FREQUENCY OF PAEDIATRIC BRAIN TUMOURS AT TWO TERTIARY REFERRAL CENTERS IN JOHANNESBURG

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DECLARATION

I, Akinola Olumide Oduntan, declare that this research report is my own work, in design and execution. It is being submitted for the degree of Master of Medicine (Neurosurgery) of the University of the Witwatersrand, Johannesburg. It has not been submitted for any degree or examination at this or any other University.

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Signature

April 2020

DEDICATION

This work is dedicated to my wife, Yolanda and my two children, Maletjatji and Akinola Jr. for their unwavering support and love.

ABSTRACT

AIM:

To determine the frequency of primary brain tumour cases among children admitted at the neurosurgical wards at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH) during 2018.

METHOD

Records of children who had primary brain tumours and met inclusion criteria were assessed for relevant data which included:

- Children's demographic profiles
- Clinical data such as Glasgow Coma Score
- presence of motor fallout
- Radiological data such as tumour size and location
- Histological data
- and WHO (World Health Organisation) histological grade

RESULT

Of the 349 children admitted during the study period, 23 had primary brain tumours, a prevalence of 6.59%. The ages of those with tumours ranged from 0 to 12 (mean = 1.87 +/- 0.87) years. The majority of primary paediatric brain tumours were found in the 0 - 3 years age group. There were more females affected with brain tumours. Of the children with brain tumours, 53% were females and 47% males. Astrocytomas (30.4%), Choroid plexus tumours (17.4%) and Medulloblastomas (17.4%) were most frequent.

In this study, more black children were affected with primary paediatric brain tumours than

white children.

CONCLUSION

The prevalence of primary paediatric brain tumours among the children was 6.59% and astrocytomas (30.4%) were most frequent. Similar studies in other referral centres are recommended.

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Finally, I sincerely wish to thank the patients and their next-of-kin / parents for giving consent without which this research report would not have been possible.

ABBREVIATIONS

ATRT: Atypical Teratoid Rhabdoid Tumour

BSG: Brain Stem Glioma

CBT: Congenital Brain Tumour

CBTRUS: Central Brain Tumor Registry of the United States

CHBAH: Chris Hani Baragwanath Academic Hospital

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

CNS: Central Nervous System

CPTs: Choroid Plexus Tumours

CT: Computed Tomography

DNET: Dysembryoplastic Neuroepithelial Tumours

GCT: Germ Cell Tumour

HIV: Human Immunodeficiency Virus

HREC: Human Research and Ethics Committee

IARC: International Agency for Research on Cancer

JPA: Juvenile Pilocytic Astrocytoma

MRC: Medical Research Council

MRI: Magnetic Resonance Imaging

NHLS: National Health Laboratory Service

NMCH: Nelson Mandela Children's Hospital

PNET: Primitive Neuroectodermal Tumours

PXA: Pleomorphic Xanthoastrocytoma

SA: South Africa

USA: United States of America

WHO: World Health Organisation

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CHAPTER ONE

INTRODUCTION

1.1 Background

Cancer in childhood is rare with the risk of developing malignancy in childhood of 1 in almost 600. [1] Cancer also is a leading cause of death in children. [2] Among all cancers in children, brain tumours are the second only to leukemias in incidence. [1] Brain tumours and paediatric brain tumours more specifically have a substantial socioeconomic burden in our communities. They also have psychosocial ramifications for patients and their families. Brain tumours currently constitute between 20 to 30 percent of all solid childhood tumours and are increasing in incidence worldwide. [2] Determining the frequency of paediatric primary brain tumours in Johannesburg is critical to address the psychosocial and socioeconomic sequelae of this often-dreadful disease.

Information on the epidemiology of brain tumours and specifically paediatric brain tumours in South Africa is quite scanty. The International Agency for Research on Cancer (IARC) based in Lyon, France publishes volumes of information from over 300 cancer registries in 60 countries every few years. Information on South Africa is lacking. This information is critical to help in the admission and consent process as it helps to contextualise a patient's disease profile and it also gives an idea of the disease burden in a specific geographical area, in this case, Johannesburg.

It is imperative to have a systematic approach to the holistic management of children with brain tumours. Currently at both Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Braragwanath Academic Hospital (CHBAH), there is synergy between the Department of Paediatrics, Department of Anatomical Pathology, Department of Paediatric Oncology and the Department of Neurosurgery in managing children with brain tumours with the aim of increased survival and quality of life.

The development of more sophisticated systems within the South African context is slow but there is progress. With the recent completion of the Nelson Mandela Children's Hospital (NMCH) in Parktown, Johannesburg, it is a huge milestone on the way to reaching better synergies.

Neurosurgeons treat a vast array of pathological entities from spine disorders to vascular anomalies to diseases unique to the paediatric population. Currently neurosurgical specialization in paediatrics is still very limited in South Africa. Hopefully with the advent of Nelson Mandela Children's Hospital (NMCH), there will be an energised focus on paediatric brain tumours and their sequelae.

Diagnostic Dilemma

A great hindrance to progress in brain tumour diagnosis is the fact that many health care facilities in Africa still lack computed tomography and magnetic resonance image scans, making the diagnosis of brain tumours impossible. It is difficult to tell whether the perceived or apparent increase in the frequency of paediatric intracranial tumours can be applied to South Africa, given the dearth of available studies on the subject.

1.2 Brain tumours

Causes of brain tumours

Various viruses have been shown to induce brain tumours in animal models; whether they cause brain tumours in humans is unclear. This is potentially where there may be a difference in the South African population: The Human Immunodeficiency Virus (HIV) is known to cause an increase in the incidence of CNS (Central Nervous System) Lymphomas in adults. While mobile telephone use remains a highly controversial causative factor regarding the development of brain tumours in the adult population, it is thought to be less important in the paediatric population for the simple reason that mobile telephone use is more common in adults than children. [13] The association between tumour development in-utero and maternal CT scans on the other hand remains strong. [13] Consumption of cured meats and exposure to pesticides by pregnant women are also thought to increase in-utero formation of brain tumours. Interestingly, there seems to be no association with maternal smoking. [12]

Classification of brain tumours

The World Health Organisation (WHO) in May, 2016 updated the classification of central nervous system tumours to reflect the increase in knowledge of the underlying genetic mutations of tumours. While this new classification is more extensive than its predecessors, it is also more specific for various tumours and will thus ultimately assist with diagnosis and management of brain tumours. Below is the summary of the updated version of the WHO grading of CNS tumours as summarized by Louis et al. [12]

Table 1. World Health Organization (WHO) classification of brain tumours

WHO grades of select CNS tumours	
Diffuse astrocytic and oligodendroglial tumours	
Diffuse astrocytoma, IDH-mutant	II
Anaplastic astrocytoma, IDH-mutant	III
Glioblastoma, IDH-wildtype	IV
Glioblastoma, IDH-mutant	IV
Diffuse midline glioma, H3 K27M–mutant	IV
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	II
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	III
Other astrocytic tumours	
Pilocytic astrocytoma	I
Subependymal giant cell astrocytoma	I
Pleomorphic xanthoastrocytoma	II
Anaplastic pleomorphic xanthoastrocytoma	III
Ependymal tumours	
Subependymoma	I
Myxopapillary ependymoma	I
Ependymoma	II
Ependymoma, *RELA* fusion–positive	II or III
Anaplastic ependymoma	III
Other gliomas	
Angiocentric glioma	I
Chordoid glioma of third ventricle	II
Choroid plexus tumours	
Choroid plexus papilloma	I
Atypical choroid plexus papilloma	II
Choroid plexus carcinoma	III
Neuronal and mixed neuronal-glial tumours	
Dysembryoplastic neuroepithelial tumour	I
Gangliocytoma	I
Ganglioglioma	I
Anaplastic ganglioglioma	III
Dysplastic gangliocytoma of cerebellum (Lhermitte–Duclos)	I
Desmoplastic infantile astrocytoma and ganglioglioma	I
Papillary glioneuronal tumour	I
Rosette-forming glioneuronal tumour	I
Central neurocytoma	II
Extraventricular neurocytoma	II
Cerebellar liponeurocytoma	II
Tumours of the pineal region	
Pineocytoma	I
Pineal parenchymal tumour of intermediate differentiation	II or III
Pineoblastoma	IV
Papillary tumour of the pineal region	II or III
Embryonal tumours	
Medulloblastoma (all subtypes)	IV
Embryonal tumour with multilayered rosettes, C19MC-altered	IV
Medulloepithelioma	IV
CNS embryonal tumour, NOS	IV
Atypical teratoid/rhabdoid tumour	IV
CNS embryonal tumour with rhabdoid features	IV
Tumours of the cranial and paraspinal nerves	
Schwannoma	I
Neurofibroma	I
Perineurioma	I
Malignant peripheral nerve sheath tumour (MPNST)	II, III or IV
Meningiomas	
Meningioma	I
Atypical meningioma	II
Anaplastic (malignant) meningioma	III
Mesenchymal, non-meningothelial tumours	
Solitary fibrous tumour / haemangiopericytoma	I, II or III
Haemangioblastoma	I
Tumours of the sellar region	
Craniopharyngioma	I
Granular cell tumour	I
Pituicytoma	I
Spindle cell oncocytoma	I

Another classification system is the International Classification of Childhood Cancer (ICCC) version with the relative frequency of the major histological subtypes of CNS tumours as presented by McKinney [13] are shown in Table 2 below.

Table 2. International Classification of Childhood Cancer (ICCC) classification and relative frequency of the major histological subtypes of Central Nervous System (CNS) tumours. *(Adapted from McKinney)* [13]

Histological Sub-type	Percentages (%)
Ependymomas	10
Astrocytomas	40 – 50
PNETs (Primitive Neuroectodermal Tumours)	25
Other Gliomas	10
Other Specified and Unspecified CNS tumours	8 – 13

Epidemiology of brain tumours

Brain tumours, which constitute between 20 to 30 percent of all solid childhood tumours are increasing in incidence worldwide. [2, 6, 10] Their incidence is thought to have gone up 2 to 3 percent since the late 1960s. [2] Whether or not this increase is due to better imaging modalities or other factors such as improved methods of registration and reporting of new cases or a reflection of true increase is debatable. A great hindrance to progress in brain cancer diagnosis in Africa is the fact that many health care facilities still lack computed tomography and magnetic resonance imaging. [3]

Among all cancers, brain tumours comprise the second largest group of childhood cancers, second only to leukemia. [1, 21] In Japan, the incidence of paediatric brain tumours increases to 20 to 30 cases per million. [28]. In China, according to Nectoux et. al, the incidence of CNS tumours is 1.31 per 100,000. [23] According to the International Association for Research on Cancer (IARC), the annual incidence of CNS tumours in children less than 15 years of age in the United States of America (USA) is 12 per 100,000. [28] Keene et al., report the incidence of childhood CNS tumours in Canada is 2.76 per 100,000. [24] Furthermore, Stiller et al., state that Nordic countries (Denmark, Norway, Sweden and Finland) have the highest incidence of paediatric CNS tumours at 3.14 per 100,000. [25]

As with many other medical conditions, information regarding tumours, including paediatric brain tumours in South Africa and Africa is limited or in many cases, non-existent. Presumably, part of the reason for this has been the focus on communicable diseases such as AIDS and Tuberculosis, which are more common in Africa.

In a study of paediatric brain tumours, Gyasi and Tettey in Ghana reported that only 32 (13%) out of 252 CNS tumours were intracranial in origin. [5] This is similar to studies reported by Mostert et al. in Western Kenya [6] and Williams et al. in Nigeria. [7]

Brain tumours affect the functional status of the patient to a varying degree. The Karnofsky Performance Score (KPS) is a grading score often used for grading functional status in patients with cancer.[22] A KPS score < 70 often identifies patients with a worse prognosis for any given treatment. [22] However, care must be taken when determining the Karnofsky of a patient, as the patient's current physical condition may appear worse than it actually is. [27] Examples of this are in patients with hydrocephalus secondary to a brain tumour obstructing normal CSF pathways or patients with hydrocephalus secondary to aneurysmal subarachnoid haemorrhage. These patients often present with low Karnofsky scores secondary to hydrocephalus but if the hydrocephalus is treated, their Karnofsy scores improve. [27] This makes them better candidates for any mode of treatment that may be chosen.

The Karnofsy performance status scale ranges from 100 to 0. A patient with a KPS score of

‘100’ is a patient with normal functional status. This patient can carry out activities of daily living and work unaided. A patient with a KPS score of ‘0’ is a patient who is dead. On average, as stated above, patient with a KPS more than 70 is implied to have normal activity. [22]

Morbidity and mortality brain tumours

In the African context, it is expected that the morbidity and mortality rates would be higher than in Western countries because of several factors on the continent that may influence presentation, diagnoses and effective management. These include socioeconomic factors like poverty, unemployment, famine, wars etc. resulting in patients presenting late to hospitals that provide imaging facilities and definitive care. Such late presentation results in advancement of tumours which in most cases would mean that their conditions are not amenable to either definitive surgical and or radiotherapeutic treatment for a chance of a cure [2, 3, 6]

1.3 Paediatric brain tumours

Paediatric versus congenital brain tumours

While this present study is based on the findings in paediatric brain tumours, a distinction at this juncture between congenital brain tumours and paediatric brain tumours must be made. A review of paediatric brain tumours will be incomplete without comments on the concept of congenital brain tumours (CBT). According to Sugimoto et al, congenital brain tumours are defined as tumours presenting within 60 days after birth. [19]. They account for less than 2% of all paediatric brain tumours with teratoma being the commonest type. [19] Differences between congenital brain tumour and paediatric brain tumours in general include location of the tumour, classification representative, histological type, imaging findings of ultrasonography treatment and prognosis. [19]

Furthermore, congenital brain tumours differ from paediatric brain tumours in terms of signs and symptoms. Congenital tumours tend to present with enlarged head circumference and a mass detected on ultrasound in addition to enlarged ventricles. Some even present with stillbirth. Paediatric tumours on the other hand can present with irritability and increased seizure activity. [19]

Differences between paediatric and adult brain tumours

There are a few differences between adult and paediatric brain tumours, for example, unlike adult brain tumours which develop in neuroepithelial tissues, paediatric tumours usually have an embryonic origin. [9] Also, adults tend to have fewer Primitive Neuroectodermal Tumours (PNETs), whereas the incidence of meningiomas in the paediatric population is quite low. [10] Metastatic brain tumours are more common in adults than in children.[13] Furthermore, the paediatric population tends to develop tumours below the tentorium cerebelli while tumours are more prevalent above the tentorium cerebelli in adults. [8]

Even though paediatric brain tumours may not be considered as important as communicable diseases, the morbidity and mortality in the paediatric population associated with them is quite high. In addition, with the current high incidence of mother-to-child HIV transmissions in South Africa, it is important to ascertain whether the frequency of paediatric brain tumours is increasing or not, and to determine whether any increase in their incidence can be correlated with the defective immunity in the paediatric population who are HIV positive. This is especially important for central nervous system lymphomas, which are known to occur most frequently among the HIV-positive population. [11]

CHAPTER TWO

2. LITERATURE REVIEW

2.1.1 Definition of a Child

According to this present study, children refer to individuals under the age of 14 years.

2.1.2 Brain Tumours in children

The frequency of brain tumours in children is on the rise worldwide. Increased surveillance in the form of diagnostic imaging for other reasons, earlier presentation of patients for central nervous system (CNS) related complaints and increased access to healthcare facilities are some of the reasons for the increase. [23, 25]

2.1.3 Causes of paediatric brain tumours

While mobile telephone use remains a highly controversial factor regarding the development of brain tumours in the adult population, it is thought to be less important in the paediatric population for the simple reason that mobile telephone use is more common in adults than children.[13] Currently, while specific causes of brain tumours in the paediatric population cannot be pin-pointed, genetics and the environment are thought to play a large role in the development of tumours. Neurofibromatosis has been positively associated with the development of paediatric brain tumours [14], as has the mutation of the TP53 gene. In the 1970s, maternal X-rays were considered to be a risk factor in brain tumour formation; this has more recently been refuted.[13] With regards to environmental factors, ionising radiation, as occurs in the treatment of other cancers or tinea capitis in children is particularly strongly associated with the development of brain tumours.[13]

2.1.4 Epidemiology of paediatric brain tumours

Epidemiological studies of paediatric brain tumours suggest that they are more prevalent in white children in comparison to other racial groups.[11] However, given that most of those studies were conducted in Western countries with lower populations of black children, these findings may not apply in the African setting. Brain tumours, which constitute between 20 to 30 percent of all solid childhood tumours are increasing in incidence worldwide. [2] Their incidence is thought to have gone up 2 to 3 percent since the late 1960s. [2] Whether or not this increase is due to better imaging modalities and registration of new cases or reflects a true increase is debatable. Among all cancers, brain tumours comprise the second largest group of childhood cancers, second only to leukemia. [21]

According to Keene et al., [24] the incidence of childhood CNS tumours in Canada is 2.76 per 100,000. Stiller et al., reported that the Nordic countries (Denmark, Norway, Sweden and Finland) have the highest incidence of paediatric CNS tumours at 3.14 per 100,000. [25] Studies on the incidence of brain tumours in paediatric patients in some regions of Africa corroborate observations of the increase in brain tumours in children. [4, 5, 6, 7,15] In Japan, the incidence of paediatric brain tumours is 20 to 30 cases per million. [27]

According to the World Health Organisation, the incidence of brain tumours cases in African children is 11 per one million. [16] According to Wessels and Hesseling, in Namibia, brain tumours were more prevalent (18%) in the paediatric population. [8]

According to the International Agency for Research on Cancer (IARC), the annual incidence of CNS tumours in the age group 0-15 between the years 1990 and 1993 for certain African countries: Algeria 2.3 per 100,000, Mali 0.4 per 100,000, Uganda 1.5 per 100,000 and Zimbabwe 10.3 per 100,000 [27]

2.1.4.1 *Frequency and pattern of paediatric tumours*

There is paucity of information on the frequency and pattern of paediatric brain tumours in the literature. According to Jahan et al, paediatric brain tumours differ in their types, location and outcomes. This study was aimed at studying the histological pattern, distribution and correlation with age and gender among children below 15 years. The most common location site was infratentorially at 59.5%. Supratentorial location was at 41%. Medulloblastomas (23%) were most common, followed by ependymomas (16.07%). The tumours were more common in males (67.3%) than females (32.7%). [58]

2.1.5 Age Distribution of various paediatric brain tumours

According to a study by Keene et al., in Canada, approximately 10% of CNS tumours occur in children under 2 years of age, 20% between 2 and 5 years, 25% between 5 and 10 years and 45% over 10 years of age. [24] Certain tumours like medulloblastomas commonly occur in children less than 8 years of age whereas 30% of ependymomas occur in children younger than 3 years of age. [27] According to a study by Davis et al., [20] medulloblastoma is the most common malignant, invasive childhood embryonal brain tumour and accounts for 16-20% of all childhood brain tumours in the USA.

Germ cell tumours commonly affect children in their teenage years. [46] The age distribution of craniopharyngioma is bimodal with a peak in childhood of 5-14 years and later in adulthood of 65-74 years. [51] Brain stem gliomas (BSGs) also have two peaks of incidence, at 5-8 years of age and another at 36-45 years of age. [52] Posterior fossa tumours like ependymomas and medulloblastomas have a mean age at diagnosis between ages 4 to 6 years and 5 to 7 years respectively. [52,53] In addition, 75% of medulloblastomas are diagnosed before the age of 15 years. [54] Pineoblastomas were commonly diagnosed in infancy and early childhood. [55] Atypical Teratoid Rhabdoid Tumour or ATRT of the CNS commonly arises in infants with the majority of patients being 3 years or younger. [56]

2.1.6 Differences between paediatric and adult brain tumours

There are a few differences between paediatric and adult brain tumours.

Unlike adult brain tumours which develop in neuroepithelial tissues, paediatric tumours usually have an embryonic origin.[9] An illustration of this example is medulloblastomas which commonly occur in children but rarely in adults. [20]

Another example is the type of brain tumours occurring across different age groups. Meningiomas occur mainly in adults whereas in children it forms 1-8% of cases. [25] According to Bondy et. al, the incidence of intracranial meningiomas in the paediatric population is quite low, at 3%. [10] Whereas, meningiomas occur almost exclusively in adults, 70% of patients with choroid plexus tumours are less than 2 years old. [21] Also, metastatic (secondary) brain tumours are more common in the adult population than in children. [13] Another critical difference between adults and children is deep white matter lesions in children often show dense contrast enhancement on neuroimaging which are often benign, unlike in adults, this often proves to be a sign of malignant transformation. [32]

In the paediatric population, tumours tend to develop infratentorially, i.e. below the tentorium cerebelli [9], under the age of 3 years, supratentorial tumours are common and between the ages of 3 and 11 years, infratentorial tumours are common. [9] According to Pollack et al., astrocytomas account for approximately 50% of hemispheric tumors in children, occurring at all ages, with a peak incidence between ages 8 and 12. [29]

Pollack et al., also reported high grade gliomas compose approximately 20% of hemispheric gliomas in children and occur at an incidence of approximately 2 cases per million per year. [40] Deeply located tumours like brain stem tumours account for approximately 10-20% of all paediatric central nervous system tumours [32] and tumours of the skull base account for about 8% of all paediatric brain tumours. [33]

The overwhelming majority of brain tumours are astrocytomas which comprise approximately 35-47% of all primary brain tumours. [34] According to Rorke et al., in a series of 1038 biopsy specimens of childhood tumours, pilocytic and grade 2 fibrillary astrocytomas each represented a third of all gliomas. [30]

Cerebellar astrocytomas represent 12-17% of all pediatric brain tumours and 20-35% of tumours in the posterior fossa of children. [35] Pleomorphic Xanthoastrocytoma (PXA) represents 0.5% of all gliomas. [36] Optic Pathway gliomas represent less than 1% of all brain tumours. [37] Craniopharyngioma has an incidence of 1.3 per 1,000,000-person years constituting 5-10% of paediatric brain tumours. [38] Oligodendrogliomas are rare in children accounting for 1-3% of hemispheric tumours [39]

Ependymomas represent 8-10% of all paediatric brain tumours. [40] and gangliogliomas account for 4-9% of all childhood brain tumours. [40] Medulloblastoma accounts for 15-30% of all brain tumours in children and 30-50% of all posterior fossa tumours in children. [41] Paediatric meningiomas exhibit a range between 0.7 and 4.2% of paediatric brain tumours. [41]. Bondy et al. put this figure at 3%. [10] Pineal Region Tumours comprise 3-8% of all intracranial tumours in children with the incidence of pinealoma and germinoma among children being 0.061 per 100000 children per year. [43] Only 2-3% brain tumours in children are pituitary adenomas. [44] Colloid Cysts form 0.3-2.0% of all brain tumours. [45]

Most of the African studies have confirmed that the commonest histological subtype of paediatric brain tumours are astrocytomas. [4,5,6,7,8] A study by Ogun et al, on paediatric CNS tumours in Ibadan, Western Nigeria over a ten-year period found an increase in incidence of brain tumours in children. [4]

2.1.7 Gender Distribution of paediatric brain tumours

There are gender differences in distribution of tumours. According to Stiller et al., the sex ratio of paediatric CNS tumours shows a male bias for all tumours except astrocytomas. [25] In a Nigerian study, it was reported that “children with gliomas had equal sex distribution and craniopharyngiomas were predominant in male children under the age of 5 years”. [4] Ghanaian researchers found “male to female ratio for tumours was 1.14:1 and 1.26:1 respectively.” [5] In a study by Rickert et al of juvenile pilocytic astrocytomas (JPAs), males and females are equally affected. [46] The same group of authors found atypical teratoid rhabdoid tumours (ATRTs) tend to be slightly more common in boys. [46] Albright et al. found medulloblastomas have a predominance in males. [47] Germinomas and other germ cell tumours (GCTs) tend to occur more commonly in males according to Matsutani et al. [48]

According to Russel and Rubenstein, pineoblastomas were commonly diagnosed in males with a 2:1 ratio. [49] Finally, across all age groups, with regards to pituitary adenomas, females tend to be affected more than males. [50]

2.1.8 Symptoms of paediatric brain tumours

The symptoms of brain tumours in children are similar to adults, with the main difference being that very young children may not be able to verbalise symptoms such as headaches effectively. The presence of seizures may be the first symptom of a brain tumour in a child. Seizures are one of the most common symptoms in paediatric brain tumours with supratentorial brain tumours involving the gray matter being more epileptogenic. [18] Also certain tumours have increased propensity for seizures like Dysembryoplastic Neuroepithelial Tumours (DNET), oligodendroglioma and ganglioglioma. [18] Other symptoms can include irritability, loss of appetite, developmental delay, and a drop in intellectual and physical abilities. In infants, parents may notice an increase in head size, sometimes along with bulging of the fontanelles. In the school-aged child, symptoms can include poor school performance, fatigue, and personality changes. Often, the lack of symptoms in what is often an enormous brain tumour is due to elasticity of a child's skull due to the open fontanelles. [21]

2.1.9 Diagnosis and management of paediatric brain tumours at two tertiary referral centres in Johannesburg

The current procedure for children with radiologically proven brain tumours at the hospitals namely: Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Braragwanath Academic Hospital (CHBAH) is to educate the caregiver and/or the patient around their diagnosis and if they understand, proceed to obtain consent from the parent/caregiver/next-of-kin to resect the brain tumour partially or whole if the brain tumour is amenable to surgery. Currently, paediatric brain tumours are managed almost similarly to adult brain tumours. Part of the armamentarium of the neurosurgeon in treating brain tumours is a) surgical resection of the tumour b) radiotherapy c) chemotherapy. Radiotherapy is generally reserved for children above the ages of 3 years because of the deleterious effects on the growing nervous system of children. [21] Some of the manifestations of radiation therapy or radiotherapy include decreased cognition, radiation necrosis, injury to optic pathways, injury to hypothalamic-pituitary axis, primary hypothyroidism, formation of new tumours and leukoencephalopathy. [21]

The choice on whether to intervene surgically or otherwise on a patient with a brain tumour must consider many factors. Some of the factors include a) location of the brain tumour b) age of the patient c) clinical condition of the patient as represented by the Karnofsy score. [21]

2.1.10 Prognosis, Morbidity and Mortality rates of paediatric tumours

Unfortunately, brain tumours in the paediatric population particularly the toddler age group are generally associated with a poor prognosis. According to Stiller et al., low survival rates continue to plague the age group less than two years of age. [24] According to the American Brain Tumour Association, intracranial tumours are the leading cause of cancer-related deaths in males and females between the ages of one and nineteen years. [17]

In the African context, it is expected that the morbidity and mortality rates would be higher than in Western countries. This is due to the prevalent issue in many African countries, including South Africa, of patients presenting late to hospitals which have access to imaging facilities and definitive care. The late presentation results in advancement of tumours which in most cases will mean they are not amenable to either definitive surgical or radiotherapeutic treatment for a chance of a cure.

2.1.11 South African Perspectives

Information on the epidemiology of paediatric brain tumours in Africa is scanty. Such information is necessary in order to monitor whether there is an increase in the frequency of brain tumours among children in South Africa. Knowledge of the increase or otherwise will be useful in determining the disease burden in our communities and to possibly reprioritise current health practices and norms.

This research report's objective was to determine the frequency of brain tumours among the South African paediatric population using the two major public referral centres in Johannesburg, as sites for data collection. The findings of this study will contribute to the existing information on the epidemiology of childhood brain tumours in Johannesburg and South Africa.

2.2 Motivation for this study

The motivation for this study is that brain tumours in both children and adults comprise a substantial burden of disease in neurosurgical and neurological practice and information on the frequency of the condition among children is scanty. For this reason, the researcher decided to look into the frequency of paediatric brain tumours at two tertiary referral centres.

2.3 Aims and objectives

Aim

The aim of this research report was to determine the frequency of primary brain tumour cases among children admitted at the neurosurgical wards at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH).

Objectives

i. To determine the pattern of different histological subtypes among the patients.

2.4 Research questions

i. What is the frequency of paediatric brain tumours among paediatric neurosurgical patients admitted at the CMJAH and CHBAH?

ii. What is the pattern of different histological subtypes the children present with?

CHAPTER THREE

3. MATERIAL AND METHOD

3.1 Research Design

This is a prospective, descriptive observational two-centre study carried out between the months of January and September, 2018, in which children diagnosed with brain tumours on computed tomography (CT) scan or magnetic resonance imaging (MRI) were studied to determine the frequency of paediatric brain tumours at two tertiary referral centres (CHBAH and CMJAH) in Johannesburg, South Africa.

3.1.1 Methods

This study was conducted at the Departments of Neurosurgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Chris Hani Baragwanath Academic Hospital (CHBAH). For context, the Department of Neurosurgery at the University of the Witwatersrand, comprises two academic hospital training sites as mentioned above. These sites were the ideal places for data collection as they are the biggest hospitals in Johannesburg in terms of bed numbers. CMJAH has just over 900 beds whereas CHBAH has almost 3000 beds making it the largest hospital in the Southern Hemisphere. For neurosurgery, at CMJAH, there are 22 adult beds of which 8 are ICU beds, and 14 are regular ward beds. The paediatric surgery wards at CMJAH houses the paediatric neurosurgery patients of which 8 beds belong to neurosurgery. Neurosurgery at CHBAH has 90 beds, 76 of which are adult beds, and 14 are paediatric.

The Greater Johannesburg Municipality (which includes the cities of Johannesburg and Ekurhuleni formerly known as the East Rand) is the largest city in South Africa with a population of almost 8 million people at the last census in 2011 according to Stats SA.[57] It is also undoubtedly the economic and financial hub of South Africa and the continent at large. Another fact to note is that a sizeable proportion (29.5%) of the South African population is younger than the age of 15 according to Stats SA. [57]

The majority of the study population were referred by our paediatric colleagues at both the CHBAH and CMJAH or referrals from district hospitals in the hospitals' drainage areas. When the patient and his/her parent/next-of-kin presented to either of the two hospitals, the patient was screened to see if he/she met the inclusion criteria of the study detailed below. The parent/next of kin was then asked to consent to participation in the study by means of use of their records i.e. patient files, CT scans, MRI scans, histopathology records etc. Informed consent was then obtained. The data sheet was then explained to the parent/next-of-kin or to the child if they were old enough to understand basic English and where their input was required, it was requested. For example: If there were any symptoms like headaches, seizures or vomiting and the duration of these symptoms? In the event where a language barrier existed, a translator was afforded to the parent/next-of-kin. The translator then signed the consent form as well as a witness.

Following all ethical processes, relevant information was obtained from the parents of each child and from the histological and radiographic profiles of each child aged 0 to 14 years.

The data sheet was completed with the assistance of the interviewee where necessary.

3.1.2 Data collection

The information collected included the following:

A. **Demographic data**: Name, age, gender, hospital file number, date of admission, admitting hospital and patient allocation tracking number.

B. **Clinical data:** The presence of raised intracranial symptoms such as headaches and vomiting, duration of these symptoms and the presence of seizures.

C. **Examination data:** Glasgow Coma Score (GCS) on arrival to the admitting hospital, pupil size and response to light, motor deficit using the Medical Research Council (MRC) scale on admission. [59]

D. **Radiological data:** CT scan and/or MRI were carefully inspected to obtain the following data:

  - Location of the tumour
  - Size of the tumour
  - presence of vasogenic edema
  - mass effect from the tumour
  - presence of midline shift
  - effacement of the basal cisterns
  - presence of calcifications
  - presence of associated bleeds (Intramural, Subarachnoid or Intraventricular).

E. Histopathological data: Information obtained by logging on to the NHLS (National Health Laboratory Services) Labtrak Pathology Portal at either hospital (CMJAH/CHBAH), entering the hospital number of the patient and retrieving the histological data of the patient included: The Diagnosis and WHO (World Health Organization) grade. Additional information such as the genetic or molecular marker was also noted. For example, if the IDH (Isocitrate Dehydrogenase) type was tested for, it was also recorded. In addition, the degree of cellularity, shape of the nuclei, presence of nuclear atypia, presence of mitotic figures, presence of necrosis and presence of endothelial proliferation were also recorded.

3.1.3 Ethical and legal considerations

Ethical approval from Human Research and Ethics Committee (HREC) before commencement of the study was done. Informed Consent was obtained from all participants**.** Confidentiality was upheld and maintained by use of only initials on the data sheets**.** Records were kept safe and private**.** The study was not invasive i.e. there was no risk of maleficence. Copies of protocols were submitted to the respective hospitals and consent granted by their respective CEOs/Clinical Directors to conduct the research as proposed and CEO/Clinical Director/Medical Advisory Committee Consent were obtained. Written consent was obtained from the Medical Superintendents of both hospitals prior to commencement of the study.

3.2 Study Site

This study was conducted at the Departments of Neurosurgery of the CMJAH and CHBAH respectively. Those sites were the ideal places for data collection as they are the largest referral hospitals in Johannesburg.

3.3 Study Population

The study population were children referred to the neurosurgery departments of both the CHBAH and CMJAH or referrals from district hospitals and the hospitals' drainage areas.

3.4 Sample Size

The sample size was the total number of new paediatric cases of children aged 0 to 14 with brain tumours in the study sites during the data collection period of January to September, 2018.

3.5 Inclusion and exclusion criteria

Inclusion criteria included the following:

i. Children between the ages of 0 and 14 years
ii. Children admitted within one year of ethics approval
iii. Consenting parent/next of kin to participate in the study
iv. Histopathologically confirmed primary brain tumour case.

Exclusion criteria included the following:

i. Children who have previously undergone treatment, either surgically and/or via radiotherapy for a brain tumour and were having a recurrence.
ii. Children with secondary (metastatic) brain diseases and with hematological malignancy.
iii. Children whose parents or next of kin refused to give consent.

3.6 Materials

A pre-designed data collection table (appendix A) was used to record demographic and other profiles of the children diagnosed with CNS tumours at the two study sites.

3.7 Method of obtaining consent/assent

The children included in the study were recruited from the two study sites only. When the patient and his/her parent or next-of-kin presented to either of the two hospitals, the patient was screened to ascertain that he/she met the inclusion criteria (as detailed above). When a suitable patient was identified and informed consent obtained, the data sheet was then explained to the parent/next-of-kin and their input requested, where necessary. The parent/next of kin was asked to consent to participation in the study by means of use of their child's records. In the event where a language barrier existed, a translator was afforded to the parent/next-of-kin. The translator signed the consent form as a witness as well. For children older than 12 but younger than 14 years, an assent form was completed. Subsequently, the demographic information of the child was obtained and recorded on the predesigned standardised data collection sheet, and subsequently captured in the Microsoft Excel spreadsheet and then exported to the Stata (Version 14) Statistical Software.

CHAPTER FOUR

4. RESULTS

4.1 Demographic profiles

Age and Gender

Twenty-three (23) children who met the inclusion criteria were enrolled for this study. 10 (43.5%) from the Chris Hani Baragwanath Academic Hospital (CHBAH) and 13 (56.5%) from Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Their ages ranged from 0 to 12 years with a mean of 1.87 years of age and standard deviation (SD) of 0.87 years. There were 10 (43.5%) males and 13 (56.5%) females. Their ages and gender distributions are illustrated in Figure 1 and Figure 2 respectively.

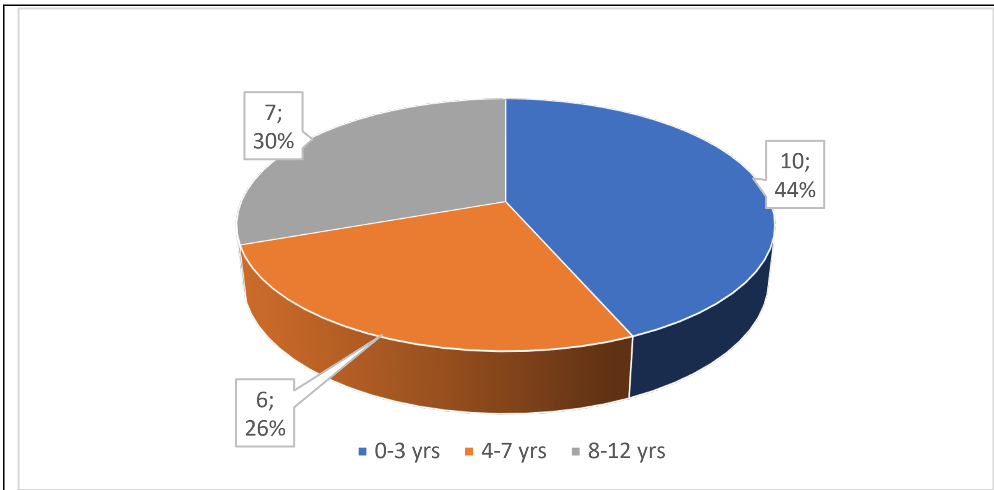

Figure 1: Illustrating the age distributions of the children. The Figure illustrates the frequencies as well as percentages of the different age groups.

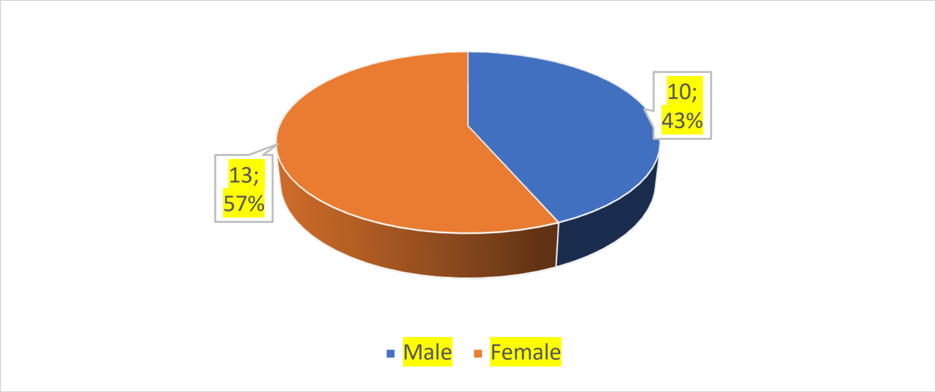

Figure 2: Illustrating the gender distribution of the children. The Figure illustrates the frequencies as well as percentages of the different genders.

Race

The races of the children were white and black. There were no Asian or Coloured children enrolled into the study. They included 22 black children (95.7%) and one white child (4.3%) with a mean of 1.04 and standard deviation (SD) of 0.209.

4.2 Clinical Findings

The Glasgow Coma Scores of the children ranged from three (4.3%) to 15 in 17 patients (73.9%). Motor Deficit using the Medical Research Council (MRC) scale on admission was present in five of the patients (21.7 %.). There were six of the 23 patients (26.1%) who had seizures and 17 (73.9%) patients who did not have seizures. The mean was 1.74 with a standard deviation 0.449.

4.3 Radiological profiles

The tumour locations were supratentorial in 11 (47.8%) and infratentorial in 12 (52.2 %). The sizes of the tumours ranged from 2.2 cm (30.4%) to more than 7.2 cm (13.0%) with a mean of 1.83 cm and SD of 0.65 cm. There was surrounding vasogenic edema in 17 (73.9 %) of the subjects. Mass effect from the tumour in the form of effacement of sulci and gyri was present in 20 (87.0%), and hydrocephalus was present in 18 (78.3%). Calcifications was present in five (21.7%). Associated bleeds (Intratumoral, Subarachnoid, Intraventricular) were present in two (8.7%) of the participants. An intratumoral and subarachnoid bleed were present in one participant and an intraventricular bleed was present in the other participant. All participants with medulloblastoma had MRI of the brain and spine and only one had drop metastasis.

4.4 Histopathological data

Of the Twenty three (23) children, seven (30.4%) of the patients were diagnosed with astrocytomas, four (17.4%) had medulloblastomas, four (17.4%) of the patients had choroid plexus tumours, two (8.7%) of the patients had craniopharyngiomas, two (8.7%) of the patients had ependymomas, one (4.3%) of the patients had ATRT (atypical teratoid rhabdoid tumour), one (4.3%) of the patients had a pineal parenchymal tumour. Two of the lesions were miscellaneous and included infantile ganglioma and epidermoid cyst.

Table 3 Frequency, with percentages (in descending order of frequency) of histological types of the brain tumours according to WHO 2016 classification among the subjects.

Tumour Type	**Frequency (N)**	**Percentage (%)**
Astrocytoma	7	30.4
Choroid Plexus Tumours	4	17.4
Medulloblastoma	4	17.4
Craniopharyngioma	2	8.7
Ependymoma	2	8.7
(Others)	2	8.7
Atypical teratoid rhabdoid tumour	1	4.3
Pineal Parenchymal tumour	1	4.3
Total	**23**	**100.0**

Histopathological diagnoses of the various types of tumours among the subjects ranged from being benign in nine (39.1%) meaning they were WHO (World Health Organization) Grade 1 to being malignant and aggressive in ten (43.5%) meaning they were WHO (World Health Organization) Grade 4.

Astrocytomas were the most common type of brain tumour among the children. Of the seven astrocytomas, 4 (57.1%) of them were pilocytic astrocytomas WHO Grade 1, one (14.3%) was a diffuse astrocytoma WHO Grade 2 and the remaining two were glioblastoma multiforme WHO Grade 4. The two choroid plexus tumours were choroid plexus carcinomas. Of the ependymomas, one was WHO Grade 2 and the other was an anaplastic ependymoma Grade 3. The pineal parenchymal tumour was a pineoblastoma WHO Grade 4.

The distributions of the ages of the children enrolled for the study in relation to the histological types of the tumours are shown in Table 4.

Table 4: Different age groups of the subjects, histological subtypes of brain tumours, their frequencies and percentages.

Age groups (years)	**Histological subtypes of brain tumours**		
	Subtypes	**Frequency (N)**	**Percentage (%)**
0-3	Astrocytoma	3	13
	Medulloblastoma	4	17.4
	Choroid Plexus Tumour	3	13
	Infantile Ganglioma	1	4.3
	Craniopharyngioma	1	4.3
4-7	Craniopharyngioma	1	4.3
	Astrocytoma	2	8.7
	ATRT	1	4.3
	Pineal Parenchymal Tumour	1	4.3
8-12	Ependymoma	2	8.7
	Astrocytoma	2	8.7
	Choroid Plexus Tumour	1	4.3
	Epidermoid Cyst	1	4.3
Total		**23**	**100.0**

4.5 Brain tumour prevalence among the participants

The total number of children admitted into the paediatric neurosurgical wards at both hospitals during the study period in 2018 are as follows:

CHBAH: 207

CMJAH: 142

Giving a total admission cohort of 349 patients, of which 23 patients had brain tumours, prevalence of 6.59%

CHAPTER FIVE

5. DISCUSSION

In this Chapter, the results of the study are discussed with focus on the objectives of this study which were, firstly to determine the frequency of paediatric brain tumours among paediatric neurosurgical patients admitted at the Charlotte Maxeke Johannesburg Academic and Chris Hani Baragwanath Academic Hospitals and secondly, to determine the pattern of presenting histological sub-types among the patients recruited for the study.

The sample population for this study were children aged 0-14 years admitted at the two study sites (Charlotte Maxeke Johannesburg Academic Hospital and Chris Hani Baragwanath Academic Hospital). This age range was chosen to correspond to the admission ages of children into paediatric wards at both hospitals.

5.1 SUMMARY OF RESULTS

1. The most frequent tumours were astrocytomas (30.4%), choroid plexus tumours (17.4%) and medulloblastomas (17.4%)

2. There were more females affected with brain tumours than males with a ratio of 1.3:1

3. Primary paediatric brain tumours generally follow the demographics of a given population. In Western populations, primary paediatric brain tumours are more common among white children. In this study, more black children were affected than white children. There were 22 black children versus one white child with brain tumours.

4. The tumours were more frequent (52.2%) among those aged 0-3 years, being three astrocytomas, four medulloblastomas, three choroid plexus tumours, one infantile ganglioglioma and one craniopharyngioma

5. The Glasgow Coma Scores of the subjects ranged from three in one patient (4.3%) to 15 in seventeen patients (73.9%).

6. Motor Deficit on admission was present in five (21.7 %.) of the patients.

7. The tumour locations were supratentorial in 11(47.8%) and infratentorial in 12 (52.2 %)

8. The tumours sizes ranged from 2.2 cm (30.4%) to more than 7.2 cm (13.0%)

9. There was surrounding vasogenic edema in 17 (73.9 %) of the subjects, hydrocephalus was present in 18 (78.3%) and calcifications was present in five (21.7%)

5.2 DISCUSSION OF RESULTS

5.2.1 PATTERN AND FREQUENCY OF HISTOLOGICAL SUBTYPES OF PAEDIATRIC BRAIN TUMOURS

In this study, there were nine different kinds of brain tumours as shown in Table 4. The most common brain tumours amongst the children enrolled into the study were astrocytomas (30.4%), medulloblastomas and choroid plexus tumours at 17.4% and 17.4% each.

This finding is consistent with other studies on the continent such as in Ibadan, Nigeria; Accra, Ghana; Western Kenya and Windhoek, Namibia all of which found that the commonest histological subtype of paediatric brain tumours were astrocytomas. [4,5,6,7,8]

It is also like the report by Pollack et al., in a study done in Pittsburgh, Pennsylvania which found that astrocytomas accounted for approximately 50% of hemispheric tumors in children, occurring at all ages. [29]

The commonest subtype of astrocytoma in this study was pilocytic astrocytoma of the cerebellum. This is consistent with the findings in a study by Rorke et al., in which in a series of 1,038 biopsy specimens of childhood tumours, pilocytic and Grade 2 fibrillary astrocytomas each represented a third of all gliomas. [30] Also, it was found in the present study that craniopharyngioma accounted for 8.7% of tumours, which is consistent with a study by Bunin et al., who found craniopharyngioma to be 5-10% of paediatric brain tumours. [38] Medulloblastoma comprised 17.4% of all paediatric brain tumours, in the present study, which is similar to the findings in a study by Schoenberg et al. at the Mayo Clinic in Rochester, Minnesota, USA in which medulloblastoma accounted for 15-30% of all brain tumours in children.

5.3 DEMOGRAPHIC PROFILES IN RELATION TO FINDINGS

5.3.1 AGE

Among the population in the present study, the majority (43.5%) of the children with primary paediatric brain tumours were between the ages of 0-3 years (Table 4). This is in contrast to the findings in a Canadian population, in which Keene et al. found that approximately 10% of CNS tumours occurred in children under two years of age, 20% between two and five years, 25% between five and ten years and 45% over ten years of age. [24] In addition, 75% of medulloblastomas were diagnosed before the age of 15 years. [54], whereas, in the present study, all the medulloblastomas were diagnosed before the age 14 years.

5.3.2 GENDER

In this study, it was found that patients with primary paediatric brain tumours had a slight female preponderance of 1.3:1 (Figure 2). This contrasts with study by Stiller et al. that found the gender ratio of paediatric CNS tumours to be male bias for all tumours except astrocytomas. [25] Also, this is in contrast with the study in Ghana by Gyasi and Tettey in which males were more likely to have brain tumours than females at a ratio of 1.14:1. [5]

5.3.3 RACE

In this study, 95.7% of the paediatric patients who had primary brain tumours were black. This finding is in sharp contrast to epidemiological studies and surveillance results in USA, which suggested that paediatric brain tumours are more common in white children in comparison to other racial groups.[11] Given that most of the studies on paediatric brain tumours were conducted in Western countries with lower populations of black children, the differences between the reports by Stiller, Gabriel, Gjerris and Schoenberg and the present study and other African studies is quite understandable. [1,11,34,41]

5.4 Clinical and radiological findings

Seizures:

Seizures are one of the most common symptoms in paediatric brain tumours with supratentorial brain tumours involving the gray matter being more epileptogenic. [18] However, only six (26.1%) of the 23 patients in the present study had seizures.

Tumour locations:

The tumour locations in the present study were supratentorial in 11 (47.8%) and infratentorial in 12 (52.2 %) of the patients. Traditionally, most paediatric brain tumours are reported to be infratentorial, but this is also dependent on the different age groups. [21]

5.5 LIMITATIONS OF THE STUDY

i. Time constraint was a major limitation of this study. If the study were carried out over a longer period e.g. five years or more, a greater number of children would have been enrolled into the study.

ii. According to the World Health Organization, persons younger than 19 years of age are considered children, but only those 14 years and below were included in this study, as that is the age limit for admission into the paediatric neurosurgery wards at both hospitals. This made comprehensive comparison of results with existing literature impossible in certain cases.

CHAPTER SIX

6. CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

1. The prevalence of primary paediatric brain tumours in this study carried out at the two biggest hospitals in Johannesburg was 6.59% and the most frequent of the types of brain tumours were astrocytomas (30.4%) and medulloblastomas and choroid plexus tumours at 17.4% each.

2. Most brain tumours in children were found in the 0 - 3 years age group.

3. More girls were affected with brain tumours than boys.

4. In this study, more black children were affected than white children.

6.2 Recommendations

1. Television media and social media awareness amongst the general public about the causes and possible prevention strategies of paediatric brain tumours can be improved. This could be done by the Department of Health in conjunction with the Nelson Mandela Children's Hospital (NMCH), CHBAH and CMJAH. Another strategy is to hold Continuous Medical Education (CME) sessions with general practitioners as they are often the first point of contact with the pediatric patients. Furthermore, one can institute an awareness campaign with the use of posters of the symptomatology of paediatric tumours and place them in paediatric casualties, and the clinical rooms of other allied health professionals.

2. It is recommended that similar studies be conducted in other referral centres around the country, so that a national frequency and tumour pattern trends can be established.

3. With the advent of Nelson Mandela Children's Hospital (NMCH) in Parktown, Johannesburg, improved synergies between the various departments namely: Paediatrics, Anatomical Pathology, Paediatric Oncology and the Department of Neurosurgery is recommended to improve research outputs related to paediatric neurosurgery.

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APPENDICES

APPENDIX A

Data Sheet/Participant Information Sheet: Page 1

Research project:

FREQUENCY OF PAEDIATRIC BRAIN TUMOURS AT TWO TERTIARY REFERRAL CENTERS IN JOHANNESBURG

Researcher:

Dr A Oduntan

Supervisor:

Dr J Ouma

Patient Details:

Name: ____

Age: ____

Gender: ____

Hospital File Number: ____

Date of admission: ____

Hospital (CHBAH/CMJAH) ____

Patient allocation tracking number: ______________________________________

Data Sheet: Page2

Patient allocation tracking number: ____

Clinical Data:

Duration of symptoms:

Raised Intracranial Pressure symptoms (Y/N):

Seizures (Y/N):

Glasgow Coma Score: ……/15

Pupil Size and Response…………….

Motor Deficit using the Medical Research Council (MRC) scale on admission:

Radiological Data:

Location of tumour: (Supratentorial/ Infratentorial) ……………………………………

Size of tumour (cm)…………………………

Surrounding vasogenic edema (Y/N) ……

Mass effect from tumour: Effacement of underlying Sulci and Gyri, Midline Shift, Effacement of Ventricle (Y/N) …………….

Presence of hydrocephalus (Y/N) ……….

Basal cisterns effaced (Y/N) ………….

Presence of calcifications (Y/N) ………..

Presence of associated bleeds: Intratumoral, Subarachnoid, Intraventricular or none…………….

Histopathological Data:

Diagnosis:

WHO Grade (if applicable):

Genetic or Molecular marker (according to WHO Classification May 2016):

Degree of cellularity:

Shape of nuclei:

Nuclear atypia (Y/N):

Mitotic Figures (Y/N):

Necrosis (Y/N):

Endothelial Proliferation (Y/N):

APPENDIX B

Data Sheet: Page 1

Consent Form: Use of clinical information for research

Good Day Madam/Sir

My name is Dr Akinola Oduntan. I am a registrar (specialist in training) in the Department of Neurosurgery at the Charlotte Maxeke Johannesburg Academic Hospital. I am conducting a research project titled below.

Your child is currently admitted at the Chris Hani Baragwanath Academic Hospital/Charlotte Maxeke Johannesburg Academic Hospital for treatment of problems he/she is currently experiencing. Chris Hani Baragwanath Academic Hospital/Charlotte Maxeke Johannesburg Academic Hospital not only renders treatment but is also actively involved in conducting research aimed at improving the quality of care that we deliver. From time to time such research involves the use of patient records from which information is extracted. The use of such information is subject to the following:

1. Approval from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand.
2. Identity of a patient from whose file information is extracted is never revealed to anyone but the researcher unless specific consent is obtained to do so. The information gathered does not contain the name of the patient.

We would like to obtain your consent to use information from your file for the purpose of research, subject to the aforementioned conditions. If you choose not to give consent, this will not compromise your treatment in any way. If at any time you choose to withdraw consent you are free to do so and will not be prejudiced in any way.

Data Sheet: Page 2

Research project title: Frequency of Paediatric Brain Tumours at two tertiary referral centers in Johannesburg

Aim

1) To determine what proportion of the total number of patients with intracranial tumours seen at the CMJAH and CHBAH are children?

2) To determine which histological subtypes (according to the new WHO classification) are these children presenting with most commonly and why?

Objectives

- Critically analyze data to objectively determine the frequency of paediatric brain tumours at the CMJAH and CHBAH

Patient requirements:

- Participation in the above study is completely voluntary. Consent may be withdrawn at any stage without prejudice. The standard of care afforded to the patient will remain the same irrespective of participation in the study.
- In cases where family members (other than parents) have consented to the use of the patient's medical records due to incapacity of the patient's parents, an attempt will be made at a later stage to obtain the parents' consent if possible.
- Clinical follow up after six months as part of routine management

Should you wish to contact us at any stage regarding consent, contact:

Researcher: Dr A Oduntan Tel: 0829262288

Charlotte Maxeke Johannesburg Academic Hospital

Data Sheet: Page 3

Parent/Next of Kin Consent form:

Use of clinical information for research

A. Consent Given

I hereby give consent for patient: ……………………………………………………………………… records to be used as per the above-mentioned conditions for the purposes of research:

PARENT/ NEXT OF KIN: ______________________________ DATE: ________________

SIGNATURE: ____

B. Consent Not Given

I hereby do not give consent for patient:……………………………………………………… records to be used:

PARENT/ NEXT OF KIN: ________________________________ DATE: ________________

SIGNATURE: ___________________________________

Data Sheet: Page 4

Deferred Consent form:

Use of clinical information for research

A. Consent Given

I hereby give consent for patient: ………………………………………………………………………… records to be used as per the above-mentioned conditions for the purposes of research:

PARENT/ NEXT OF KIN: ________________________________ DATE: __________________

SIGNATURE: ____

B. Consent Not Given

I hereby do not give consent for patient:……………………………………………………… records to be used:

PARENT/ NEXT OF KIN: ___________________________________ DATE: __________________

SIGNATURE: ______________________________________

APPENDIX C

Data Sheet: Page 1

Information and Assent Form for Children Old Enough To Understand The Study: Use of clinical information for research

Good Day

My name is Dr Akinola Oduntan. I am a specialist doctor in training in the Department of Neurosurgery at the Charlotte Maxeke Johannesburg Academic Hospital. I am conducting a research project titled below.

You are currently admitted at the Chris Hani Baragwanath Academic Hospital/Charlotte Maxeke Johannesburg Academic Hospital for treatment of problems you are currently experiencing. Chris Hani Baragwanath Academic Hospital/Charlotte Maxeke Johannesburg Academic Hospital not only gives treatment but is also actively involved in conducting research aimed at improving the quality of care that we deliver. From time to time such research involves the use of patient records from which information is taken from. The use of such information is subject to the following:

4. Approval from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand.
5. Identity of a patient like you from whose file information is taken from and is never revealed to anyone but the researcher unless specific consent is obtained to do so. The information gathered does not contain the name of the patient.

We would like to obtain your permission to use your information from your file for the purpose of research, subject to the aforementioned conditions. If you choose not to give permission, you won't get into any trouble. If at any time after giving permission, you choose to stop participating in the study you are free to do so and will not be prejudiced in any way.

Data Sheet: Page 2

Research project title: Frequency of Paediatric Brain Tumours at two tertiary referral centers in Johannesburg

Researchers: Dr A. Oduntan and Dr J. Ouma

Address: Department of Neurosurgery, Charlotte Maxeke Johannesburg Academic Hospital, Jubilee Road, Parktown

What is Research?

Research is something we do to find new knowledge about the way things (and people) work. We use research projects or studies to help us find out more about disease and illness.

What is this research project all about?

The research project is about collecting information about children like you with the same condition i.e. with brain tumours

Who is doing the research?

As noted above (Page 1)

What will happen to me in this study?

You as the participant will just be required to answer a few questions about your condition like how long you have been ill and when you first sought medical attention etc. In addition, if consent is granted, information about your condition will be collected along with other children's information.

Can anything bad happen to me?

No. Nothing bad will happen to you. The study's aim is to add more information to studies that can benefit other children like you.

Will anyone know I am in the study?

No. Your participation will be kept strictly confidential

What if I do not want to do this?

You have a right to refuse to take part in the study. You also can stop being in the study at any time without getting into trouble.

Patient requirements:

- Participation in the above study is completely up to you. You are not forced to take part. You may take away your permission at any time without getting into trouble. The care afforded to you will remain the same

Should you wish to contact us at any stage regarding this consent, contact me:

Researcher: Dr A Oduntan Tel: 0829262288

Charlotte Maxeke Johannesburg Academic Hospital

Data Sheet: Page 3

Patient Consent/Assent form:

Use of clinical information for research

C. Consent Given

I hereby give consent for patient: ……………………………………………………………………… records to be used as per the above-mentioned conditions for the purposes of research:

PATIENT: ________________________________ DATE: __________________

SIGNATURE: ____

D. Consent Not Given

I hereby do not give consent for patient:……………………………………………………… records to be used:

PATIENT: ___________________________________ DATE: __________________

SIGNATURE: _______________________________________

APPENDIX D

Superintendent Consent from Chris Hani Baragwanath Academic Hospital

APPENDIX E

Superintendent Consent from Charlotte Maxeke Johannesburg Academic Hospital

Appendix F

Permission from Prof Hale to conduct study using NHLS records