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EPIDEMIOLOGY OF PRIMARY PAEDIATRIC BRAIN TUMOURS AT JOHANNESBURG AND CHRIS HANI BARAGWANATH HOSPITALS FROM APRIL 1995 TO APRIL 2005

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirement for the degree of Master of Medicine in the branch of Neurosurgery, Johannesburg, 2008

DECLARATION

I, Agabe Emmy Nkusi, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine (Neurosurgery) of the University of the Witwatersrand, Johannesburg.

It has not been submitted before for any degree or examination at this or any other University.

_____

(Signature)

_____ **day of** _____ **2008.**

DEDICATION

To Anita my wife, and children, Daniel, Andrew and Natasha for their love, patience and support.

ABSTRACT

Epidemiology of primary paediatric brain tumours has been studied extensively in developed countries of the west. Such studies are lacking in developing countries especially sub-Saharan Africa.

This study seeks to establish the epidemiology of primary brain tumours seen among children that were treated at Chris Hani Baragwanath and Johannesburg Hospitals from April 1995 to April 2005.

The records of 252 patients who presented with this condition during the study period were reviewed, for the following details:

- Demographic details such as age, gender and race
- Diagnosis and the date when it was made
- The follow-up period at the hospital(s)/clinic(s)
- The anatomical location of the tumours; supratentorial or infratentorial
- The treatment that was given which included mainly surgery for tumour removal or biopsy, radiotherapy, chemotherapy and others which included ventriculoperitoneal shunt, external ventricular drain insertion.
- The outcome of treatment included:
  - alive
  - dead
  - presumed alive
  - lost to follow-up

It was found:

- That 225 patients had full demographic details of race, gender and age.
- That there was a slight male predominance among children with primary brain tumour.

- That the majority of children with brain tumours were black, followed by whites which is in keeping with the country's demographics.
- The three most common tumours were astrocytomas, medulloblastomas and brainstem gliomas in the descending order of frequency.
- Medulloblastomas were the commonest tumours in the infratentorial region while craniopharyngiomas were commonest tumours in the supratentorial region.
- More children had infratentorial tumours
- Younger children were more likely to have infratentorial tumours.
- Majority of patients had surgery either for diagnosis or for diagnosis and treatment.
- Few patients were presumptively diagnosed clinically and by imaging modalities
- Combination therapy of surgery, chemotherapy and radiotherapy had the best survival outcome while chemotherapy as the only form of treatment had the worst outcome.
- The overall 5 year survival rate for all the study participants was much lower than that of their counterparts in the literature.
- Children who had craniopharyngiomas and astrocytomas had better survival.
- Mortality incidence was slightly higher for whites than blacks but that could have been skewed by a high number of blacks that was lost to follow-up.
- A higher infratentorial tumour prevalence than in the literature was noted.

It was noted that racial prevalence of primary paediatric brain tumours follows population demographics.

From the results of this study, there is a need for a better record keeping and improved patients follow-up.

There is also a need for a larger epidemiological study in the two hospitals.

There is need to establish a specialized paediatric unit which will help start a paediatric team comprising of a paediatric neurosurgeon, paediatric oncologist, paediatric intensivist and neuroradiologist with dedicated neuropaediatric ICU. Such a team given resources will improve survival outcome of children with brain tumours.

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LIST OF ABBREVIATIONS

CNS	=	Central Nervous System
Neuro ICU	=	Neurosurgical Intensive Care Unit.
PNET	=	Primitive Neuroectodermal Tumour
PY	=	Person-Years
SA	=	South Africa
USA	=	United States of America.

DEFINITION OF TERMS

Glioma: In this research report, the term glioma was found to be used as a presumptive diagnosis for lesions in brainstem and thalamus based on clinical and radiological grounds.

Primitive neuroectodermal (PNET) occurs in both supratentorial and infratentorial regions. The commonest PNET in the infratentorial region is Medulloblastoma. In this research report Medulloblastoma is specified from general PNETs by writing the name or putting PNET and then Medulloblastoma in blackets.

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND

Primary paediatric brain tumours have been studied extensively in the developed countries in the last 2 decades, but such studies are few or lacking in the developing world. Comparison of data from the two worlds may not give the true picture because of small numbers reported in the developing countries especially sub Sahara Africa. However, one is able to compare the trends of the prevalence of the brain tumours.

The author's experience while working at Chris Hani Baragwanath and Johannesburg hospitals regarding national and provincial epidemiology of primary paediatric brain tumours was found to be inadequate. Due to inadequacy of epidemiological data on primary childhood brain tumours, the author developed interest in studying primary paediatric brain tumours. The epidemiology of primary paediatric brain tumours and the associated morbidity and mortality rate are important for counselling and obtaining consent for surgery from caregivers and to predict diagnosis, which may influence treatment outcome. These data are particularly important for tertiary hospitals where a high number of children with primary brain tumours are referred.

Paediatric brain tumours are the second most common type of cancer after leukaemia and the leading cause of mortality among children[1]. In the same study it was reported that infratentorial tumours comprised 50-55% and were the most common. They comprised of medulloblastomas (20%), astrocytomas (15%), brainstem gliomas (10%) and ependymomas (6%). Supratentorial tumours (45 - 50%) were the second common and included astrocytomas (23%), malignant gliomas (6%), craniopharyngioma (6%), primitive neuroectodermal

tumours (PNET)(4%), pineal region intracranial germ cell tumours (4%), ependymomas (3%), and others 4%[1].

A Korean study[7] found Pilocytic astrocytomas, medulloblastomas, craniopharyngiomas and germ cell tumours were commonest of brain tumours. In this multicentre study overall male to female ratio of 1.4:1 among children with primary paediatric brain tumours was noted.
Similarly, in a German study by Kaatsch et al[6] the most common tumours were astrocytomas (41.7%), medulloblastomas(18.1%), ependymomas (10.4%), supratentorial PNETs (6.7%) and craniopharyngiomas (4.4%).
In developing countries, community based epidemiological data about childhood primary brain tumours is lacking, and where studies have been done, they concentrated on adult central nervous system tumours or on childhood cancers in general. Examples of such studies are:

"Tumours of childhood in Ibadan, Nigeria" by A.Olufemi, W[9]. In this study 1325 cases were analyzed and intracranial tumours were only 29(2.2%). In the same study, the commonest tumours were astrocytomas (37.9%) followed by craniopharyngiomas (24.1%),medulloblastomas and pineolomas were of equal proportion (10.3%) ependymomas (6.9%) gliomas (3.4%), and teratomas (3.4%).

In a Ghanian study by R K Gyasi,and Y Tettey[10], out of 252 cases only 32(13%) were brain tumours.The modal age group was 11-14 years with modal age of 11years. Histological types were gliomas 21(65.6%), meningioma 2(6.3%),and pituitary adenoma 1(3.1%). The histological type was not stated in 25%(8/32) of cases. The male:female ratio for CNS tumours was 1.14:1.

In South Africa and in particular the two tertiary hospitals (Chris Hani Baragwanath and Johannesburg), there is little documented epidemiological data about paediatric brain tumours. Sparrow[14] in 1986 studied central nervous tumours and found only 49 paediatric brain tumours. The tumour composition

was as follows; astrocytomas 26(53%), medulloblastomas 12(25%), craniopharyngiomas 7(14%), ependymomas, oligodendrogliomas, meningioma and pineal tumours were 1(2%) each.

This study determined the epidemiology of primary brain tumours among children treated at Chris Hani Baragwanath and Johannesburg hospitals from April 1995 to April 2005 by analyzing patients' records.

1.2 PROBLEM STATEMENT

Although there is literature about epidemiology of paediatric brain tumours in other countries, to the author's knowledge there is no study that has been done at the two mentioned tertiary hospitals of Johannesburg and Chris Hani Baragwanath to establish such epidemiological data.

This study was carried out so that the prevalence, the type of common tumours, treatment modalities and the survival periods are established.

1.3 RESEARCH QUESTION AND OBJECTIVES

1.3.1 Specific questions

What is the epidemiology of primary brain tumours in children of 0 ─14 years?

1.3.2 Specific objectives

(i) To determine the prevalence of primary brain tumours in paediatric age group of 0 ─14 years
(ii) To identify the types and frequency rates of paediatric brain tumours.
(iii) To establish the common anatomic locations of paediatric brain tumours.

(iv) To identify differences in ages affected by different paediatric brain tumours.

(v) identify various treatment modalities used in the management of paediatric brain tumours

(vi) To establish the mortality and survival rates associated with childhood brain tumours.

1.4 SIGNIFICANCE

The information gained from the study will be valuable in the management of subsequent patients, planning for treatment and further managerial follow-up of the children with primary paediatric brain tumours.

Furthermore, the information gained will be important to obtain informed consent from caregivers including parents and guardians. These data will be used in the appropriate management of patients with similar conditions while explaining the possible diagnoses and possible treatment outcomes.

In comparison with data from other countries and institutions, different treatment options that have been proven effective elsewhere would be introduced to improve the treatment outcome among the affected children.

The author is optimistic that these data will contribute in future management of children with brain tumours and that it will stimulate more research in this field.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 PREVALENCE OF PAEDIATRIC BRAIN TUMOURS

Primary paediatric brain tumours have been studied extensively in the developed countries in the last 2 decades, but such studies are few or lacking in the developing world. Comparison of data from the two worlds may not give a true picture because of small numbers reported in the developing countries especially sub Saharan Africa. However, one is able to compare the trends of the prevalence of the brain tumours and other epidemiological data. In this chapter, larger studies are considered first because of their significance, and then studies from other African countries and finally the South African studies are reviewed.

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Brain tumours are the most common group of solid tumours in childhood according to studies in the developed countries of USA, Europe and Japan[1,2,8,3]. It is also evident that children with brain tumours have a relatively poor survival rate[5]. In most countries the commonest childhood tumours are leukemias followed by brain tumours[4,8]. The childhood brain tumours typically account for about 20-25% of all childhood cancers[4,8].

In a study by Stiller CA and Parkin DM[4], the most common category of CNS tumour in childhood was astrocytoma, followed by medulloblastomas, while ependymomas were rare.

Greta R.Bunin[2] also reported that the commonest brain tumours are astrocytomas and primitive neuroectodermal tumour (PNET)/ medulloblastomas, which accounted for about 50% and 20% of childhood brain tumours respectively.

Similarly, Melissa and Julianne[8] showed that from 1975 to 1995 astrocytomas accounted for 52% of central nervous system malignancies, primitive neuroectodermal tumour [PNET] including medulloblastomas 21%, gliomas 15%, ependymomas 9%, and other CNS tumours 3%. These authors also reported that the overall annual incidence in the United States of paediatric malignant CNS tumours was about 28 per million in children younger than 14 years of age. Primary malignant tumours of the central nervous system were found to account for about 16% of childhood malignancies[6] and it was found to account for about 19 – 22 % of all reported incidences of malignancies in children[1].

Feltbower et al[5] in their study on the epidemiology of central nervous system tumours in children and young adults (0-29years), reported a higher incidence of childhood CNS tumours at 32.7 (28.9-36.5) per million compared to the 28 per million of USA[8.] They also found that astrocytomas and medulloblastoma/PNET comprised the majority of childhood CNS tumours at 41% and 25% respectively.

A German study by Kaatsch et al[6] on epidemiology of brain tumours in German children, like other studies from developed countries, found the incidence rate of 2.6 per 100,000(26 per million). They also found that the most common brain tumours were astrocytomas (41.7%), medulloblastomas (18.1%), ependymomas (10.4%), supratentorial PNETs (6.7%) and craniopharyngiomas (4.4%).

In a Korean Study by Suh et al[7] on central nervous system tumours, 3221 cases were studied and only 273 (8.5%) cases were children under 15 years of age. Pilocytic astrocytomas, medulloblastomas, craniopharyngiomas, germ cell tumours and ependymomas were common types of tumours found.

In a Nigerian study by Olufemi A[9] on tumours of childhood in Ibadan, a total of 1325 children with cancer were analyzed. In this study, intracranial tumours accounted for only 2.2% (29). They comprised astrocytomas 37.9%, craniopharyngiomas 24.1%, medulloblastomas and pineolomas each at 10.3%,

ependymomas 6.9%, gliomas and intracranial teratomas each at 3.4%. Contrary to studies from western countries, lymphomas were more than leukemias at 59% and 4.5% respectively, of the total childhood cancers.

Gyasi and Tettey[10] in their study on childhood deaths from malignant neoplasms in Accra found most common malignancy was lymphoma at 54% of cases followed by CNS tumours at 13%. Leukemias were fourth common at 6.7%. Gliomas (65.6%) were the most common brain tumours, meningiomas (6.3%), and pituitary adenoma (3.1%). Histologic types were not stated in 25% of cases[10].

Wiredu and Armah[11] in their study on cancer mortality patterns in Ghana, analysed 375 children (<15 years), and only 19 children had brain tumours. The commonest cause of death was reported to be haematopopoietic in origin (57.8% in females and 60.3% in males.).

Wessels and Hesseling[12] studied the incidence and frequency rates of childhood cancer in Namibia.

In this study, central nervous system CNS) tumours occurred most commonly (18%), followed by renal tumours (14%), leukaemia 9(12%) and lymphoma (11.5%). The incidence rate of CNS tumours was only 9.3 per million, much lower than that reported in western countries[2,3,4,5,6,7,8].

In a study by Peacock, Lazareff and Levin[13], 145 cases were studied. Ninety one (63%) were infratentorial while 54(37%) were supratentorial in location. Of the supratentorial tumours 24(44.4%) were in parasellar region, 14(24.9%) in cerebral hemispheres, 8(14.8%) in pineal region and 4(7.4%) in third ventricles. The posterior fossa included medulloblastomas (41.8%), brainstem gliomas (25.3%), ependymomas (16.5%) and cerebellar astrocytomas (15.4%).

In Sparrow's[14] report out of 49 cases, 26(53%) were astrocytomas, 12(25%) medulloblastomas, 7(14%) craniopharyngiomas and only 1 case (2%) each for ependymoma, oligodendroglioma, meningioma and pineal tumours.

2.2 AGE DISTRIBUTION

The overall prevalence of central nervous system (CNS) tumours is highest in children younger than 8 years of age[8]. The difference was attributed to cerebellar PNET [medulloblastoma], brainstem gliomas and ependymomas that occur almost exclusively in children less than 10 years old. According to these authors, the average annual incidence of CNS cancer between 1986 to 1994 varied only slightly by age of diagnosis from infancy through age 7 years [36 per million]. For all CNS tumours from age 7 to 10 years, a 40% drop in the incidence rate was observed, with a slight increase from ages 10 to 12, and a second decline from ages 12 to 20. For all ages the incidence of astrocytomas was highest, peaking at age 5 and 13 years [70 per million]. For ages 0 - 3 years PNET and ependymoma rates were highest [11 and 7 per million respectively] and then steadily declined. Gliomas had the lowest incidence during infancy with peaks at ages 8 and 17[9 and 7 per million]. Overall, ependymoma was the rarest type of brain tumour in children ages 3 to 20 years.

Olufemi[9] in his study reported that children with gliomas were over the age of 7 years.

Gyasi and Tettey[10] reported that the modal age group for childhood CNS neoplasms was 11-14 years with a modal age of 11 years .

Wessel and Hesseling[12] found the median age for children with central nervous system (CNS) tumours to be 7.8 years, similar to that found in Nigerian[9] children and much lower than among children in Ghana[10].

2.3 GENDER DISTRIBUTION

Melissa and Julianne[8] in their study, reported overall incidence of invasive CNS tumours between 1990 - 1995 for children ages 0 – 20 years was 24% higher in males than females, with rates of 30 and 24 per million respectively. PNETS showed the largest difference between males and females, followed by ependymomas. There were more males than females with CNS tumours for both white and black children, with greater difference between boys and girls seen among white children[8].

Feltbower et al[5] reported a male:female ratio of 1.3:1 and a striking sixfold male excess was observed for ependymomas in children aged under 10 years.

In a Korean multicentre study[7], the overall male to female ratio of 1.4:1 among children with brain tumours was observed. Furthermore, most tumour types in children showed a distinct predilection for males with exception of pilocytic astrocytomas [0.7:1], which was more common in girls than boys.

In one study on childhood cancer in Nigerian[9] children, it was demonstrated that children with gliomas had equal sex distribution. Craniopharyngiomas were also predominant in male children under the age of 5 years.[9] On the other hand, in Ghanian[10,11] studies male to female ratio for tumours was 1.14:1 and 1.26:1 respectively.

2.4 RACE DISTRIBUTION

Melissa and Julianne[8] while studying epidemiology of brain tumours in children found that CNS tumours are more common in white children compared to black children, with an 18% higher rate between 1990 -1995. The greatest difference was seen in white males at a 26% higher rate, compared to an 8% higher rate for white females.

Stiller and Parkin [4] also found that black children in Britain have significantly low relative frequency of brain tumours than their white counterparts.

2.5 ANATOMIC LOCATIONS

Kline and Sevier [3] in their study on solid tumours in children found that approximately 55% of the tumours arose in the posterior fossa, and 45% were supratentorial. Kaatsch et al[6] reported a nearly equal tumour distribution between supratentorial and infratentorial regions. They reported that, among children with infratentorial tumours, 56.0% had ependymomas, and 44.0% had astrocytomas. Among children with PNETs, 70.2% had infratentorial PNETs (medulloblastoma), and 26.0% supratentorial PNETs.

In the group of children with other brain tumours, Supratentorial tumours were preponderant. Suh et al[7] reported 42% of paediatric brain tumours to be infratentorial and 68% to be supratentorial contrary to reports from western countries[3,6]. Peacock et al[13] in their study "childhood brain tumours in Cape Town" found that 63% of the tumours were located in the infratentorial region and 37% in the supratentorial region.

2.6 MORTALITY AND SURVIVAL RATES ASSOCIATED WITH PAEDIATRIC BRAIN TUMOURS

Melissa S and Julianne B[8] in their study on the epidemiology of brain tumours in children reported that although children with malignant CNS tumours did not have as favourable prognosis as children with other cancers, 5 year relative survival rates increased from 59% between 1975 -1984 to 67 % between 1985 - 1994. During these time periods, the greatest increase in survival by age was seen in ages 15-19 by 10 % [from 67 - 77 %] with only 2 % increase in ages 0 - 5 [from 54 -56 %]. Males had a greater increase in survival of 9% compared to 2% for females. White and black children had similar increase in survival of 6% and

5% respectively. These increases were seen in all tumour types with the greatest improvement in ependymomas [39 % to 56 %], followed by gliomas [46% to 57%].

Survivors of paediatric brain tumours may have significant long-term morbidity from their disease and treatment. Fortunately, survival rates for childhood CNS tumours continues to be on the rise as improvements in therapy are being pursued to improve patient survival.

Kline and Sevier[3] reported that survival rate for children with brain tumours varies widely depending on histology, degree of surgical resection, and level of metastasis.

Feltbower et al[5] reported one-and 5-year survival rates for children 0-14 years with CNS tumours as 82% and 67% respectively.

Similarly, Kaatsch et al[6] reported a 5 year survival of 64% for all brain tumours which is comparable to that from other developed countries. Of the most frequent brain tumours, children with craniopharyngiomas had the best prognosis (10-year survival rate ,87%) followed by children with astrocytomas (73%). Within 10 years after diagnosis more than 50% of children with ependymomas, medulloblastomas and supratentorial PNETs had died. Kaatsch et al[6] also reported that for the whole group of children with brain tumours, girls showed a somewhat better prognosis than boys. They also found in the same study that CNS tumours showed somewhat a better prognosis with increasing age.

According to the above literature review, the need for an epidemiological study of brain tumours among children in South Africa became necessary to establish the prevalence, types, locations, treatment options used and outcomes of the different brain tumours. This will help clinicians in proper planning of treatment and also the government in availing resources. Knowledge of the disease

problem will help in establishing public awareness of brain tumours and this will in turn help in early diagnosis of the tumours and treatment which in turn improves survival rates.

CHAPTER THREE

3.0 METHODOLOGY

3.1 STUDY SETTING

The target population comprised of all children between 0 and 14 years of age, treated at Chris Hani Baragwanath and Johannesburg Hospitals with diagnoses of primary brain tumours from April 1995 to April 2005.

Chris Hani Baragwanath is the largest hospital in South Africa and one of the largest hospitals in sub-Saharan Africa. It is located in South-Western townships (SOWETO) in Johannesburg. It serves as a teaching hospital of the University of the Witwatersrand, and as a tertiary hospital for Gauteng Province. Chris Hani Baragwanath hospital serves mainly the black poor living in SOWETO and the surrounding areas who often do not have medical insurance facilities. Besides being a referral hospital for smaller hospitals in Gauteng, it also serves as a referral hospital for Mpumalanga and North West provincial hospitals particularly for neurosurgical conditions.

Johannesburg hospital is also a teaching hospital of the University of the Witwatersrand, and also serves as tertiary hospital for Gauteng Province. However, the hospital serves both the poor and middle class people who may have medical insurance facilities. It is located in Johannesburg city, and further serves as a neurosurgical referral for other provincial hospitals in Mpumalanga and North West provinces.

Consequently, it was important for the author to study epidemiology of primary paediatric brain tumours at Chris Hani Baragwanath and Johannesburg Hospitals since these are the largest and major referral hospitals for neurosurgical

conditions in Johannesburg and surrounding areas, and therefore information obtained from this study was considered to be representative of the greater Johannesburg and surrounding areas' population.

3.2 STUDY DESIGN

A retrospective study design was used to study the epidemiology of primary paediatric brain tumours from April 1995 to April 2005.

A review of patients' records enabled the author to establish the epidemiology of paediatric primary paediatric brain tumours among the study population. The author considered this ten-year period of follow-up to be adequate and the neurosurgical conditions received at the hospitals during that time was considered to be a representative sample of the communities served by the hospitals.

Data from a retrospective study is fairly representative and minimizes possibilities of bias compared to a cross-sectional study.

3.3 STUDY POPULATION

Children that were admitted to Chris Hani Baragwanath and Johannesburg hospitals during the period April 1995 to April 2005 with diagnoses of primary brain tumours were studied.

3.3.1 Inclusion criteria

Children were included if they met the following criteria:

- Male or female children between ages 0 and 14 years with primary brain tumours

- Children admitted to Chris Hani Baragwanath and Johannesburg Hospitals between April 1995 and April 2005.

3.3.2 Exclusion criteria

The following subjects were excluded:

- Children with brain tumours other than primary brain tumours
- Children above 14 years.
- Children with incomplete records.

3.4 SAMPLES AND SAMPLING METHODS

There was no sampling of subjects to include in the study. All children who fulfilled inclusion criteria with primary brain tumours between 0 and 14 years admitted to Baragwanath and Johannesburg hospitals between April 1995 and April 2005, were studied.

3.5 INSTRUMENTS

Data capture sheet based on study objectives was developed (Annex 1) and used. Data obtained from the retrospective review included subjects' demographics, number and type of tumours, anatomic locations of the tumours, treatment modalities and follow-up period.

The demographic data particularly assessed different age groups, gender and races of the subjects. Demographic data together with follow-up period were used to ascertain mortality and survival rates associated with childhood brain tumours.

3.6 DATA ANALYSIS

Data was entered into Microsoft Excel where preliminary cleaning was done before being transferred to STATA version 9.0 where more data management and all statistical analyses were carried out. Graphs were plotted using both Excel and STATA version 9.0 programs.

Descriptive statistics were first carried out for key variables. The descriptive statistics employed depended on the variable. Means and standard deviations were used for continuous variables while proportions and graphs were used for categorical variables.

Statistically significant differences in continuous variables were assessed using the Student t-test while for categorical variables, the Chi-squared test was used. Test for significant difference were done at a confidence level of 0.05. A p-value less than 0.05 indicated a statistically significant finding.

For mortality from brain tumours, incidence rates and Kaplan-Meier survival estimates were carried out using survival analysis. Incidence rate and Kaplan-Meier survival curves were estimated for all study participants for whom time of follow-up information was available, and were also estimated by key explanatory variables including diagnosis and treatment received.

A participant's person-years (py) is length of time for which the participant was under observation. For participants who were still alive, length of time of observation was truncated at the end of the study period of 30th April 2005.

3.7 ETHICAL CONSIDERATIONS

Considerations to protect the rights of human subjects and standards of any scientific enquiry were taken into consideration.

However, since this study was a retrospective study there was no direct contact with the subjects. Permission was obtained from hospital administration at Chris Hani Baragwanath and Johannesburg Hospitals where the study took place (Annexes 2 and 3). Besides, ethical clearance (number M051128) was obtained from ethics committee at University of the Witwatersrand (Annex 4).

Although this study was a retrospective review of subjects' records without direct contact with patients, data remained anonymous. The author will make all attempts to share the data findings obtained from this study are shared with various professional colleagues, such as those at University of the Witwatersrand, Baragwanath and Johannesburg hospitals. The author will endeavour to write articles for publications in professional peer review journals.

CHAPTER FOUR

4.0 RESULTS

4.1 INTRODUCTION

This chapter comprises the following sub-sections:

(i) Description of study participants
(ii) Types and frequencies of brain tumours by age and location
(iii) Description of treatment modalities used in the management of primary paediatric brain tumours
(iv) Mortality incidence presented by crude proportion of all participants
(v) Refined incidence rate by person years and survival estimates

4.2 DESCRIPTION OF STUDY PARTICIPANTS

Initially, 348 children were found to have had primary brain tumours from April 1995 to April 2005 with 196(56.3%) at Chris Hani Baragwanath hospital and 152(43.7%) at Johannesburg hospital. One hundred twenty three (35.5%) were excluded because they did not meet the inclusion criteria. A total of 225 participants were included in this study.

4.2.1 Subjects' demographic characteristics (n= 225)

Table 4.2.1 shows subjects' demographic characteristics. There was a significant difference in race distribution of tumours, with the majority of tumours (n=182) affecting blacks (80.9%). Thirty four (15.1%) of tumours affected the whites and the least affected were the coloured (n=5, 2.2%) and the Asians (n=4, 1.8%).

The mean age of the study participants was 7.1 years with a standard deviation of 3.8 years. The youngest participant was 0.2 years while the oldest was 14 years.

One hundred and fifteen (52.1%) of the subjects were males and one hundred and ten were females (48.9%). The male to female ratio was 1.05:1.

Table 4.2.1. Subjects' gender and race characteristics

Characteristics	n	%
Gender		
Males	115	52
Females	110	48
Race		
Black	182	80.9
Asian	4	1.8
White	34	15.1
Coloured	5	2.2

n=number; %= percentage

4.3 RELATIVE PREVALENCE FOR DIFFERENT TYPES OF BRAIN TUMOURS

Table 4.2.2 shows the prevalence of paediatric brain tumours. The commonest brain tumours were astrocytomas (25.7%), whereas medulloblastomas (21.2%) were second commonest, followed by gliomas (brainstem and thalamic) (19.9%), craniopharyngiomas (11.5%) and ependymomas (7.5%). The rare ones were meningiomas (0.9%), pituitary adenomas (0.9%) and gangliogliomas (0.9%).

About eighty percent (80.1%)of the tumours were histologically diagnosed. The remainder, the gliomas (19.9%) were diagnosed clinically and by imaging techniques. The commonest imaging modality used was magnetic resonance

imaging (MRI). Gliomas were diagnosed using MRI because they are found in deep and delicate structures; brainstem and thalamus.

Table 4.2.2: Prevalence of primary paediatric brain tumours

Diagnosis	Relative prevalence (%)	Confidence Interval (CI)
Medulloblastoma	21.2	16.1 – 27.1
Glioma	19.9	14.9 – 25.7
Astrocytoma	25.7	20.1 – 31.9
Ependymoma	7.5	4.4 – 11.8
Craniopharyngioma	11.5	7.7 – 16.4
Meningioma	0.9	0.1 – 3.2
Pituitary adenoma	0.9	0.1 – 3.2
Ganglioglioma	0.9	0.1 – 3.2
PNET	3.5	6.2 – 14.4
Pineoblastoma	8.0	0.5 – 4.5

PNET, Primitive neuroectodermal tumour, Glioma =Brainstem gliomas+thalamic gliomas.

4.4 ANATOMIC LOCATIONS OF THE TUMOURS

Intracranial cavity is divided into two parts, namely, supratentorial and infratentorial regions. This was done to facilitate tumour analysis in different locations.

Majority of the tumours were found in the infratentorial region (67%) whereas the supratentorial region comprised the remaining 33%. There were 151 (67%) infratentorial and 74 (33%) supratentorial brain tumours.

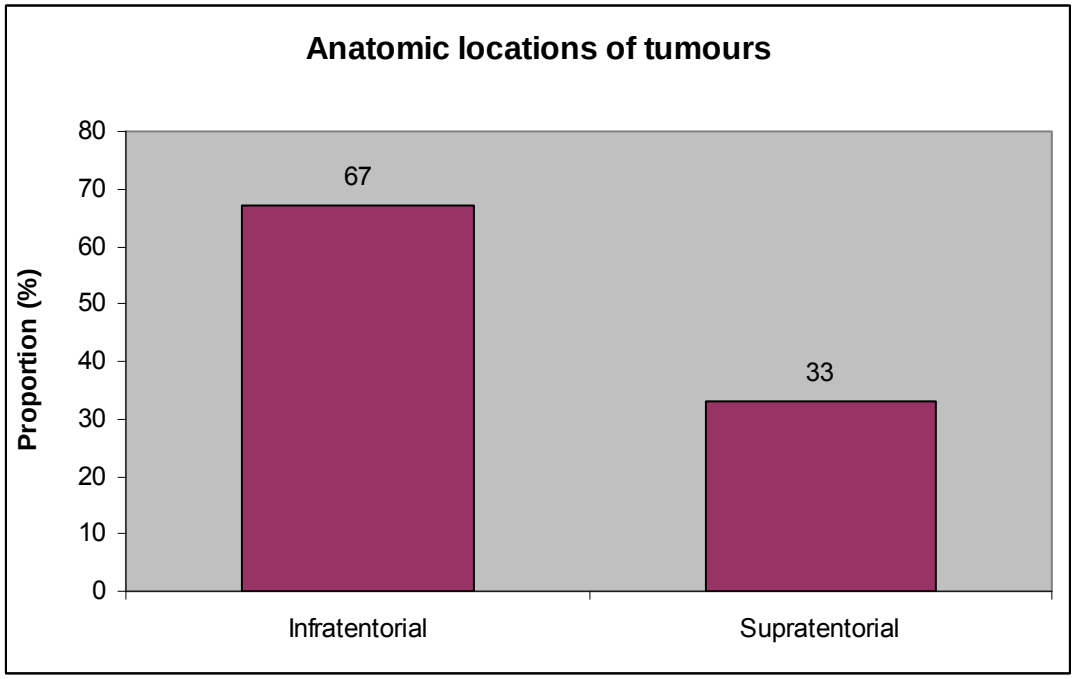


Figure1: The different anatomic locations of childhood brain tumours.

4.4.1 Tumours in infratentorial region

The majority of the tumours (67%) were found in the infratentorial region. Medulloblastomas were the commonest (34%), followed by brainstem gliomas (30%), astrocytomas (19%), ependymomas (12%), and PNET (other than medulloblastoma) were only 5%.

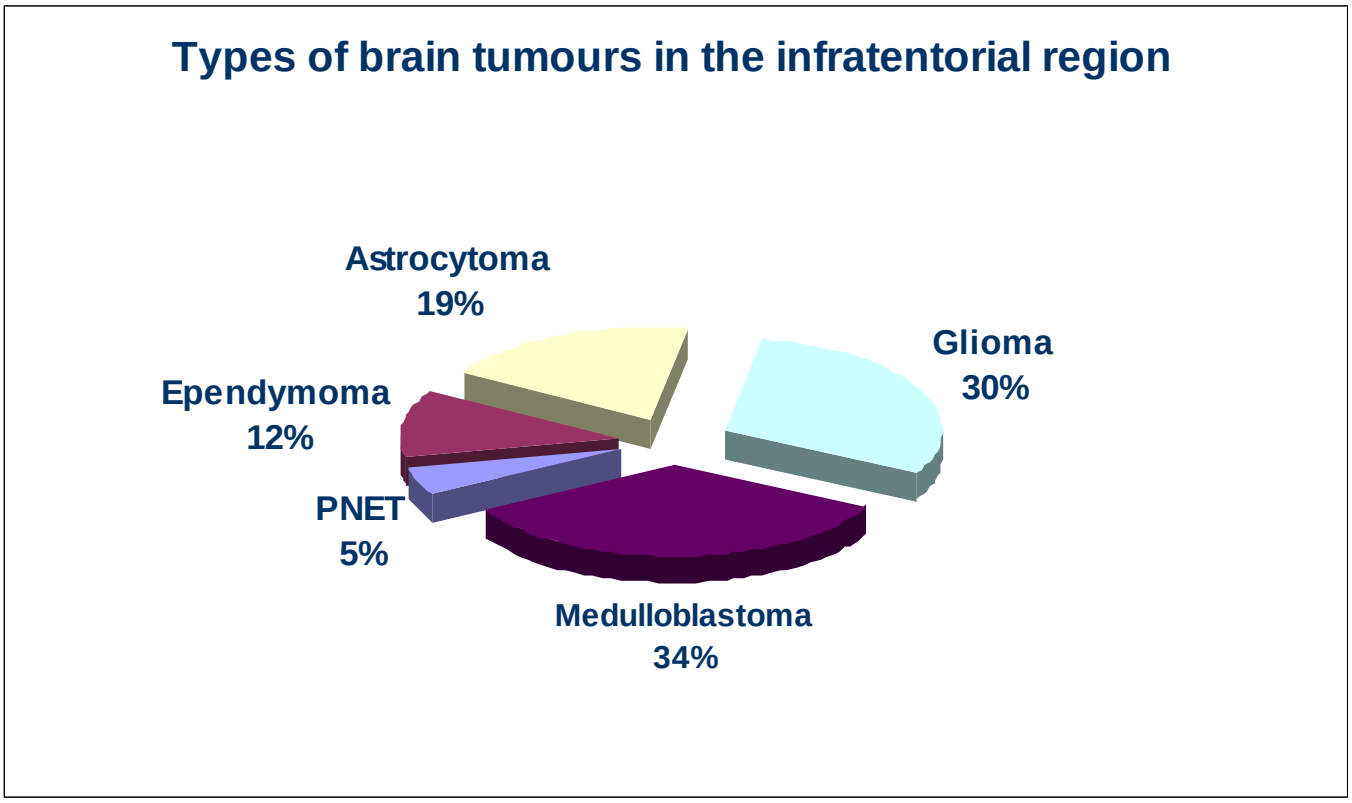


Figure 2: Brain tumour profiles in the infratentorial region of the brain

4.4.2 Tumours in the supratentorial region

This region had the highest number of histochemically diagnosed tumours because of easy accessibility of most parts in this region which is exemplified by the low number of gliomas (4.2%).

The commonest tumour in the supratentorial region was craniopharyngiomas (36.6%), followed by pineoblastomas (25.4%), astrocytomas (21.1%), gliomas (4.2%) and the remaining tumours comprising of supratentorial PNET, pituitary adenomas, gangliogliomas, ependymomas and meningiomas making the remaining 12.6%.

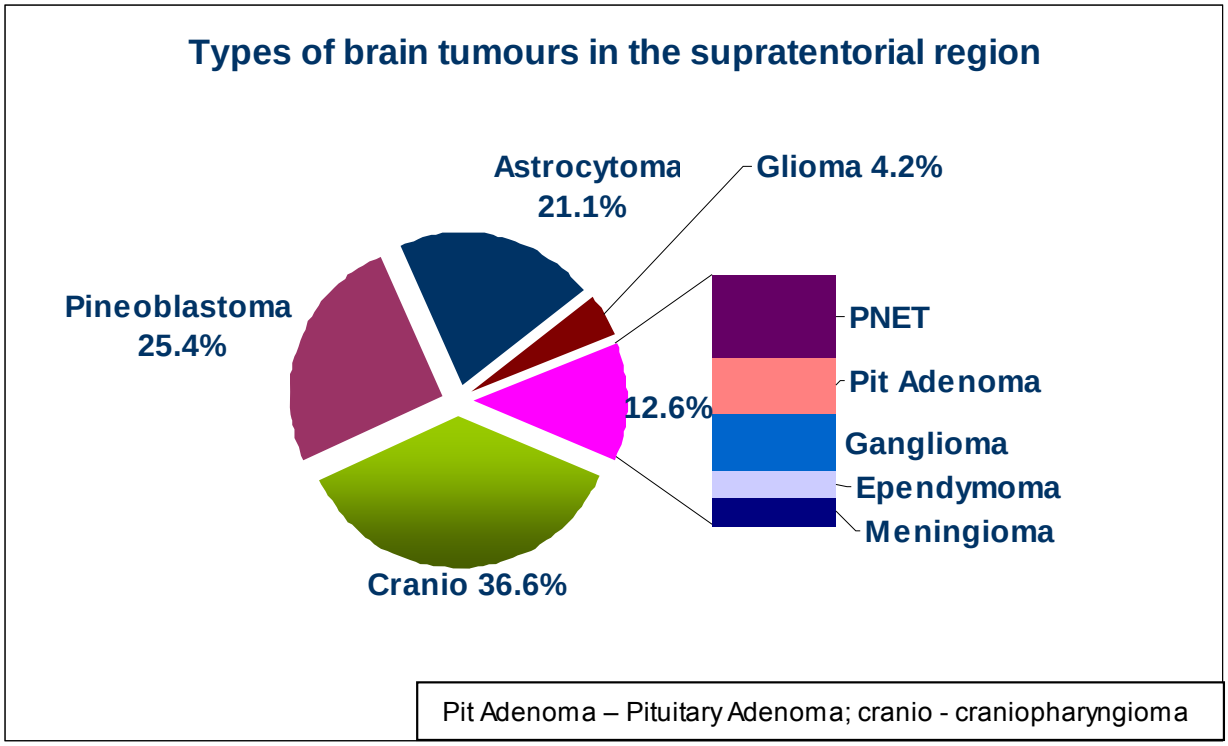


Figure 3: Brain tumour profiles in the supratentorial region of the brain

4.5 AGE AND BRAIN TUMOUR DISTRIBUTION

Figure 4 shows tumour distribution in different age groups. Participants' age groups were as follows: 0-2.0 years, 2.1-6.0 years, 6.1-9.0 years, 9.1-12.0 years, and 12.1-14.0 years. Different tumours affected different age groups differently. For example, medulloblastomas affected all children, and the most affected children were in the age groups between 2.1 and 9.0 years.

Gliomas included mainly brainstem gliomas which were over 90%, the others were thalamic gliomas. In this study group, gliomas affected ages from 0 to 12 years, and the most affected age group was 2.1 to 6.0 years.

Astrocytomas affected all age groups but peaked in age group 2.1 to 6.0 years and started slowly to decline.

Ependymomas affected all age groups but peaked in the age group of 2.1 to 6.0 years and then peaked again in the age group of 9.1 to 12.0 years.

Craniopharyngiomas affected mainly ages between 2 to 12 years.

Pineoblastomas were common among ages between the age 6 to 14 years. PNETs other than medulloblastomas and pineoblastomas affected mainly children of ages between 2 to 12 years, and were uncommon between the age groups of 0 to 2.0 years and 12.1 -14 .0 years.

The numbers for pituitary adenomas, meningiomas and gangliogliomas were too small to be analysed.

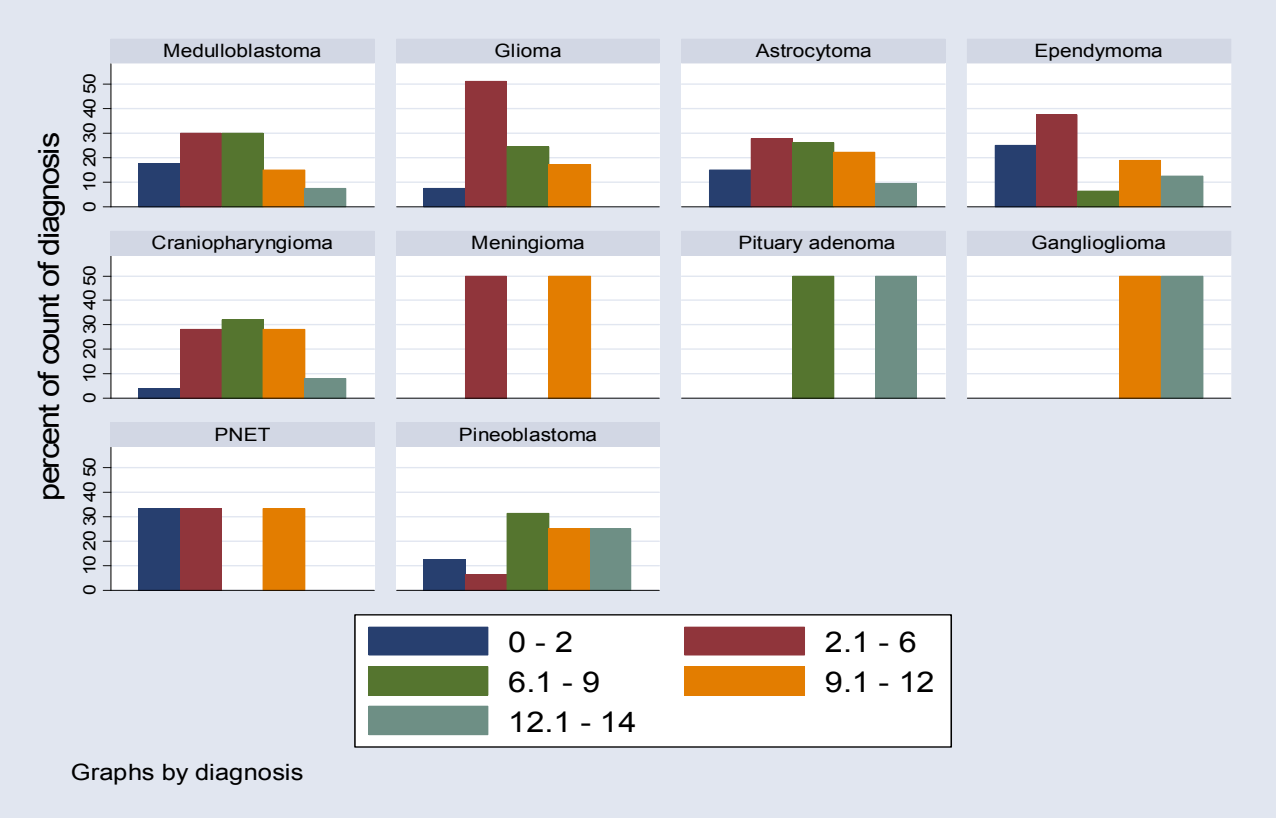


Figure 4: Subjects' age groups in relationship to the types of brain tumours

Age seems to affect the location of brain tumours in children (Table 4.5.1.). The mean age of the subjects who had brain tumours in the supratentorial location was significantly higher than the mean age of those who had brain tumours in the infratentorial location.

Also, there was a significant difference between age distribution of supratentorial brain tumours (7.9 ± 0 45) and Infratentorial brain tumours (6.4 ± 0.32) (p=0.009).

An epidemiological cross-tabulation was then carried out to quantify this risk of brain tumour location by age. The 2 by 2 table below (table 4.5.1) revealed that children who were older than 7 years were about 2.4 times more likely to have a supratentorial brain tumour than children who were younger.

Table 4.5.1: The Odds ratio of anatomical location of brain tumour by age group

	Supratentorial	Infratentorial	Total
Older than 7	41 (44.6)	51 (55.4)	110
Younger than 7	28 (25.5)	82 (74.6)	92
Total	133 (66)	69 (34)	202

Data is presented as n (%) OR = 2.35 (95% CI = 1.28 – 4.32), p-value = 0.004.

4.6 DIFFERENT TREATMENT MODALITIES EMPLOYED

Figure 5 shows different treatment modalities which were employed in the management of primary paediatric brain tumours. Majority of participants were treated by surgical intervention alone (49.2%).

During surgery, either a total tumour was removed and required no other treatment or surgery was followed by other treatment modalities, radiotherapy or chemotherapy or a combination of the two modalities. Ten percent of the participants received radiotherapy alone. These were children diagnosed with brainstem gliomas. Chemotherapy was used for subjects who had braistem gliomas but were 3 years or younger and could not receive radiotherapy.

Combination therapy: This modality of treatment was commonly given to subjects with malignant tumours. In this study group combination therapy comprised 25.5%.

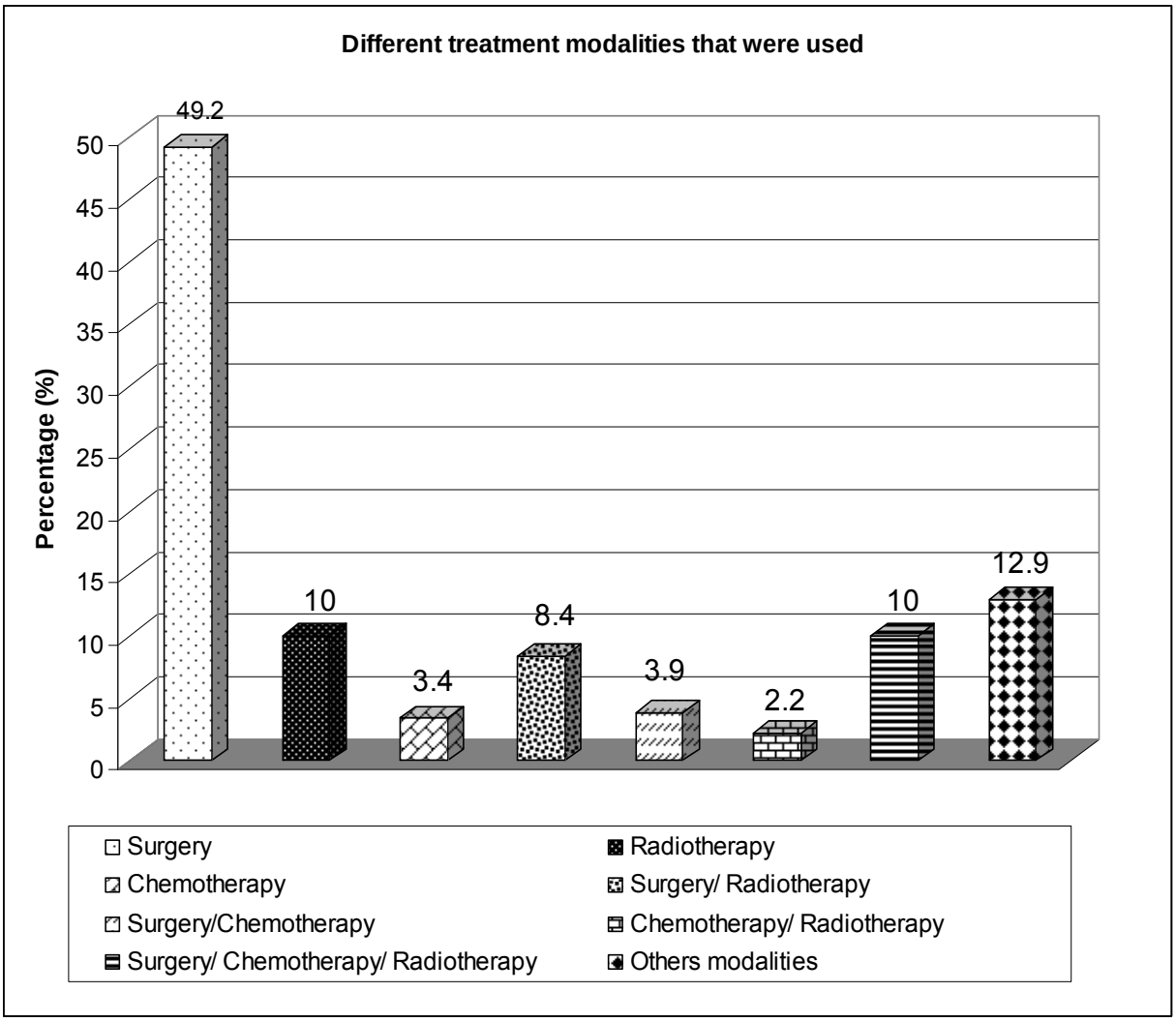


Figure.5 The different treatment modalities that were used.

4.7 MORBIDITY AND MORTALITY FROM CHILDHOOD BRAIN TUMOURS

Outcome was defined as: 1) Died, 2) Alive (alive at the end of study follow-up – 30 April 2005), 3) Presumed alive (Fact of death is unknown – patient discharged or last known to be alive before end of study follow-up), and 4) lost to follow-up (No data on discharge date or outcome).

Figure 6 shows overall outcome from childhood brain tumours.

Figure 7 also shows survival outcome by race groups.

4.7.1 Overall outcome

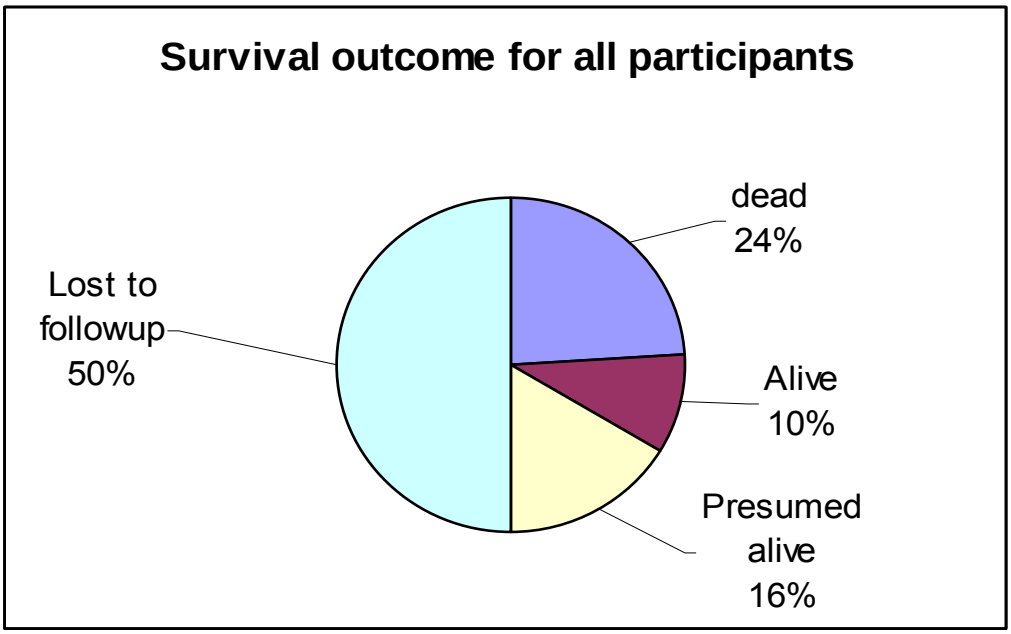


Figure 6 The overall outcome from childhood brain tumours

Outcome information is not available for about half of the study participants while 24% were dead (cumulative incidence in mortality) and 10% were alive while16% of study participants were presumed alive.

4.7.2 Outcome by race

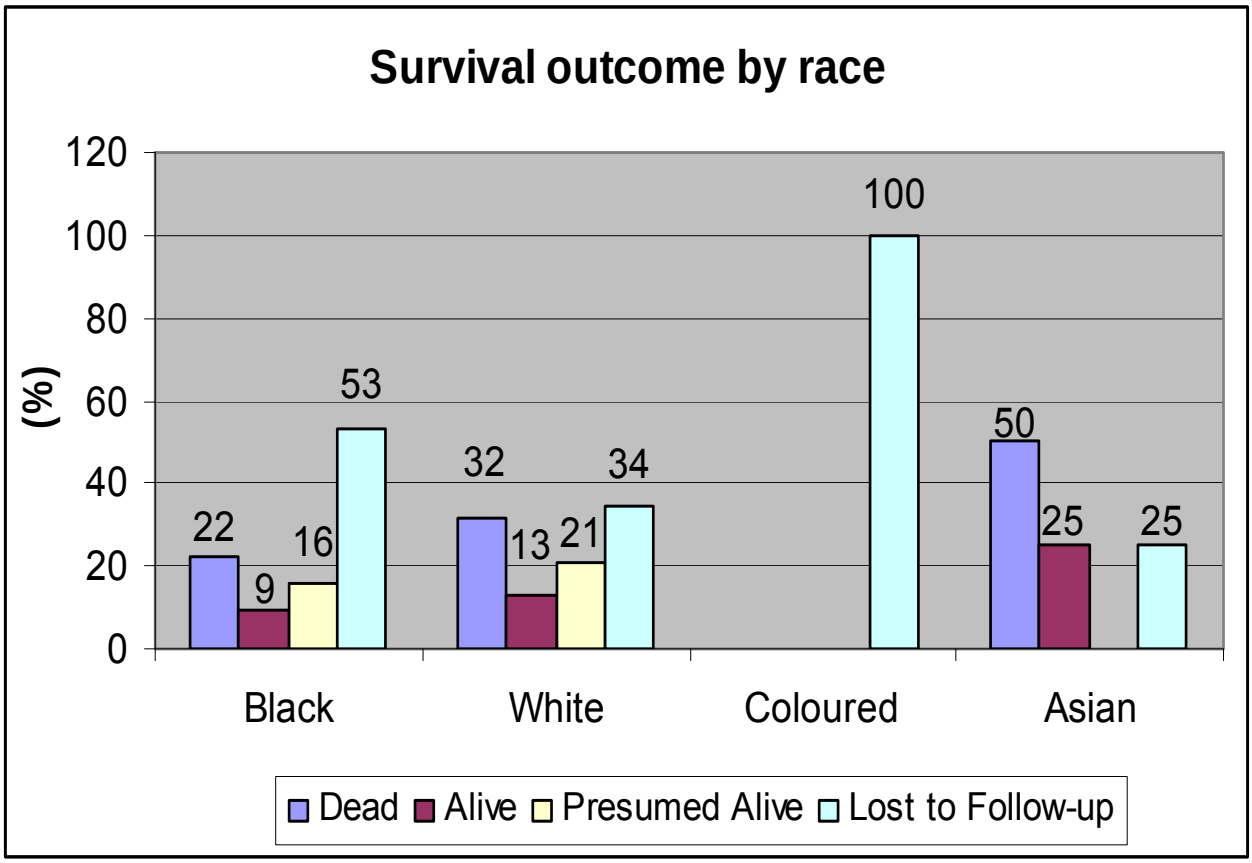


Figure 7 shows survival outcome by race groups.

4.7.3 Outcome by gender

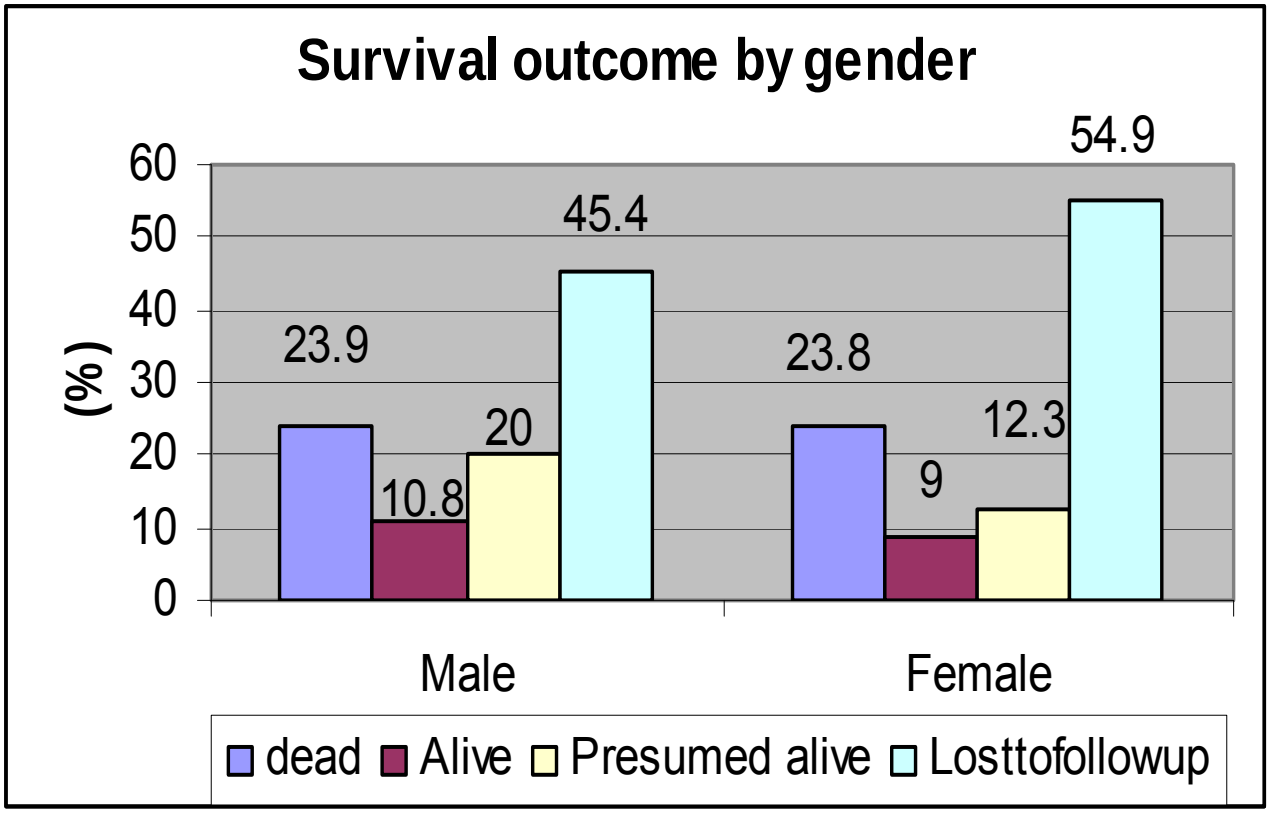


Figure 8 shows outcome by gender

The pattern of mortality is similar for males and females.

4.7.4 Outcome by treatment modalities

This study showed that the best of treatment modalities was combination therapy of surgery, radiotherapy and chemotherapy where 38.8% were alive at the end of the study, whereas the worst was treatment by chemotherapy alone where there were no survivors.

Table 4.7.1.Outcome by treatment in percentage

Treatment	n	Percentages (%)			
		Dead	Alive	Pre-alive	Lost to FU
Surgery	88	13.6	4.6	20.5	61.4
Radiotherapy	18	50.0	11.1	33.3	5.6
Chemotherapy	6	66.7	-	16.7	16.7
Surgery/Radiotherapy	15	33.3	13.3	20.0	33.3
Surgery/Chemotherapy	7	14.3	28.6	-	57.1
Chemotherapy/Radiotherapy	4	50.0	25.0	-	25.0
Surgery/Chemotherapy/Radiotherapy	17	22.2	38.9	-	38.9
Other modalities	23	43.5	26.1	8.7	21.7

n=number, FU=Follow-up, Pre-alive=Presumed alive

4. 7.5 Outcome by diagnosis

When one considers outcome based on diagnosis table 4.7.2. It is difficult to make a proper assessment because of a big number of study participants who were lost to follow-up. Different methods were used to analyse the data as shown in the following subsections.

Table 4.7.2. Outcome by diagnosis in percentage

Diagnosis	n	Percentages (%)			
		Dead	Alive	Pre-alive	Lost to FU
Medulloblastoma	48	25	21.8	10.4	43.8
Glioma (brainstem + thalamic)	45	40	6.7	15.6	37.8
Astrocytoma	58	8.6	6.9	24.1	60.3
Ependymoma	16	29.4	17.7	5.9	47.1
Craniopharyngioma	26	15.4	7.7	23.1	53.9
Meningioma	2	-	-	-	100
Pituitary adenoma	2	-	50	-	50
Ganglioglioma	2	50	-	-	50
PNET	8	25	-	12.5	62.5
Pineoblastoma	18	38.9	11.1	5.6	44.4

PNET= Primitive neuroectodermal tumours

4.8 MORTALITY INCIDENCE

For this analysis of mortality incidence and survival analysis, persons lost to follow-up were excluded from the analysis as no further visit information was available for them after first report to the hospital. As a result, there were no person years of follow-up information on them.

It is however, assumed that the survival outcome in persons for which data was available might not be different from those lost to follow-up. Person- years is total length of time for which a participant was under observation. For participants still alive, length of time was truncated at the end of the study period; 30th April 2005. Incidence of mortality was done using Poisson regression.

4.8.1 Overall mortality incidence

Total person years of observation (n = 114) = 207.7 years (min = 0.005 and max = 8.5 years)

Mortality cases = 60
Incidence of mortality = 28.4 per 100 person years (95% CI; 21.6 – 36.6). These results indicate that if 100 people diagnosed with a brain tumour were followed up (100 person-years), about 28 of them will die in a year.

Table 4.8.1 Mortality incidence by race and gender

Variable	*IR (per 100 person years)	95% CI
Race		
Blacks	26.2	19.1-35.2
Whites	32.6	16.8-58.9
Asian	61.6	7.4-222.7
Gender		
Males	27.8	18.9-39.4
Females	29.1	19.3-42.1

*Incidence rate

Table 4.8.1 Shows mortality incidence rate being higher among whites 32.6 per 100 person years (CI 16.8-58.9) compared to blacks 26.2per 100 person years. The numbers for Asians and coloured were too small for analysis (non-significant).

Also, this study showed that there was more mortality incidence among females than males, 29.1 and 27.8 per 100person years respectively (non-significant).

Table 4.8.2 Mortality incidence by diagnosis

Treatment	*IR (per 100 person years)	95% CI
Medulloblastoma	16.0	8.3-27.9
Glioma (Brain Stem + thalamic	67.8	40.2-107.1
Astrocytoma	15.6	5.1-36.4
Ependymoma	65.2	17.8-167
Craniopharyngioma	18.8	5.1-48
Meningioma	*	
Pituitary adenoma	*	
Ganglioglioma	*	
PNET	*	
Pineoblastoma	32.9	13.3-67.9

- No event * negligible no of person-years

Table 4.8.2 Shows mortality incidence rate being highest among children with gliomas 67.8 per 100 person years followed by ependymomas, 65.2 per 100 person years and pineoblastomas, 32.9 per 100 person years. Craniopharyngiomas, medulloblastomas and astrocytomas had low mortality incidence rates,18.8,16.0 and 15.6 per 100 person years respectively.

Table 4.8.3 Mortality incidence by treatment modality

Treatment	Proportion (%)	95% CI
Surgery	21.3	11-37.1
Radiotherapy	55.8	25.5-105.8
Chemotherapy	83.9	22.9-214
Surgery/Radiotherapy	32.6	10.6-76.1
Surgery/Chemotherapy	*	
Chemotherapy/Radiotherapy	*	
Surgery/Chemotherapy/Radiotherapy	9.8	2.6-25.1
Other modalities	21.6	10.3-39.7

4.9 WAITING TIME TO MORTALITY – KAPLAN-MEIER SURVIVAL CURVE

Figure 9 shows general survival estimates for primary childhood brain tumours. The 5 year survival for the study participants that were analysed was about 37.5%

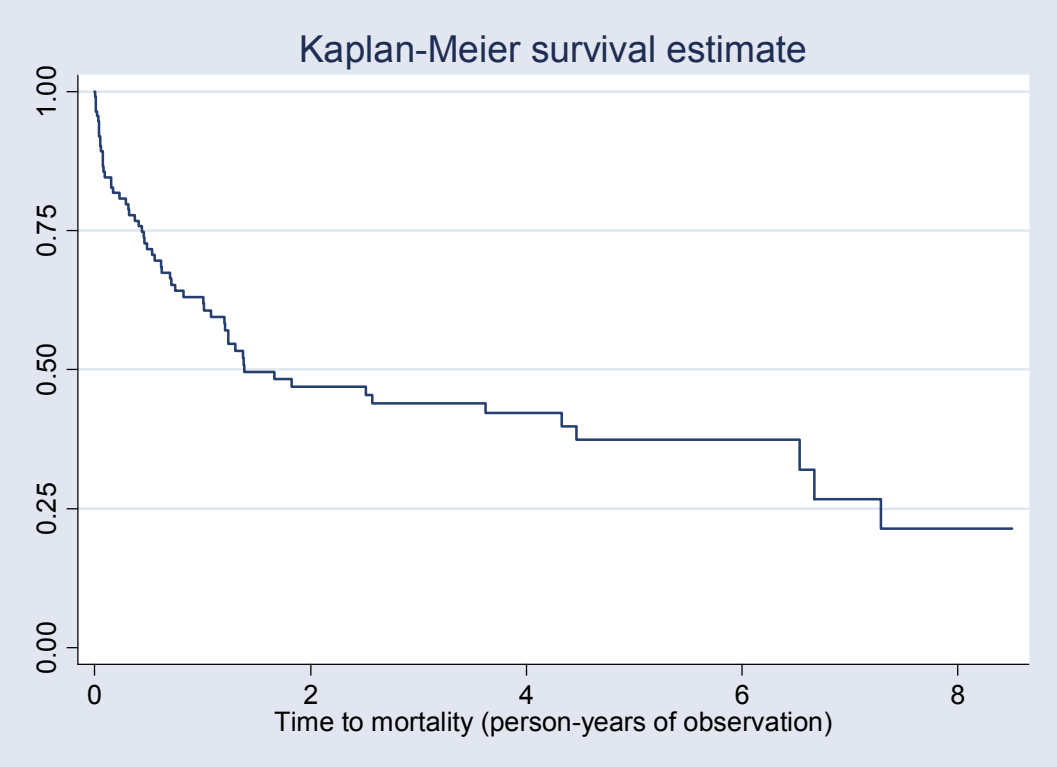


Figure.9 shows the Kaplan-Meier survival curve for the study participants whose follow-up time was known.

The general 5 year survival rate for the study participants who were analysed was about 37.5%.This is a low survival rate.

4.9.1 Survival estimates by gender

Figure 10 shows survival estimates by study participants' gender.

The curves show a slight better male survival rate than females.

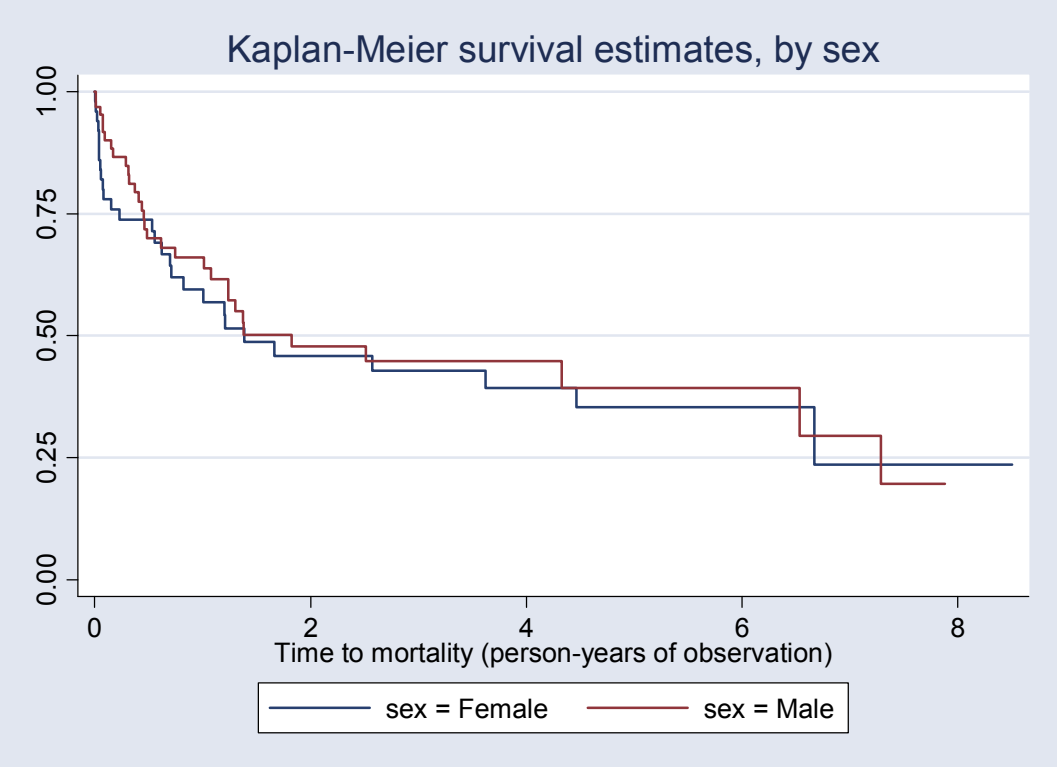


Figure10 shows time to mortality curves by gender

4.9.2 Survival estimates by race

Figure 11 shows survival estimates by race. From the figure, one sees that the blacks survived longer than whites. The other races were small for comparison.

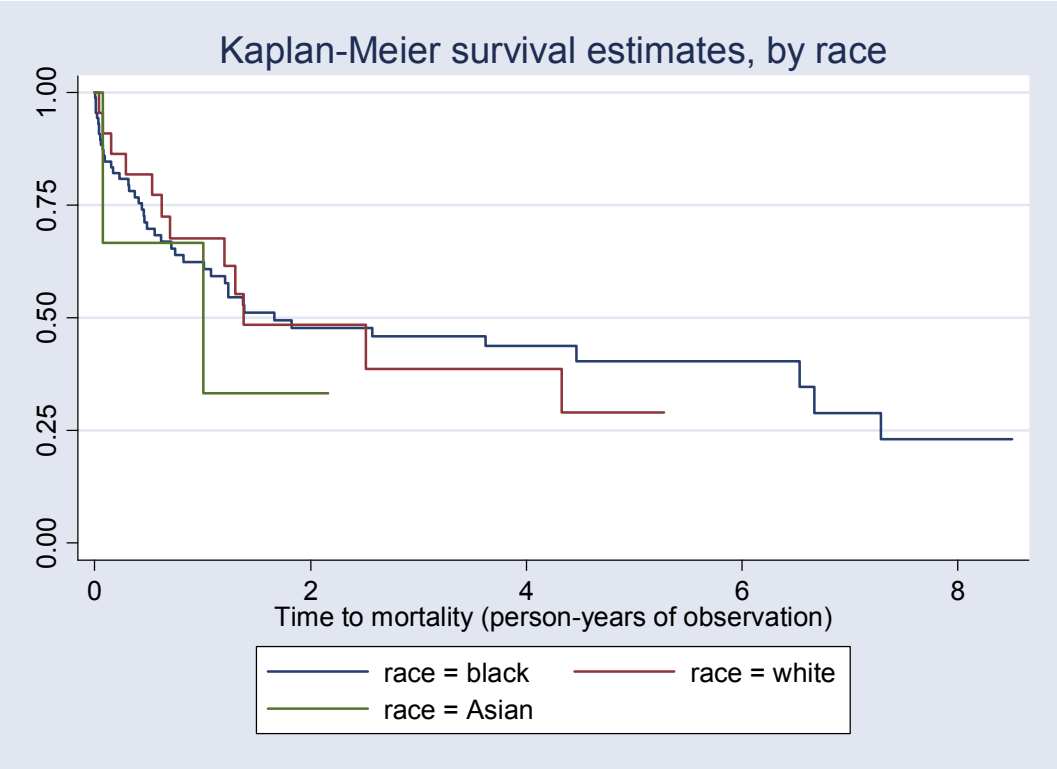


Figure.11 shows survival curves by race

4.9.3 Survival estimates by Diagnosis.

The survival analysis by diagnosis suggests that survival was longest among children with astrocytomas and craniopharyngiomas with about 55% 5-year survival, then medulloblastomas with about 45% 5-year survival and gliomas with about 20% 5-year survival. The small number of participants for PNET, gangliogliomas and ependymoma makes it difficult to analyse.

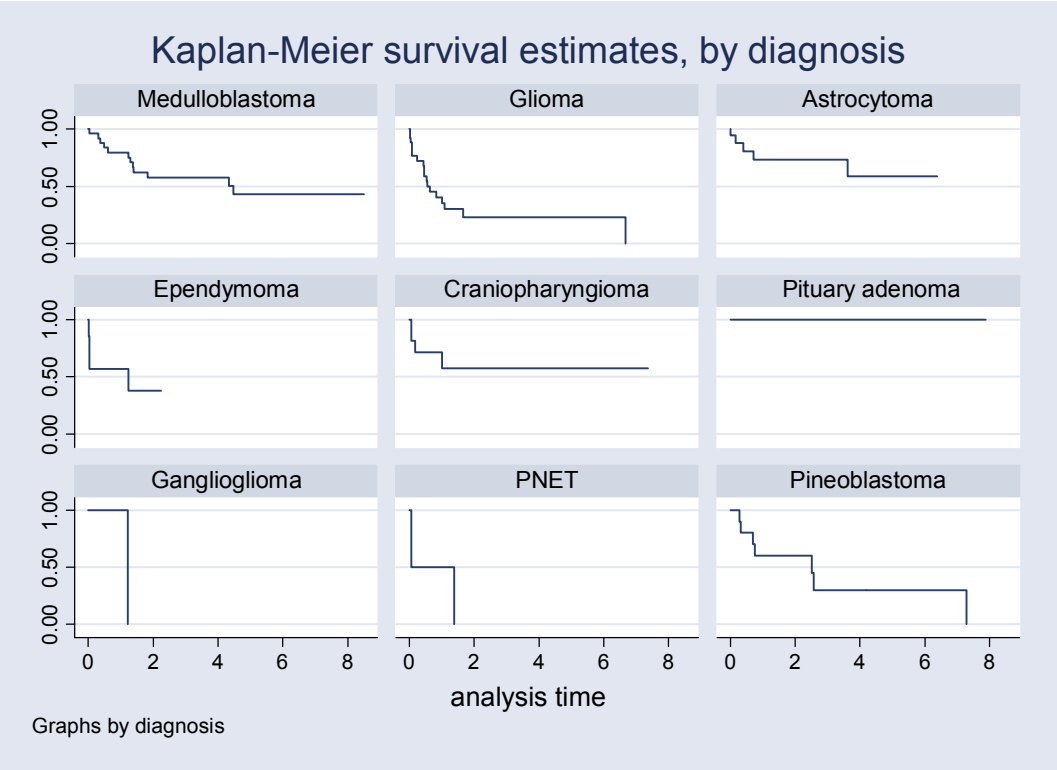


Figure.12 shows survival curves by diagnosis

4.9.4 Survival estimates by treatment modalities

Survival estimates were also carried out by treatment received (Figure 13). The results indicate that survival is longest for participants who had combination of surgery, chemotherapy and radiotherapy, with around 70% five-year survival. Survival was also high for participants who had surgery alone at about 55%five-year survival while the worst was for chemotherapy alone, where there was no survivors by the end of second year, after diagnosis.

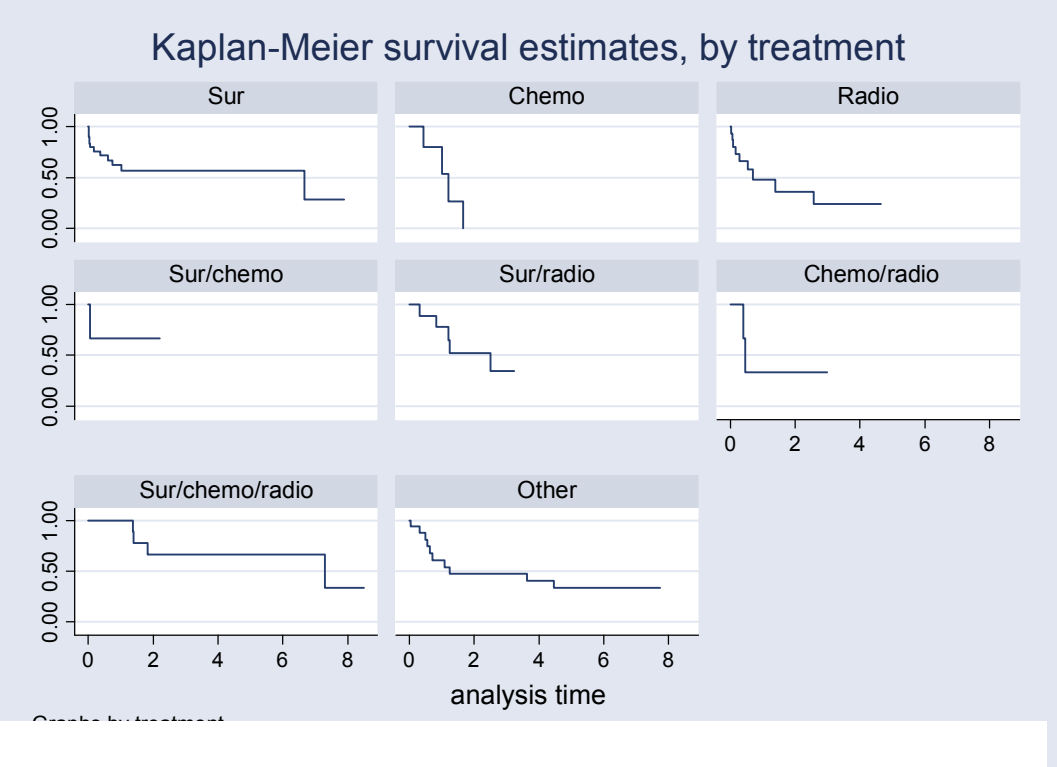


Fig.13 shows survival estimates by different treatment modalities.

Figure legend:

Sur=	Surgery;
Chemo=	Chemotherapy;
Radio=	Radiotherapy;
Sur/chemo=	Surgery/Chemotherapy;
Sur/radio=	Surgery/Radiotherapy;
Chemo/radio=	Chemotherapy/Radiotherapy;
Sur/chemo/radio=	Surgery/Chemotherapy/Radiotherapy

5.0 DISCUSSION

Epidemiology of primary paediatric brain tumours has been studied extensively in the developed countries. Studies from these countries show that these brain tumours are the most common group of solid tumours in childhood[1,2,3,8]. Different epidemiological details of the children harbouring primary brain tumours have also been analysed in those studies. Such studies are few or lacking in the developing countries especially in sub-saharan Africa.

This study analysed epidemiological data of the study participants and the following is a discussion of the findings on each item and comparison with other studies is done.

5.1 AGE, GENDER AND RACE IN RELATION TO CHILDHOOD BRAIN TUMOURS

5.1.1 Age

The mean age of study participants was 7.1 years. This is lower than the findings in other studies[10,12].

The findings of this study show that different types of tumours affect different ages and age groups differently.

For example, medulloblastomas were found to be commonest among children aged between 2 years and 9 years.

Gliomas included mainly brainstem gliomas which were over 90%. The others were thalamic gliomas. These tumours were diagnosed clinically and by radiological techniques because of their deep location in the brain In this study,

gliomas were commonest between ages of 2 years and 6 years and there were no children diagnosed with gliomas above the age of 12 years.

Astrocytomas affected all age groups but peaked in age group 2 to 6 years and started slowly to decline.

Ependymomas affected all age groups but peaked in the age group of 2 to 6 years and then peaked again in the age group of 9 to 12 years.

Craniopharyngiomas affected mainly ages between 2 to 12 years.

Pineoblastomas were common among ages between the age 6 to 14 years.

PNETs other than medulloblastomas and pineoblastomas affected mainly children of ages between 2 to 12 years, and were uncommon between the age group of 0 to 2 years and 12 to 14 years.
The numbers for pituitary adenomas, meningiomas and gangliogliomas were too small to be analysed.

Age was found to have significant impact on the distribution of primary childhood brain tumours between the supratentorial and infratentorial regions. The mean age of the subjects who had brain tumours in the supratentorial location was significantly higher than the mean age of those who had brain tumours in the infratentorial location; (7.9 ± 0 45) and (6.4 ± 0.32) (p=0.009) respectively.
Data from this study demonstrates that older children above seven years are more likely to suffer from supratentorial tumours than children less than seven years. In fact the mean age in years of the children with supratentorial tumours was approximately eight years compared to the mean age of children suffering from infratentorial tumours, which was about six years. This study also shows that childhood brain tumours are commoner among children younger than 7 years.(54.5% below 7 years compared to 45.5% above 7 years). When age was

categorized into two, with children less than seven years and those above seven years, children above seven years were 2.4 times more likely to develop supratentorial tumours than children younger than seven years. Similarly, Mellisa and Julianne[8] in their study found that the overall prevalence of central nervous tumours was highest in children younger than 8 years of age.

5.1.2 Gender

There were more males than females in this study, although not significantly different, with a male to female ratio of 1.04:1. Although this study found a slight male predominance, other studies show a clear male predominance among children with brain tumours[5,7,8,10,11.]

5.1.3 Race

Data from this study on race distribution of paediatric brain tumours show majority being blacks (80.9%), followed by whites (15.1%), with coloured (2.2%) and the Asians(1.8%) being the least. This is in contrast with studies from the USA[8] and Britain[4] where white children were more affected by brain tumours than their black counterparts. Looking at these studies, one may attribute the differences to the racial demographics of these countries; in South Africa and in particular Greater Johannesburg metropolitan area[18], african blacks constituted 73%, whites 16%, coloured 6% and asians 4%. On the other hand, in the UK[15], whites are the majority constituting 92%, asians 4.4%, blacks 2% and others 2.6%. In the USA[16], the majority are also whites constituting 73.9%, black americans 12.2%, asians 4.4%, alaskan natives 0.14% and mixed races 6.3%.

5.2 THE PREVALENCE OF PRIMARY PAEDIATRIC BRAIN TUMOURS

The commonest primary paediatric brain tumours in this study were astrocytomas followed by medulloblastomas. This was true for most studies that were reviewed[2,4,5,7,8,14]. However, Gyasi and Tettey[10] in their study found gliomas and meningiomas to be the most common childhood brain tumours. On the other hand, Peacock et al[13] found medulloblastomas, followed by brainstem gliomas to be more common.

5.3 TYPES FREQUENCY AND ANATOMIC LOCATIONS OF PAEDIATRIC BRAIN TUMOURS

Infratentorial tumours were the commonest compared to supratentorial tumours; 67% and 33% respectively. This predominance of infratentorial tumours over supratentorial tumours was reported by other authors.[3,6,13.] However, the difference in numbers of tumours between the infratentorial and supratentorial regions was higher than in any other study. The closest was a study from Cape Town[13] where infratentorial tumours were 63% and supratentorial tumours were 37%. Contrary to the above findings, Kaatsch et al[6] reported a near equal distribution of tumours between supratentorial and infratentorial regions and Suh et al[7] in their study reported that more tumours were found in supratentorial (68%) than in the infratentorial region (42%).

In the infratentorial region, medulloblastomas (34%) were the commonest followed by brainstem gliomas (30%), astrocytomas (19%), ependymomas (12%) and PNET other than medulloblastomas (5%). The Cape Town study[13] also found medulloblastomas (41.8%) were commonest followed by brainstem gliomas(25.3%), ependymomas(16.5%) and cerebellar astrocytomas(16.5%). This was contrary to some studies in the literature[6] where ependymomas (56%) were commonest followed by astrocytomas (44%)

In supratentorial region, the commonest tumours were craniopharyngiomas (36.6%) followed by pineoblastomas (25.4%), astrocytomas (21.1%), thalamic gliomas (4.2%), and others (12.6%). Peacock et al[13] in their study also found craniopharyngiomas to be the commonest tumours in the supratentorial region.

5.4 TREATMENT MODALITIES USED IN MANAGEMENT OF PAEDIATRIC BRAIN TUMOURS

Majority of the study participants (95.8%) had surgery as part of their treatment but surgical intervention alone was offered to about one half of that number (49.2%). During surgery, either a total tumour was removed and required no other treatment or surgery was followed by other treatment modalities; radiotherapy or chemotherapy or a combination of the two modalities. This was reported to be the practice in other studies[13.]

Ten percent of the participants received radiotherapy alone. These were children diagnosed with brainstem gliomas and thalamic gliomas and were above 3 years of age.
Chemotherapy alone was offered to 3.4% of the study population and was used for subjects who had braistem gliomas but were 3 years or younger and could not receive radiotherapy.

Combination therapy of chemotherapy and radiotherapy was given to subjects with gliomas who were older than 3 years. In this study group combination therapy comprised 2.2%. This modality of treatment for brainstem gliomas was confirmed in literature[13].

Combination therapy comprising surgery, chemotherapy and radiotherapy was offered to 10% of the study participants. These were children with malignant tumours like medulloblastomas and ependymomas.

5.5 MORTALITY AND SURVIVAL RATES ASSOCIATED WITH CHILDHOOD BRAIN TUMOURS

This study shows mortality incidence rate being slightly higher (non-significant) among whites 32.6 per 100 person years(CI 16.8-58.9) compared to 26.2per 100 person years for blacks whereas in the literature mortality was the same for white and black children[8].
The numbers for Asians and coloured were too small for analysis.

Also, this study showed that there was a non significant mortality incidence difference with more females than males dying, 29.1 and 27.8 per 100 person years respectively.
Contrary to the above findings, Kaatsch et al[6] reported a slightly better prognosis for girls than boys.

This report also shows mortality incidence rate being highest among children with gliomas (67.8 per 100 person years) followed by ependymomas (65.2 per 100 person years) and pineoblastomas, (32.9 per 100 person years). Craniopharyngiomas, medulloblastomas and astrocytomas had low mortality incidence rates (18.8,16.0 and 15.6 per 100 person years) respectively.

The overall five year survival rate for the study participants was 37.5%. This is much lower than that seen in the developed countries[5,6,8].
Looking at individual tumours, astrocytomas and craniopharyngiomas had the longest 5-year survival (55%), followed by medulloblastomas (45%). This is still very low compared to that in literature[5,6,8].
Speculation as to why there was high mortality rates among children treated for childhood tumours in this study include:

- Low social economic status and cultural beliefs: Some parents and caregivers do not consider taking children to hospital when they are ill as the first thing to

do. They take them to traditional healers first and only when there is no response to the traditional healer's treatment the child is taken to hospital. Sometimes there may be no money to take a child to hospital for treatment or for follow-up:

- Late presentation. Many children present with advanced disease and this makes it difficult to treat these children and reduces their time of survival.
- Lack of specialized paediatric neurosurgical units may be a big contributing factor in low survival outcomes. This may be due to divided attention and resources while the children are under the care of general neurosurgical units.

5.6 LIMITATIONS OF STUDY

The study participant numbers were small as to make reasonable conclusions from it. A bigger study needs to be carried out so that firmer conclusions can be made.

There was incomplete data in patients' records and this led to exclusion of many patients, almost one third of the children who had brain tumours were excluded.

Loss of patients to follow-up was also found to be a major problem in this study; half of the study participants were lost to follow-up.

Grading of tumours that have grades like astrocytomas, ependymomas was not stated. This might have affected the outcome results negatively where high grade tumours were compared with low grade ones.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Introduction

This study is hospital based and carries the limitations of hospital based studies. However, important conclusions and recommendations can be made.

6.2 Conclusions

- The average age of children who had primary brain tumours was 7.1 years.

- The average age of children with infratentorial tumours was 6 years while that for children with supratentorial tumours was 8 years.

- The older the child the higher was the likelihood of being diagnosed with supratentorial tumour than infratentorial tumour. Over 7 years of age a child was 2.4 times more likely to have a supratentorial tumour than infratentorial tumour.

- There was a slight male predominancy amongst children with primary brain tumours.

- Primary paediatric brain tumours prevalence, in general, follows population demographics. This is evident in this study and studies from the USA and Britain that looked at race and prevalence of the tumours. In the USA and Britain these tumours are more common among white children than among black children while in this study blacks are more affected than whites.

- The common supratentorial tumours were craniopharyngiomas, astrocytomas and pineoblastomas in that order of frequency while the common infratentorial tumours were medulloblastomas, brainstem gliomas and astrocytomas in descending order of frequency.

- The treatment modalities were similar to those given in similar patients in the literature.

- There was very high mortality rate and poor survival rates than those recorded in the literature.

- There was very poor patients follow-up.

- Record keeping was inadequate.

6.3 Recommendations

- A much bigger follow up study needs to be undertaken to confirm or disprove the above findings.

- Record keeping in the two hospitals needs to be improved.

- There is need to establish a specialized paediatric unit which will help start a paediatric team comprising paediatric neurosurgeon(s), paediatric oncologist(s), paediatric intensivist(s) and neuroradiologist(s) with the dedicated paediatric neuro ICU. Such a team given resources will improve survival outcome of children with brain tumours.

- Public awareness about childhood brain tumours should be improved by teaching public the symptoms and signs of these diseases. Also making

the public aware that when these tumours are diagnosed early, the treatment outcome is much better.

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ANNEXURE ONE

SHOWS DATA COLLECTION SHEET.

DATA COLLECTION SHEET

CODE NO	DATE OF DIAGNOSIS	AGE	SEX	RACE	DIAGNOSIS	ANATOMIC LOCATION	TREATMENT GIVEN	FOLLOW-UP PERIOD	OUTCOME
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									

ANNEXURE TWO.

SHOWS ETHICS COMMITTEE CLEARENCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Nkusi

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M051128**
PROJECT	Epidemiology of Primary Paediatric Brain Tumours among Children Treated at Johannesburg and CH Baragwanath...
INVESTIGATORS	Dr AE Nkusi
DEPARTMENT	Neuroscience
DATE CONSIDERED	05.11.25
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 05.11.28 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr J Ouma

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

ANNEXURE THREE

SHOWS PERMISSION LETTER FROM BARAGWANATH HOSPITAL ADMINISTRATION AUTHORISING USE OF PATIENTS' RECORDS.

GAUTENG
PROVINCIAL GOVERNMENT

Department Of Neurosurgery
CHRIS HANI BARAGWANATH HOSPITAL
October 31, 2005

The Clinical Director
CHRIS HANI BARAGWANATH HOSPITAL

Dear Sir

Re: Access medical records for research

Dr Nkusi is doing a research on paediatric tumours for his M.Med dissertation.

I have agreed for him to access our records as he works in the neurosurgery department and the information will be useful for us to manage our future cases.

I kindly request that he be allowed to access our hospital records for the purpose of clinical research.

Many thanks

.....
PROFESSOR R GOPAL
HEAD OF NEUROSURGERY DEPARTMENT
CHRIS HANI BARAGWANATH HOSPITAL

Approved

Dr. M.P.E. DDUNGU
Senior Clinical Executive

CHIEF EXECUTIVE SUPERINTENDENT
CHRIS HANI BARAGWANATH HOSPITAL
PK BERTSHAM
P.O. 2013
31 OCT 2005

ANNEXURE FOUR

SHOWS LETTER OF PERMISSION FROM JOHANNESBURG HOSPITAL ADMINISTRATION AUTHORISING USE OF PATIENTS' RECORDS.

DEPARTMENT OF NEUROLOGICAL SURGERY
JOHANNESBURG GENERAL HOSPITAL
PARKTOWN

P/BAG X39
JOHANNESBURG 2000

TEL: (011) 488 3663/43565
FAX: (011) 647 1612

November 1, 2005

THE CHIEF EXECUTIE OFFICER
JOHANNESBURG GENERAL HOSPITAL
PARKTOWN

Dear Sir,

RE: REQUEST FOR PERMISSION TO CONDUCT RESEARCH

DR. A.E. NKUSI

Dr. Nkusi is a Registrar in our department.

He is preparing to undertake a research project in order to fulfill part of the requireme for the M.Med (Neurosurgery) degree of the University of the Witwatersrand.

He intends to conduct a retrospective study into paediatric brain tumours treated over past ten years at the Johannesburg and Baragwanath hospitals.
I will be one of his supervisors.

Patient records will be studied. The patients will not be identified, contacted or in any way inconvenienced or compromised.
A copy of his research protocol is attached hereto for your perusal.

Formal permission from you is required prior to the commencement of this study in te of the rules of the research ethics committee.

Anticipating your understanding,

Yours truly,

DR. JOHN OUMA
PRINCIAL SPECIALIST