CLINICOPATHOLOGICAL FEATURES AND EARLY SURGICAL OUTCOME OF POSTERIOR CRANIAL FOSSA TUMOURS IN CHILDREN AT KENYATTA NATIONAL HOSPITAL

DEPARTMENT OF SURGERY

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DECLARATION

I declare that this dissertation is my own original work and to the best of my knowledge, it has not been presented elsewhere for consideration of publication or award of another degree.

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DEDICATION

This is dedicated to children with posterior fossa tumours and their families

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LIST OF ABBREVIATIONS

KNH…… Kenyatta National Hospital

PCF……. Posterior Cranial Fossa

ICU ……. Intensive Care Unit

EVD ……. External Ventricular Drain

KNH/UON ERC……. Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

KPS……. Karnofsky Performance Score

LPS……...Lansky Performance Score

CNS……...Central Nervous System

CSF……Cerebrospinal fluid

WHO……. World Health Organization

CPA……. Cerebellopontine Angle

CBTRUS ……. Central Brain Tumour Registry of the United States

ATRT……Atypical teratoid rhabdoid tumour

PA……. Pilocytic Astrocytoma

ABSTRACT

Study Background: Posterior cranial fossa (PCF) tumours account for 54 – 70% of brain tumours in children. The pattern of presentation is variable and is dependent on the location of tumour within the PCF, however, a triad of early morning vomiting, headache and gait imbalance is common. Radiologically, these tumours have a variable pattern of appearance that is useful for surgical planning, predicting diagnosis and outcome. Surgery is key in the management of these tumours, either for CSF diversion or tumour removal.

Broad Objective: To describe clinicopathologic features and early surgical outcome of children managed surgically for PCF tumours in KNH

Methodology: Nine months observational prospective cohort study at Kenyatta National Hospital. Children aged 12 years and below managed surgically at KNH for PCF tumour. Informed consent was obtained from the next of kin. At admission, data collected included patient demographics, presenting signs and symptoms, radiological details, surgical intervention, and post-operative management. The follow up period was in hospital up to 1 month with an end point of death or discharge.

The main outcome measures included, length of ICU stay, length of hospital stay and complication rate. Other outcomes included the patterns of clinical and radiologic presentation, the various histologic types, and change in GCS and KPS.

Data management and results: Data was collected using predesigned data collection forms, then entered Stata version 16.

Results: Twenty-eight children with PCF tumours were analysed. The mean age was 6.49 years and the male to female ratio was 1:1.33. All the children presented with cerebellar signs and

symptoms; features of raised ICP were seen in 96.4% with an average duration before diagnosis of 40 days (1.5 months); motor signs were seen in 75% with a mean duration of 54.1days (2.5 months) before diagnosis; cranial nerve dysfunction was present in 67.9%; 85.7% of the patients had hydrocephalus. 78.6% had a GCS of >13 and 75% had a KPS >60 at admission.

All patients had imaging done with 60.71% having both CT and MRI. The vermis was the most common location of PFT on imaging. Medulloblastoma was the most common radiologic diagnosis and histopathological tumour type at fifty percent and 35.7% respectively. The level of agreement between histopathological diagnosis and radiological diagnosis was 97.4% ($p<0.001$) and Kappa statistic 0.68.

Eighty five percent had CSF diversion with majority being VP shunting. It took a mean of 18 days between CSF diversion and definitive surgery. 75% had a craniotomy for exposure and 21% had craniotomy plus C1 laminectomy. Telovelar approach was used 42.9%, transvermian in 39.3% and transcortical in 17.9%. Extubation was done in 53.6% of patients post operatively in theatre. Those who had delayed extubation remained intubated for a mean of 11.5 days.

All patients were managed in ICU. The overall mean length of ICU stay was on 10.6 days, patients with delayed extubation had a mean length of ICU stay 18.4 days with those extubated early having a mean ICU stay of 3.8 days.

The mean overall length of hospital stay was 24 days. The complication rate was 32.1%.
Hydrocephalus was the most common complication at 77.8% followed by wound complications at 22.2%. Young age, less than 4.7 years, duration of hospital stay, and ICU stay were the main risk factors associated with developing complications. The 30-day mortality was 10.7%.

Conclusion: This study shows that, more female patients present with PCF in this population. Cerebellar signs and symptoms are the most common pattern of clinical presentation. The symptom duration before diagnosis is long. The most common imaging location is the vermis with medulloblastoma being is the most common radiological and histological tumour type. Long stay in ICU and long admission duration are associated with increased complication occurrence.

CHAPTER 1: INTRODUCTION

One of the earliest series of posterior cranial fossa (PCF) tumours was done by Cushing in which he published a paper on 61 patients with medulloblastoma. In this series, the mortality at 1 year was 68% (1,2). Now, years later, the understanding of pathological patterns, clinical presentation, diagnostic imaging, tumour biology and various treatment modalities of PCF tumours has greatly advanced. Additionally, treatment outcomes have improved due to anaesthesia, neurologic localization, asepsis, surgical technique, postoperative critical care, and adjuvant treatment.

The PCF is one of the three cranial fossae. The space is found below the tentorium cerebelli and extends to the foramen magnum. As such, this fossa is also referred to as infratentorial compartment or fossa.(3)

PCF tumours are either intraaxial, tumour arising from the brain parenchyma, or extraaxial, tumour that is not arising from the parenchyma but within the cranial cavity. Overall, PCF tumours account for 16 – 23 % of all central nervous system (CNS) tumours. They are more common in children representing 54 – 70% of all childhood brain tumours(2). There are various histopathologic tumour types present in the PCF among children (4).

PCF tumours often present as an emergency with intraventricular obstructive hydrocephalus. A triad of early morning vomiting, ataxia and headache is seen in patients with PCF tumours (4–6). Surgery is the mainstay in the treatment of PCF tumours. The surgical treatment involves a suboccipital or retrosigmoid craniotomy or craniectomy and tumour excision. An external ventricular drain (EVD) may be used to divert the CSF reducing the intracranial pressure which relaxes the brain during surgery. Ventriculoperitoneal shunting has also been used to manage hydrocephalus. Post operatively patients are managed in the intensive care unit for a variable

duration of time. This is dependent on the preoperative performance status, intraoperative events such as duration of surgery, intraoperative bleeding, and proximity of surgery to vital centres within the brainstem.(3,7)

A few studies have been done in Kenyatta national hospital (KNH) that evaluate paediatric PCF tumours. Wanyoike et al did a retrospective analysis in 2003 of paediatric patients with PCF tumours(8). Other studies that have evaluated paediatric PCF tumours were by Kwasi et al(9) and Tracy et al(10).

This study aims at describing the pattern of clinical presentation, the histopathologic types, and early surgical outcomes in children with PCF tumours managed at the Kenyatta National Hospital (KNH).

CHAPTER 2: LITERATURE REVIEW

2.1 THE POSTERIOR CRANIAL FOSSA

The PCF is the most posterior and deepest part of the cranial fossae. The extents include the tentorial incisura and tentorium cerebelli superiorly to the foramen magnum inferiorly. Anteriorly, lies the dorsum sellae, (which is the posterior part of the sphenoid body), and the clival part of occipital bone; and on each side, is the petrous and mastoid parts of the temporal bone, the lateral part of occipital bone, and above and behind a small part of mastoid angle of the parietal bone. The lower portion of the squamosal part of the occipital bone forms the posterior boundary(3).

The PCF has various anatomic regions that are of surgical importance these include the cerebellum and vermis, the fourth ventricle, the cerebellopontine angle (CPA), the brainstem, CSF spaces and foramen magnum. The main structures within the fossa include neural structures, arteries and veins of the posterior cerebral circulation, exiting cranial nerves, and meninges that cover and form part of the anatomic boundaries of the fossa. It communicates through various foramina, canals and fissures with the supratentorial compartment, spinal canal, and neck. The posterior fossa is also referred to as the infratentorial compartment. The term infratentorial compartment will be used interchangeably with PCF(3).

The diagram below shows the bony anatomy of the PCF

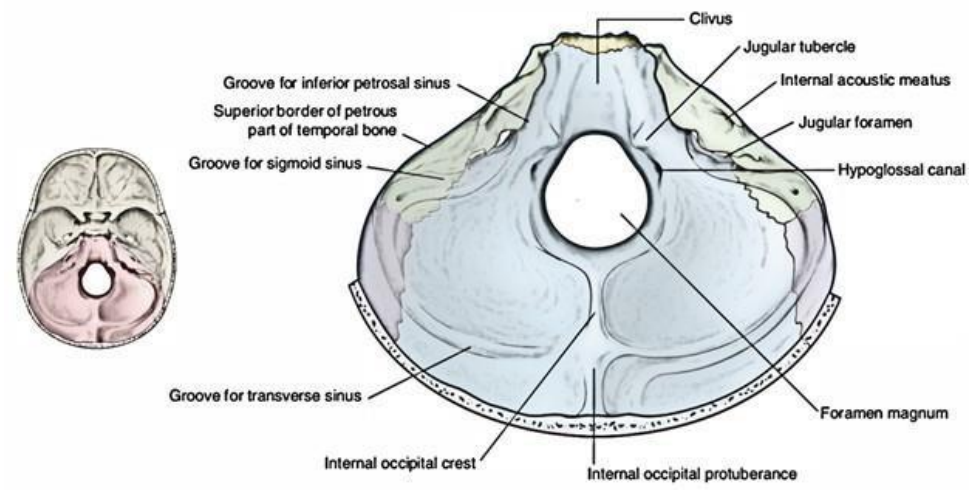


Figure 1*:* An illustration showing the bony anatomy of the Posterior Cranial Fossa adapted from (11)

2.2 EPIDEMIOLOGY OF PCF TUMOURS IN CHILDREN

Lesions present in the PCF have histologic similarities with lesions in the supratentorial compartment. However, others are unique, in that they only occur in the PCF and may have a specific age range of occurrence. Diagnosis is guided by location of lesion within the infratentorial compartment, age of the patient, associated clinical history that includes signs and symptoms and duration, and imaging studies.

Overall, brain tumours are the most common solid tumours in children comprising of 40-50% of all tumours. Additionally, brain tumours are now the leading cause of cancer related deaths in children due to improved survival of hematologic malignancies(12). PCF tumours account for 54 – 70% of brain tumours in children(2). Various brain tumour registries and studies report on various aspects of PCF tumours in children.

The National brain tumour registry shows a decreasing incidence of PCF tumours with increasing age. PCF tumours accounted for 30% of brain tumours between the ages 0 – 14 year, 9% between 14 – 24

years and 2% between 25 – 85 years. Medulloblastoma and pilocytic astrocytoma remain the most common in the early childhood and adolescent group of patients.(13).

The Central Brain Tumour Registry of the United States (CBTRUS) 2019 report summarizes CNS tumours as malignant and non-malignant tumours, and further characterised them based on site in the CNS. Cerebellar and brainstem location account for 3.7% of all primary brain tumours. The incidence of malignant brain tumours, defined as WHO grade II, III, and IV, in the cerebellum and brainstem was 8.2% and that of non-malignant tumours was only 1.3% (14).

In Nigeria, Salami et al, in a 10-year retrospective study, analysed data from 72 patients with PCF tumours, adult and paediatric, who underwent neurosurgical intervention and found that 44.4% of PCF tumours were in children aged 14 years and below, the male to female ratio was 2.56:1 in paediatric patients. In addition, the most common anatomic location for occurrence of PCF tumour in children was cerebellar hemisphere at 56.94%. Other anatomic locations in descending frequency were 4^{th} ventricle, CPA, vermis, brainstem and foramen magnum. The most common histological tumour types reported was medulloblastoma and pilocytic astrocytoma at 20.8% and 18.6% respectively. Others noted were diffuse astrocytoma, ependymoma, glioblastoma, and atypical teratoid and rhabdoid tumour (ATRT). (15)

In a 17-year retrospective study in Sudan, 31 children aged between 1 and 15 years were diagnosed and treated for PCF tumour. The mean age of presentation was 7.9 years, female patients were more common at 51%. The most common tumours were brainstem tumours at 48% followed by medulloblastoma at 36%. This study reported a pre diagnostic interval of 3.6 months.(16)

In Egypt, a 2 year retrospective study reported children were most commonly affected by PCF tumours at 73.3%.(17)

2.3 PCF TUMOURS IN CHILDREN AT KNH

KNH has a busy neurosurgical centre with a countrywide catchment area. Several studies been done in KNH both published and unpublished manuscripts on brain tumours and have reported on infratentorial tumours.

Wanyoike et al, in a retrospective analysis of 46 paediatric patients treated for PCF tumours between 1996 and 2003, found that the mean age was 6.7 years, cerebellar symptoms were most common and the histologic tumour types included mainly astrocytomas and medulloblastoma with equal occurrence. Other histologic types noted were ependymoma, tuberculoma and meningioma.(8)

In a retrospective analysis of 54 children treated for PCF tumour in KNH between 2009 and 2012, V. Kwasi reported a male to female ratio of 1.25:1, mean age of 7.4 years, 32% had cerebellar symptoms, and mean duration of symptoms was 5.4 months and mean of 6 weeks between diagnosis and treatment.(9)

In a study by Tracy John and Mwang'ombe, through a cross sectional study on childhood brain tumours the pattern of clinical presentation and pre-symptomatic interval was reviewed. In this study, in which age limit was 0 to 12 years, results from 61 children were analysed. The presymptomatic interval ranged from 1 week to 3 years with a median of 3 months, the main reason for the delay was attributed to lack of health care expertise. Up to twenty-five signs and symptoms were recorded with headache being the most common at 75.4%. PCF tumours were the most common representing 21 out of 61 representing 34%. Based on histological types medulloblastoma, pilocytic astrocytoma and ependymomas constituted 38.4%, these were the commonest PCF tumour types.(18)

In a 2-year cross-sectional retrospective study on histopathologic spectrum and neuroradiologic correlation of childhood intracranial brain tumours, Omuok et al, analysed 87 histopathologic samples in KNH and Moi Teaching and Referral office (MTRH). Of the 87 patient samples analysed 67 were from KNH. PCF tumours were most the common at 48.8%. Pilocytic astrocytomas and medulloblastoma were the most common histological tumour types.

2.4 PATHOLOGY OF PCF TUMOUR IN CHILDREN

2.4.1 THE WHO CNS TUMOUR CLASSIFICATION AND GRADING

The WHO CNS tumour classification is a widely used system. The basis of this classification has been histological, cell of origin of the tumour. In 2016, the revised 4th edition incorporated molecular parameters into the classification. Additionally, this classification further describes various tumour grades, grade I to IV, within a particular histological classification(19).

Table 1: WHO CNS tumour grading system: Summarized from WHO classification of CNS tumours 4th Edition Revised (19)

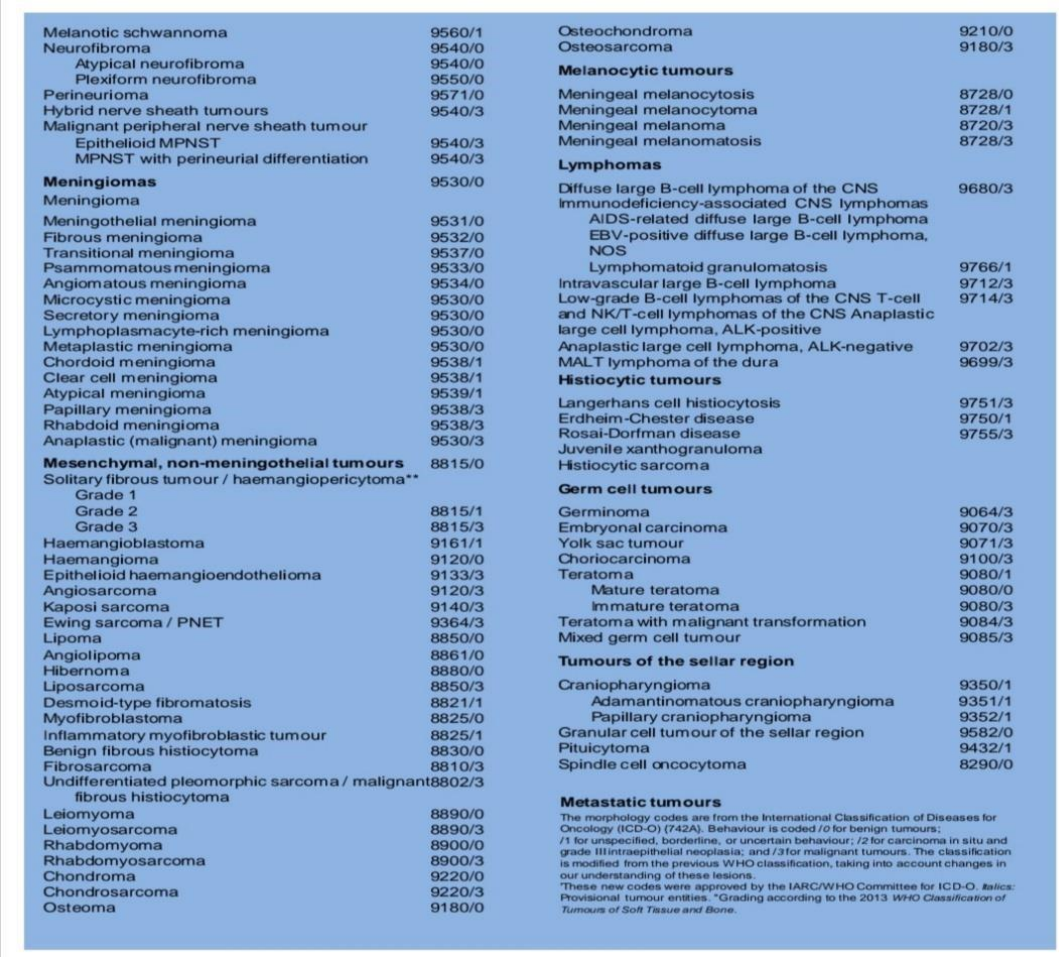
Tumour Grade	**Grade Description**
Grade I	Lesions with low proliferative potential. Cure can be achieved with complete resection
Grade II	Lesions are infiltrative in nature and have a tendency to recur. They have low proliferative potential. They may progress to malignancy
Grade III	Lesions have clear histologic evidence of malignancy. These include nuclear atypia, and brisk mitosis.
Grade IV	This applies to lesions that are cytologically malignant. They are mitotically active, demonstrate necrosis.

	They progress rapidly in the pre and postoperative periods

Tumour grade is one of the factors used in setting criteria to predict response to therapy and outcome. Other components include clinical findings (such as patient's age, performance status, and tumour location), radiological features (pattern of contrast enhancement, presence of edema), extent of surgical resection, proliferation index values, and genetic alteration.(19)

Table 2*:* WHO CNS tumour classification: Adapted from WHO classification of CNS tumours 4th Edition Revised (19)

Diffuse astrocytic and oligodendroglial tumours		**Neuronal and mixed neuronal-glial tumours**	
Diffuse astrocytoma, IDH-mutant	9400/3	Dysembryoplastic neuroepithelial tumour	9413/0
Gemistocytic astrocytoma, IDH-mutant	9411/3	Gangliocytoma	9492/0
Diffuse astrocytoma, IDH-wildtype	*9400/3*	Ganglioglioma	9505/1
Diffuse astrocytoma, NOS	9400/3	Anaplastic ganglioglioma	9505/3
		Dysplastic cerebellar gangliocytoma	
Anaplastic astrocytoma, IDH-mutant	9401/3	(Lhermitte-Duclos disease)	9493/0
Anaplastic astrocytoma, IDH-wildtype	*9401/3*	Desmoplastic infantile astrocytoma and	
Anaplastic astrocytoma, NOS	9401/3	ganglioglioma	9412/1
		Papillary glioneuronal tumour	9509/1
Glioblastoma, IDH-wildtype	9440/3	Rosette-forming glioneuronal tumour	9509/1
Giant cell glioblastoma	9441/3	*Diffuse leptomeningeal glioneuronal tumour*	
Gliosarcoma	9442/3	Central neurocytoma	9506/1
Epithelioid glioblastoma	*9440/3*	Extraventricular neurocytoma	9506/1
Glioblastoma, IDH-mutant	9445/3*	Cerebellar liponeurocytoma	9506/1
Glioblastoma, NOS	9440/3	Paraganglioma	8693/1
Diffuse midline glioma, H3 K27M-mutant	9385/3*	**Tumours of the pineal region**	
		Pineocytoma	9361/1
Oligodendroglioma, IDH-mutant and		Pineal parenchymal tumour of intermediate	
1p/19q-codeleted	9450/3	differentiation	9362/3
Oligodendroglioma, NOS	9450/3	Pineoblastoma	9362/3
		Papillary tumour of the pineal region	9395/3
Anaplastic oligodendroglioma, IDH-mutant			
and 1p/19q-codeleted	9451/3	**Embryonal tumours**	
Anaplastic oligodendroglioma, NOS	*9451/3*	Medulloblastomas, genetically defined	
		Medulloblastoma, WNT-activated	9475/3*
Oligoastrocytoma, NOS	*9382/3*	Medulloblastoma, SHH-activated and	
Anaplastic oligoastrocytoma, NOS	*9382/3*	*TP53*-mutant	9476/3*
		Medulloblastoma, SHH-activated and	
Other astrocytic tumours		*TP53*- wildtype	9471/3
Pilocytic astrocytoma	9421/1	Medulloblastoma, non-WNT/non-SHH	9477/3*
Pilomyxoid astrocytoma	9425/3	*Medulloblastoma, group 3*	
Subependymal giant cell astrocytoma	9384/1	*Medulloblastoma, group 4*	
Pleomorphic xanthoastrocytoma	9424/3	Medulloblastomas, histologically defined	
Anaplastic pleomorphic xanthoastrocytoma	9424/3	Medulloblastoma, classic	9470/3
		Medulloblastoma, desmoplastic/nodular	9471/3
Ependymal tumours		Medulloblastoma with extensive nodularity	9471/3
Subependymoma	9383/1	Medulloblastoma, large cell / anaplastic	9474/3
Myxopapillary ependymoma	9394/1	Medulloblastoma, NOS	9470/3
Ependymoma	9391/3		
Papillary ependymoma	9393/3	Embryonal tumour with multilayered rosettes,	
Clear cell ependymoma	9391/3	C19MC-altered	9478/3*
Tanycytic ependymoma	9391/3	*Embryonal tumour with multilayered*	
Ependymoma, *RELA* fusion-positive	9396/3*	*rosettes, NOS*	*9478/3*
Anaplastic ependymoma	9392/3	Medulloepithelioma	9501/3
		CNS neuroblastoma	9500/3
Other gliomas		CNS ganglioneuroblastoma	9490/3
Chordoid glioma of the third ventricle	9444/1	CNS embryonal tumour, NOS	9473/3
Angiocentric glioma	9431/1	Atypical teratoid/rhabdoid tumour	9508/3
Astroblastoma	9430/3	*CNS embryonal tumour with rhabdoid features*	*9508/3*
Choroid plexus tumours		**Tumours of the cranial and paraspinal nerves**	
Choroid plexus papilloma	9390/0	Schwannoma	9560/0
Atypical choroid plexus papilloma	9390/1	Cellular schwannoma	9560/0
Choroid plexus carcinoma	9390/3	Plexiform schwannoma	9560/0



Melanotic schwannoma	9560/1
Neurofibroma	9540/0
Atypical neurofibroma	9540/0
Plexiform neurofibroma	9550/0
Perineurioma	9571/0
Hybrid nerve sheath tumours	9540/3
Malignant peripheral nerve sheath tumour	
Epithelioid MPNST	9540/3
MPNST with perineurial differentiation	9540/3
Meningiomas	9530/0
Meningioma	
Meningothelial meningioma	9531/0
Fibrous meningioma	9532/0
Transitional meningioma	9537/0
Psammomatous meningioma	9533/0
Angiomatous meningioma	9534/0
Microcystic meningioma	9530/0
Secretory meningioma	9530/0
Lymphoplasmacyte-rich meningioma	9530/0
Metaplastic meningioma	9530/0
Chordoid meningioma	9538/1
Clear cell meningioma	9538/1
Atypical meningioma	9539/1
Papillary meningioma	9538/3
Rhabdoid meningioma	9538/3
Anaplastic (malignant) meningioma	9530/3
Mesenchymal, non-meningothelial tumours	8815/0
Solitary fibrous tumour / haemangiopericytoma**	
Grade 1	
Grade 2	8815/1
Grade 3	8815/3
Haemangioblastoma	9161/1
Haemangioma	9120/0
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma	9120/3
Kaposi sarcoma	9140/3
Ewing sarcoma / PNET	9364/3
Lipoma	8850/0
Angiolipoma	8861/0
Hibernoma	8880/0
Liposarcoma	8850/3
Desmoid-type fibromatosis	8821/1
Myofibroblastoma	8825/0
Inflammatory myofibroblastic tumour	8825/1
Benign fibrous histiocytoma	8830/0
Fibrosarcoma	8810/3
Undifferentiated pleomorphic sarcoma / malignant fibrous histiocytoma	8802/3
Leiomyoma	8890/0
Leiomyosarcoma	8890/3
Rhabdomyoma	8900/0
Rhabdomyosarcoma	8900/3
Chondroma	9220/0
Chondrosarcoma	9220/3
Osteoma	9180/0
Osteochondroma	9210/0
Osteosarcoma	9180/3
Melanocytic tumours	
Meningeal melanocytosis	8728/0
Meningeal melanocytoma	8728/1
Meningeal melanoma	8720/3
Meningeal melanomatosis	8728/3
Lymphomas	
Diffuse large B-cell lymphoma of the CNS	9680/3
Immunodeficiency-associated CNS lymphomas	
AIDS-related diffuse large B-cell lymphoma	
EBV-positive diffuse large B-cell lymphoma, NOS	
Lymphomatoid granulomatosis	9766/1
Intravascular large B-cell lymphoma	9712/3
Low-grade B-cell lymphomas of the CNS T-cell and NK/T-cell lymphomas of the CNS Anaplastic large cell lymphoma, ALK-positive	9714/3
Anaplastic large cell lymphoma, ALK-negative	9702/3
MALT lymphoma of the dura	9699/3
Histiocytic tumours	
Langerhans cell histiocytosis	9751/3
Erdheim-Chester disease	9750/1
Rosai-Dorfman disease	9755/3
Juvenile xanthogranuloma	
Histiocytic sarcoma	
Germ cell tumours	
Germinoma	9064/3
Embryonal carcinoma	9070/3
Yolk sac tumour	9071/3
Choriocarcinoma	9100/3
Teratoma	9080/1
Mature teratoma	9080/0
Immature teratoma	9080/3
Teratoma with malignant transformation	9084/3
Mixed germ cell tumour	9085/3
Tumours of the sellar region	
Craniopharyngioma	9350/1
Adamantinomatous craniopharyngioma	9351/1
Papillary craniopharyngioma	9352/1
Granular cell tumour of the sellar region	9582/0
Pituicytoma	9432/1
Spindle cell oncocytoma	8290/0
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (742A). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification, taking into account changes in our understanding of these lesions.
†These new codes were approved by the IARC/WHO Committee for ICD-O. *Italics:* Provisional tumour entities. *Grading according to the 2013 *WHO Classification of Tumours of Soft Tissue and Bone*.

2.4.2 PCF HISTOLOGICAL TUMOUR TYPES IN CHILDREN

The most common histological tumour types of the PCF in children include pilocytic astrocytoma, brainstem gliomas, medulloblastoma and ependymoma. Other less common are atypical teratoid and rhabdoid tumour (ATRT), hemangioblastoma, teratoma, metastasis and epidermoid. 30 - 55% are medulloblastomas, 25% cerebellar astrocytomas and 20% ependymomas.(2)

Pilocytic astrocytoma (PA) is a common infratentorial neoplasm in children. It is a WHO grade 1 tumour. PAs account for 5.4% of all gliomas and are common during the first two decades of life. The mean age of presentation is 7 years(20). They are the most common gliomas in children accounting for 33.2% of all gliomas(19). They are found in the cerebellum and as part of the

brainstem glioma spectrum in which case they present as dorsal exophytic brain stem glioma.(21,22)

Medulloblastoma is a malignant embryonal neuroepithelial tumour arising in the cerebellum. It is the most common CNS embryonal tumour and the most common malignant tumour of childhood. It has histologic and molecular classification regardless of which, it is regarded a WHO grade 4 tumour. It accounts for 25% of all intracranial tumours with a median age of diagnosis at 9 years and peaks at 3 and 7 years. It may grow into the fourth ventricle or remains within the cerebellar parenchyma. It has a propensity to spread through CSF pathways.(19,23–25).

Ependymoma is a circumscribed intra axial tumour of glial origin made of uniform small cells with pseudorosettes. They are graded into WHO grade I, II or III based on cellular atypia. They account for 6.8% of all neuroepithelial tumours. 60% are found in the posterior fossa. Infratentorial ependymomas are more common in children, accounting for 30% of all CNS tumours. The mean age of presentation is 6.4 years. The male to female ratio is 2:1.(19,26). They are usually compressive rather than infiltrative lesions with slow growth.(27)

Brainstem gliomas are more common in paediatric than adults patients. They affect the midbrain, pons, medulla and cervicomedullary junction. They account 10 -20 % of CNS tumours in children. They are either diffuse intrinsic pontine glioma (DIPG) 75%, dorsal exophytic glioma 10 - 20% or cervicomedullary glioma 5 – 10%. The mean age of presentation is 6.5 years with equal male:female ratio.(28,29)

Atypical teratoid/rhabdoid tumour (AT/RT) is a malignant embryonal tumour that displays poorly differentiated elements and frequently includes rhabdoid cells. They are most frequently seen in young children. They correspond to WHO grade IV. They account for 1 – 2% of paediatric brain

tumours and are exceedingly rare in adults. The high preponderance in children < 3 years makes them account for 10% of tumours in infants. They are more common in male patients. They are found both in the supratentorial and infratentorial compartment in a ratio of 4:3. Infratentorial ATRT is found in the cerebellar hemispheres, cerebellopontine angle and brainstem.(19,30)

Hemangioblastoma is a WHO grade 1 tumour that consists of neoplastic stromal cells and abundant small vessels. It is slow growing and is mostly seen in adults. In children the occurrence is lower than 1/1000000. When they occur 50 – 65% are sporadic while 35 – 50% are in association with Von Hippel Lindau (VHL) syndrome. They are more common in adolescence. In the infratentorial compartment they affect the brainstem or cerebellum.(19,31–33)

Brain metastases which are the most common PCF tumour in adults, account for only 2% of all paediatric CNS tumours(34). Infratentorially, these metastases may be in the brainstem accounting for 5% of all brain metastasis and cerebellar hemispheres accounting for 15% of all brain metastasis. Dural and leptomeningeal metastasis is much less common and associated with extension into other compartments(35). The primary sources in children are hematopoietic cancers such as leukaemia and lymphoma and non – hematopoietic sources, such as germ cell tumours, rhabdomyosarcoma, Ewing sarcoma, neuroblastoma and osteosarcoma. In up to 10% of patients with brain metastasis no primary tumour is found at presentation.(19,36–40)

2.5 PATHOPHYSIOLOGY OF PCF TUMOURS

There are numerous neural structures within the limited space in the posterior cranial fossa, majorly, the brainstem, cerebellum and cranial nerves. Tumours occurring in this compartment produce mass effect with compression of structures. Additionally, some infiltrate these structures and cause dysfunction. The signs and symptoms that arise are not specific to the tumour but the effect it has on the contents within the compartment.

A lesion within the PCF causes an increase in compartmental pressure. This leads to herniation of structures, cerebellar tonsils, through the foramen magnum, often referred to as tonsillar herniation. Tonsillar herniation causes obstruction of the flow of CSF at the craniovertebral junction causing obstructive hydrocephalus. The cardiac and respiratory centres are found in the pons and medulla. These structures are compressed against the clivus when there is increased PCF compartment pressure. Moreover, blood vessels supplying this vital structure within the brainstem are compressed leading to hypoxic injury. Tonsillar herniation and its consequence can lead to decreased consciousness, impaired respiration and cardiac function, and sudden death. Compression of the cerebellum and cranial nerves leads to neuronal dysfunction and associated clinical signs and symptoms. (41)

2.6 CLINICAL PRESENTATION OF PCF TUMOURS

A triad of headache, nausea/vomiting and gait imbalance is the most common manifestation of posterior fossa tumours. The signs include: -

Cerebellar signs: Ataxia – this is a disturbance in performance of voluntary motor acts smoothly. It may affect the tracts, as seen in cerebellar lesion in the midline, the limb, typically seen in cerebellar lesion within the hemispheres or gait. Ataxia includes many other disorders of synergistic muscle movement and other signs related to ataxia include decomposition of movement, dysmetria, dysdiadochokinesia, and past pointing. *Hypotonia and reflexes* – reduced tone and reflexes is apparent in the lower limbs in cerebellar disease. Hyperactive reflexes and spasticity (increased tone) is found in brainstem compression or infiltration. *Intention tremor* – the tremors are non-rhythmic and appear with action. *Torticollis and neck stiffness* – torticollis is a hyperkinesia associated with contraction of neck musculature. Among other conditions, it may be a sign of PCF tumour. Neck stiffness results from extension of tumour into the foramen magnum

and/or tonsillar herniation. *Weakness* - compression of descending corticospinal tracts leads to upper motor neuron weakness. *Eye abnormalities* – these include abducens nerve palsy, papilledema, reduced visual acuity and nystagmus. Nystagmus is rapid rhythmic involuntary movement of the eyes. PCF tumours can cause various types of nystagmus including upbeat or down beat nystagmus.(1,5,29)

Symptoms include: -

Features of raised ICP and hydrocephalus: Headache – This is the most common symptom in patients with PCF tumour. Its occurrence was reported at 63.6%(6). The headache is insidious and intermittent. It is worse in the morning and after a period of recumbence. This is attributed to hypoventilation during sleep. The headache due to PCF tumours is associated with neck pain, stiffness and head tilt, findings that indicate the mass is causing compression at foramen magnum. In children younger than 2 years, it manifests as irritability, poor response to handling and prolonged inconsolable crying. *Nausea and vomiting* – This occurs due to generalized increased intracranial pressure, irritation of the vagal nucleus in the medulla and area postrema. Some relief to the headache occurs following vomiting. *Lethargy* – This was reported in 28.8%(6). Low energy levels may be the only symptom indicating increased intracranial pressure. *Strabismus* – This result from abducens nerve palsy. It is preceded by diplopia. *Enlarging head size attributable to hydrocephalus in children* – Progressive macrocephaly is a common presenting symptom in children. Radiological evidence of hydrocephalus is present in more than 80% of children with PCF tumour. Hydrocephalus contributes to development of raised intracranial pressure. *Seizures* – PCF tumours rarely cause seizures.(1,5,42)

Certain patterns of presentation may be more common in some tumours due to location and growth pattern. The pattern of signs and symptoms in a cerebellar hemispheric tumour is different from

that of midline cerebellar tumours. Brainstem tumours will involve the reticular activating system producing drowsiness and loss of attention in patients. Additionally, they will involve cranial nerve nuclei and white matter tracts, producing cranial nerve palsies and hemiparesis early in the presentation. Cerebellar and 4th ventricular tumours produce mass effect and obstruct CSF flow causing hydrocephalus early in the disease. Children less than 2 years of age present with nonspecific signs and symptoms that can pass for any other childhood and infant illness. These include irritability, vomiting, unsteadiness, lethargy, macrocephaly, ataxia, hypereflexia, and cranial nerve palsies. (1,5,6)

Signs and symptoms of infratentorial tumours can be grouped as features of raised intracranial pressure (this include headache, nausea, vomiting, increasing head size, blurred vision and neck stiffness), cranial nerve dysfunction (this include diplopia, dysphagia, dyspnoea, loss of hearing, strabismus), cerebellar dysfunction (such as ataxia, hypotonia, dysdiadochokinesia, hypotonia, intention tremors and pendulous reflexes), motor signs (due to involvement of pyramidal tracts) and hydrocephalus (2,4). Additionally, the patient GCS and KPS are taken as part of evaluation.

2.7 EVALUATION OF PATIENTS WITH PCF TUMOURS

Thorough history, neurologic examination and imaging are the mainstay of evaluation of patients with infratentorial tumours. Multiple signs and symptoms may be apparent in patients with posterior fossa tumours. The pattern of signs and symptom occurrence, duration and progression help in understanding the location of the lesion within the posterior fossa. Brainstem lesions will, in addition to long tract signs and cranial nerve palsies, cause drowsiness and inattention that are due to involvement of the reticular formation; purely cerebellar lesions will cause cerebellar signs such as intention tremors, ataxia, and slurred speech and the associated mass effects will lead to obstructive hydrocephalus thus causing features of raised intracranial pressure.(42)

2.7.1 ASSESSMENT OF FUNCTIONAL STATUS

The pre-treatment patient condition is important in determining prognosis, that is, beyond the local burden of the disease, the general patient outlook and quality of life thereafter. Patient performance status has long been used to assess the patient pre-operatively and compare with post-operative treatment, and to guide physicians in having candid discussions on outcome with patients and next of kin. In adults, the Karnofsky performance score (KPS) index is used. Initially adapted in the management of cancer patients with chemotherapeutic agent, the KPS has widely been used in pre and post-operative assessment of neurosurgical patients(43). KPS describes the patients' functional status as an 11-point scale with corresponding percentages ranging from 100% (where there is no evidence of disease and symptom) to 0 (death). KPS is therefore a decision aid on modality of treatment to be instituted and also has a role in prognosis(43,44). The table below show the various elements in the scale.

Table 3: Karnofsky Performance Score

Condition	% value	Level of functional capacity
Able to carry on normal activity and to work; no special care needed	100	No complaints; no evidence of disease
	90	Able to carry on normal activity; minor signs or symptoms of disease
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	70	Cares for self; unable to carry on normal activity or to do active work
	60	Requires occasional assistance but is able to care for most personal needs
	50	Requires considerable assistance and frequent medical care
	40	Disabled; requires special care and assistance

Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	30	Severely disabled; hospital admission indicated although death not imminent
	20	Very sick; hospital admission necessary; active supportive treatment necessary
	10	Moribund; fatal processes progressing rapidly
	0	Dead

In patients less than 16 years, the Lansky performance status (LPS) is used. It is a play – performance scale administered to parents and produces reproducible and reliable functional status. It uses the parents' description of the child to assess response to treatment. The LPS is favourable in children because certain information necessary for completing the KPS are directly solicited from the patient which would not be feasible in children (45). The table below depicts the LPS: -

Table 4: Lansky performance status

Condition	**% value**	**Level of functional capacity**
Able to carry out normal activity; no special care needed	100	Fully active
	90	Minor restriction in physically strenuous play
	80	Restricted in physical play. Tires more easily. Otherwise active.
Mild to moderate restriction	70	Both greater restriction of, and less time spent in active play
	60	Ambulatory only 50% of the time, limited active play with assistance or supervision
	50	Considerable assistance required for any active play, fully able to engage in quiet play.
Moderate to severe restriction	40	Able to initiate quiet activities
	30	Needs considerable assistance for quiet activity
	20	Limited by very passive activities initiated by others

	10	Completely disabled, not even passive play.

2.7.2 RADIOLOGICAL EVALUATION

Optimal imaging of the posterior fossa is achieved by use of magnetic resonance imaging (MRI). MRI is best because it has multi planar capability, improved soft tissue contrast and resolution and lacks scanning artefacts that are apparent on computed tomography (CT) scans due to the osseous skull base. Additional benefits of MRI include multiple sequences that characterise tumour cellularity, possible grade, necrosis, and haemorrhage. Its use extends beyond diagnosis to surgical and radiation therapy planning. MRI is expensive and takes time to perform. As such, CT scans have a role in screening emergent situations and follow up post operatively. CT scans are also complementary to MRI in highlighting features such as calcification and remodelling of bone which is not apparent on MRI. (46,47)

2.8 SURGERY FOR PCF TUMOURS

2.8.1 GOALS OF SURGERY

Surgery is often inevitable for most PCF tumours due the emergent pattern of symptoms. Gross total resection is the appropriate treatment for all PCF tumours however may not be achievable. Depending on the radiological assessment of tumour, that is, tumour size, location, extent and association with the infratentorial structures; an appropriate surgical strategy is chosen

The goals are surgical decompression of the posterior fossa structures, relief of obstructive hydrocephalus and to obtain tissue for histologic diagnosis. In patients with medulloblastomas and ependymomas, the extent of resection provides the best treatment outcome for the patients.

2.8.2 SURGICAL APPROACH

PCF surgery can be done in the supine, prone, sitting, lateral and park bench position. Depending on the epicentre of the tumour as guided by radiologic investigation the appropriate position is chosen. The supine position is useful for accessing lesions in the CPA. In this position the head is

turned to the opposite side. The prone position provides access to the midline structures. The lateral position allows gravity assisted blood and CSF drainage and affords excellent access to unilateral structures. In the park bench, the patient is placed in a semi-prone position with the head flexed and facing the floor, it is a modification of the lateral position. It provides access to midline structures while avoiding the prone position. The sitting position has several advantages, there is improved surgical access, gravity assisted drainage of blood and CSF and decreased intracranial pressure. This positioning is associated with intraoperative venous air embolism.(48)

A craniotomy or a craniectomy may be completed to open the PCF. The craniotomy is referred to as a sub-occipital craniotomy. The bone is usually replaced upon completion of the operation. When craniectomy is done the bone is not replaced. Both approaches are equally effective for exposure. However, sub-occipital craniectomy is associated with more post-operative complications such as CSF leak and pain. (49,50)

Tumour removal is done microscopically through transcortical, transvermian, telovelar or retrosigmoid approach depending on the anatomic location, size and extent of the tumour within the PCF. Tumour within the cerebellar cortex is removed by a transcortical approach. The transvermian approach involves splitting the cerebellar vermis to access the tumour. Telovelar approach is through natural planes without cerebellar splitting and has fewer complications.(17,51)

The immediate post-operative care is continued in the intensive care unit. The decision to extubate or maintain patient on intubation is made. Preoperative patient condition, intraoperative events and postoperative imaging are important factors to consider when planning postoperative management. The duration of stay in the intensive care unit and the duration of hospital stay vary from patient to patient. This is affected by development of post-surgical complications.(52)

2.9 EARLY SURGICAL OUTCOME AND COMPLICATIONS

In patients who have had PCF surgery for PCF tumours, early surgical outcome can be evaluated by assessing morbidity and mortality. The post-operative period regarded as early is variable, however the immediate post-operative period is considered to extend up to 4 weeks postoperatively. The morbidity parameters include duration of intubation, length of stay in intensive care unit, length of hospital stay, development of complications, change in KPS/LPS, and need for reoperation.(7)

Posterior cranial fossa surgery is associated with certain complications that contribute to morbidity and mortality. Complications are either intraoperative or postoperative. These include haemorrhage, injury to structures on the floor of the fourth ventricle and brainstem, injury to cranial nerves, CSF leak, wound infection, meningitis, hydrocephalus and cerebellar mutism (7,48,52,53). These complications have the potential to affect the duration of ICU and hospital stay and the long-term quality of life of the patients. Injury to the lower cranial nerves affects muscle control of the upper aero-digestive tract that usually leads to patients' dependence on tracheostomy tubes and feeding tubes post operatively.

The occurrence of these complications has been reported by Dubey et al in a 10 year retrospective study, the overall complication rate was 31.8% and overall mortality rate related to surgery was 2.6%. Individual complications included CSF leak 13%, wound infection 7%, meningitis 9%, cranial nerve palsies 4.8% and hydrocephalus at 4.2%, cerebellar hematoma 3% and cerebellar mutism 1.2%. (54)

Kanna et al showed the mean duration of hospital stay in children after posterior fossa surgery varied between craniectomy and craniotomy. They reported increased complication rate and duration of stay in patients who underwent craniectomy (17.5 days) compared to craniotomy (14

days). CSF leak, CSF infection, wound infection and hydrocephalus were the most common complications. (50)

Ali et al in a 2-year retrospective study in Egypt, reported 20% of patients developed post-operative hydrocephalus, 13.3% developed CSF leak, 10% bulbar palsy and mortality was 6.6%. Other complications included wound infection and mutism.(17)

Surgical techniques, anaesthesia, aseptic techniques, biological understanding of individual tumours in the PCF, critical care, and diagnostic technology have improved over the years since Cushing's first series. The outcome of posterior cranial fossa surgery has in turn significantly improved. Upon gross total resection, there is up to a 60% 5year survival rate of patients with PCF tumours and up to 80% in certain cases(55).

CHAPTER 3: JUSTIFICATION, RESEARCH QUESTION AND OBJECTIVES

3.0 JUSTIFICATION

Paediatric PCF tumours are a common neurosurgical indication at Kenyatta National Hospital. There is paucity of recent information regarding the early surgical outcome of management of these tumours. This study will provide information on early surgical outcomes that will help improve surgical management and post-surgical care of posterior fossa tumours.

3.1 RESEARCH QUESTION

What is the clinical pattern of presentation and early surgical outcome of PCF tumours in children at KNH?

3.2 BROAD OBJECTIVE

To describe clinicopathologic features and early surgical outcomes of children managed surgically for PCF tumours in KNH

3.3 SPECIFIC OBJECTIVES

1. To describe the pattern of clinical presentation in children with PCF tumours at KNH
2. To describe the imaging pattern of PCF tumours in children at presentation to KNH
3. To describe the histopathological tumour types of PCF tumours managed surgically in children at KNH
4. To determine early surgical outcomes and complications following surgery in children with PCF at KNH

CHAPTER 4: METHODOLOGY

4.1 STUDY DESIGN

Prospective cohort study

4.2 STUDY AREA AND STUDY SITES

Kenyatta National Hospital Accident and Emergency Department, Paediatric Emergency Unit, Paediatric Neurosurgery Clinic, Paediatric wards, Adult Medical wards, Operating theatre, Neurosurgical ward 4C, Paediatric intensive care unit, Intensive care unit, Pathology department, and KNH records department

4.3 STUDY POPULATION

Children aged 12 years and below managed surgically at KNH for PCF tumours

4.4 INCLUSION CRITERIA

Children with a clinical and/or radiologic diagnosis of PCF tumour managed surgically at KNH who consent to participate in the study during the study period.

4.5 EXCLUSION CRITERIA

The exclusion criteria were patients with recurrent PCF tumours

4.6 SAMPLE SIZE

The sample size was computed to test the hypothesis that the anticipated incidence rate of complications in PCF tumours is 50% at the 5% level of significance. A study in Pakistan had estimated the incidence rate of complications at 30% (56). The desired power of this study was 90% for detecting a true incidence rate of 50% and will reject the null hypothesis if the true value is greater than 30% (one-sided test).

The required sample size was determined as follows(57);

$$n= (z_{1-\alpha}\lambda_0 + z_{1-\beta}\lambda_a)_2/(\lambda_0-\lambda_a)_2$$

Where;

$z_{1-\alpha}$ = z statistic at 95% confidence level

(1.96) $z_{1-\beta}$= Power of the test (90%) α =

Level of significance (5%)

λ_a = Anticipated incidence rate of complications (50%) λ_0

=Test value of the incidence rate of complications (30%)

Subtituting the parameters in the formula, the required minimum sample size was 33.

4.7 STUDY PROCEDURE

Children aged 0 -12 years with a clinical diagnosis/radiologic diagnosis of PCF tumour were identified from study areas, the cut-off age for children at KNH is 12 years. Consent was taken from the parents, guardian or next of kin. Data on clinical information was sought by the principal investigator, which included patient demographics, features of raised intracranial pressure (which are a combination some or all of the following: headache, irritability, nausea and vomiting, blurred vision), Long tract symptoms and signs (which include weakness, spasticity, broad based ataxic gait, cerebellar signs, and hydrocephalus. An admission GCS score and KPS were ascertained and recorded.

The preoperative imaging data on radiological pattern was extracted from the CT scan and MRI reports, which had been reported by a qualified radiologist. In the absence of such a report, the images were discussed in the neuroradiology conference and findings documented and captured. The CT scan data included location (epicenter) of tumour (which was described as cerebellar hemisphere, vermis, 4th ventricle, brainstem, and CPA); extension of tumour from the epicenter (to cerebellar hemisphere, brainstem, CPA, foramina of Luschka and Magendie); attenuation on

non-contrast CT (described as hypodense, isodense or hyperdense); and the pattern of contrast enhancement on Contrast Enhanced CT described as either present or absent, and if present homogenous, heterogenous or rim enhancement.

The MRI data from the report included T1 and T2 imaging characteristics described as hypointense, isointense, hyperintense or mixed intensity; T1 with contrast characteristics which include presence and pattern of contrast uptake described as mild, moderate or avid with homogenous, heterogenous, or rim/ring pattern; location (epicenter) of tumour; extension of tumour to other anatomic regions in the PCF and characteristic of diffusion weighted image as either restriction or no restriction.

The patient was prepared for surgery according to the standard pre – operative work up at KNH. The principal investigator extracted information on the surgery from the theatre notes and discussion with primary surgeon. This included date of surgical procedure; the surgical procedures were CSF diversion procedure and definitive tumour surgery. Type of bone exposure, craniotomy or craniectomy. Type of surgical approach, telovelar, transvermian, retrosigmoid, or transcortical. Extent of resection gross total resection, maximal safe resection or biopsy.

Postoperatively, the patient was followed up and patient care was observed in the intensive care unit and neurosurgical ward. The end points to follow-up were death, discharge or 30 days postoperatively. The following information was captured, length of intubation post-operatively in days, the length of stay in ICU, the length of hospital stays, and complication occurrence (the complications included CSF leak, wound infection, hydrocephalus, and wound dehiscence. The GCS and KPS at discharge were also noted.

The histopathology report from the pathologist was used to capture data on histological tumour type and the post-operative scan report was used to capture the extent of resection.

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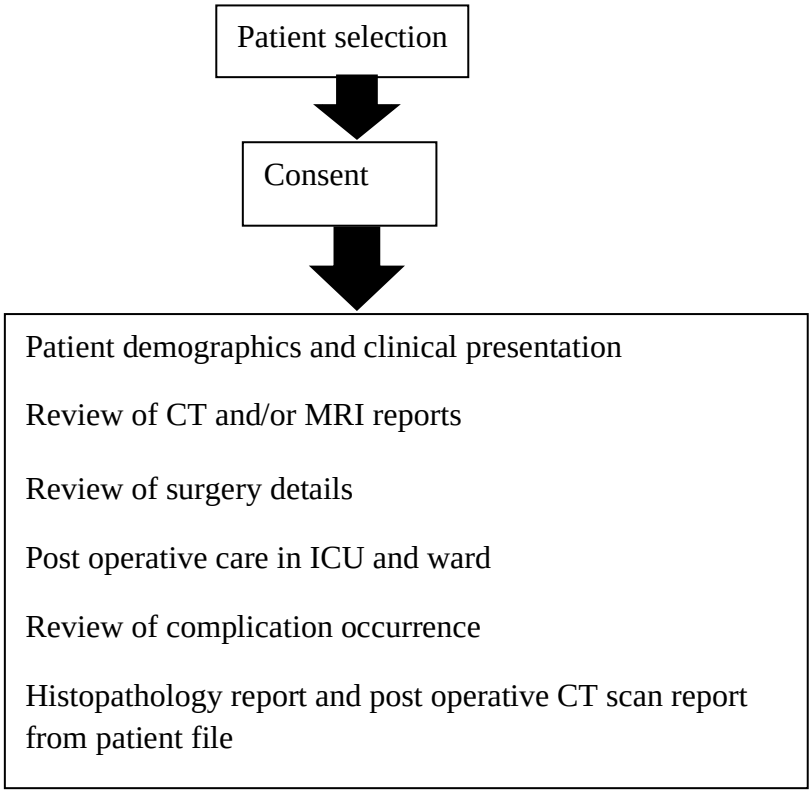


4.8 STUDY MATERIALS

- Data collection tool.

- Patients' record files at KNH, radiology reports and histopathology report

4.9 DATA MANAGEMENT

The data was captured in a Microsoft Excel data sheet that had information on the patient's details, presentation patterns, radiologic patterns, intraoperative and postoperative details including length of stay and complications. Patient details were coded (de-identified). The raw data was stored securely by the lead investigator in a password protected computer to maintain patient confidentiality.

4.10 DATA ANALYSIS

Demographic and clinical data were summarized using means or medians for continuous variables and proportions for categorical variables. The pattern of clinical presentation in children with PCF tumours was analyzed using proportions based on features of raised ICP and long tract signs and symptoms among others. Proportions were used to describe the imaging patterns of PCF tumours in children at presentation based on CT scan and MRI data. The histopathological tumour types of PCF tumours managed surgically were described using proportions based on surgical data from theatre notes and histopathology reports.

Continuous outcomes like length of stay (length of intubation, length of ICU stay, and length of hospital stay) and GCS were summarized using means and medians while categorical outcomes like incidence rate of complications from surgical outcomes of PCF tumours were summarized using proportions and presented as pie charts.

At bivariate analysis, Independent t tests was used to correlate length of stay outcomes with independent variables, while chi-square tests (or Fisher's exact test) were used to test for association between categorical independent variables and complications of PCF tumours following surgical interventions.

At multivariable level, linear regression was to evaluate effects of covariates on length of stay, and logistic regression analysis was used to evaluate the effect of covariates on complications of PCF tumours. Statistical significance was interpreted at 5% level (p value < 0.05). Analysis was done using Stata version 16(58)

4.11 ETHICAL CONSIDERATIONS

Institutional consent was obtained from the Department of Surgery, University of Nairobi (UON) and Kenyatta National Hospital Ethics and Research Committee. Informed consent was obtained

from the next of kin of the patients. Confidentiality was ensured by non-disclosure of data collected to third parties, data collected was used for this research purposes only and anonymity was ensured by use of patient codes for identification instead of participants' names. Patients had a right to withdraw from the study at any stage.

Patients' confidentiality was observed by coding patients' names and the codes subsequently used for analysis, reference, and presentation of the findings of this study. The data and information were available only to the statisticians and the lead investigator. All raw data, both soft and hard copies will be destroyed after presentation of the results.

4.12 QUALITY ASSURANCE AND CONTROL MEASURES

The principal investigator carried out all the interviews and physical examinations. The data collection tools were cross checked for completeness and any missing entries corrected. The quantitative and qualitative data collected were cross checked for any inconsistencies and outliers rectified. All CT, MRI and radiology reports were discussed by an appointed radiologist from UON/KNH radiology department. All histopathology specimens and reports thus generated were processed in the UON/KNH histopathology laboratory by an appointed pathologist.

4.13 STUDY RESULTS DISSEMINATION PLAN

The study findings will be presented to the department of surgery, University library, and Kenyatta National Hospital. Manuscripts will also be submitted to scientific journals for publication or conference presentations.

4.14 STUDY LIMITATION

The ideal would be to cover a much longer period (e.g. 5 years), but due to budgetary and time constraints, the study was limited to one year. However, we are confident that results will achieve objectives of the study and will provide useful, actionable information to guide diagnosis and

improved management of this condition in our setup. It will also serve as a baseline study for future enquiry on the subject.

The study is limited to Kenyatta National Hospital hence the results may not represent what happens in the whole country

CHAPTER 5: RESULTS

There were 32 patients whose data was collected; however, 4 patients were excluded for failure to meet the inclusion criteria. Therefore, final analysis was done for 28 patients.

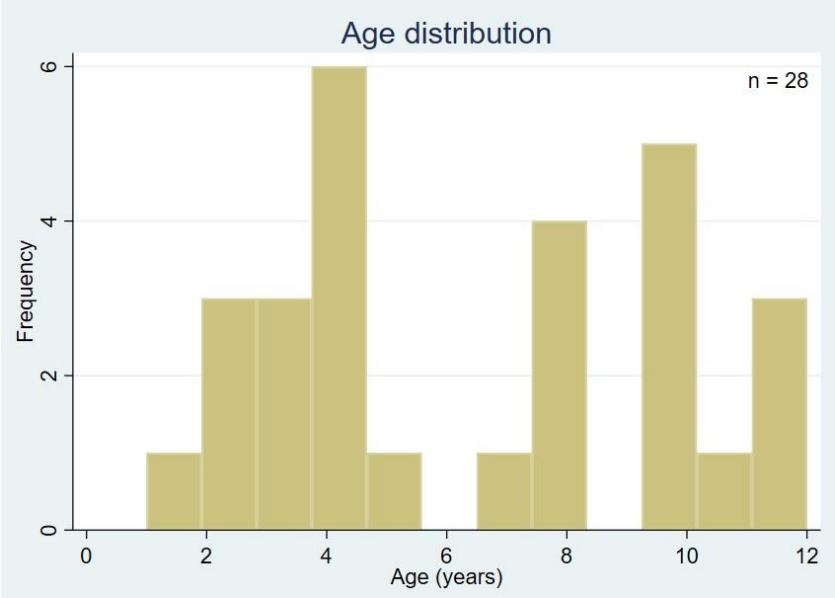
PATIENT'S DEMOGRAPHICS

A. PATIENT DETAILS

Age

The mean age of the patients was 6.46 years (SD 3.60, Range 1-12) (Figure 2)

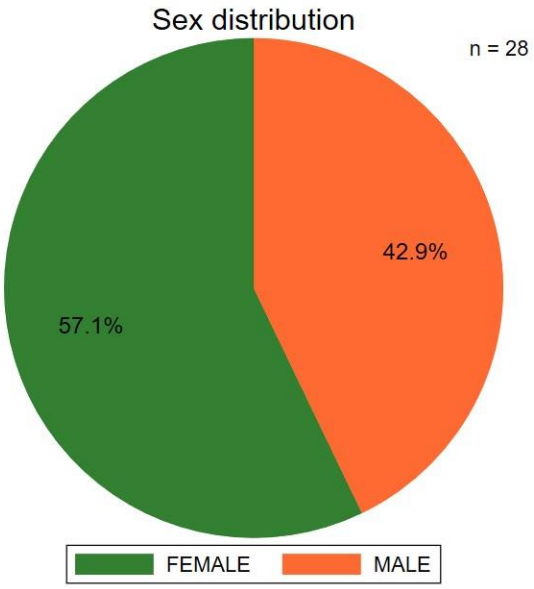
Figure 2: Histogram showing age distribution



Sex

There were more female patients 16 (57.1%) who had posterior cranial fossa tumours than the males who were 12 (42.9%) as shown by the figure below.

Figure 3: Pie chart showing sex distribution among patients

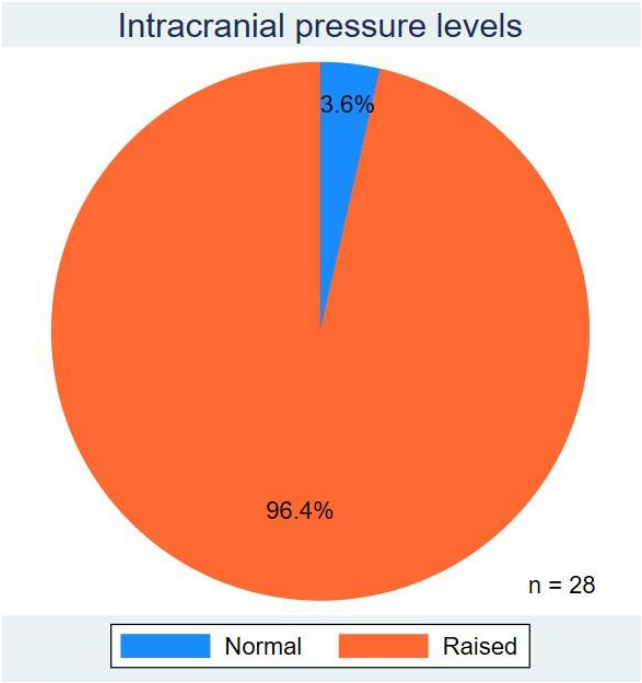


B. CLINICAL PATTERN: SYMPTOMS AND SIGNS

Raised ICP

Out of 28 participants, 27 (96.4%) had raised ICP compared to 1 (3.6%) who had normal intracranial pressure.

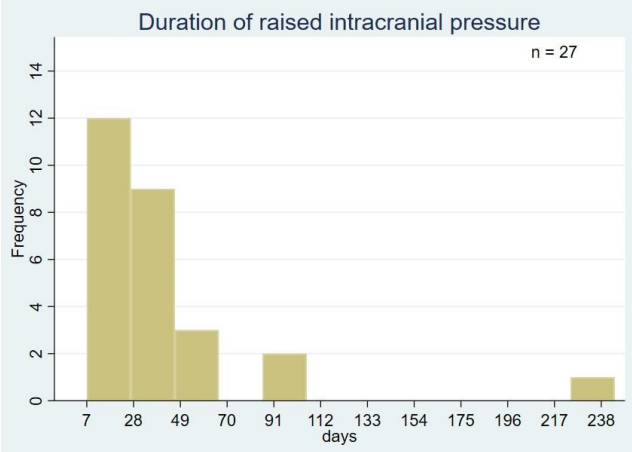
Figure 4 : Intracranial pressure levels



Duration of raised intracranial pressure

The mean number of days for the raised intracranial pressure among the 27 patients with the condition was 40 days (SD 46.9, Range 7-244).

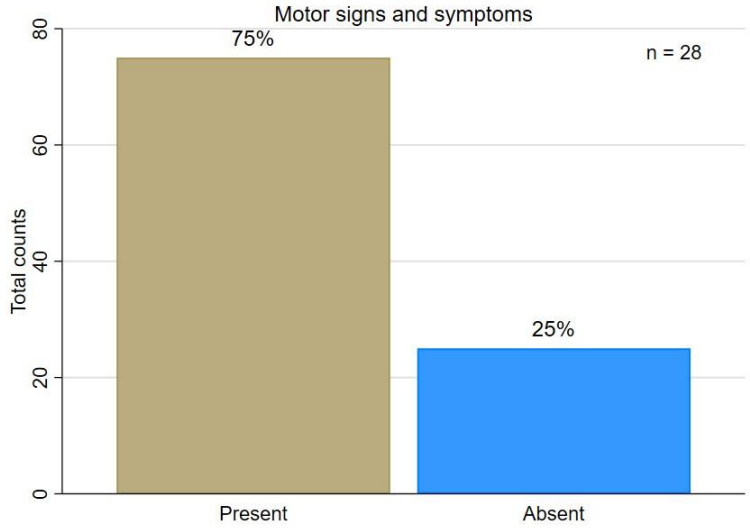
Figure 5: Duration of raised Intracranial pressure



Motor Signs

Presence of motor signs and symptoms among the study group was seen in 21 patients (75%) while 7 (25%) of the patients had none.

Figure 6: Showing motor signs and symptoms

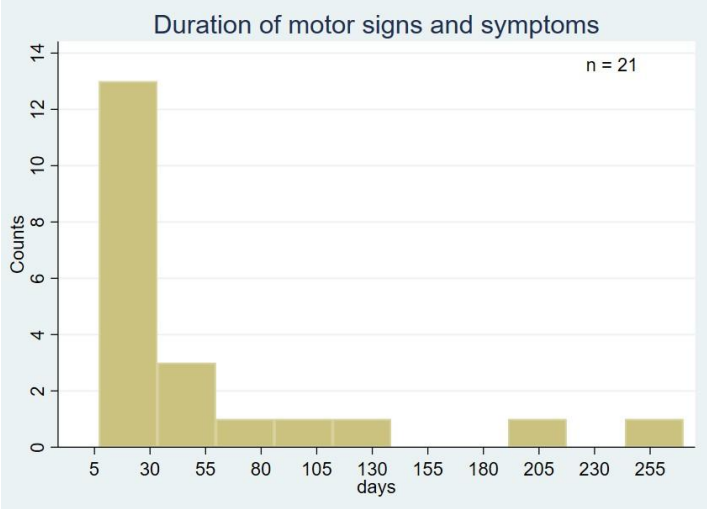


Duration of the Motor Signs and Symptoms

The mean number of days to presentation of motor signs and symptoms was 54.1 days (SD 68.7,

Range 7 – 270, median 25)

Figure 7: Duration of motor signs and symptoms



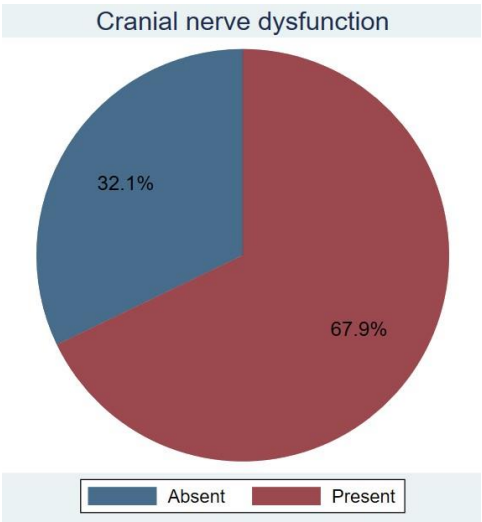
Cerebellar Signs

All the PCF patients (100%) had cerebellar signs.

Cranial nerve dysfunction

The patients who experienced cranial nerve dysfunction were 19 (67.9%) whereas 9 (32.1%) had no cranial nerve dysfunction.

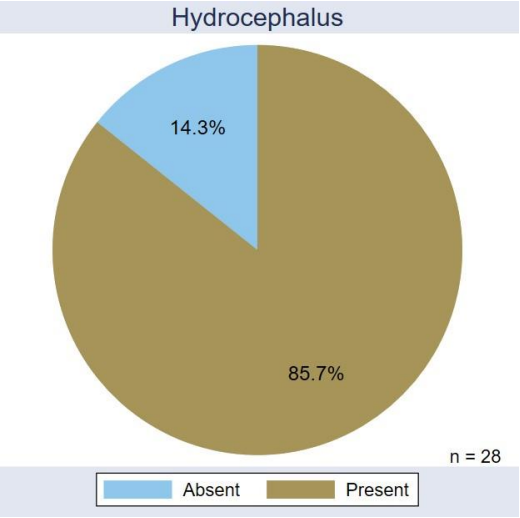
Figure 8: Pie chart showing cranial nerve dysfunction occurrence



Hydrocephalus

Out of the 28 patients 24 (85.7%) had hydrocephalus while 4 (14.3%) did not.

Figure 9: Pie chart showing presence of hydrocephalus



GCS and KPS at admission

Majority of patients, 22 had a GCS of 13 – 15 with 5 having a score of 9 -12 and only 1 patient with a score of less than 9. Majority had a Karnofsky performance status score of 61-70.

Table 5: Admission GCS and KPS

Variable	Category	Frequency	Percent
GCS	13-15 9-12 0-8	22 5 1	78.6 17.9 3.6
KPS	41-50 51-60 61-70 71-80 91-100	1 6 11 6 4	3.6 21.4 39.3 21.4 14.3

Table 6: Summary table of clinical and demographic characteristics

Variable	Category	Frequency	Percent
Sex	Male Female	12 16	42.9 57.1
Raised ICP	Present Absent	27 1	96.4 3.6
Motor signs	Present Absent	21 7	75 25
Cerebellar signs	Present Absent	28 0	100
Cranial nerve dysfunction	Present Absent	19 9	67.9 32.1
Hydrocephalus	Present Absent	24 4	85.7 4
GCS	13-15 9-12 0-8	22 5 1	78.6 17.9 3.6
KPS	41-50 51-60 61-70 71-80 91-100	1 6 11 6 4	3.6 21.4 39.3 21.4 14.3

C.RADIOLOGIC PATTERN

Scans Done

Most of the patients 17 (60.7%) had both CT and MRI scans done. The patients who had the MRI alone were 5 (17.9%) while those who had only CT scan were6 (21.4%).

Figure 10: Types of scans done

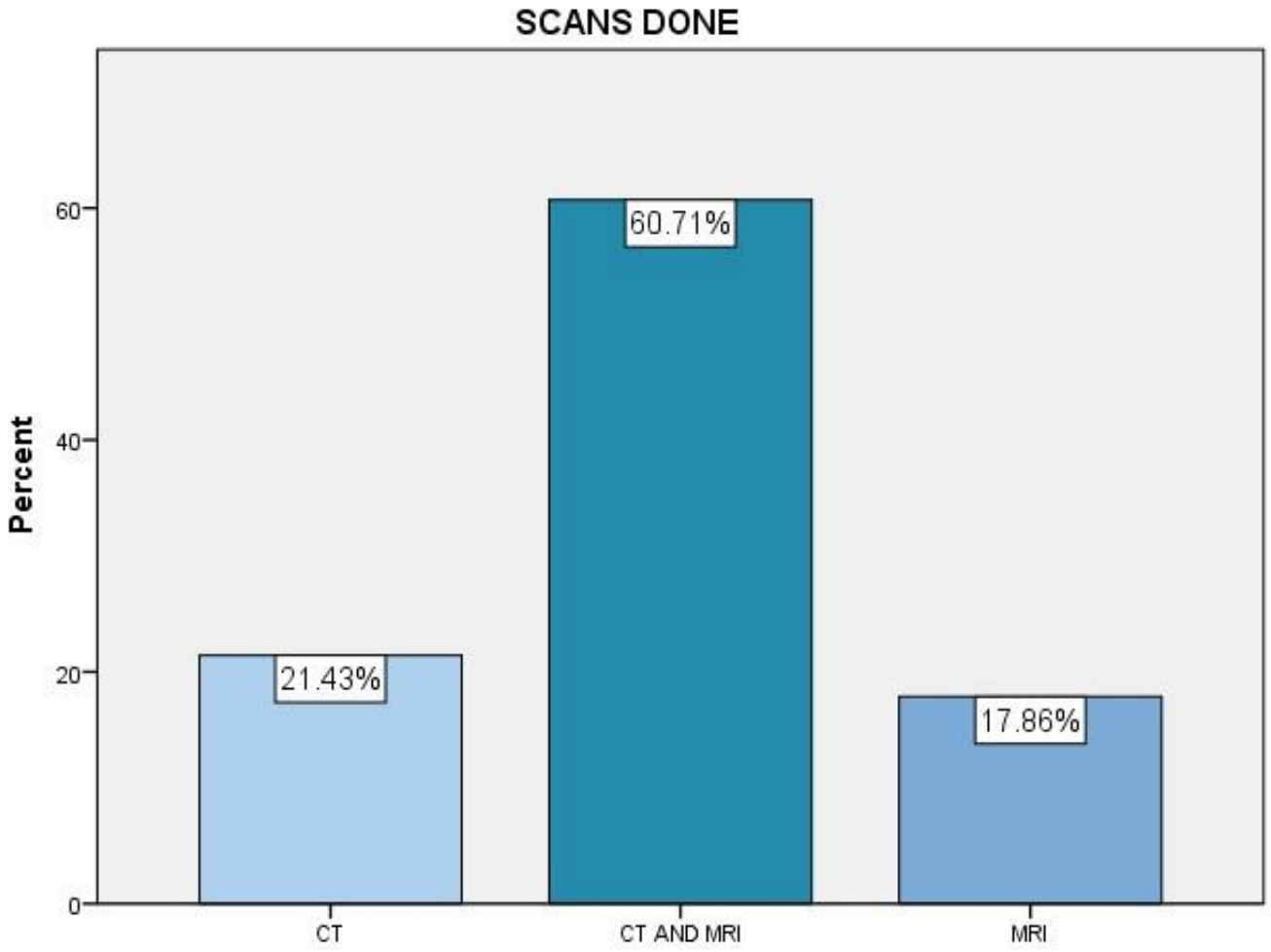

SCANS DONE
Percent
60
40
20
0
60.71%
21.43%
17.86%
CT
CT AND MRI
MRI

Table 7: CT patterns

CT scan imaging attributes	Categories	Tumour type on histopathology					
			Medulloblastoma	**Pilocytic astrocytoma**	**Ependymoma**	**Brainstem glioma**	**Hemangioblastoma**
Location Epicenter	Vermis	16 (69.6%)	7 (77.8)	6 (85.7%)	2 (50%)		1 (100%)
	4th Ventricle	5(21.7%)	2 (22.2)		2 (50%)	1 (50%)	
	Cerebral hemisphere	1(4.3%)		1 (14.3%)			
	Brainstem	1(4.3%)				1 (50%)	
	Total	**23(100%)**	**9**	**7**	**4**	**2**	**1**
Extension	Present	73.9%	6 (66.7)	5 (71.4)	3 (75%)	2 (100%)	1 (100%)
	Absent	26.1%	3 (33.3)	2 (28.6)	1 (25%)		
	Total	**23**	**9**	**7**	**4**	**2**	**1**
NCCT	Hyperdense		8 (88.9)		2 (50)		
	Isodense		1 (11.1)		1 (25)		
	Hypodense			7 (100)		2 (100)	
	Mixed density				1 (25)		1 (100)
	Total		**9**	**7**	**4**	**2**	
Pattern of CECT	Homogenous		5 (62.5)		1 (25)		
	Heterogenous		3 (37.5)	4 (57.1)	3 (75)		1 (100)
	RIM			3 (42.9)			
	Total		**8**	**7**	**4**		**1**

Table 8: MRI patterns

	Categories	**Tumor type on histopathology**

MRI scan imaging attributes			**Medulloblastoma**	**Pilocytic astrocytoma**	**Ependymoma**	**Brainstem glioma**	**Hemangioblastoma**
Location Epicenter	Vermis	10(45.5 %)	6 (60)	2 (33.3)	1 (33.3)		1 (100)
	4th Ventricle	6(27.3 %)	3 (30)	1 (16.7)	2 (66.7)		
	Cerebral hemisphere	4(18.2 %)	1 (10)	3 (50)			
	Brainstem	2(9.1%)				2 (100)	
	Total	**22**	**10**	**6**	**3**	**2**	**1**
Extension	Present	68.2%	6 (60)	3 (50)	3 (100)	2 (100)	1 (100)
	Absent	31.8%	4 (40)	3 (50)			
	Total		**10**	**6**	**3**	**2**	**1**
T1 WEIGHTED	Hyperintense						
	Isointense		4 (40)		1 (33.3)		1 (100)
	Hypointense		5 (50)	6 (100)	1 (33.3)	2 (100)	
	Mixed intensity		1 (10)		1 (33.3)		
	Total		**10**	**6**	**3**	**2**	**1**
T2 WEIGHTED	Hyperintense		5 (50)	5 (83.3)	2 (66.7)	2 (100)	

	Hypointense		1 (10)				
	Isointense		3 (30)				
	Mixed Intensity		1 (10)	1 (16.7)	1 (33.3)		1 (100)
	Total		**10**	**6**	**3**	**2**	**1**
T1 + GD	Heterogenous		9 (90)	2 (33.3)	1 (33.3)		1 (100)
	Homogenous		1 (10)	2 (33.3)	2 (66.7)		
	RIM			2 (33.3)		2 (100)	
	Total		**10**	**6**	**3**	**2**	**1**
DWI	Restriction		7 (77.8%)	1 (25)			
	No Restriction		2 (22.2%)	3 (75)	1 (100)		
	Total		**9**	**4**	**1**		

Tumour Size on MRI

The tumour sizes on MRI for varied histological tumour types are indicated in the table below. **Table 9: Tumour size based on histopathological diagnosis**

Tumour type	Observations	Mean	SD	Min	Max
Medulloblastoma	10	133	89.7	23	331
Pilocytic astrocytoma	6	147.5	36.7	97	190
Ependymoma	4	177.75	23.5	143	195
Brainstem glioma	2	106.5	26.2	88	125
Hemangioblastoma	1	184	-	184	184

Diagnosis on Imaging

Medulloblastoma was the most common diagnosis on MRI at 50.00%.

Table 10*:***Imaging diagnosis**

Imaging diagnosis	Frequency	Percentage
MEDULLOBLASTOMA	14	50.00
EPENDYMOMA	7	25.00
PILOCYTIC A	3	10.71
BSG	2	7.14
ATRT	1	3.57
HEMANGIOBLASTOMA	1	3.57
Total	28	100.00

HISTOPATHOLOGICAL DIAGNOSIS

Table 11: Histopathological diagnosis

Tumour type	Frequency	Percent
Medulloblastoma	12	42.9
Pilocytic Astrocytoma	9	32.1
Ependymoma	4	14.3
Brainstem glioma	2	7.1
Hemangioblastoma	1	3.6
Total	**28**	**100**

AGREEMENT BETWEEN IMAGING AND HISTOPATHOLOGICAL DIAGNOSIS

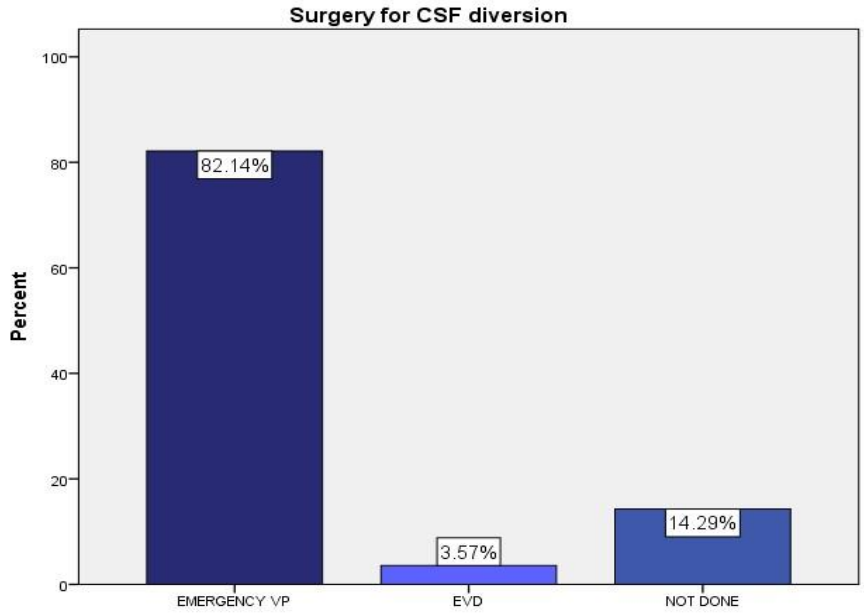
Cohen's Kappa was carried out to assess agreement between the MRI and the histopathological diagnosis. There was substantial agreement between the two methods in determining the diagnosis with an agreement level of 97.4%, $p<0.001$ and Kappa statistic 0.68 which indicated moderate level of agreement between the two methods.

D. SURGERY

The most common type of surgery done for CSF diversion was Emergency VP shunt insertion 23 (82.14%) followed by EVD 1 (13.6%). However, 4 (14.3%) did not have CSF diversion prior to definitive surgery.

Figure

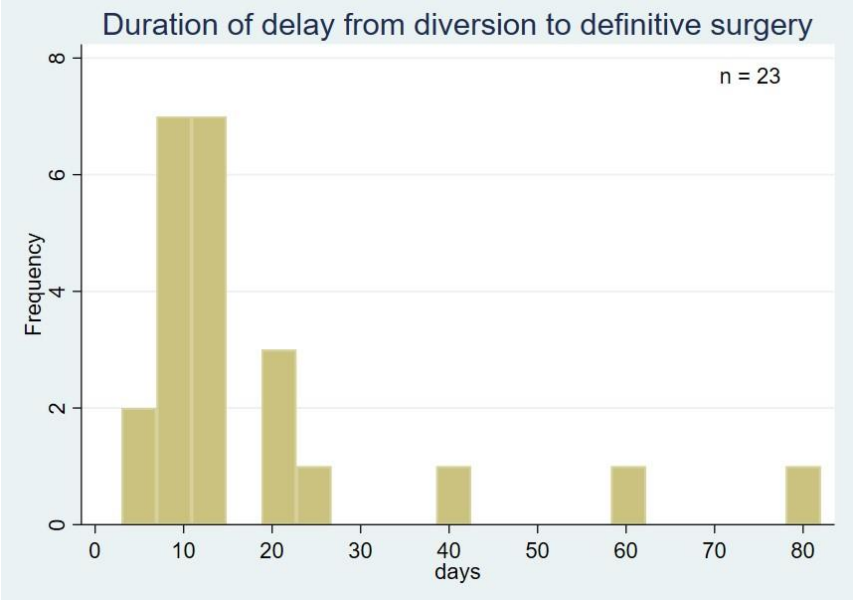
11: Surgery for CSF diversion



DURATION OF DELAY FROM DIVERSION TO DEFINITIVE SURGERY

Mean duration from diversion to definitive surgery from 23 observations was 18.3 days (SD 18.7, Range 3 – 82, median 12)

Figure 12: Duration of delay from CSF diversion to definitive surgery



SURGICAL APPROACHES

The most common surgical approach used was telovelar in 12 (42.9%) of study participants, followed by Transvermian at 11(39.3%) and Transcortical at 5 (17.9%) of study subjects.

Table 12: The surgical approaches for PCF tumors used.

Surgical Approach	Frequency	Percent
Telovelar	12	42.9
Transvermian	11	39.3
Transcortical	5	17.9
Total	**28**	**100**

BONY EXPOSURE METHOD AND OCCURRENCE OF COMPLICATIONS

Method of bony exposure as compared to occurrence of complications **Table 13: Method of bony exposure compared to occurrence of complications.**

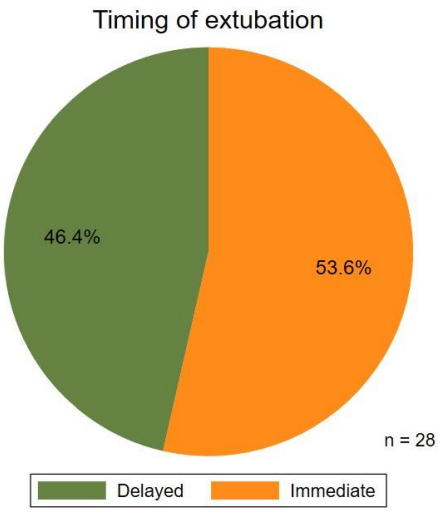
Bony exposure method	Complications occurrence		
	Present	Absent	Total
Craniectomy	1 (5.3)		1 (3.6)
Craniotomy+C1 laminectomy	3 (15.8)	3 (33.3)	3 (21.4)
Craniotomy	15 (79.0)	6 (66.7)	21 (75)
Total	19	9	28

EXTUBATION TIMING

The patients who were extubated immediately post op were 15 (53.6%) as compared to 13 (46.4%) who were extubated later in the ICU (Figure 13)

13: Pie chart showing immediate vs delayed extubation

Figure



LENGTH OF EXTUBATION

Patients with delayed extubation, were 13, mean duration to extubation was 11.5 days (SD 11.9, Range 1 – 42, Median 9).

LENGTH OF ICU STAY AMONG DELAYED EXTUBATION

For the 13 patients with delayed extubation, the mean length of ICU stay was 18.4 days (SD 15.7, Range 4 – 54, Median 12) whereas the 15 patients who underwent immediate extubation had a mean ICU stay of 3.8 days (SD 3.5, Range 1 – 16, Median 3).

OVERALL DURATION OF ICU STAY

Among the 28 patients, mean duration of ICU stay was 10.6 days, (SD 13.1, Range 1-54, Median 4). Long duration of ICU stay defined as greater than 72 hours was associated with increased risk of occurrence of complications, HR 6.0 (1.6-23.0), p=.009, under 5 years, HR 4.2 (1.2 – 14.4), p=0.020, mortality HR 4.5 (1.2 – 16.6), p=.022,

Figure

14: Kaplan Meir survival estimate of duration of ICU stay by complications

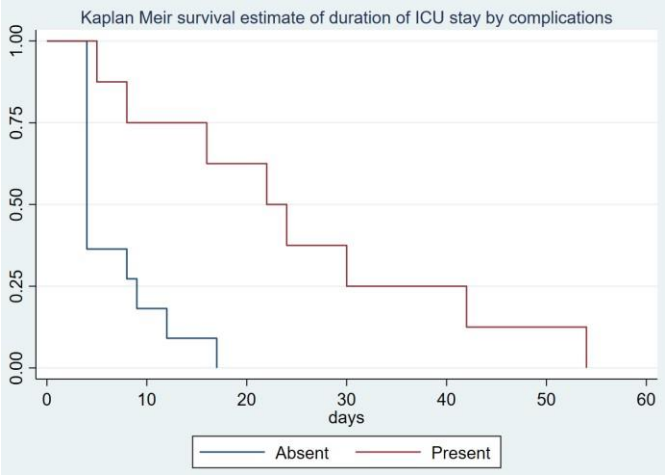
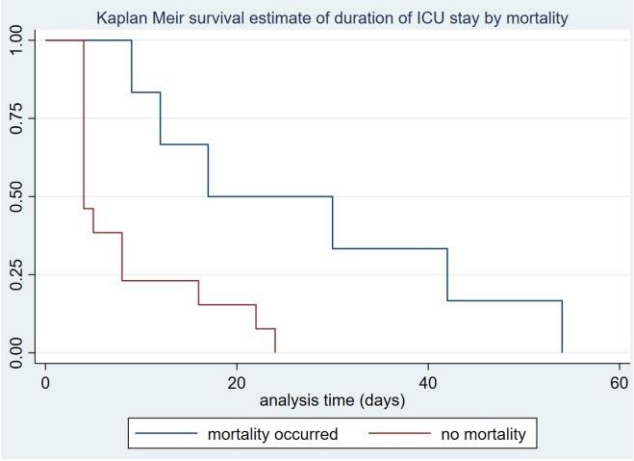
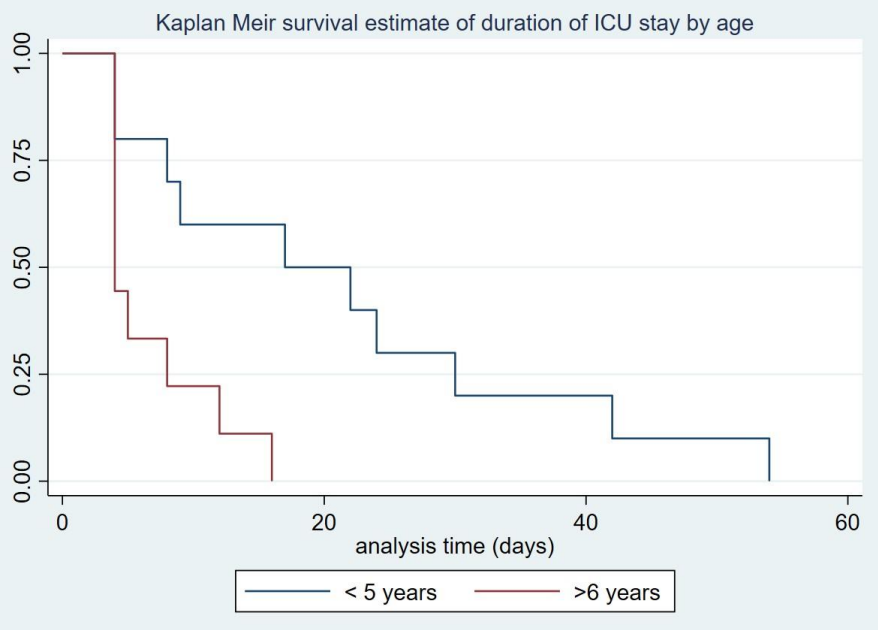


Figure 15: Kaplan Meir survival estimate of duration of ICU stay by mortality



16: Kaplan Meir survival estimate of duration of ICU stay by age

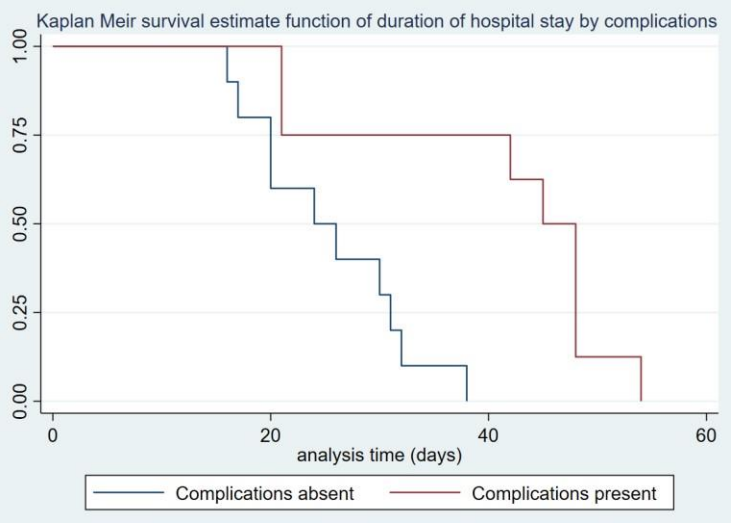
Figure



OVERALL DURATION OF HOSPITAL STAY

Among the 28 patients, mean duration of hospital stay was 24 days, (SD 15.2, Range 4 - 54, Median 20.5). Long hospital stay duration was associated with occurrence of complications, HR 8.0 (1.7 – 38.3), p=.009

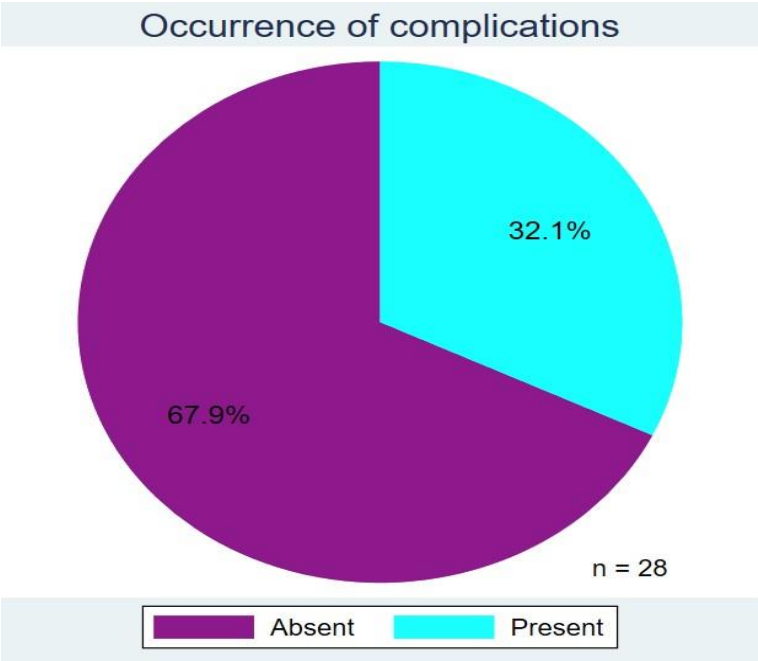
Figure 17: Kaplan Meir survival function of duration of hospital stay by complications



RATES OF COMPLICATIONS

Among the 28 study participants, complications were present in 9 (32.1%) as compared to 19 (67.9%) who had no complications (Figure 18).

Figure 18: Pie chart showing occurrence of complications.

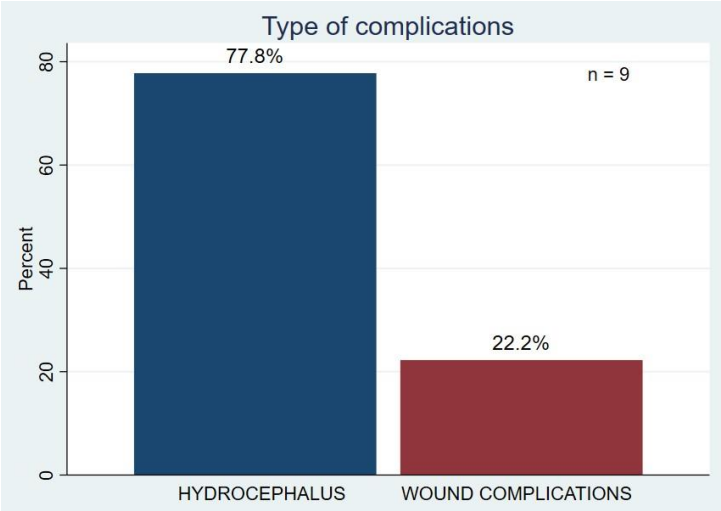


TYPE OF COMPLICATION

Among the 9 with complications, 7 (77.8%) had hydrocephalus compared to 2 (22.2%) without complications.

19: Bar graph showing type of complications

Figure



FACTORS ASSOCIATED WITH OCCURRENCE OF COMPLICATIONS

Factors associated with occurrence of complications included age (p=.34) with older participants having no complications compared to younger participants, Mean age 7.3 vs 4.7

Other factors associated with complications included duration of hospital stay (p<.001) and length of ICU stay (p<0.001)

Duration of signs and symptoms, tumour location and size, presence of tumour extension, histopathological diagnosis, extent of resection and surgical approach were not significantly associated with occurrence of complications in the bivariate analysis.

According to a multivariate logistic regression model, age and duration of hospital stay were the strongest predictors of complications.

Table 14: Logistic regression model for risk of complication

Risk factor for complication	Adjusted Odds ratio	95% confidence Interval	P value

Age	157	36.8 – 673.8	0.001
Duration of hospital stay	2.9	1.5 – 5.7	0.002
Duration of ICU stay	1.1	0.4 – 2.8	0.890

RATE OF MORTALITY

The overall rate of mortality among the 28 study participants was 6 / 26 (23.1%).

The risk factors associated with occurrence of mortality in the bivariate analysis included extubation status (p=0.015), age (p=0.041), Karnofsky score (p=0.013), duration of ICU stay (p<0.001). Other factors were not associated with occurrence of mortality.

In the multivariate analysis, the strongest risk factors for mortality were length of ICU stay and low Karnofsky performance score

Table 15: Logistic regression model for risk or mortality

Risk factor for complication	**Adjusted Odds ratio**	**95% confidence Interval**	**P value**
Duration of ICU stay	1.3	1.01 – 1.62	0.038
Admission Karnofsky	1.4	1.3 – 1.5	0.001
Age	1.3	0.7 – 2.3	0.479
Extubation status	26.5	0.4 – 1633.4	0.119

CHANGE IN GCS AND KPS BEFORE AND AFTER DISCHARGE

Table 16: Change noted in GCS and KPS at discharge

Variable	Category	Obs	Mean	Std. Err.	Std. Dev.	95% Conf. Interval	P value
GCS	At admission	28	13.4	0.35	1.85	12.7 – 14.1	0.004
	At discharge	22	14.7	0.15	0.72	14.4 – 15.0	
KPS	At admission	28	73.6	2.53	13.4	68.4 – 78.8	0.001
	At discharge	22	90	1.47	6.9	86.9 – 93.1	

COMPARISON BETWEEN EXTENT OF RESECTION AND POST-OPERATIVE SCAN

The level of agreement between the extent of resection and post op scan was 80.8%, p<.001, Kappa statistic 0.64 which implies substantial agreement.

CHAPTER 6: DISCUSSION

PCF tumours account for 54 – 70% of brain tumours in children worldwide, thus contributing significantly to cancer related deaths among children. In Kenya, studies have shown an occurrence of 34 to 50%(18,59)

6.1 PATTERN OF CLINICAL PRESENTATION

In this study, 28 patients with PCF tumors were followed up at KNH, of these, 16 (57.1%) were female while 12 (42.9%) were male, with a male to female ratio of 1:1.3. Across the literature the male to female ratio is variable. Female preponderance compares to findings of other similar studies on PCF tumors(8)(16). In some studies however, there was a higher male to female ratio(2)

The mean age at presentation was 6.49 years in this study. This is similar to other studies both local and international that report a mean age range of 6 to 8 years(60)(15). Elhassan et al showed a mean age of 7.9 years(16).

In this study, the clinical pattern of presentation was grouped into presentation with cerebellar signs (100%), features of raised ICP (96.4%), hydrocephalus (85.7%), motor signs (75%), and cranial nerve dysfunction (67.9%). Kadali et al showed a similar pattern of presentation but with a slightly different occurrence, in their study, features of raised ICP were most common at 70.3%, hydrocephalus at 70.3%, cerebellar signs at 57%, cranial nerve palsy at 46% and motor signs at 27%(2).

The duration of occurrence of features of raised ICP and motor signs prior to diagnosis was evaluated in this study. Features of raised ICP were present for an average of 40 days (1.5 months) with a wide range 7 days to 244 days; motor signs and symptoms had been present for an average of 54.1 days (2.5 months). The long duration of symptoms prior to presentation has been attributed

to diagnostic delays due to similar presentation pattern of other diseases. Additionally, the pediatric skull provides compliance with increasing intracranial pressure. This is much better than prior studies in the same institution. This long durations of signs and symptoms is apparent in childhood brain tumours and constitutes the pre-diagnostic symptomatic interval (PSI). PSI was evaluated by Tracy et al and was found to have a mean of 7.7 +- 9.6months for all childhood brain tumours(18). Wanyoike et al found the mean duration of symptoms to be 3.7 months and median interval of 3.7 months for PCF tumors. The duration to diagnosis of PCF tumours is shorter due to early symptom occurrence(8).

6.2 IMAGING PATTERN OF PCF TUMOUR

In this study, 60.71% had both CT and MRI scans, 21.4% had CT scan only, and 17.9% had MRI scans only. All patients had some form of radiological investigation prior to management. PCF is best evaluated using MRI scans due to the limitations of CT scan. However, in some situations management decision and management strategy can be made using CT.

6.2.1 PATTERN ON CT SCAN

In the 23 (82.1%) patients who had a CT scan done, the most common tumour location (epicenter) was the vermis (69.6%), 4th Ventricle (21.7%), cerebellar hemisphere (4.3%) and brainstem (4.3%) in that order. Extension of tumour beyond the epicenter was documented in 73.9%. The series by Kadali found similar results where the vermis and cerebellar hemisphere were the most common location followed by 4th ventricle(2)

Based on the histopathological diagnosis, 77.8% of medulloblastomas were in the vermis while 22.2% were in the 4th ventricle, this places the tumour in the midline position of PCF. This location for medulloblastoma has also been reported by other authors, Donati et al reported an 80% midline occurrence(46,47). Pilocytic astrocytomas, 85.7% were in the vermis and 14.3% were in the

cerebellar hemisphere. Ependymomas were reported to occur equally in the vermis and 4th ventricle at 50%. Extension of tumor beyond the epicenter was noted in all tumour types. Medulloblastoma and pilocytic astrocytoma mostly displayed extension (64.7%) this is because they accounted for most of the tumours noted.

On NCCT, 88.9% of medulloblastoma were hyperdense while 11.1% were hypodense, all pilocytic astrocytomas were hypodense. This is consistent with findings from other radiological studies such that a hyperdense midline PCF tumour is highly likely to be a medulloblastoma. Plaza et al reports 89% of cases are hyperdense on NCCT(61). Ependymomas were hyperdense in 50%, isodense in 25%, and mixed density in 25% of the patients. In general, Kadali reports that majority of PCF are hypodense on CT with contrast enhancement(2).

6.2.2 PATTERN ON MRI

Twenty-two (78.6%) of patients had an MRI done. The most common location of the tumour was in the vermis in 45.5% followed by 4th ventricular in 27.3%, cerebellar hemisphere in 18.2% and brainstem in 9.1%. Most medulloblastomas (60%) were in the vermis while most pilocytic astrocytomas were in the cerebellar hemisphere (50%).

All ependymomas and brainstem gliomas extended beyond the epicenter on MRI evaluation, while only 60% of medulloblastomas and 50% of PA reported extension beyond the tumour epicenter.

6.2.3 TUMOR SIZE

The overall average tumor size in the PCF was 144.5cc. The average size of medulloblastoma was 133cc (23 – 331), pilocytic astrocytoma was 147.5cc (97 – 190), and ependymoma was 177.75cc (143 – 195)

6.3 HISTOPATHOLOGICAL TUMOUR TYPES

The most common tumors in this study were medulloblastoma (42.9%), PA (32.1%) and ependymoma (14.3%). These are the main tumour types found in the posterior fossa as reported in other studies(4,8,9,59,62). In a retrospective study by Wanyoike et al at KNH, medulloblastoma and pilocytic astrocytoma occurred equally at 37.9%.(8). Based on Sutton et al, a similar histopathologic pattern was seen, with medulloblastoma being most common at 36%, PA at 28% and ependymoma at 4%(63).

When compared to the preoperative diagnosis on imaging, there was substantial agreement of 97.4% ($p < .001$) and Kappa statistic 0.68 indicating a moderate level of agreement. Similar levels of agreement were reported by Omuok et al in a study at the same institution. (59).

6.4 EARLY SURGICAL OUTCOMES AND COMPLICATIONS FOLLOWING SURGERY OF PCF TUMOURS

This study evaluated various outcome measures for children with PCF tumours. These were, the duration of hospital stays, duration of stay in intensive care unit, occurrence of complication, change in pre- and post-operative GCS and KPS, and 30-day mortality.

In addition to definitive surgery, 85.7% of patient had a CSF diversion procedure. Majority had emergency ventriculoperitoneal shunting and 3.57% had intra operative EVD placement during definitive surgery. CSF diversion is often inevitable as obstructive hydrocephalus accompanies clinical and emergent presentation. In this study, all patients who had hydrocephalus had a CSF diversion procedure. Emergent tumor removal relieves obstructive hydrocephalus in PCF tumours. At KNH, ventriculoperitoneal shunting is offered as an emergency procedure for PCF tumour due to logistical constraints while tumour surgery is done electively. Bernt et al, reported an overall cure rate of symptomatic HCP of 87% by tumor removal but noted much lower cure rates for

patients with medulloblastoma and ependymoma who required VP shunting(64). 75% of our patients had a preoperative MRI diagnosis of medulloblastoma and ependymoma. Notably, ventriculoperitoneal shunting is a safe method of CSF diversion prior to surgery that reduces morbidity and mortality during definitive surgery(65).

All patients were admitted to ICU post operatively. The overall mean duration of ICU stay was 10.6 days and a median of 4 days. This duration was affected by whether the patient had immediate post-operative extubation or delayed extubation. Fifteen (53.6% of) patients were extubated immediately, the average duration of ICU stay was 3.8 days with a median 3 day stay. Thirteen (46.4%) patients had delayed extubation, with an average ICU stay of 18.4 days and a median of 12 days. Additionally, longer duration of ICU stay was associated with occurrence of complications and increased mortality.

The mean duration of hospital stay was 24 days, with a median of 20 days. Long hospital stay was associated with occurrence of complication. This is close to what Kanna et al reported, a mean duration of 14 days for patients who had craniotomy and 17.5 days for patients who had craniectomy(66).

In this study the surgery significantly improved GCS and KPS. The mean KPS when reviewed at discharge or 30-day follow up was 90 compared to 70 at admission. This represents excellent surgical outcome that was seen in 22 of 28 (78.5%) patients. In a study by Shaikh et al, 66 patients were reviewed and concluded good surgical outcome in 77%, similar results were reported by Emara et al at 77.3%.(67,68). The subjective intraoperative assessment of extent of resection was found to have an 80.8% level of agreement when compared to post-operative imaging.

Complications were reported in 9 patients (32.1%). This compares to a study done by Dubey et al reported overall complication of 31.2% like this study. The most common complication was hydrocephalus (77.8%) and wound complications (22.2%).

In this study, all patients with hydrocephalus as a complication had emergency VP shunting prior to definitive surgery. This means that postoperative hydrocephalus was due to shunt failure. A study by Emara et al on surgical outcomes of PCF tumour reported similar outcome with the most reported complication being shunt obstruction at 18.2%(67). Dubey et al also reported hydrocephalus being a common type of complication following PCF tumor surgery(54).

Factors noted to be associated with occurrence of complications in this study were age and duration of hospital and ICU stay. Mean age for complication occurrence was 4.7 years. Older children showed no significant occurrence of complication.

The overall mortality rate was 23.1%. The 30-day mortality was 10.7%. In this study, mortality was associated with delayed extubation, young age, lower KPS at admission and longer duration of ICU stay, with lower KPS and longer ICU stay being the greater risk factors. Shaikh et al reported a mortality of 4.87% in their study which included adult patients and grouped them into extra axial and intraaxial tumours. They also identified age >10 years and tumour type as factors affecting good outcome.

6.5 CONCLUSION

This study shows that, more female patients presented with posterior fossa tumors. Cerebellar signs and symptoms were the most common pattern of clinical presentation. The symptom duration ranged from 1.5 to 2.5 months. The most common imaging location was the vermis.

Medulloblastoma was the most common histological tumour type. Length of stay in ICU and hospital was long and was associated with complication occurrence. The overall complication rate was 32.1% and the 30-day mortality was 10%.

6.6 RECOMMENDATION

1. Follow up beyond 30 days to evaluate patient survival.
2. Study outcome of other treatments that are part of management such as radiotherapy and chemotherapy
3. An extensive pathological study on the various molecular aspects of posterior fossa tumours in line with the 2016 WHO CNS tumor classification 4. A review on cost of surgical treatment

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APPENDICES

APPENDIX 1: STUDY TOOL

FORM NUMBER_____

A. PATIENT DETAILS

1. Date of Birth _____
2. Age (in years) _____
3. Sex_____
4. Date of first consultation_____

B. CLINICAL PATTERN: SYMPTOMS AND SIGNS

B.1 Features of raised intracranial pressure: Y/N Duration(days) _____

(*nausea, vomiting, headache, blurred vision, neck stiffness*)

B.2 Motor (Long tracts) signs and symptoms: Y/N Duration(days)_____

(*weakness, ataxia, spasticity*)

B.3 Cerebellar signs: Y/N

(*Ataxia (limb or truncal), past-pointing, dysdiadochokinesia, intention tremor*)

B.5 Cranial nerve dysfunction: Y/N

(*diplopia, strabismus, dysphagia, difficulty swallowing*)

B.6 Hydrocephalus: Y/N

B.7 GCS at admission_____

B.8 KPS at admission_____

C. RADIOLOGIC PATTERN

Imaging modality □CT scan □MRI

If CT is available: Tumour details from Imaging Report	
Location (Epicentre) of tumour in PCF (*choose one)*	□ Cerebellar hemisphere □ Vermis □ 4th ventricle □ Brainstem □ CPA
Extension of tumour beyond epicentre	□ Cerebellar hemisphere Y/N □ 4th ventricle Y/N □ Foramen Luschka Y/N □ Foramen Magendie Y/N
Attenuation of lesion Non contrast CT	□ Hypodense □ Isodense □ Hyperdense □ Mixed intensity
Enhancement on CT *(choose one)*	Yes No <u>Pattern of enhancement reported</u> □ Homogenous □ Heterogenous □ Rim/ring
Diagnosis on CT	

If MRI is available: Tumour details from imaging Report	
Location (Epicentre) of lesion (*choose one)*	☐ Cerebellar hemisphere ☐ Vermis ☐ 4th ventricle ☐ Brainstem ☐ CPA
Extension of lesion from epicentre	• Cerebellar hemisphere Y/N • 4th ventricle Y/N • Foramen Luschka Y/N • Foramen Magendie Y/N
T1 weighted characteristic *(choose one)*	☐ Hypointense ☐ Isointense ☐ Hyperintense ☐ Mixed intensity
T2 weighted characteristic (*choose one)*	☐ Hypointense ☐ Isointense ☐ Hypeintense ☐ Mixed intensity
T1 + contrast	Present Absent ☐ Pattern ☐ Homogenous ☐ Heterogenous ☐ Rim
Diffusion weighted imaging	☐ Restriction ☐ No restriction ☐ Not reported
Tumour size	Volume in cc_____ Size not given

Diagnosis on MRI	

D.

SURGERY

Surgery for CSF diversion	
Surgery for CSF diversion	Yes No If yes: *(choose one of the operations)* □ Emergency VP shunting □ EVD Date of procedure:_____
Definitive surgery	
Date of surgery	
Bony Exposure	□ Craniotomy

(choose one)	☐ Craniectomy ☐ C1 laminectomy
Surgical Approach (*choose one*)	☐ Telovelar ☐ Transvermian ☐ Transcortical ☐ Retrosigmoid
Extent of resection reported *(choose one)*	☐ Gross total resection ☐ Maximal safe resection ☐ Biopsy

E. POSTOPERATIVE MANAGEMENT

Successful extubation post-surgery (dayon of surgery)	Yes No If No Length of intubation in days: _____
Duration of ICU stay (days)	_____
Duration of hospital stay (days)	_____
Death or Discharge	
Complications in post- in operative hospital stay	☐ CSF leak ☐ Wound infection ☐ Hydrocephalus ☐ Wound breakdown ☐ Skull Pressure sores ☐ Aseptic meningitis ☐ External ventricular drain complication
GCS at Discharge	
KPS at Discharge	
Post-operative imaging	GTR: Yes or No

Histological diagnosis from pathologist report	

APPENDIX 2: PARENTAL CONSENT FORM - ENGLISH

Patient's Study Number: _____ Date:_____ Study

Title:

CLINICOPATHOLOGICAL FEATURES AND EARLY SURGICAL OUTCOME OF POSTERIOR CRANIAL FOSSA TUMOURS IN CHILDREN AT KENYATTA NATIONAL HOSPITAL

Investigators/Researchers:

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Department of Surgery, University of Nairobi

Dr. Karanja Susan Wanjiru MBChB, M. Med Neurosurgery (UKZN), FC Neurosurgery (SA) Consultant Neurosurgeon, Kenyatta National Hospital

Introduction:

The purpose of this consent form is to provide you with the information you will need to assist you in deciding whether you want to participate in the study. This process is called 'Informed Consent'. Please read this consent information carefully and ask any questions or seek clarification on any matter concerning the study with which you are uncertain.

What is the purpose of the study?

Posterior cranial fossa tumors are debilitating, incapacitating neurological condition causing significant morbidity and mortality. This study aims at providing information that will guide the development of strategies that will help in identification and managing posterior cranial fossa tumors in our setup with a view of improving management and outcomes.

What will happen if you decide you want to be in this research study?

If you agree your child to participate in this study, the following things will happen:

You will be interviewed by the investigator in a private area where you feel comfortable answering questions. The interview will last approximately 15 minutes. The interview will cover the child's clinical presentation. Then the principal investigator will examine the child and record the clinical and radiological imaging findings. During your treatment, the investigator will note and record the progress of your treatment that will include treatment in operating theatre, treatment in intensive care unit and treatment in the ward. At the point of discharge from the hospital, the investigator will also record the clinical management administered and the outcome.

Are there any risks, harms, discomforts associated with this study?

The study carries no extra risk to the patient. Refusing to take part in this study will not jeopardize your treatment in any way.

Confidentiality

The information obtained about you will be kept in strict confidence. No specific information regarding your child will be released to any person without your written permission. We will, however, discuss general overall findings of the study regarding all patients assessed but nothing specific will be discussed regarding your child.

Are there any benefits being in this study?

The results obtained from the study will be used as a basis to improve the quality of care offered to children being managed for posterior cranial fossa tumors at Kenyatta National Hospital. The information will be shared among treating clinicians and the hospital.

Will being in this study cost you anything?

Being in this study will cost you nothing.

Is there reimbursement for participating in this study?

There is no reimbursement for participating in this study.

What if you have questions in future?

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, **Dr. NJERU, Tel. 0720170962,** or his supervisors**, Dr. KITUNGUU, Tel. 0722881405, Dr. Wekesa, Tel. 0721585535 and Dr. KARANJA Tel. 0722643000**. If any queries arise regarding your rights as a research participant, you can contact the **Kenyatta National Hospital Ethics and Research Committee (KNH- ESRC)** by calling **2726300 Ext. 44355.**

Voluntariness of participation and right to withdrawal

Your decision to participate in this research is voluntary. **You are free to decline or withdraw participation in the study at any time without injustice or loss of benefits. Just inform the investigator and the participation in the study will be stopped**. You do not have to give reasons for withdrawing if you do not wish to do so. Withdrawal from the study will not affect the services you or your child is otherwise entitled to in this health facility or other health facilities.

CONSENT FORM (STATEMENT OF CONSENT)

The persons being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include them in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study investigator. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that the participation of my child in this study is voluntary and that I may choose to withdraw it any time. I understand that all information regarding my child's personal identity will be confidential.

By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my / my child's participation in this research study:

Yes No

Parent/Guardian signature /Thumb stamp: _____ Date _____

Parent/Guardian printed name: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent.

Name: _____ Date: _____

Signature: _____

Role in the study: _____

APPENDIX 3: PARENTAL CONSENT FORM - SWAHILI

IDHINI KUTOKA KWA MZAZI YA KUJIHUSISHA NA UTAFITI

Namba ya utafiti:_____ Tarehe:_____ Jina la utafiti:

Vipimo vya kliniki na matokeo ya upasuaji ya mapema ya fossa ya nyuma ya kichwa katika Hospitali ya Kitaifa ya Kenyatta Wachunguzi/watafiti:

Dr. Njeru Peter Kimathi, MB ChB (UON)

Wasimamizi:
Dr. Kitunguu Peter Kithikii Bsc, (MB ChB), M. Med Neurosurgery (UON), Neurosurgeon. Department of Surgery, University of Nairobi
Dr. Dismas Vincent Wekesa (MB ChB), M. Med Neurosurgery (UON), Neurosurgeon.
Department of Surgery, University of Nairobi
Dr. Karanja Susan Wanjiru (MB ChB), M. Med Neurosurgery (UKZN), FC Neurosurgery (SA) Consultant Neurosurgeon, Kenyatta National Hospital

Utangulizi

Madhumuni ya fomu hii ya idhini ni kukupa maelezo unayohitaji ili kukusaidia kuamua kama utashiriki katika utafiti huu. Utaratibu huu unaitwa 'Mtaalam wa Kibali'. Tafadhali soma habari hii ya ridhaa kwa uangalifu na uulize maswali yoyote au utafute ufafanuzi juu ya suala lolote linalohusu kujifunza ambayo huyajui.

Kusudi la utafiti ni nini?
Tumor za nyuma za cranial fossa ni dhaifu, husababisha hali ya neva kusababisha ugonjwa mbaya na vifo. Utafiti huu unakusudia kutoa habari itakayoongoza ukuzaji wa mikakati ambayo itasaidia katika kutambua na kutibu tumors za nyuma za cranial fossa katika usanidi wetu kwa lengo la kuboresha usimamizi na matokeo.

Je, Nini kitatokea ikiwa utaamua kuwa katika utafiti huu?

Ikiwa unakubali mtoto wako kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

Utahojiwa na mpelelezi katika eneo la kibinafsi ambapo unahisi vizuri kujibu maswali. Mahojiano yatadumu takriban dakika 30. Mahojiano yatashughulikia uwasilishaji wa kliniki ya mtoto. Halafu mpelelezi mkuu atakuchunguza mtoto na kurekodi matokeo ya kliniki na ya uchunguzi wa kiinolojia. Wakati wa matibabu, mpelelezi atabaini na kurekodi maendeleo ya matibabu ya mtoto ambayo ni pamoja na upasuaji, matibabu katika kitengo cha utunzaji mkubwa na matibabu katika wadi. Katika hatua ya kutokwa kutoka kwa hospitali, mchunguzi pia atarekodi usimamizi wa kliniki uliyosimamiwa na matokeo

Je, kuna hatari yoyote, madhara, kutokuwepo na uhusiano na utafiti huu?

Utafiti huu hauna hatari zaidi kwa mgonjwa. Kukataa kushiriki hakutahatarisha matibabu ya mtoto wako kwa njia yoyote.

Usiri

Taarifa itakayopatikana kuhusu mtoto wako itahifadhiwa kwa siri. Hakuna taarifa maalum kuhusu yeye itatolewa kwa mtu yeyote bila idhini yako iliyoandikwa. Hata hivyo, tutajadili matokeo ya jumla ya utafiti kuhusu wagonjwa wote watakayopimwa lakini hakuna kitu kitajadiliwa kuhusu yeye.

Je, kuna faida yoyote kuwa katika utafiti huu?

Matokeo yaliyopatikana kutoka kwa utafiti huo yatatumika kama msingi wa kuboresha huduma inayotolewa kwa wagonjwa wanaosimamiwa kwa tumors za nyuma za cranial fossa katika Hospitali ya Kitaifa ya Kenyatta. Habari hiyo itashirikiwa kati ya madaktari na hospitali.

Je, kuwa katika utafiti huu unadai gharama yoyote?

Kuwa katika utafiti huu hakutakupa gharama yoyote.

Je, Kuna malipo kwa kushiriki katika utafiti huu?

Hakuna malipo ya kushiriki katika utafiti huu.

Ikiwa una maswali baadaye?

Ikiwa una maswali yoyote kuhusu utafiti au juu ya matumizi ya matokeo unaweza kuwasiliana na mpelelezi mkuu, **Dr. NJERU**, Tel.**0720 - 170962**, au wasimamizi wake, **Dr KITUNGUU**, Tel.**0722-881405**, Dr. WEKESA, Tel, 0721-585535 **Dr. KARANJA**, Tel.**0722-643000**. Ikiwa una maswali yoyote kuhusu haki zako kama mshiriki wa utafiti unaweza kuwasiliana na **Kenyatta National Hospital Ethics and Research Committee (KNH- ESRC)** kwa kupiga **2726300 Ext. 44355.**

Hiari na haki ya kujiondoa

Uamuzi wako wa kushiriki katika utafiti huu ni ya hiari. **Uko huru kupungua au kuondoa ushiriki katika masomo wakati wowote bila dhulma au upotezaji wa faida. Mjulishe tu mchunguzi na ushiriki katika utafiti utasimamishwa. Sio lazima kutoa sababu za kujiondoa ikiwa hutaki kufanya hivyo**. Kujiondoa kwenye utafiti haitaathiri huduma ambazo wewe au mtoto wako ana haki nyingine katika kituo hiki cha afya au vituo vingine vya afya.

FOMU YA IDHINI

Mtu anayezingatiwa kwa utafiti huu hawezi kujikubali kwa sababu yeye ni mdogo (mtu chini ya miaka 18). Unaombwa ruhusa kuwajumuisha katika utafiti huu.

Taarifa ya mzazi / mlezi

Nimesoma fomu hii ya idhini au nimesomewa. Nimepata nafasi ya kujadili utafiti huu na mpelelezi wa masomo. Nimepata maswali yangu kujibiwa naye kwa lugha ambayo naelewa. Nimeelezewa hatari na faida. Ninaelewa kuwa nitapewa nakala ya fomu hii ya idhini baada ya kusaini. Ninaelewa kuwa ushiriki wa mtoto wangu kwenye utafiti huu ni ya hiari na kwamba naweza kuchagua kuiondoa wakati wowote. Ninaelewa kuwa juhudi zote zitafanywa kuweka habari kuhusu mimi au mtoto wangu siri.

Kwa kusaini fomu hii ya idhini, sijapeana haki za kisheria zangu au za mtoto wangu kama mshiriki katika utafiti huu.

Mimi kwa hiari ninakubali kusiriki au ushiriki wa mtoto wangu katika utafiti huu:

Ndio la

Sahihi ya Mzazi / Mlinzi / Thumb stamp: _____ Tarehe _____

Mzazi / Mlinzi jina la kuchapishwa: _____

Taarifa ya Mtafiti

Mimi, jina langu hapo chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki jina lake hapo juu na kuamini kuwa mshiriki ameelewa na amepeana idhini yake.

Jina: _____ Tarehe: _____

Sahihi: _____

Jukumu katika utafiti: _____

APPENDIX 3: CHILD ASSENT FORM - ENGLISH

Project Title: **CLINICOPATHOLOGICAL FEATURES AND EARLY SURGICAL OUTCOME OF POSTERIOR CRANIAL FOSSA TUMOURS IN CHILDREN AT KENYATTA NATIONAL HOSPITAL**

Investigator: Dr. Njeru Peter Kimathi, MB ChB (UON)

I am doing a research study about children with a swelling inside the back of the head such as yours. Permission has been granted to undertake this study by the Kenyatta National HospitalUniversity of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol No. _____)

This research study is a way to learn more about people. At least thirty-three children will be participating in this research study with you.

If you decide that you want to be part of this study, I will ask you questions about how you feel, and I will examine you for 30 minutes.

There are some things about this study you should know. During your treatment, I will keep checking on you and asking some questions. You will undergo surgery as part of the treatment and stay in ICU and the ward. There are no harmful things, or any cause of discomfort by the study.

Not everyone who takes part in this study will benefit. A benefit means that something good happens to you. We think these benefits might be helping the doctors here take greater care of children who are like you.

When we are finished with this study, we will write a report about what was learned. This report will not include your name or that you were in the study.

You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. Your parents know about the study too.

If you decide you want to be in this study, please sign your name.

I, _____, want to be in this research study.
_____ _____ (Signature/Thumb stamp)
(Date)

APPENDIX 4: CHILD ASSENT FORM - SWAHILI

<u>Jina la utafiti</u>: Vipimo vya kliniki na matokeo ya upasuaji ya mapema ya fossa ya nyuma ya kichwa katika Hospitali ya Kitaifa ya Kenyatta

Wachunguzi/watafiti: Dr. Njeru Peter Kimathi, MB ChB (UON)

Ninafanya utafiti kuhusu watoto walio na uvimbe ndani ya nyuma ya kichwa kama wako. Nimepewa ruhusa kufanya utafiti huu na, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol No. _____).

Utafiti huu ni njia ya kujifunza zaidi juu ya watu. Angalau watoto thelathini na tatu watashiriki katika utafiti huu na wewe.

Ukiamua kuwa unataka kuwa sehemu ya utafiti huu, nitakuuliza maswali juu ya jinsi unavyohisi, na nitakuchunguza kwa dakika 30.

Kuna mambo kadhaa kuhusu utafiti huu unapaswa kujua. Wakati wa matibabu yako, nitaendelea kukuangalia na kuuliza maswali kadhaa. Utafanyiwa upasuaji kama sehemu ya matibabu na utakaa ICU na wodi. Hakuna vitu vyenye madhara, au sababu yoyote ya usumbufu kwa utafiti.

Sio kila mtu anayeshiriki katika utafiti huu atafaidika. Faida inamaanisha kuwa kitu kizuri kinakutokea. Tunafikiria faida hizi zinaweza kuwa kusaidia madaktari hapa kutunza zaidi watoto ambao ni kama wewe

Tutakapomaliza na utafiti huu, tutaandika ripoti juu ya kile tulichojifunza. Ripoti hii haitajumuisha jina lako au kwamba ulikuwa kwenye utafiti.

Sio lazima uwe katika utafiti huu ikiwa hautaki kuwa. Ukiamua kuacha baada ya kuanza, hiyo ni sawa pia. Wazazi wako pia wanajua kuhusu utafiti huu.

Ikiwa unaamua unataka kuwa katika utafiti huu, tafadhali saini jina lako:

Mimi, _____, nimekubali kuwa Katika utafiti huu.

_____ _____

Tarehe **Signature/ Stempu ya kidole gumba**