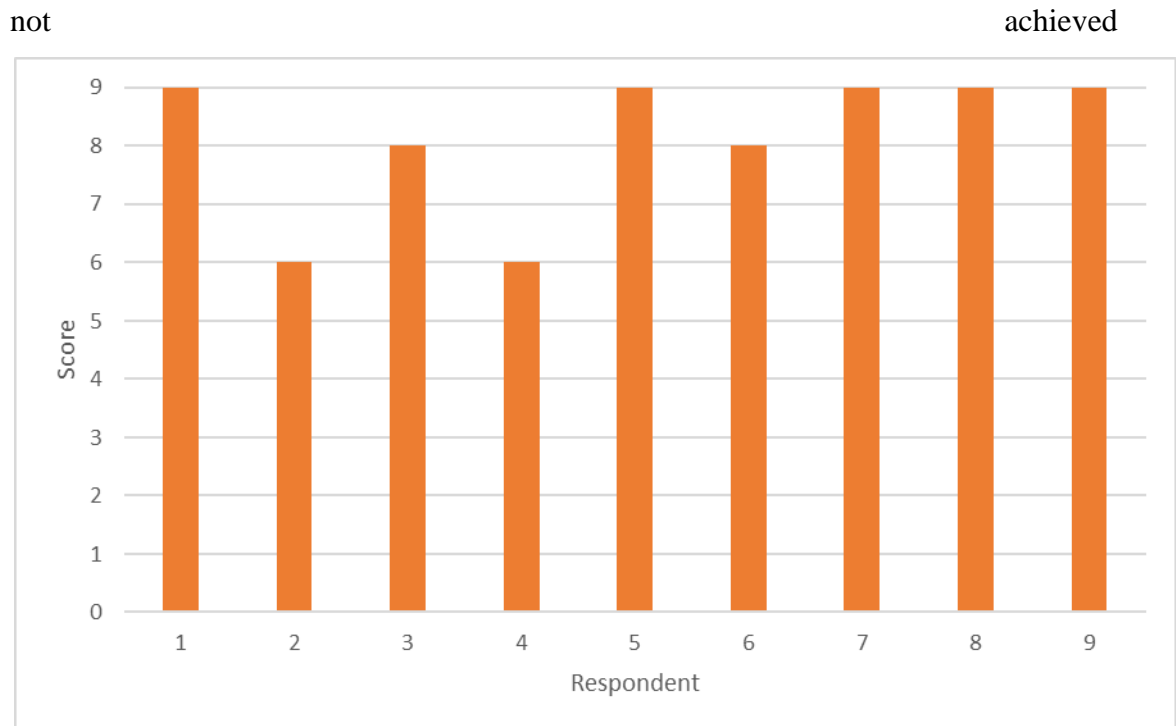
**Figure 16: Persistent Nausea and/or vomiting**

12. Persistent nausea and/or vomiting in the absence of confirmatory history, examination or investigation findings should not be associated with a gastrointestinal or other systemic infective cause. Seven (77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was not achieved



**Figure 17: Unconfirmed cause of nausea and/or vomiting**

13. Persistent vomiting on awakening requires Brain imaging. Seven (77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was

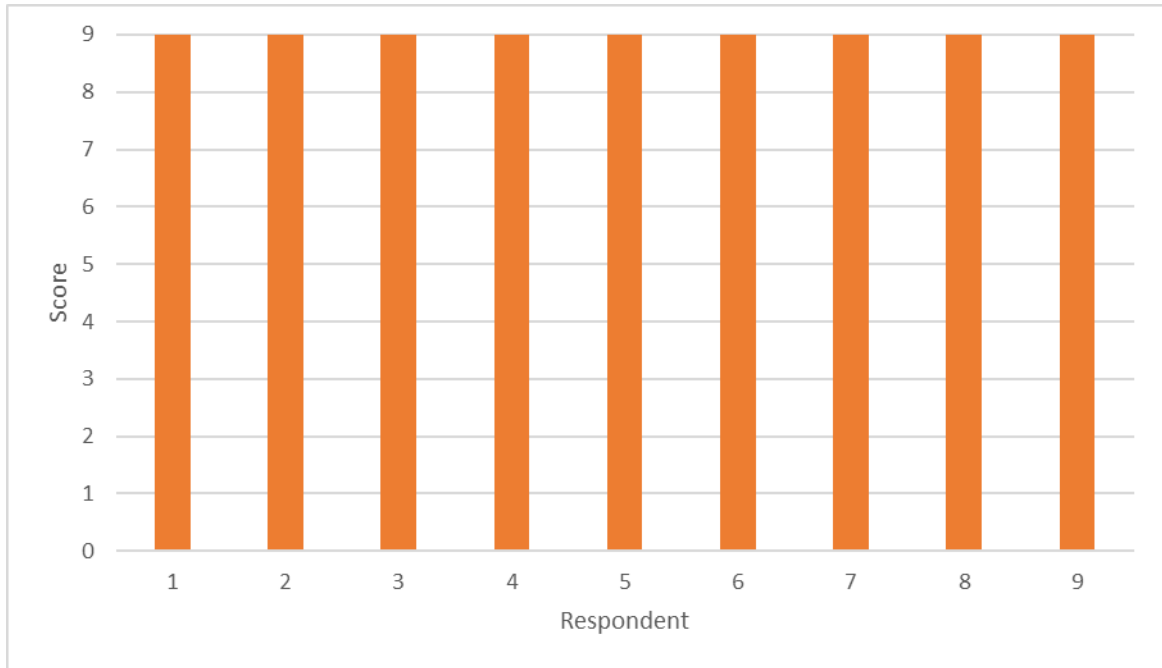


**Figure 18: Imaging in persistent nausea and/or vomiting**

14. Visual assessment of a child with a different diagnosis of a brain tumor must include assessment of:

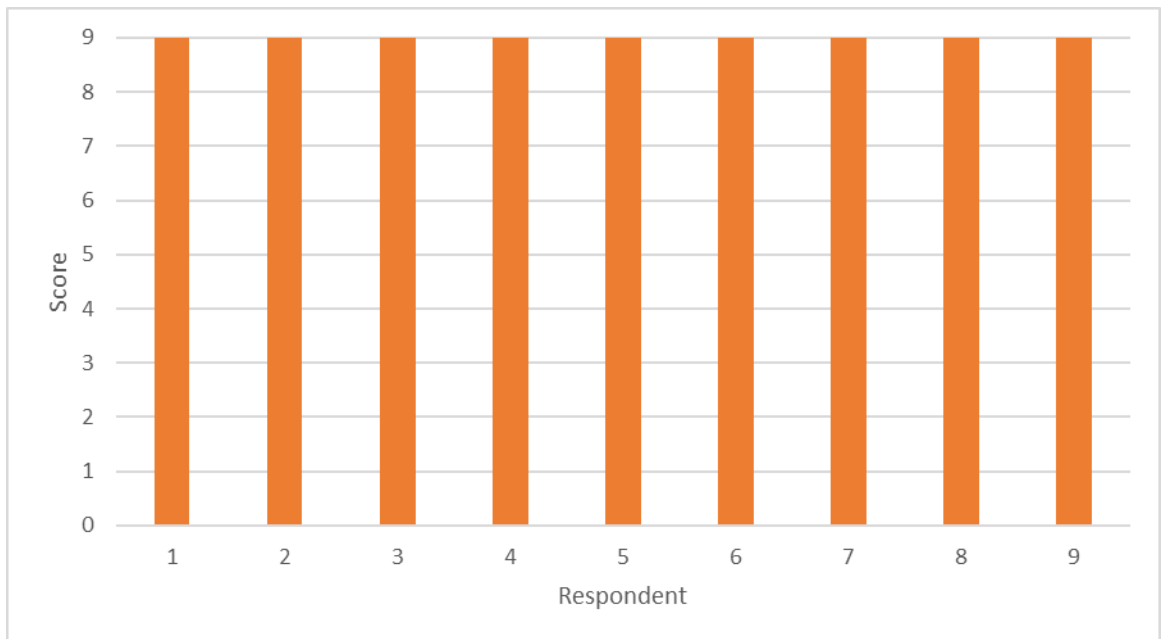
- Visual acuity
- Eye movements
- Pupil responses
- Optic disc appearance
- Visual fields (in children > 5 years)

All the 9(100%) respondents scored between 7-9. Consensus was achieved.



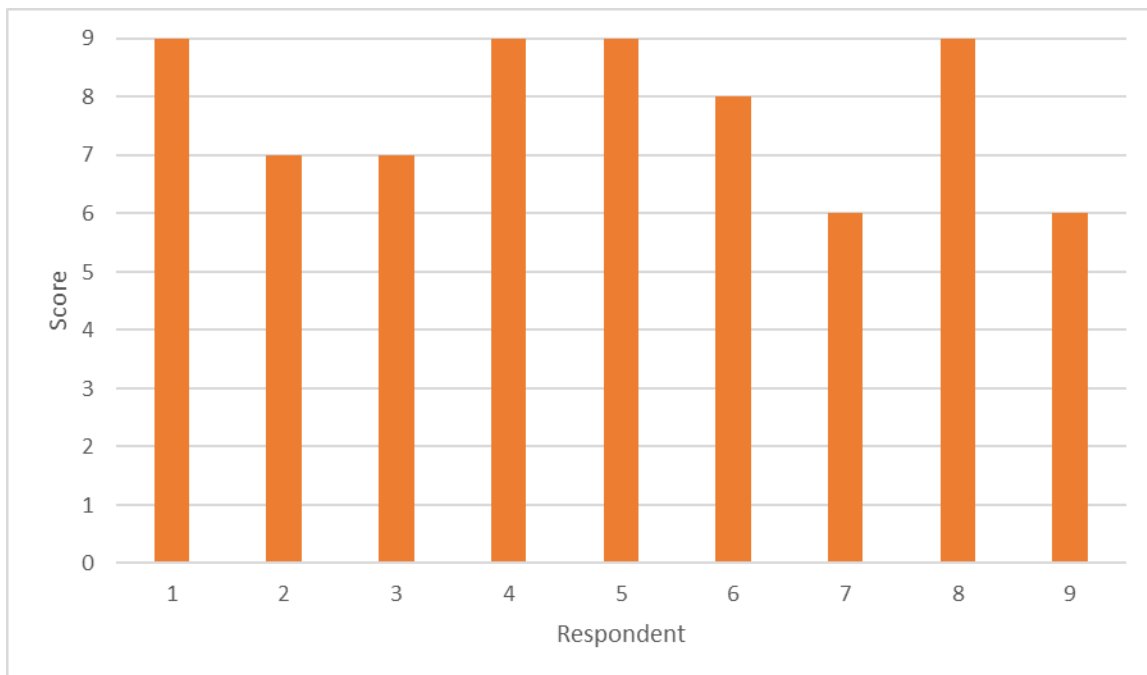
**Figure 19: Visual assessment in brain tumor**

15. Brain imaging is required in papilledema, optic atrophy, proptosis and reduced visual field. All the 9(100%) respondents scored between 7-9. Consensus was achieved.



**Figure 20: Brain imaging in visual finding**

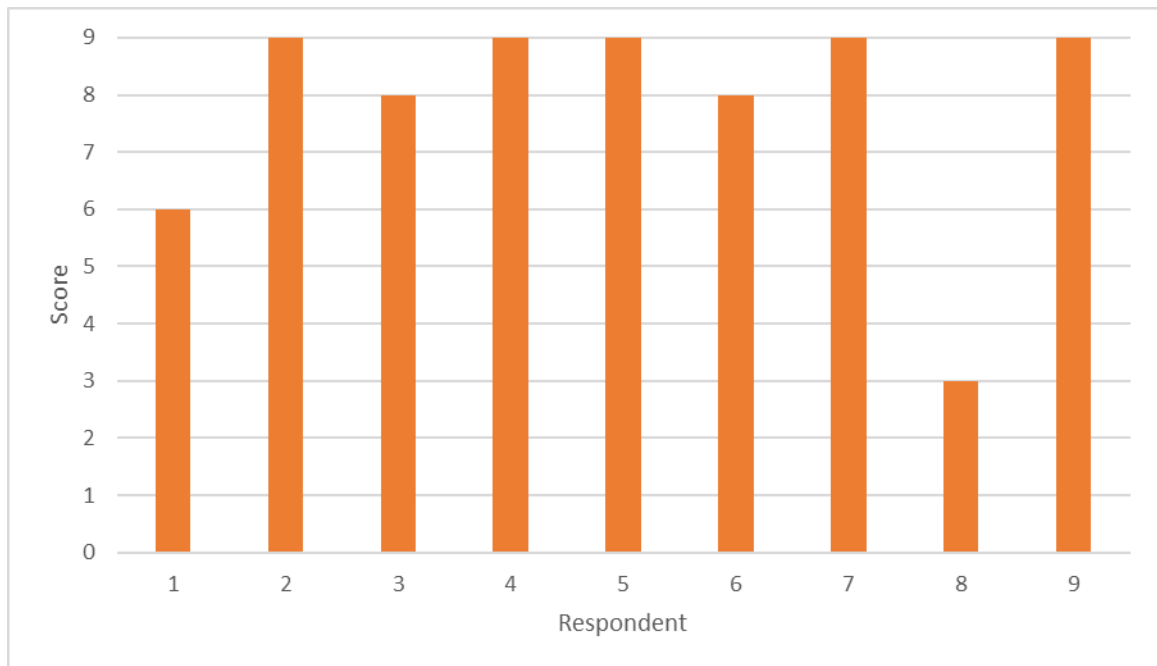
16. Brain imaging is needed in new onset non paralytic squint and nystagmus. Seven (77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was not achieved.



**Figure 21: Brain imaging in squint**

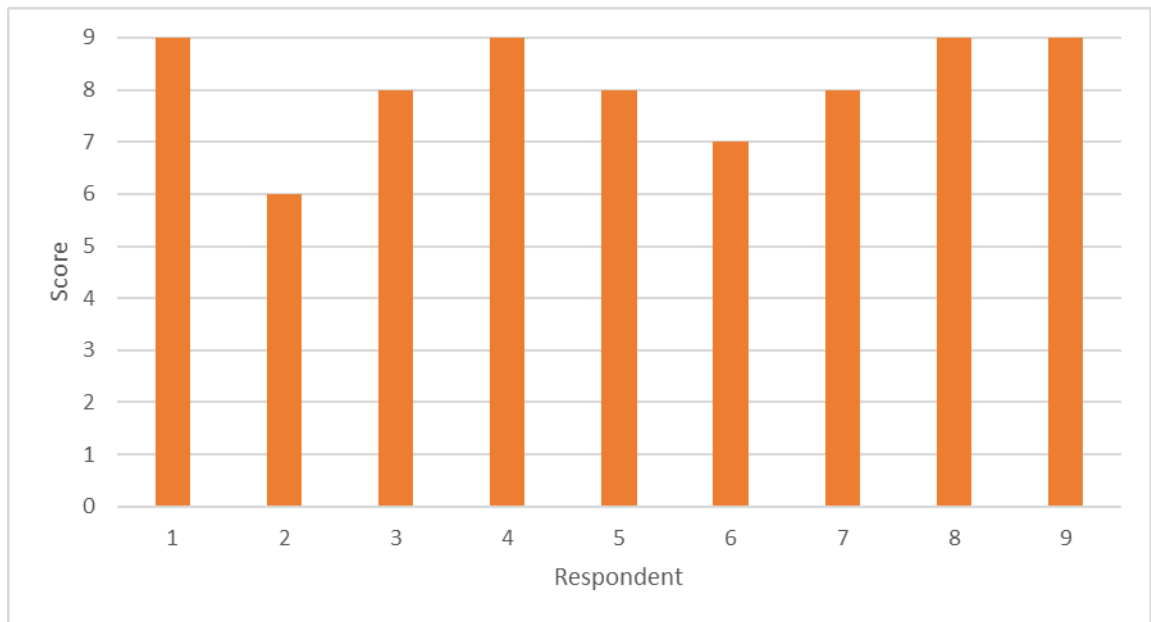
17. Brain imaging is required in reduced visual acuity not caused by a refractive error. 7(77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was not achieved.





**Figure 22: Brain imaging in reduced visual acuity**

18. History should enquire into minor changes in motor skills e.g. change of hand or foot preference, loss of learned skills. Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved

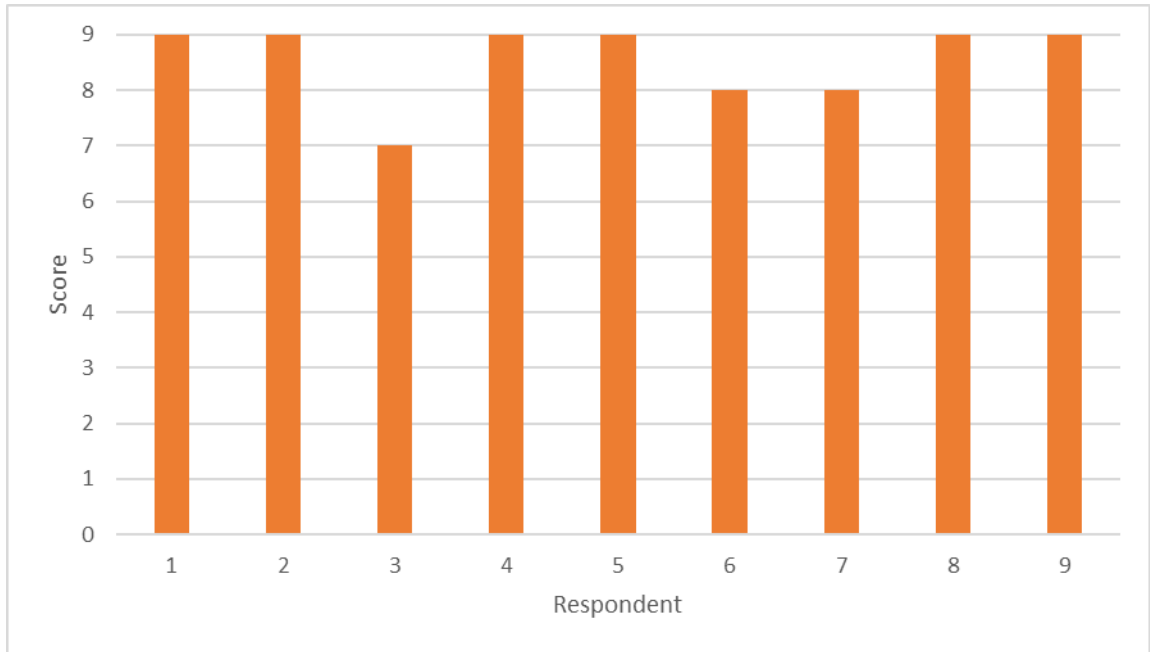


**Figure 23: Minor changes in motor skills**

19. Assessment of the gross motor skills of a child who may have a brain tumor should include observation of:

- Sitting or crawling in infants
- Walking or running
- Gross motor coordination.

All the 9(100%) respondents scored between 7-9. Consensus was achieved.



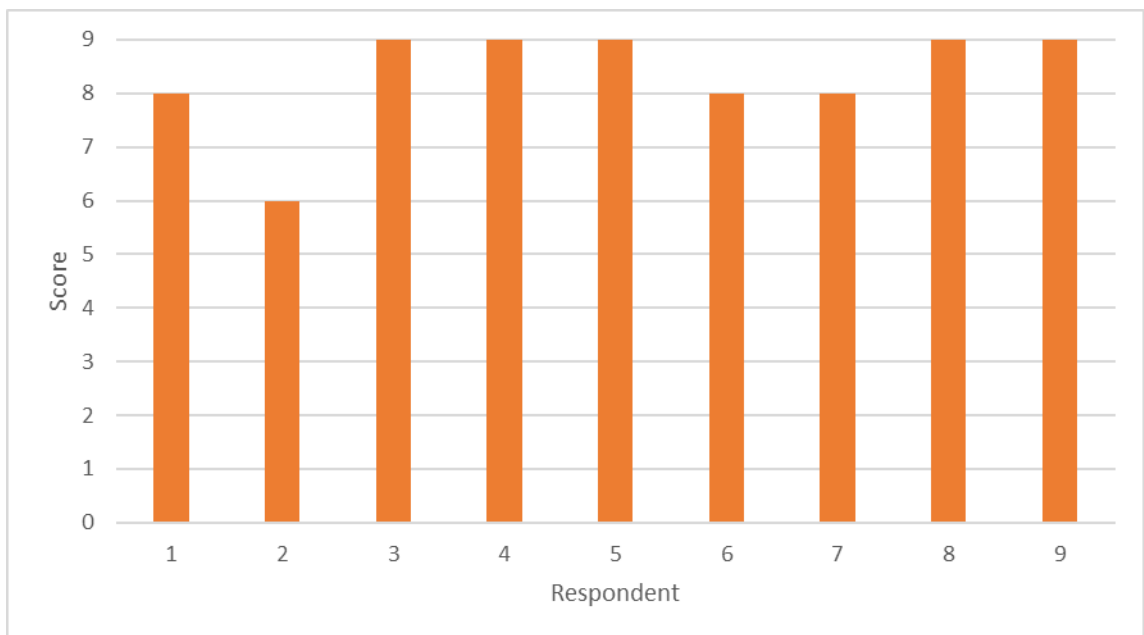
**Figure 24: Assessment of the gross motor skills**

20. Assessment of a child’s fine motor skills should include observations of:

- Handling of small objects e.g. cup, spoon
- Handwriting in older children

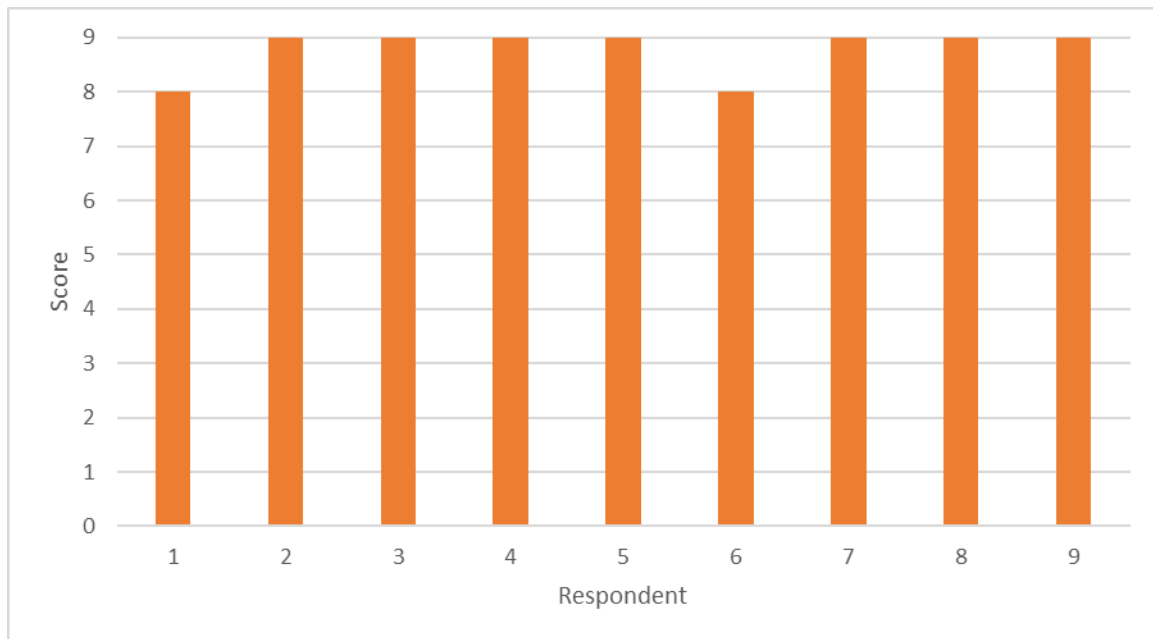
Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-

6. Consensus was achieved



**Figure 25: Assessment of fine motor skills**

21. Abnormal balance or gait is not an indication of inner ear disease in the absence of confirmatory history, examination or investigation findings. All the 9(100%) respondents scored between 7-9. Consensus was achieved.

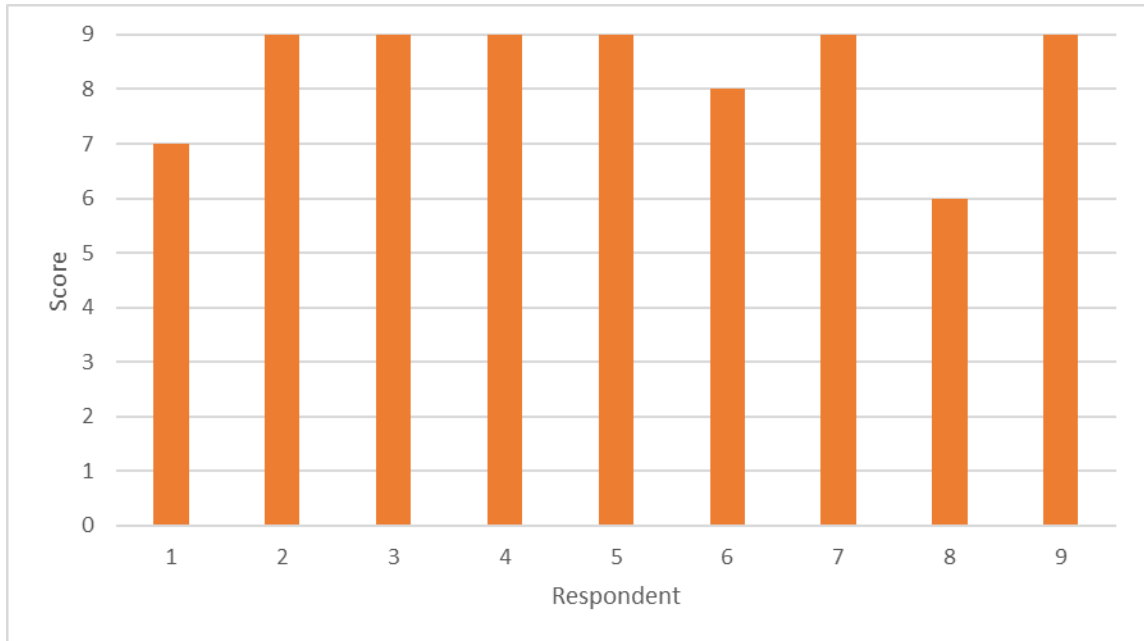


**Figure 26: Unconfirmed abnormal balance or gait**

22. Brain imaging is required for any child with

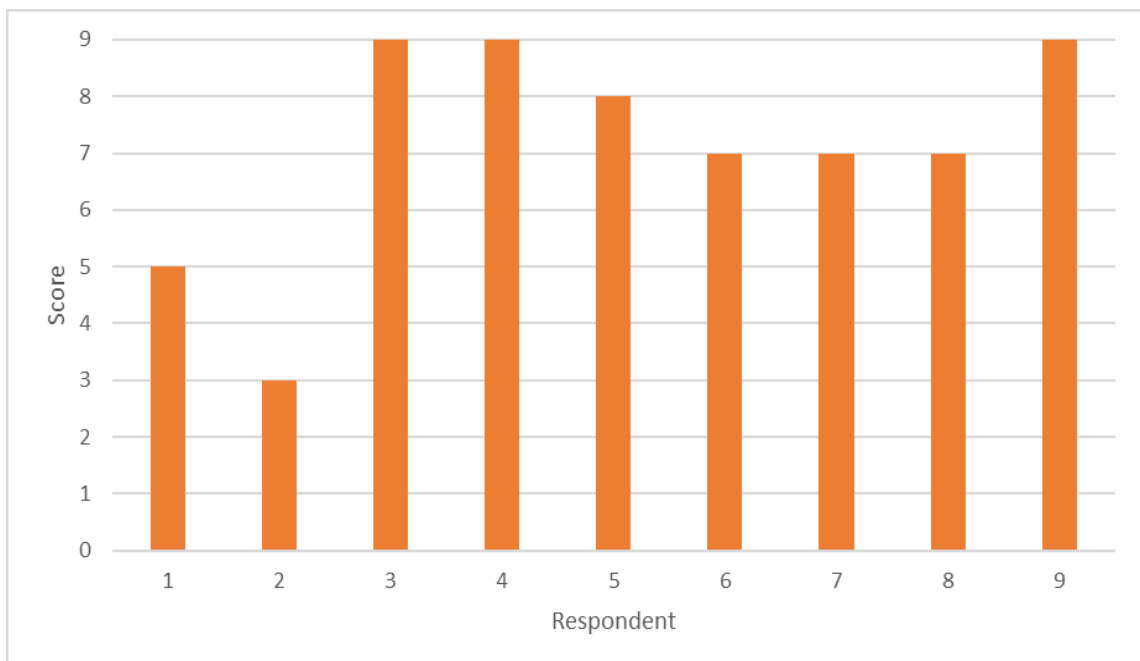
- Regression in motor skills
- Abnormal gait or co-ordination unless there is an indication of a non-neurological cause
- Focal motor weakness

Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.



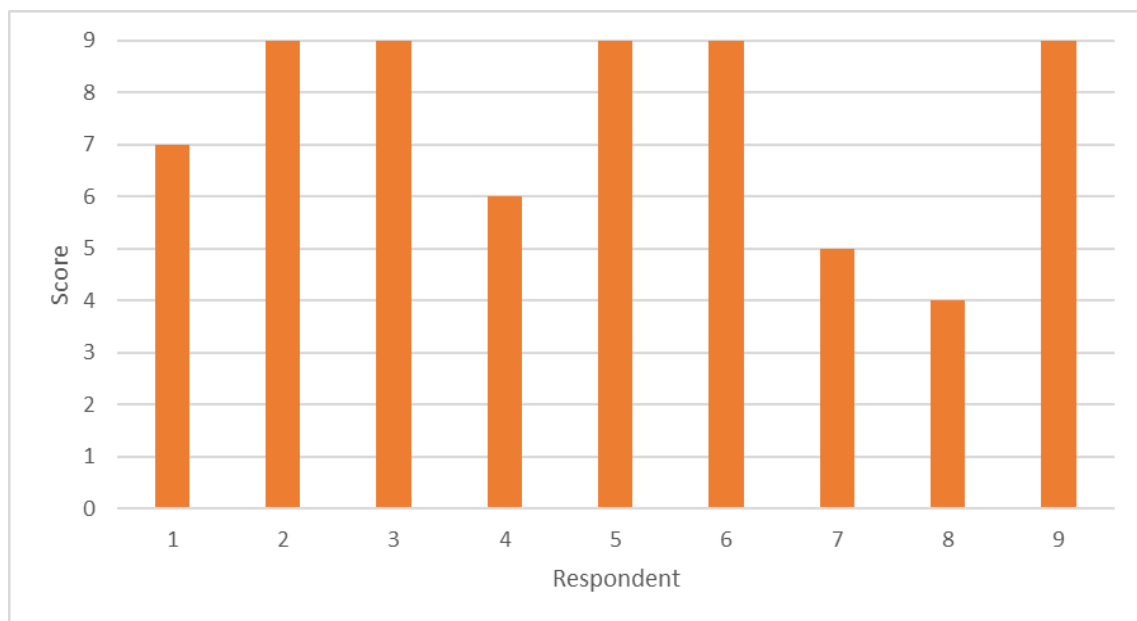
**Figure 27: Imaging in abnormal motor findings**

23. A child with impaired growth with no clearly identifiable psychosocial or physical cause should have Brain imaging. Seven (77.8%) respondents scored between 7-9 while 2(22.2%) respondents scored between 0-6. Consensus was not achieved.



**Figure 28: Imaging in abnormal growth**

24. MRI is the imaging modality of choice for a child who may have a brain tumor. Six (66.7%) of the respondents scored between 7-9 while 3(33.3%) respondents scored between 0-6. Consensus was not achieved.



**Figure 29: MRI as the imaging modality of choice**

25. If MRI is not available a contrast enhanced CT scan should be performed in a child who may have a brain tumor. Eight (88.9%) respondents scored between 7-9 while 1(11.1%) respondent scored between 0-6. Consensus was achieved.

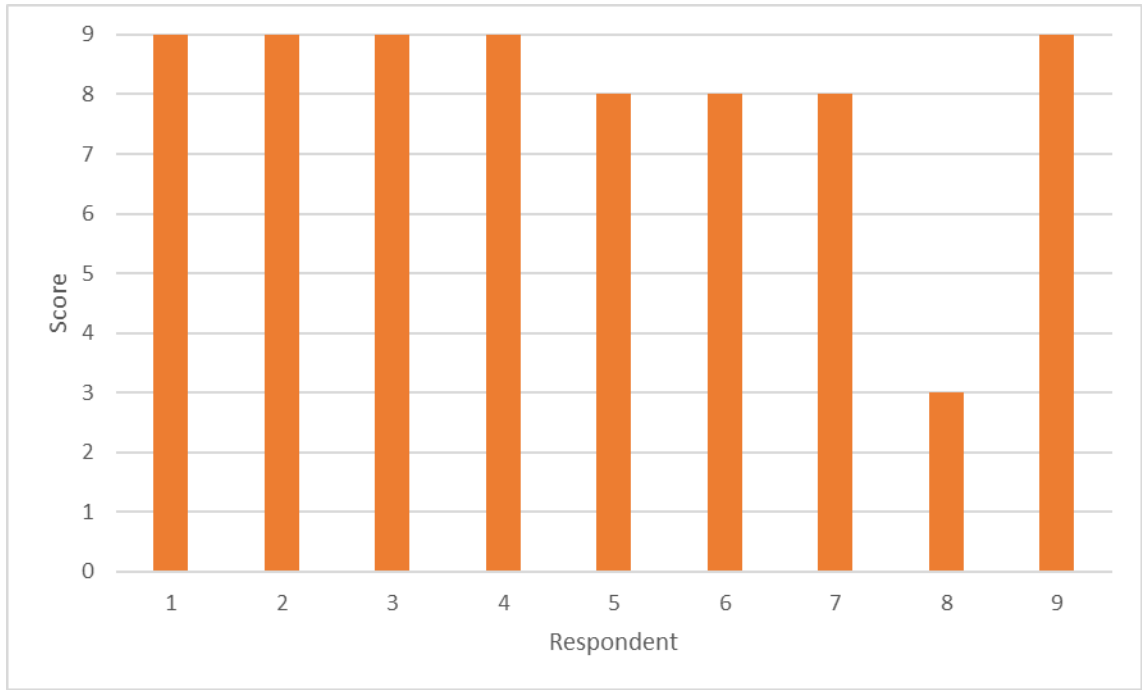
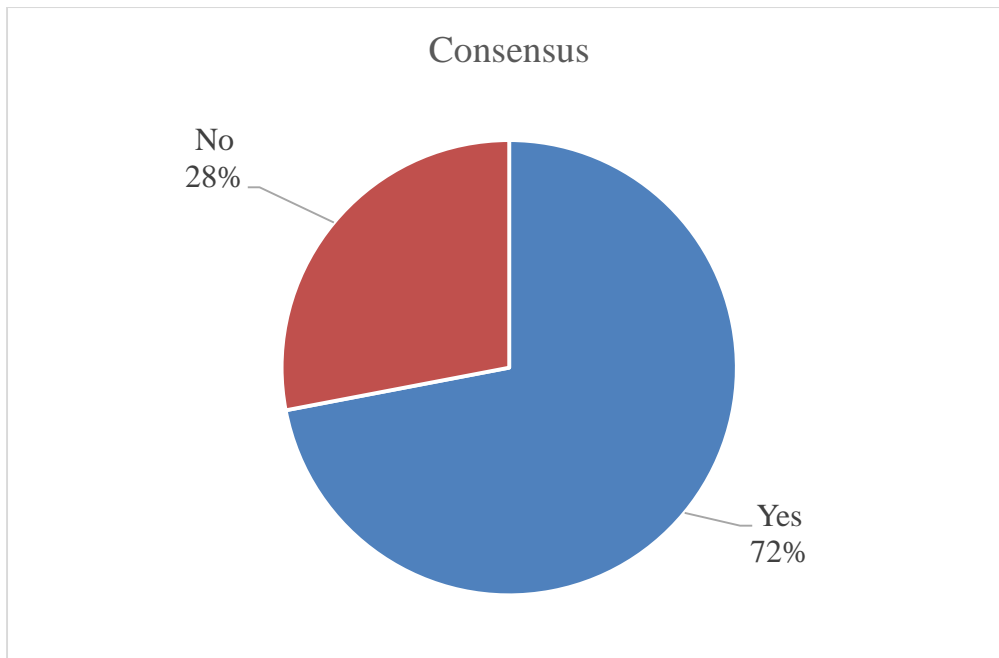


Figure 30: CT scan modality

**Table 11: Consensus Table**

STATEMENTS	SCORE 0-6	SCORE 7-9	CONSENSUS	
			YES	NO
1	0 (0.0)	9 (100.0)	YES	
2	1 (11.1)	8 (88.9)	YES	
3	1 (11.1)	8 (88.9)	YES	
4	1 (11.1)	8 (88.9)	YES	
5	0(0.0)	9 (100.0)	YES	
6	0(0.0)	9 (100.0)	YES	
7	1 (11.1)	8 (88.9)	YES	
8	0 (0.0)	9 (100.0)	YES	
9	2 (22.2)	7 (77.8)		NO
10	1 (11.1)	8(88.9)	YES	
11	0 (0.0)	9 (100.0)	YES	
12	2 (22.2)	7 (77.8)		NO
13	2 (22.2)	7 (77.8)		NO
14	0 (0.0)	9 (100.0)	YES	
15	0 (0.0)	9 (100.0)	YES	
16	2 (22.2)	7 (77.8)		NO
17	2 (22.2)	7 (77.8)		NO
18	1 (11.1)	8 (88.9)	YES	
19	0 (0.0)	9 (100.0)	YES	
20	1 (11.1)	8 (88.9)	YES	
21	0 (0.0)	9 (100.0)	YES	
22	1 (11.1)	8 (88.9)	YES	
23	2 (22.2)	7 (77.8)		NO
24	3 (33.3)	6 (66.7)		NO
25	1 (11.1)	8 (88.9)	YES	
<b>TOTAL</b>			<b>18(72%)</b>	<b>7(28%)</b>





**Figure 31: Consensus**

The 18 statements that achieved consensus (80% or more of the respondents scored between 7-9) constituted the final guideline statements. The 7 statements that had less than 80% of the respondents score between 7-9 did not achieve consensus and were eliminated.

### **5.5 Guidelines**

Eighteen (72%) of the statements achieved consensus while 7(28%) did not meet the consensus threshold and were eliminated. The 18 statements formed the final guideline.

- 1. The initial symptoms of a brain tumor may resemble symptoms that occur with other more common and less serious childhood conditions.**
- 2. Symptoms of brain tumors in children may fluctuate in severity.**
- 3. The absence of neurological abnormalities does not exclude a brain tumor.**
- 4. Children aged 3 years and below with a brain tumor may present differently from older children.**
- 5. A child with a brain tumor who is symptomatic will have one or more of the following symptoms and or signs:**
  - Headache**
  - Nausea & Vomiting**
  - Focal motor abnormalities**
  - Abnormal vision, eye movements and fundoscopy findings**

- Altered consciousness.
  - Abnormal gait and co-ordination
  - Seizures
  - Abnormal behaviour including lethargy.
  - Abnormal growth
6. A child presenting with any of the symptoms and signs listed in 5 above requires the following:
- a detailed history including specific enquiry for associated symptoms
  - a complete neurological assessment
  - assessment of height, weight & head circumference in a child aged < 2 years
  - assessment of developmental stage in a child < 5 years
7. A continuous or recurrent headache lasting more than 4 weeks should be regarded as persistent.
8. Persistent(more than 4 weeks) headache require brain imaging
9. A child with headache and episodes of confusion requires brain imaging.
10. Nausea and/or vomiting for longer than 2 weeks should be regarded as persistent and possibility of a brain tumor should be considered.
11. Visual assessment of a child with a differential diagnosis of a brain tumor must include assessment of:
- Visual acuity
  - Eye movements
  - Pupil responses
  - Optic disc appearance(Fundoscopy)
  - Visual fields (in children > 5 years)
12. Brain imaging is required in a child with papilloedema, optic atrophy, proptosis and reduced visual field.
13. History should enquire into minor changes in motor skills e.g. change of hand or foot preference, loss of learned skills.
14. Assessment of the gross motor skills in a child who may have a brain tumor should include observation of:
- sitting or crawling in infants
  - walking or running
  - gross motor coordination

**15. Assessment of a child's fine motor skills should include observation of:**

- **handling of small objects e.g. cup, spoon**
- **handwriting in older children**

**16. Abnormal balance or gait is not an indication of inner ear disease in the absence of confirmatory history, examination or investigation findings**

**17. Brain imaging is required for any child with:**

- **regression in motor skills**
- **abnormal gait or co-ordination unless there is an indication of a non-neurological cause**
- **focal motor weakness**

**18. If MRI is not available a contrast enhanced CT scan should be performed in a child who may have a brain tumor.**

## CHAPTER 6: DISCUSSION

During the study period, a total of 61 patients presented with childhood brain tumors at the Kenyatta National Hospital, of which 38 (62.3%) were male while 23 (37.7%) were female, with a male to female ratio of 1.7:1. The male predominance compares to other findings of childhood brain tumors (11).

Pre-Diagnostic Symptomatic Interval (PSI) ranged from as low as 1 week to 3 years with a median PSI of 3 months. The mean PSI was  $7.7 \pm 9.6$  months.

The time to diagnosis for brain tumors is one of the longest of all childhood cancers. The study finding compared with the mean and median symptom interval for cohorts and case series of children with central nervous system (CNS) tumors published over a duration of 15 years' ranges from 1.8 to 9.8 and 1 to 3 months respectively (4-17). A study done by Wanyoike et al (43) on children with infratentorial tumours at KNH showed a mean duration of symptoms of 3.7 months and the symptom median interval was 3.7 months.

In this study only, 11 (18%) of the patients were diagnosed within a month of the onset of symptoms while 50 (82%) were diagnosed after a month from the onset of symptoms. Another study found that only 33% of CBT are diagnosed within one month after the onset of symptoms (10). This shows that at KNH the PSI is within the range but on the higher end of the range. Opala et al (44) conducted a study in childhood cancers at KNH and found the symptom interval in KNH to be comparable to other developing countries but longer compared to more developed countries.

On the factors for late diagnosis, the study found out that 36 (59%) patient's late diagnosis was due to lack of expertise by the health worker, 12 (19.7%) patients did not provide a reason since they felt the diagnosis was timely, 5 (8.2%) respondents lacked awareness on the illness, 4 (6.6%) patients lacked awareness and professional expertise, 2 (3.3%) patients lacked finance and professional expertise. One (1.6%) patient lacked finance and another 1 (1.6%) patient lacked awareness, professional expertise and availability of CT scan. In the study by Wanyoike et al (43).

The reasons for late diagnosis included lack of knowledge and awareness by the caregivers and inadequate diagnostic tools especially in the rural areas. The high level of lack of professional expertise can be explained by the fact that there are only two Neurosurgical centres in Kenya; KNH and MTRH Eldoret. Patients are seen in the peripheral facilities before need for referral to KNH is established where the majority of health workers in contact

with the patients are clinical officers and Nurses who lack the expertise on childhood brain tumors.

The study identified 25 signs and symptoms. The top two signs and symptoms were headache from 46 (75.4%) patients, followed by nausea and vomiting 43 (70.5%) patients. The other prevalent signs and symptoms exhibited were lethargy and school difficulties from 24 (39.3%) patients, focal motor weakness from 20 (32.8%) patients, abnormal gait from 18 (29.5%) patients, seizures from 17 (27.9) of the patients and reduced visual acuity from 16 (26.2%) patients. Others signs and symptoms were alteration in or loss of consciousness 11(18%), abnormal co-ordination and cranial nerve palsies 10(16.4%)patients each, nystagmus 5(8.2%) patients, abnormal handwriting ,diplopia, endocrine and growth anomalies 4(6.6%) patients each, abnormal tone, squint, papilledema, and optic atrophy 3(4.9%) patients each, abnormal speech and exophthalmia 2(3.3%)patients each while abnormal reflexes, reduced visual fields, eye pain, unequal pupils and sunset eyes had 1 (1.6%) patients each. The varied pattern of presentation of CBT at KNH was clearly established and was similar to earlier studies (4, 39) where the commonest presenting symptoms were headache, nausea and or vomiting and a total of 56 signs and symptoms (39).

In the Delphi survey 18(72%) of the statements achieved consensus while 7(28%) did not meet the consensus threshold and were eliminated. The 18 statements formed the final guideline. The professional expertise helped to determine the specificity of symptoms and signs associated with childhood brain tumors and to advise on appropriate indications for imaging.

Guidelines development was based on high level of evidence through combination of a cross sectional study and Delphi survey (48).

## **6.1 Conclusion**

The study clearly established the varied pattern of presentation of CBT at KNH, the delayed diagnosis of CBT (prolonged PSI) at KNH and the main reason for delayed diagnosis (lack of health worker expertise). Therefore, the guidelines will assist the health professionals in early diagnosis of CBT by providing the common signs and symptoms associated with CBT and indications for brain imaging.

## **6.2 Recommendation**

1. Dissemination of guidelines through a combined effort between the department of surgery UoN/KNH by forwarding the document to the Ministry of Health
2. MOH to endorse the document and distribute it to the County, National, Faith based and Private hospitals for implementation.
3. MOH may be required to train health professionals on the utilization of the guidelines.

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## APPENDIX 1: ETHICAL APPROVAL LETTER



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Ref: KNH-ERC/A/302

10<sup>th</sup> August, 2016

Dr. Trizah Tracey John  
Reg. No. H58/69329/2011  
Dept. of Surgery  
School of Medicine  
College of Health Sciences  
University of Nairobi

Dear Dr. John,

**REVISED RESEARCH PROPOSAL: DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS AT KENYATTA NATIONAL HOSPITAL (P125/02/2016)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 10<sup>th</sup> August 2016 – 9<sup>th</sup> August 2017.

This approval is subject to compliance with the following requirements:

- a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
- c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
- d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
- e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
- f) Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
- g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

"Protect to discover"

For more details consult the KNH- UoN ERC website <http://www.erc.uonbi.ac.ke>

Yours sincerely,



**PROF. M.L. CHINDIA**  
**SECRETARY, KNH-UoN ERC**

c.c.     The Principal, College of Health Sciences, UoN  
          The Deputy Director, CS, KNH  
          The Assistant Director, Health Information, KNH  
          The Chair, KNH- UoN ERC  
          The Dean, School of Medicine, UoN  
          The Chair, Dept. of Surgery, UoN  
          Supervisors: Prof. N.J. Mwang'ombe, Mr. P.O. Akuku

"Protect to discover"

## **APPENDIX 2: CONSENT FORM**

This Informed Consent form is for parents/guardians of pediatric neurosurgical patients with brain tumors at the Kenyatta National Hospital. We are requesting these patients to participate in this research project whose title is “. DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS IN AT KENYATTA NATIONAL HOSPITAL.

Principal investigator: Dr. Trizah Tracey John

Supervisors:

1. Prof.N.J. Mwangombe
2. Mr. P.O Akuku

This informed consent has three parts:

- Information sheet (to share information about the research with you)
- Certificate of Consent (for signatures if you agree to take part)
- Statement by the researcher

You will be given a copy of the full Informed Consent Form.

### **Part I: Information sheet**

#### **Introduction.**

My name is Dr. Trizah Tracey John. I am a post graduate student at the University of Nairobi, Department of Surgery, Division of Neurosurgery. I am carrying out a study to develop clinical guidelines for early diagnosis of childhood brain tumors at KNH. This will be possible through data collection by filling in a questionnaire.

#### **Procedure**

The following information will be recorded in the questionnaire:

- Age and gender of the patient.
- Highest level of education of parent/guardian
- How the patient feels since the illness

- Duration of the illness
- Reasons for prolonged duration of illness before diagnosis
- Neurological examination (eyes, face, legs, hands, posture) and documentation of the findings.
- Available records (radiological images, laboratory histological results, patient's file) will be reviewed and information documented in the questionnaire.

**Delphi process:** The final results will be discussed by a panel of specialists from the University of Nairobi and Kenyatta National Hospital.

### **Purpose of the Research.**

Information obtained from this study will help in the creation of guidelines that will be used by health workers in Kenya to promote early diagnosis of brain tumors in children. This study is also a requirement for any doctor who aspires to graduate from our college as a surgeon.

### **Voluntary participation/right to refuse or withdraw.**

An invitation for your patient to participate in this study is hereby extended to you. You will have the opportunity to ask questions before you decide on your patient's participation. You may seek clarification regarding any bit of the study should any part be unclear.

### **Confidentiality.**

All the information which you provide regarding your patient will be kept confidential; only the researchers will access this information. The questionnaire will be identified by a number and only the researchers can relate the number to the patient. All the information you give us will be used for research only.

### **Risks.**

This study will not expose your patient to any risk.

### **Sharing of the results.**

The information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UoN-ERC).

This proposal has been reviewed and approved by the KNH/UoN-ERC which is a committee whose work is to make sure research participants are protected from harm.

**Cost and compensation.**

There will be no extra cost incurred for participating in this study nor is there compensation offered.

**Who to contact.**

The contact information is given below if you wish to contact any of them for whatever reason;

Secretary, KNH/UoN-ERC

P.O. Box 20723 KNH, Nairobi 00202

Tel 726300-9

Email: [uonknh\\_erc@uonbi.ac.ke](mailto:uonknh_erc@uonbi.ac.ke)

University of Nairobi research supervisors

1. Professor N. J. Mwangombe,

Professor of Surgery,

Head, Thematic Unit of Neurosurgery,

Department Of Surgery,

University Of Nairobi.

P.O. Box 19676 KNH, Nairobi 00202

Tel # 0202726300

2. Mr.P.O Akuku,

Senior Lecturer,

Thematic Unit of Neurosurgery,

Department of Surgery,

University of Nairobi.

P.O. Box 19676 KNH, Nairobi 00202

Tel # 0202726300

Principle researcher:

Dr. Trizah Tracey John

Division of Neurosurgery, Department of Surgery, University of Nairobi

P.O. Box 19676 KNH, Nairobi 00202

Mobile phone 0722203025

**Part II certificate of consent.**

I have read the above information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction.

I consent voluntarily to for my patient to participate in this research.

Name of Parent/guardian \_\_\_\_\_

Signature \_\_\_\_\_

Date \_\_\_\_\_



If Illiterate;

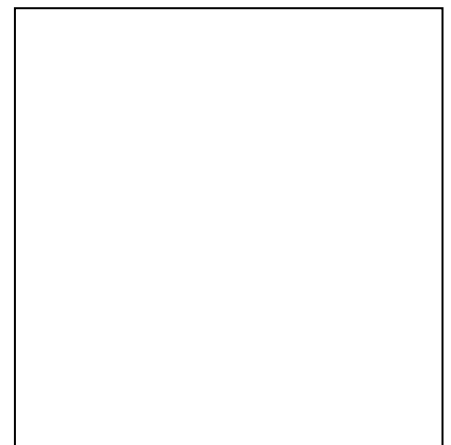
I have witnessed the accurate reading of the consent form to the potential participant's parent/guardian, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print Name of witness \_\_\_\_\_

Left thumb print of  
participant

Signature of witness \_\_\_\_\_

Date \_\_\_\_\_



**PART III: Statement by the researcher**

I have accurately read out the information sheet to the parent/guardian of the participant, and to the best of my ability made sure that the he/she understands that the following will be done:

- Refusal to participate or withdrawal from the study will not in any way compromise the care of treatment.
- All information given will be treated with confidentiality.
- The results of this study might be published to facilitate knowledge of clinical presentation and reasons of delayed diagnosis of brain tumors in children at KNH.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the patient's parent/guardian have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Name of researcher taking consent \_\_\_\_\_

Signature of researcher taking consent \_\_\_\_\_

Date \_\_\_\_\_

## **FOMU YA MAKUBALIANO YA MZAZI/MLEZI**

**KICHWA CHA UTAFITI:** DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS IN AT KENYATTA NATIONAL HOSPITAL.

Fomu hii ya makubaliano ni kwa wazazi/walezi wa wale watoto wanaouguua saratani ya ubongo wanaotibiwa hospitalini kuu Kenyatta. Namualika mtoto wako kuwa mmoja wa wale watakaofanyiwa uchunguzi huo katika utafiti huu kwa hiari yako.

**Mtafiti mkuu:**Dkt. Trizah Tracey John

**Wasimamizi:** 1.Prof.N.J. Mwang’ombe

2. Mr. P.O Akuku

Fomu hii ya makubaliano ina sehemu tatu:

- 1) Habari itakayo kusaidia kukata kauli
- 2) Fomu ya makubaliano (utakapoweka sahihi)
- 3) Ujumbe kutoka kwa mtafiti

Utapewa nakala ya fomu hii.

## **SEHEMU YA KWANZA: Ukurasa wa habari**

### **Kitambulizi**

Jina langu ni Dkt.Trizah Tracey John. Mimi ni daktari ninayesomea uzamili katika idara ya upasuaji Chuo Kikuu cha Nairobi. Ninafanya utafiti kwa anwani ya, “**DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS AT KENYATTA NATIONAL HOSPITAL**”. Dhamira ya utafiti huu itawezekana kupitia kujaza dodoso.

### **Utaratibu**

Ujumbe ufuatao utajazwa kwenye dodoso:

- Umri na jinsia ya mgonjwa.
- kiwango cha juu cha elimu ya mzazi/mlezi
- dalili za ugonjwa tangu mwanzo.

- muda wa dalili za ugonjwa
- sababu ya muda mrefu ya ugonjwa kabla ya utambuzi.
- uchunguzi wa mishipa ya fahamu(uso,miguu,mikono)
- rekodi za matibabu zitaangaliwa na majibu kujazwa kwenye dodoso na mtafiti.

Baadaye, majibu yatazungumziwa na kikundi cha wataalamu wa chuo kikuu cha Nairobi na Hospitali kuu ya Kenyatta (Delphi process)

### **Nia ya utafiti huu**

Ujumbe utakaopatikana kutokana na utafiti huu utasaidia kutengeneza miongozo ya kusaidia katika utambuzi wa haraka wa ugonjwa saratani ya ubongo. Aidha, utafiti huu ni mojawapo ya mahitaji anayohitajika mtafiti kuhitimisha katika kiwango cha uzamili kama daktari wa upasuaji.

### **Haki ya kukataa utafiti**

Kushiriki kwa mtoto wako kwa utafiti huu ni kwa hiari yako. Una uhuru wa kukataa ashriki, na kukataa kwako hakutatumiwa kumnyima tiba. Unayo haki ya kumtoa katika utafiti wakati wowote unapoamua.

### **Taadhima ya siri**

Ujumbe kuhusu majibu yako yatahifadhiwa vyema. Ujumbe kuhusu ushiriki wa mtoto wako katika utafiti huu utaweza kupatikana na wewe na wanaoandaa utafiti na wala si yeyote mwingine. Jina la mtoto halitatumika bali ujumbe wowote kumhusu utapewa nambari badili ya jina lake.

### **Hatari unayoweza kupata**

Hakuna hatari yoyote ambayo yaweza kutokea kwa sababu ya kuhusishwa kwa utafiti huu. Aidha, kukataa au kujitoa katika ushiriki kwa huu utafiti kwa wakati wowote ule hakutamletea hatari yoyote ya matibabu.

### **Hifadhi ya matokeo.**

Matokeo ya utafiti huu yatachapishwa kwa nukuu mbali za sayansi kupitia kwa idhini ya mtafiti mkuu. Nakala za chapisho zitahifadhiwa katika idara ya upasuaji, chuo kikuu cha

Nairobi na katika maktaba ya sayansi za Afya, kitivo cha utabibu. Hivyo basi, matokeo ya utafiti huu hayatasambazwa kwa umma au jukwaa lisiloidhinishwa kihalali. Ujumbe ulio kwa dodoso hautahifadhiwa baada ya uchanganuzi wa matokeo

### **Gharama au fidia.**

Utafiti huu hautakugharimu zaidi ya matibabu ya mtoto ya kawaida. Vilevile, hakuna malipo yoyote au fidia utakayopokea kutokana na kujiunga kwako katika utafiti huu. Muda wako ndio utakaotumiwa wakati wa kukubali mtoto ashiriki katika utafiti.

### **Anwani za Wahusika**

Ikiwa uko na maswali ungependa kuuliza baadaye, unaweza kuwasiliana na:

1. Mtafiti Mkuu:

Dkt. Trizah Tracey John

Idara ya upasuaji, Shule ya Afya, Chuo Kikuu cha Nairobi,

SLP 19676 KNH, Nairobi 00202.

Simu: 0721203025

2. Wahadhiri husika:

Prof. N.J Mwang'ombe,

Profesa wa Upasuaji,

Mkuu wa Mgawayo wa upasuaji wa mfumo mkuu wa neva,

Idara ya upasuaji,

Shule ya Afya, Chuo Kikuu cha Nairobi,

SLP 19676 KNH, Nairobi 00202.

Simu: # 0202726300

3. Dkt. P.O Akuku

Mhadhiri mkuu,

Mgawayo wa upasuaji wa mfumo mkuu wa neva,

Idara ya Upasuaji

Shule ya Afya, Chuo Kikuu cha Nairobi

SLP 19676 KNH, Nairobi 00202.

Simu: # 020 272 6300

Wahusika wa maslahi yako katika Utafiti:

Karani,

KNH/UoN-ERC

SLP 20 723 KNH, Nairobi 00202

Simu: +254-020-2726300-9 Ext 44355

Barua pepe: [uonknh\\_erc@uonbi.ac.ke](mailto:uonknh_erc@uonbi.ac.ke)

**SEHEMU YA PILI: Fomu ya makubaliano**

Nimeelezwa utafiti huu kwa kina. Nakubali mtoto wangu kushiriki katika utafiti huu kwa hiari yangu. Nimepata wakati wa kuuliza maswali na nimeelewa kuwa iwapo nina maswali zaidi, ninaweza kumwuliza mtafiti mkuu au watafiti waliotajwa hapa juu.

Jina la

Mshiriki \_\_\_\_\_

Sahihi ya mshiriki

\_\_\_\_\_

Tarehe \_\_\_\_\_

Kwa wasioweza kusoma na kuandika:

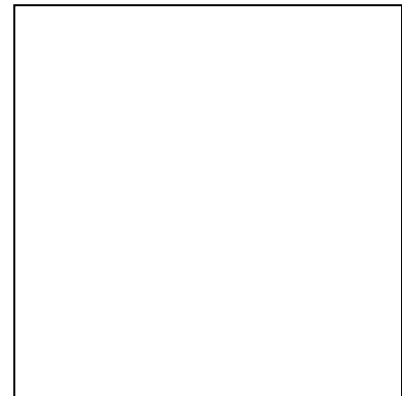
Nimeshuhudia usomaji na maelezo ya utafiti huu kwa mshiriki. Mzazi/mlezi wa mshiriki amepewa nafasi ya kuuliza maswali. Nathibitisha kuwa mzazi/mlezi alipeana ruhusa ya motto kushiriki bila ya kulazimishwa.

Jina la shahidi \_\_\_\_\_  
cha

Alama ya kidole cha gumba

Sahihi la shahidi \_\_\_\_\_

Mzazi/mlezi wa mshiriki



Tarehe \_\_\_\_\_

### **SEHEMU YA TATU: Ujumbe kutoka kwa mtafiti**

Nimemsomea mzazi/mlezi wa mshiriki ujumbe kiwango ninavyoweza na kuhakikisha kuwa amefahamu yafuatayo:

- Kutoshiriki au kujitoa kwenye utafiti huu hakutadhuru kupata kwa mtoto matibabu.
- Ujumbe kuhusu majibu yatahifadhiwa kwa siri.
- Matokeo ya utafiti huu yanaweza chapishwa kusaidia kuhamasisha uwepo na uzito wa ugonjwa.

Ninathibitisha kuwa mzazi/mlezi wa mshiriki alipewa nafasi ya kuuliza maswali na yote yakajibiwa vilivyo. Ninahakikisha kuwamzazi/mlezi wa mshiriki alitoa ruhusa bila ya kulazimishwa.

Mzazi/mlezi wa mshiriki amepewa nakala ya hii fomu ya makubaliano.

Jina la mtafiti

---

Sahihi ya Mtafiti

---

Tarehe

---



### **APPENDIX 3: ASSENT FORM**

**STUDY TITLE:** DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS IN AT KENYATTA NATIONAL HOSPITAL.

#### **INVESTIGATORS**

Principle investigator:

Dr. Trizah Tracey John

Supervisors:

3. Prof. N.J. Mwang'ombe
4. Mr. P.O Akuku

#### **1. Why are you here?**

The doctor wants to tell you about a study concerning children with brain tumors in Kenyatta National Hospital. The doctor wants to see if you would like to be in this study. This form tells you about the study; if there is anything you do not understand, please ask your parent/guardian or the doctor.

#### **2. Why are they doing the study?**

The investigators want to create a guideline to help in early diagnosis of brain tumors in children.

#### **3. What will happen to you?**

The interview will last about 2 hours.

The following information will be filled in a questionnaire:

- Your age and gender
- Highest level of education level of your parent/guardian
- Duration of sickness and reasons for long duration before diagnosis
- How you feel since you were unwell
- The doctor will examine your body and record the findings

- The doctor will look at your tests and fill the results.

The results will be discussed by a selected group of doctors from the University of Nairobi and Kenyatta National Hospital. (Delphi process)

**4. Will the study hurt?**

No. You might feel a bit tired during the interview period.

**5. Will you get better if you are in the study?**

During the study, you receive the usual treatment of your condition.

**6. What if you have any questions?**

You can ask any time, now or later. You can talk to the doctors, parent or guardian.

**7. Who will know what I did in the study?**

Any information you give to the study staff will be kept private.

Your name will not appear in the study papers.

No one except the study staff and your parent/guardian will know that it was you who was in the study.

**8. Do you have to be in the study?**

No. No one will be angry at you if you do not want to do this.

I will also ask your parent/guardian if they would like you to be in the study.

Even if your parent/guardian want you to be in the study, you can still say no.

Even if you say yes now, you can change your mind later.

The doctor will still treat you for the brain tumor even if you say no to the study.

**Assent**

I want to take part in this study. I know I can change my mind at any time.

A) Verbal assent. (Print name of child) ..... verbal  
assent given.

B) Written Assent

Sign.....Age.....Date.....

I confirm that I have explained the study to the participant to the extent compatible with  
the participant's understanding, and that the participant has agreed to be in the study.

Name.....Sign.....Date.....

## **FOMU YA MAKUBALIANO**

**KICHWA CHA UTAFITI:** DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD BRAIN TUMORS IN AT KENYATTA NATIONAL HOSPITAL.

### **Watafiti**

Mtafiti mkuu: Dkt. Trizah Tracey John

Wasimamizi: 1. Prof. N. J. Mwang'ombe

2. Mr. P. O Akuku

### **1. Mbona uko hapa?**

Daktari anataka kukueleza kuhusu utafiti wa watoto wanaouguua saratani ya ubongo hospitali ku ya Kenyatta. Daktari anataka kujua kama ungependa kuhusika kwa huu utafiti. Fomu hii ina maelezo kuhusu utafiti huu: ikiwa kuna jambo usilolielewa, tafadhali uliza kutoka kwa mzazi/mlezi au madaktari.

### **2. mbona utafiti huu?**

watafiti wanataka kuunda miongozo ya kusaidia katika utambuzi wa haraka wa saratani ya ubongo

### **3. Mwelekeo**

Mahojiano yatachukua mda wa karibu masaa mawili.

Ujumbe ufuatao utajazwa kwenye dodoso:

- Umri na jinsia yako
- kiwango cha juu cha elimu ya mzazi/mlezi
- dalili za ugonjwa tangu mwanzo.
- muda wa dalili za ugonjwa
- sababu ya muda mrefu ya ugonjwa kabla ya utambuzi.
- uchunguzi wa mishipa ya fahamu (uso, miguu, mikono, legs,)
- rekodi za matibabu zitaangaliwa na majibu kujazwa kwenye dodoso na mtafiti.

Baadaye, majibu yatazungumziwa na kikundi cha wataalamu wa chuo kikuu cha Nairobi na Hospitali kuu ya Kenyatta (Delphi process).

#### **4. Iko hatari yoyote?**

Hakuna hatari yoyote utakayoipata.  
Unaweza kupata uchovu wakati wa mahojiano.

#### **5. Iko matibabu kwa utafiti?**

Utapata matibabu ya kawaida wakati wa utafiti.

#### **6. Maswali?**

Unaweza kuuliza maswali wakati wowote. Utapata majibu kutoka kwa madaktari, mzazi/mlezi.

#### **7. Nani atajua kuhusika kwangu?**

Ujumbe kuhusu majibu yako yatahifadhiwa vyema. Ujumbe kuhusu ushiriki wako katika utafiti huu utaweza kupatikana na wewe, mzazi/mlezi na wanaoandaa utafiti na wala si yeyote mwingine. Jina lako halitatumika kwenye utafiti.

#### **8. Kuhusika ni kwa lazima?**

Hapana. Hakuna yeyote atakayekulaumu usiposhiriki kwa utafiti.

Mzazi/mlezi wako ataulizwa ruhusa ya kushiriki pia; si lazima ushiriki hata ikiwa mzazi/mlezi wako amekubali.

Unayo haki ya kujitoa katika utafiti wakati wowote unapoamua na kukataa kwako hakutatumiwa kukunyima tiba.

#### **Makubaliano**

nimeamua kushiriki kwa utafiti huu, naelewa ninaweza kujitoa wakati wowote.

A) makubaliano ya matamshi (jina la mtoto) .....

B) makubaliano kwa maandishi

Sahihi.....umri.....Tarehe.....

Nimethibitisha ya kwamba nimemweleza mshiriki kuhusu utafiti huu kulingana na kuelewa kwake na amekubali kushiriki.

Jina.....Sahihi.....Tarehe.....

**APPENDIX 4: QUESTIONNAIRE**

**DEVELOPMENT OF GUIDELINES FOR EARLY DIAGNOSIS OF CHILDHOOD**

**BRAIN TUMORS**

**INSTRUCTIONS**

1. Read and listen carefully to each of the questions before responding.
2. Ask for clarification from the interviewer where required.
3. Respond to each question as correctly as possible, do not guess or give false information.

**1. GENERAL INFORMATION**

Date.....

Study serial number.....

Age(years).....months.....

Gender (tick appropriately)  Male  Female

**2.How long did it take from the onset of illness to diagnosis? (FILL APPROPRIATELY)**

DAYS.....MONTHS.....

**3.WHAT DO YOU FEEL ARE THE REASONS FOR THE PROLONGED PERIOD FROM ONSET OF ILLNESS TO DIAGNOSIS(LIST IN THE APPROPRIATE CATEGORY)**

A) Patient/ caregiver factors

1.....

2.....

3.....

B) Health professional factors

1.....

2.....

3.....

C)Health system factors

1.....

2.....

3.....



**4. WHAT ARE THE PRESENTING SYMPTOMS AND SIGNS?(TICK APPROPRIATELY)**

YES NO N/A

Headache

Nausea and vomiting

Seizures

Alteration in or loss of consciousness

**MOTOR SYSTEM ABNORMALITIES**

Abnormal gait

Abnormal co-ordination

Focal motor weakness

Abnormal tone

Abnormal reflexes

Abnormal speech

Abnormal handwriting

**VISUAL SYSTEM ABNORMALITIES**

Reduced visual acuity

Reduced visual fields

Nystagmus/Other abnormal eye movements

Squint

Exophthalmia

Diplopia

Eye pain

Papilloedema

Optic atrophy

Unequal pupils

Sunsetting

**CRANIAL NERVE PALSIES**

**BEHAVIOURAL CHANGE**

(including lethargy and school difficulties)

**ENDOCRINE AND GROWTH ABNORMALITIES**

**5. LOCATION OF TUMOR(TICK APPROPRIATELY)**

Posterior Fossa

Pineal Gland

Supratentorial hemispheric Pituitary fossa

Brainstem Tumours

Thalamus

Third Ventricle

Hypothalamus

Tectum

Optic Pathway

Basal Ganglia

Others (Specify).....

**6.TYPE OF TUMOR(FILL APPROPRIATELY)**

.....

**APPENDIX 5: DELPHI QUESTIONNAIRE**

**1. The initial symptoms of a brain tumor may resemble symptoms that occur with other more common and less serious childhood conditions**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**2. Symptoms occurring with brain tumors may fluctuate in severity.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**3. The absence of neurological abnormalities does not exclude a brain tumor.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**4. Children aged 3 years and under with a brain tumor may present differently from older children**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**5. A symptomatic child with a brain tumor will have one or more of the following symptoms and/or signs:**

- **Headache**
- **Nausea & Vomiting**
- **Focal motor abnormalities**
- **Abnormal vision, eye movements and fundoscopy findings**
- **Altered consciousness**
- **Abnormal gait and co-ordination**
- **Seizures**
- **Abnormal behaviour including lethargy.**
- **Abnormal growth**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**6. A child presenting with any of the symptoms and signs listed in 5 above requires the following:**

- **a detailed history including specific enquiry for associated symptoms**
- **a complete neurological assessment**
- **assessment of height, weight & head circumference in a child aged < 2 years**
- **assessment of developmental stage in a child < 5 years**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**7. A continuous or recurrent headache lasting more than 4 weeks should be regarded as persistent.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**8. Persistent headache require Brain imaging**

1 2 3 4 5 6 7 8 9  
Strongly Disagree           Strongly Agree

**9. A young child who is unable to complain of headache may demonstrate head pain by holding their head, lethargy or withdrawal**

1 2 3 4 5 6 7 8 9  
Strongly Disagree           Strongly Agree

**10. A child with headache and episodes of confusion requires Brain imaging**

1 2 3 4 5 6 7 8 9  
Strongly Disagree           Strongly Agree

**11. Nausea and/or vomiting for longer than 2 weeks should be regarded as persistent and possibility of a brain tumor considered.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree           Strongly Agree

**12. Persistent nausea and/or vomiting in the absence of confirmatory history, examination or investigation findings should not be associated with a gastrointestinal or other systemic infective cause**

1 2 3 4 5 6 7 8 9  
Strongly Disagree           Strongly Agree

**13. Persistent vomiting on awakening requires Brain imaging.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**14. Visual assessment of a child with a differential diagnosis of a brain tumor must include assessment of:**

- Visual acuity
- Eye movements
- Pupil responses
- Optic disc appearance
- Visual fields (in children > 5 years)

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**15. Brain imaging is required in papilloedema, optic atrophy, proptosis and reduced visual field**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**16. Brain imaging is needed in new onset non paralytic squint and nystagmus.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**17. Brain imaging is required in reduced visual acuity not caused by a refractive error**

1    2    3    4    5    6    7    8    9  
Strongly Disagree               Strongly Agree

**18. History should enquire into minor changes in motor skills e.g. change of hand or foot preference, loss of learned skills.**

1    2    3    4    5    6    7    8    9  
Strongly Disagree               Strongly Agree

**19. Assessment of the gross motor skills of a child whomay have a brain tumor should include observation of:**

- **sitting or crawling in infants**
- **walking or running**
- **gross motor coordination**

1    2    3    4    5    6    7    8    9  
Strongly Disagree               Strongly Agree

**20. Assessment of a child's fine motor skills should include observation of:**

- **handling of small objects e.g. cup, spoon**
- **handwriting in older children**

1    2    3    4    5    6    7    8    9  
Strongly Disagree               Strongly Agree



**21. Abnormal balance or gait is not an indication of inner ear disease in the absence of confirmatory history, examination or investigation findings.**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**22. Brain imaging is required in any child with:**

- regression in motor skills
- abnormal gait or co-ordination unless there is an indication of a non-neurological cause
- focal motor weakness

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**23. A child with impaired growth with no clearly identifiable psychosocial or physical causes should have brain imaging**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**24. MRI is the imaging modality of choice for a child who may have a Brain tumor**

1 2 3 4 5 6 7 8 9  
Strongly Disagree          Strongly Agree

**25. If MRI is not available a contrast enhanced CT scan should be performed for a child who may have a brain tumor.**

	1	2	3	4	5	6	7	8	9	
Strongly Disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly Agree

## **APPENDIX 6: ELIMINATED DELPHI STATEMENTS**

- 1. A young child who is unable to complain of headache may demonstrate head pain by holding their head, lethargy or withdrawal.**
- 2. Persistent nausea and/or vomiting in the absence of confirmatory history, examination or investigation findings should not be associated with a gastrointestinal or other systemic infective cause**
- 3. Persistent vomiting on awakening requires Brain imaging**
- 4. Brain imaging is needed in new onset non paralytic squint and nystagmus.**
- 5. Brain imaging is required in reduced visual acuity not caused by a refractive error**
- 6. A child with impaired growth with no clearly identifiable psychosocial or physical cause should have brain imaging.**
- 7. MRI is the imaging modality of choice for a child who may have a brain tumor**

## **APPENDIX 7: LIST OF DELPHI PARTICIPANTS**

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