PATTERN OF BRAIN TUMOURS IN KENYATTA NATIONAL HOSPITAL: A 3 YEAR CROSS-SECTIONAL STUDY.

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN NEUROSURGERY FROM THE UNIVERSITY OF NAIROBI

DR MURIITHI SOLOMON WAHOME

MBCHB (UON 2001)

SUPERVISORS

DR J. KIBOI,

SENIOR LECTURER OF NEUROSURGERY,

DEPARTMENT OF SURGERY,

UNIVERSITY OF NAIROBI

SIGNATURE……. DATE……..

PROF NIMROD J. MWANGOMBE,

PROFESSOR AND THEMATIC HEAD NEUROSURGERY,

DEPARTMENT OF SURGERY,

UNIVERSITY OF NAIROBI

SIGNATURE……. DATE……..

DECLARATION

I declare that this research proposal is my own original work and has not been presented for a degree in any other University.

Dr. Solomon Wahome Muriithi

H58/79009/2009

Signature…….. Date…….

DEDICATION

To my late father for his love, care and encouragement

ACKNOWLEDGEMENT

I would like to express my heartfelt thanks and appreciation to my supervisors Prof Mwang'ombe and Dr Kiboi for their kind advice and professional guidance.

I sincerely want to thank the Ministry of Defence for their financial support to enable me cater for the budgeted items in my thesis and in paying fees for my post graduate studies.

I would also wish to thank my wife, mum and my son for their moral support and prayers all through my post graduate studies.

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LIST OF ABBREVIATIONS

CSF-CEREBROSPINAL FLUID

KNH- KENYATTA NATIONAL HOSPITAL

ASIR- AGE STANDARDIZED INCIDENCE RATE

WHO- WORLD HEALTH ORGANIZATION

PMBTs- PRIMARY MALIGNANT BRAIN TUMOURS

NF- NEUROFIBROMATOSIS

ASM- ANNUAL STANDARDIZED MORTALITY

CBTRUS- CENTRAL BRAIN TUMOUR REGISTRY of the UNITED STATES

GBM- GLIOBLASTOMA MULTIFORME- WHO GRADE IV

MRS- MAGNETIC RESONANCE SPECTROSCOPY

NSAIDS- NON STEROIDAL ANTI INFLAMMATORY DRUGS

ICP- INTRACRANIAL PRESSURE

PPI- PROTON PUMP INHIBITOR

CT SCAN- COMPUTERIZED TOMOGRAPHY SCAN

MRI SCAN- MAGNETIC RESONANCE IMAGING

DEFINITION OF TERMS

I. PRIMARY BRAIN TUMOURS- any type of tumour that starts from the brain either from the glial cells, meninges, glands or nerves

II. METASTATIC BRAIN TUMOUR- any type of brain tumour that originates from outside the neuriaxis

III. GLASGOW COMA SCALE- neurological clinical scale used to evaluate in a reliable and objective way the conscious state of a person for initial as well as subsequent assessment

ABSTRACT

Background

The burden of brain tumours in Kenya is still largely unknown though information from the Nairobi Cancer Registry suggests that they form about 2.3% of all reported male cancers and 0.9% of all female cancers. Kenyatta National Hospital (KNH) remains the main centre for neurosurgery in Kenya and as a result, the majority of patients with brain tumours continue to present at the hospital.

Objective

To describe the characteristics of brain tumours including clinical presentation, radiological and histological patterns in patients aged 13 years and more presenting at the Kenyatta National Hospital over a period of three years from January 2012 to December 2014.

Study methods and design

This was a 3-year hospital-based descriptive cross-sectional study. The study was conducted at Kenyatta National Hospital amongst patients aged 13 years and above with brain tumours that underwent surgery confirmed by histology from January 2012 to December 2014. The clinical syndromes, radiological features and histological types were described. The prevalence rates of the different brain tumours were given and tests of association (chi-square or Fischer's exact test) where possible were performed to explore the relationship between the three features. Significant associations were explored further using logistic regression.

Results

It was found that there was an overall mean age of 40.63 yrs for all brain tumours with a range of 13-70 years. Peak was at 40 years. Overall male to female ratio was 1:1.49. Main occupations seen with brain tumours were farmers and housewives. Kikuyu ethnic group were seen more at 53.29%. Headache and visual deficits were the chief complaints at presentation. Familial history of brain tumours only occurred in 2.63% of our patients. Most patients operated on had a good performance score with GCS of 15/15. Most of the tumours seen were supratentorial. Only 1.31% of brain tumours presenting in our setup had any familial associations. Meningiomas at 41.4% and gliomas at 26.3% were the most common tumours seen. Glioblastoma accounted for 55% of all gliomas seen. Male to female ratio for meningiomas was 1: 3.2 with a mean age of

43.97 years. Gliomas had a male to female ratio of 1.35: 1 with an average age of 39.65 years. Most meningiomas were located in the sphenoid wing and convexity locations while most gliomas were frontal and temporal.

Conclusion

It was found that we are seeing brain tumours at a younger age at KNH compared to the average age of brain tumour presentation in the western world with most studies quoting an average age of above 59 years with glioblastomas and meningiomas having an average of 64 and 65 years respectively. Females are presenting more commonly with meningiomas while males are presenting more commonly with gliomas. Ethnic and geographic variables are a key determinant to access to neurosurgical care in our local setup. Headache and visual deficits are a key indicator of presence of brain tumour. A lower proportion of brain tumours with familial associations are been seen in KNH when compared to averages from western studies at 5%. Most of the tumours seen in the adult population are supratentorial. Meningiomas and gliomas are the commonest tumours seen in our set up accounting for 67.7% of all brain tumours. Glioblastoma are still the commonest gliomas seen and carry a grave prognosis. Gliomas occur in a younger age group compared to meningiomas. More metastatic tumours are been offered surgical care compared to previous studies done in KNH. Supratentorial tumours are the commonest tumours in adults. Proximity to neurosurgical care and the socioeconomic status has a bearing on access to neurosurgical services. Many of the neurosurgical patients from far flung areas away from Nairobi county where KNH is located are been seen in Eldoret referral hospital or are not getting proper neurosurgical services due to under diagnosis and lack of specialist services.

Recommendations

More vigilance needed in our local setup as patients are presenting with brain tumours at a much younger age. The patients to be empowered economically so that they can be able to access neurosurgical care promptly which has a direct effect on outcomes and prognosis. Neurosurgical services need to be decentralized too.

CHAPTER ONE: INTRODUCTION

1.0 BACKGROUND

It is generally accepted that metastatic or secondary brain tumours are the commonest type of brain tumours from various studies done in the western world. However, the central role of the brain and the functional consequences of neuronal loss explain the severity of primary brain tumours. In the United States, 70,000 new cases of primary malignant and benign brain and CNS tumours are diagnosed each year, and 14000 patients die annually; 31% of these tumours are gliomas and 37% are meningiomas[1]

The burden of brain tumours in Kenya remains largely unknown though information from the Nairobi Cancer Registry suggests that they form about 2.3% of all reported male cancers and 0.9% of all female cancers. Kenyatta National Hospital (KNH) remains the main centre for neurosurgery in Kenya and as a result, the majority of patients with brain tumours continue to present at the hospital.

The clinical presentation of a brain tumour which includes the age and gender of the patient, occupation and clinical signs and symptoms of the brain tumour on presentation can impact on diagnosis and hence treatment and prognosis. In addition to this, the radiological presentation of brain tumours also impacts diagnosis and there is uncertainty over what histological types of tumour are present in Kenya. Also the geographical distribution and occupational patterns of patients presenting in KNH needs to be analyzed with a view of understanding the impact of this critical variable and its effects on brain tumour diagnosis and management.

CHAPTER TWO: LITERATURE REVIEW

2.0 EPIDEMIOLOGY OF BRAIN TUMOURS

Most large-scale epidemiological studies for brain tumours have been conducted in the developed world. Metastatic tumours are the commonest brain tumours in adults, and their incidence is increasing. Local studies, however, have painted a totally different picture and this has been attributed to the patients with brain metastases presenting too late or with multiple intracranial lesions and hence neurosurgeons are unwilling to operate on these patients due to the limited benefit of surgery. Stereotactic biopsy, which is a minimally invasive technique of getting tissue biopsy safely, is also rarely done in Kenya with one machine available in Nairobi county in a private hospital. Less effective treatment and control of the primary tumour has also been cited as a reason for the under reporting of metastatic brain tumours as these patients die before specialist neurosurgical care is given. Brain metastases from systemic cancer are upto 10 times more common than primary malignant brain tumours and are a significant burden in the management of patients with advanced cancer.[2]

In the Mwang'ombe et al. study done locally in KNH in 2005 retrospectively, metastatic brain tumours accounted for 2.8% of all brain tumours[3]. Primary malignant or benign brain tumours represent only 2% of all cancers, with more than 35,000 new cases diagnosed each year in the United States (CBTRUS in the year 2000 recorded 35,519 cases). However, in the CBTRUS 2005-2009, 70,000 new cases of primary brain tumours were diagnosed each year, and 14000 patients died per year; 31% of these tumours are gliomas and 37% are meningiomas[4]. The annual global age-standardized incidence of primary malignant brain tumours is 3.7 per 100,000 for males and 2.6 per 100,000 for females. These rates are said to be higher in more developed countries (males 5.8 vs. females 4.1 per 100,000) than in less developed countries (males 3.0 vs. females 2.1 per 100,000)[5]. This may be due to under diagnosis in less developed countries and ethnic differences in susceptibility to development of brain tumours as reported by Yaari et al in 2011[6]. This was also reported in other studies that regions with the highest reported rates of malignant brain tumours e.g. Northern Europe, the US white population, and Israel with rates of 11 to 20 per 100,000 people, generally have more accessible and developed medical care than areas with the lowest rates e.g. India and the Philippines with rates of 2-4 per 100,000 people[7]. However, some of the variations suggest ethnic differences in inherited susceptibility or cultural

or geographic differences in risk factors.[8,9] Among the most consistent finding in the epidemiology of brain tumours is the difference in incidence rates between genders; gliomas are more common in men and meningiomas more common in women.[10]

Global age-standardized mortality rate for PMBT is 2.8 for males and 2.0 for females per 100,000, and estimated mortality is higher in developed countries than in less developed countries[5]. This could be attributed to a variety of factors including late diagnosis, poor access to quality neurosurgical services for diagnosis and few specialists available in the developing countries. The figures differ significantly in relation to histology and age; glioblastoma has a five year survival rate of approximately 30% while low grade gliomas such as pilocytic astrocytomas, oligodendrogliomas and ependymomas have five year survival rates of over 70%[11]. In another study, high grade gliomas and anaplastic astrocytomas have 5 year survival rates of less than 40%.[12]

The Central Brain Tumour Registry of the United States, CBTRUS, in its report for the period 2005-2009 reported an overall incidence rate of 26.81 per 100,000 adults aged above 20 years. The distribution of these primary brain tumours by site was reported to be 35.2% in the meninges, 15.3% sellar-suprasellar region, 8.9% in the frontal lobes, 6.6% temporal lobe, 4.3% parietal lobe, 1.2% occipital lobe, 1.2% intraventricular, 1.6% brainstem, 6.9% involving the cranial nerves, 2.8% cerebellum, 0.4% pineal region and 9.7% other brain[4].

Only about 5% of primary brain tumours have known hereditary factors. Specifically, the Li-Fraumeni syndrome, *p53* defects, NF1, NF2, tuberous sclerosis, von Hippel-Lindau disease, Turcot's syndrome, and familial polyposis coli increase the risk of brain tumours. In particular, optic pathway gliomas have been linked to in NF1.[13] Studies of syndromes, familial aggregation and linkage and mutagen sensitivity in adults suggest genetic susceptibility to gliomas although the mechanisms are not clear.[13] People with certain mutations in the NF2 gene have a substantial risk of developing schwannoma, ependymomas and meningiomas. High dose ionizing radiation is an established risk factor for meningiomas. However, brain tumours aggregate in families and this may be as a result of multifactorial inheritance where genetic factors determine the degree of risk from exposure to exogenous environmental factors such as irradiation.[13]

2.1 CLASSIFICATION OF PRIMARY BRAIN TUMOURS- WHO GRADING 2007

Primary brain tumours (PBT) are classified histologically as (WHO grade is shown in brackets):

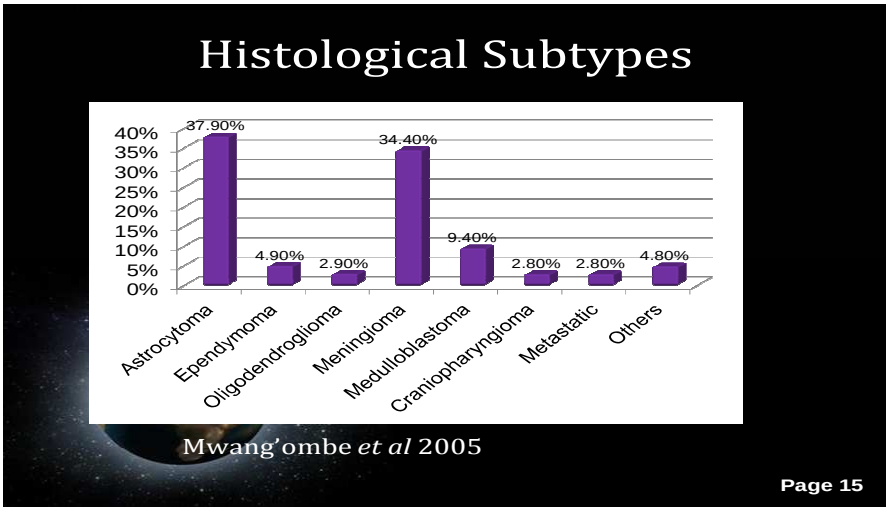
1. Astrocytic tumours:
    - Pilocytic astrocytoma (grade I);
    - SEGA(grade I);
    - Diffuse astrocytoma (grade II);
    - Anaplastic astrocytoma (grade III);
    - Glioblastoma (grade IV)
2. Oligodendroglial tumours:
    - Oligodendrogliomas (grade II);
    - Anaplastic oligodendrogliomas (grade III)
3. Mixed gliomas:
    - Oligoastrocytoma (grade II);
    - Anaplastic oligoastrocytoma (grade III)
4. Ependymal tumours
5. Choroid plexus tumours
6. Pineal parenchymal tumours
7. Embryonal tumours:
    - Medulloblastoma
    - Primitive neuroectodermal tumours
8. Meningeal tumours:
    - Meningioma
9. Primary CNS lymphoma
10. Germ-cell tumours
11. Tumours of the sellar region

The World Health Organization (WHO) classifies meningiomas into 3 categories:

1. Typical or benign (88-94%),
2. Atypical (5-7%), and
3. Anaplastic or malignant (1-2%).

In the USA, according to the CBTRUS 2005, the distribution of tumours by histology was gliomas at 29%, meningiomas 35.5%, pituitary tumours at 14.1%, craniopharyngioma at 0.9%, and lymphomas at 2.2% and germ cell tumours at 0.5%. Notably, glioblastomas accounted for 54% of all gliomas followed by diffuse astrocytomas at 9.5%.

In a retrospective study performed at the Kenyatta National Hospital between 1983 and 1994, gliomas were found to be the commonest intracranial tumours (45.8%).[17] Meningiomas were the next common tumours (34.4%). In another study conducted at the same hospital by Boore et al., meningiomas were the most frequently diagnosed, accounting for 40.8% (29) of cases, followed by astrocytomas at 26.8%.[18] The difference in findings between these two studies could be attributed to the fact that, at that particular time period, meningiomas were the most frequent tumours operated on in KNH and the study used intraoperative cytological smear as study specimens. Males were most affected by gliomas with a male to female ratio of 1.4:1[3] in the Mwang'ombe et al study in 2005 depicted below with permission.



Ruberti and Moppi, in 1971, found gliomas formed 45% of all intracranial tumours seen at KNH. Similarly, Kasili in 1973 reported that gliomas formed 45% of all intracranial tumours and 87% were astrocytomas and 13% ependymomas. Both of these studies were retrospective studies.

2.2 CLINICAL PRESENTATION AND DIAGNOSIS

The lower-grade glial tumours and most meningiomas have a more indolent course that may persist over years, whereas the more aggressive tumours (e.g., anaplastic oligodendrogliomas, anaplastic astrocytomas, glioblastoma multiforme) may have a rapid onset of neurologic decline.

Whatever the type of brain tumour, four main circumstances lead to diagnosis on clinical presentation. Firstly, patients have partial or generalized seizures, which are more frequent when the neoplasm is cortical and slowly growing (80% low grade vs. 30% high grade). Secondly, raised intracranial pressure generally reveals rapidly growing tumours, especially when located in silent areas of the brain e.g. right frontal and temporal lobes and posterior cranial fossa. Thirdly, progressive focal neurological deficits generally show the tumour site. Supratentorial tumours can induce motor or sensory deficits, hemianopia visual field defects, expressive or receptive aphasia or a combination of these, whereas posterior fossa tumours or brainstem tumours are revealed by various combinations of cranial nerve palsies, cerebellar dysfunction, and long-tract signs. Finally, cognitive dysfunction which has an implication on behaviour, learning ability and intellect of variable severity is common in frontal lobe syndrome, leptomeningeal spread of the tumour, or diffuse brain infiltration. Other common manifestations include hormonal disturbances with obesity, decreased libido, amenorrhoea, etc.

Overall, the median age of onset for brain tumours is 59 yrs, and the median ages of onset for glioblastoma and meningioma are 64 and 65, respectively.[5] As with other types of cancer, the increased incidence of most types of brain tumours with increasing age could be due to length of exposure required for neoplastic transformation, necessity of many genetic alterations prior to onset of clinical disease, or diminished immune surveillance.[20] Interestingly, there is a decline in the incidence of glioblastoma and astrocytoma among those aged 85 and older.[21] Oligodendrogliomas and ependymomas have been found to peak in middle age.[21]

2.3 IMAGING AND HISTOPATHOLOGY

When a brain tumour is clinically suspected, magnetic resonance imaging (MRI) of the brain, with and without gadolinium infusion is the best method to define the characteristics of the mass (location, size, degree of oedema, contrast enhancement). T1 weighted images are used to define the normal anatomy better whereas the T2 weighted series and FLAIR (fluid attenuation inverse ratio) are more useful to describe the tumour pathology including peri tumoural vasogenic oedema and if tumour is cystic or solid or heterogeneous. Gradient and susceptibility weighted series (SWI) series helps us to define if there is any calcification or haemorrhage in the tumour. In DWI or diffusion weighted imaging, restriction occurs in highly cellular tumours as hyperintense images on MRI although it is good to note that pyogenic and tuberculous abscesses also restrict on diffusion. Contrast uptake is seen on malignant primary brain tumours with the breakdown of the blood brain barrier eg GBM or in highly vascular tumours e.g. meningiomas.

CT scanning, although less sensitive than MRI, is appropriate as a first-line procedure to obtain a quick assessment of the lesion. CT scans are useful in characterizing bony involvement e.g. in meningioma bony hyperostosis or in tumoural calcification eg in oligodendrogliomas which account for 5-10% of all primary intracranial neoplasms and 70-90% calcify.

The parietal region was the commonest site of intracranial gliomas (37.5%) in the Mwang'ombe et al study. [4]. Most western studies have the frontal lobes as the most common site for gliomas.[22] Anatomic location of gliomas or meningiomas influences prognosis and treatment options. It is widely believed that gliomas develop in different lobes with frequencies relative to the volume of glial tissue, reflected in the ratio of grey to white matter. Revealing differences in the anatomic location of gliomas may provide further insight into the aetiology and pathogenesis of gliomas and, for example, give clues about the role of highly local external exposures such as trauma or electro-magnetic radio frequency fields from mobile phones. Another possibility is that anatomic structures provide physiologic stimuli to adjacent glial tissue, which affects the susceptibility to malignant transformation. A third possibility is the effect of functional differences amongst tissues and cells in different areas of the brain on the development of gliomas. Several studies have shown differences in biologic characteristics with molecular alterations amongst gliomas arising from different locations.[22] Suuvi L et al. (2007) found most gliomas were located in the cerebral lobes in 86% and most common was in the frontal lobe at 40%, temporal lobe 29%, parietal lobe 14% and occipital in 3%. 6.4% were deep seated, 1.5% in the cerebellum and 4.1%

in the brainstem. Gliomas were located more frequently in the right hemisphere in51% than the left at 40% and 4.9% were bilateral.[22]

However, imaging patterns are not specific and diagnosis must be confirmed by histological examination of tumour biopsy samples or by surgical resection tissue samples. Newer tissue diagnosis techniques, for example immunohistochemistry, are currently been used to better characterize tissues by use of proliferative markers e.g. Ki-67 and MiB and glial tissue markers e.g. GFAP or glial fibrillary acid protein, S-100 and vimentin with neuronal markers eg synaptophysin and neuron specific enolase. Meningiomas are positive for EMA or epithelial membrane antigen and primary CNS lymphomas for CD45 markers.

Spontaneous (or steroid-induced) disappearance of lesions is classic to primary CNS lymphomas, hence the term 'ghost' tumours. Thus a biopsy should be taken before commencing any steroids. 80-90% is malignant large diffuse B cell lymphomas[23].

2.4 TREATMENT

Initial therapy is symptom based and usually involves the use of steroids and anticonvulsant medication with dexamethasone preferred as the steroid of choice due to its superior glucocorticoid effect and less mineralcorticoid effect. The American Academy of Neurology issued a position statement in May 2000 recommending avoidance of prophylactic anticonvulsants in patients who have newly diagnosed brain tumours and who have never had a seizure.[24]

Most patients will undergo a surgical procedure for diagnostic and treatment purposes. Low grade tumours grow very slowly and regular monitoring with serial MRI or CT scan images is an option that can be offered to the patient. If the tumour is causing symptoms, is enlarging, or has signs on the scan that suggests tumour de-differentiation to a higher grade lesion, then the doctor can suggest a biopsy or surgery to remove the tumour. For patients with malignant brain tumours, the location of the tumour usually defines the surgical risk. Tumours in eloquent areas or deep seated tumours convey a higher surgical risk. Tumours that cross the midline eg lymphomas, butterfly glioblastomas or metastatic tumours also convey a high surgical risk and the only option would be CT guided biopsy only. Surgeons may elect to perform cerebral

angiography and have the patient undergo tumour embolization before surgical resection to decrease bleeding complications eg in large convexity meningiomas.

For individuals with malignant brain tumours, histological type of tumour and the age at presentation are strong prognostic factors.[25] In addition, grade of the tumour, extent of lesion resection, tumour location, administration of radiotherapy for high grade tumours and some chemotherapy protocols have been consistently linked with better overall survival rates in both population registry and clinical trial data.[25]

Postsurgical treatments include focused external beam or stereotactic radiation therapy for symptomatic tumours that cannot be resected or tumours that are incompletely resected eg parasagittal or cavernous sinus meningiomas, recurrent tumours or highly aggressive tumours. Chemotherapy can also be offered eg temozolomide, PCV (procarbazine/lomustine/vincristine) regimen for GBM and anaplastic astrocytomas. For anaplastic oligodendrogliomas with the 1p19q co-deletion, the preferred regimen is PCV given before or after radiotherapy.

Mwang'ombe et al found 15 patients with high grade glioma alive after 24 months and that 20% had undergone biopsy and radiotherapy, 7% debulking of the tumour only, 20% debulking and radiotherapy, 26.5% total excision and 26.5% total excision and radiotherapy. This suggests that total excision of the tumour may be associated with better long term outcomes especially in combination with radiotherapy.[3]

CHAPTER THREE: STUDY RATIONALE

3.0 JUSTIFICATION OF THE STUDY

The clinical presentation of a primary brain tumour can impact on diagnosis and hence treatment and prognosis. In addition to this, the radiological presentation of brain tumours also impacts diagnosis and there is uncertainty over what histological types of tumour are present in Kenya. The last descriptive study done on the neuroepidemiology of brain tumours was in 2005 by Mwang'ombe et al. This was before the current advancement in neurosurgery resident training in Kenya with the introduction of the Masters in Neurosurgery training at the University of Nairobi in 2006. In addition, no study has reported its findings in a way that relates clinical presentation, to radiological and histological findings in patients aged 13 years and above.

The information from this study will be used to form a blueprint on which to perform other descriptive epidemiological studies of brain tumours in Kenya and elsewhere that is crucial in understanding brain tumour behaviour and to aid in tailoring various targeted therapies and to prognosticate various brain tumour presentations.

The three-year period has been chosen because KNH records department has been attempting to computerize all patient medical records over the past few years. The process is not yet complete. These records will form the backbone of future research and this study will go some way in indirectly auditing the quality of this digital records.

3.1 RESEARCH QUESTION

What are the characteristics of brain tumours in patients aged 13 years and above presenting at Kenyatta National Hospital?

3.2 STUDY OBJECTIVES.

3.2.1 The Primary Objective

To describe the pattern of brain tumours in patients above the age of 13 years presenting at the Kenyatta National Hospital

3.2.2 Specific Objectives

I. To describe the clinical syndromes of brain tumours in patients above the age of 13 years presenting at the Kenyatta National Hospital.

II. To describe the radiological features of brain tumours amongst patients above the age of 13 years presenting at the Kenyatta National Hospital.

III. To determine the histological types of brain tumours in patients above the age of 13 years presenting at the Kenya National Hospital.

CHAPTER FOUR: METHODS

4.0 STUDY SETTING

This study was conducted in the following units at Kenyatta National Hospital:

1. All wards in KNH with brain tumour patients admitted and operated on.
2. Neurosurgical outpatient clinic no 24 where most patients are admitted to wards from.
3. Main intensive care unit KNH where patients go post operatively.
4. Main theatre no 9.
5. Pathology department KNH.
6. Records department KNH.

4.1 STUDY POPULATION

All patients with suspected brain tumours admitted at KNH from January 2012 to December 2014 formed the study population.

The inclusion criteria for study subjects were:

1. Patients aged 13 years and older with brain tumours.
2. Patient with the relevant imaging studies done to diagnose the brain tumour.
3. Patient had tumour debulking or excision surgery performed for suspected brain tumour.
4. Patient whose histopathology report is available and signed by a pathologist.

The exclusion criteria for the study were:

1. Patients lacking a histological diagnosis of their tumour will be excluded from the study.
2. Patients who lack the relevant radiological investigations for the diagnosis of the brain tumour.
3. All patients younger than 13 years at the time of admission.

4.2 STUDY DESIGN

This was a descriptive cross-sectional study. Data on clinical syndromes, radiological and histological diagnosis were collected.

4.3 SAMPLING

4.3.1 Sampling procedure

Clustered random sampling was used to select the sample. The clusters selected were the 3 years: 2012, 2013, and 2014. All patients with suspected brain tumours admitted at KNH during the period of the study and who met the inclusion criteria were randomly selected until the required sample size was reached.

4.3.2 Sampling Size Determination

The desired sample size was calculated using the formula;

$$n_0 = \frac{p(1-p)}{e^2}$$

Where:

n_0 = sample to be selected before the finite population correction is used

p =Proportion of interest. This will be given by 0.8

e=Required size of standard error. This will be given 0.07

The proportion of 0.80 was obtained from a retrospective study performed at the Kenyatta National Hospital between 1983 and 1994 by Mwang'ombe et al which found that gliomas represented 45.8% of primary brain tumours and that meningiomas were the next most common tumours at 34.4%.[16] The required size of the standard error of 0.07 was selected so that the 95% confidence interval will be no wider than the standard error of +/- 0.07.

Thus our sample size became 33. Since the sample was drawn from a finite population, the finite population correction was used.

$$n = \frac{n_0 N}{n_0 + (N - 1)}$$

Where:

n_0 = sample to be selected before the finite population correction is used

N =Total population size given by 73 in each year. Over the three years the total is 219.

The sample was thus 23. An increment of 20% was also included in the sample size so as to account for missing data and interaction between the clusters .Thus the total sample size became 28 people within each cluster.

A consistent number of records within each cluster were selected to account for the lack of the interclass correlation coefficient and variation within and between the clusters. This means that we targeted to collect 28 records at random from each year to get a total of 84 over the three years.

4.4 STUDY PROCEDURES

A list of records of all patients fitting the inclusion criteria in the study period were obtained from the records department. After this, the list was separated into the three years (clusters) from which a list of 28 records for each year were selected through random sampling. The inpatient records of these patients were obtained and used to populate the fields in the data collection tool. Any missing data was supplemented by linking with data held in other departments such as outpatient clinics, ICU department, admission wards and the pathology department.

We anticipated that clinical presentation data was collected on admission to ward 4C, the primary neurosurgical ward in Kenyatta National Hospital and other relevant wards that the patients could have been admitted to due to various reasons. Radiological data from MRI brain and/or CT head scan images was also collected from patient records. Finally, histological data was captured from the post-operative examination of specimens in the KNH pathology department. Data collection was performed by the primary investigator on this study and captured in the data collection tool (Appendix 1).

4.5 DATA MANAGEMENT AND ANALYSIS

All data collected using the data collection tool was entered into the Statistical Package for Social Scientists (SPSS USA Inc) Version 16.0. All data was anonymized. Each record was assigned a unique identifier at the time of data entry to maintain patient confidentiality. Data was checked for consistency and errors and any issues resolved before the data was cleaned and readied for analysis.

Descriptive analysis was made of the data. The primary outcomes were a description of the clinical syndromes, radiological features and histological types of primary brain tumours in patients aged 13 years and more presenting as the Kenyatta National Hospital. This was to be presented in prose and through bar graphs and pie charts. We performed tests of association (chi-square or Fischer's exact test) where possible to explore the relationship between the three features and death and other functional outcomes where applicable. Significant associations were explored further using logistic regression.

CHAPTER FIVE: ETHICAL CONSIDERATIONS

5.0 DECLARATION OF HELSINKI

The investigator ensured that this study was conducted in full conformity with the current revision of the Declaration of Helsinki in terms of patient confidentiality and respect.

5.1 ETHICS COMMITTEE APPROVAL

Permission to carry out the study was obtained from the Kenyatta National Hospital Ethical and Research Committee and no study procedures commenced before this permission had been received.

5.2 PATIENT CONFIDENTIALITY

Because the study was a descriptive cross sectional study based on de-identified patient data, informed consent was not required from individual patients once ethical approval was received. However, the investigator ensured that the patient's privacy was maintained. No data obtained from this study will be used for any other purpose other than meeting the objectives stated in this proposal. The data collection tool was stored securely in a lockable cabinet in the department of surgery. All data was anonymized and de-identified with a unique study identification number assigned to each record. Only the principal investigator and data manager had access to the information collected. Data entered into SPSS was kept in a password protected computer.

5.3 DISCLOSURE OF INFORMATION

In order to allow the use of the information derived from this study, the investigator understands that he has the obligation to provide complete results and all data generated from this study to the department of Surgery University of Nairobi and KNH in order to aid in policy change.

CHAPTER SIX: RESULTS

This study collected data from 152 patients over the study period. A descriptive analysis was done on the age, sex, occupation, ethnicity, clinical presentation, GCS at presentation, radiological features of the brain tumour, prior history of brain or other tumour in the family and the histopathology tumour type.

6.1 AGE ASSESMENT OF ALL BRAIN TUMOURS

The patients had a mean age of 40.63 years with a standard deviation of 15.36. The ages ranged from 13 years to 70 years. The table generally shows a small peak at around 20 years of age with a larger peak at 40 years of age then two smaller peaks at 50 and 60 years of age.

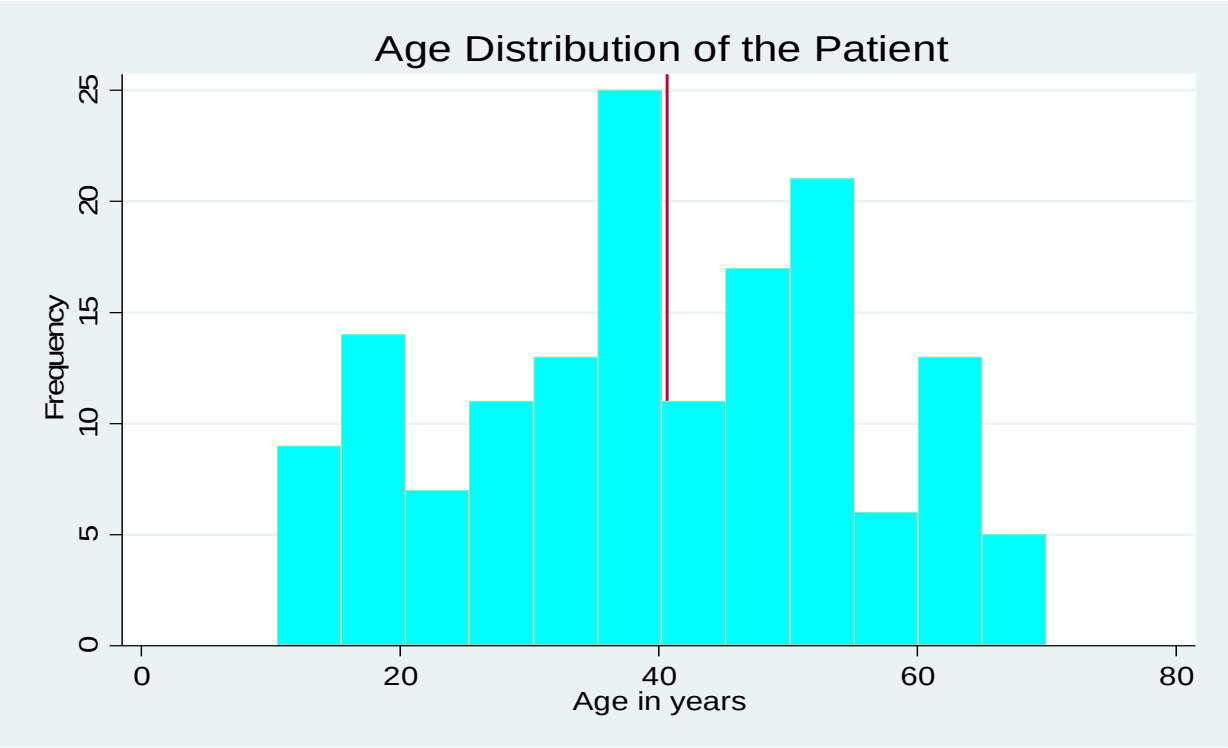


Figure 1: Histogram of age distribution of patients

6.2 SEX PREPONDERANCE IN ALL BRAIN TUMOURS

The sample had 61 male cases, constituting 40.13% of the patients and 91 female cases, constituting 59.87% of the patients in adult patients between the ages of 13 years and above presenting at KNH from January 2012 to December 2014. The male to female ratio was 1:1.49.

Table 1: Patient distribution by gender

	Frequency	Percentage
Female	61	40.13
Male	91	59.87
Total	**152**	**100**

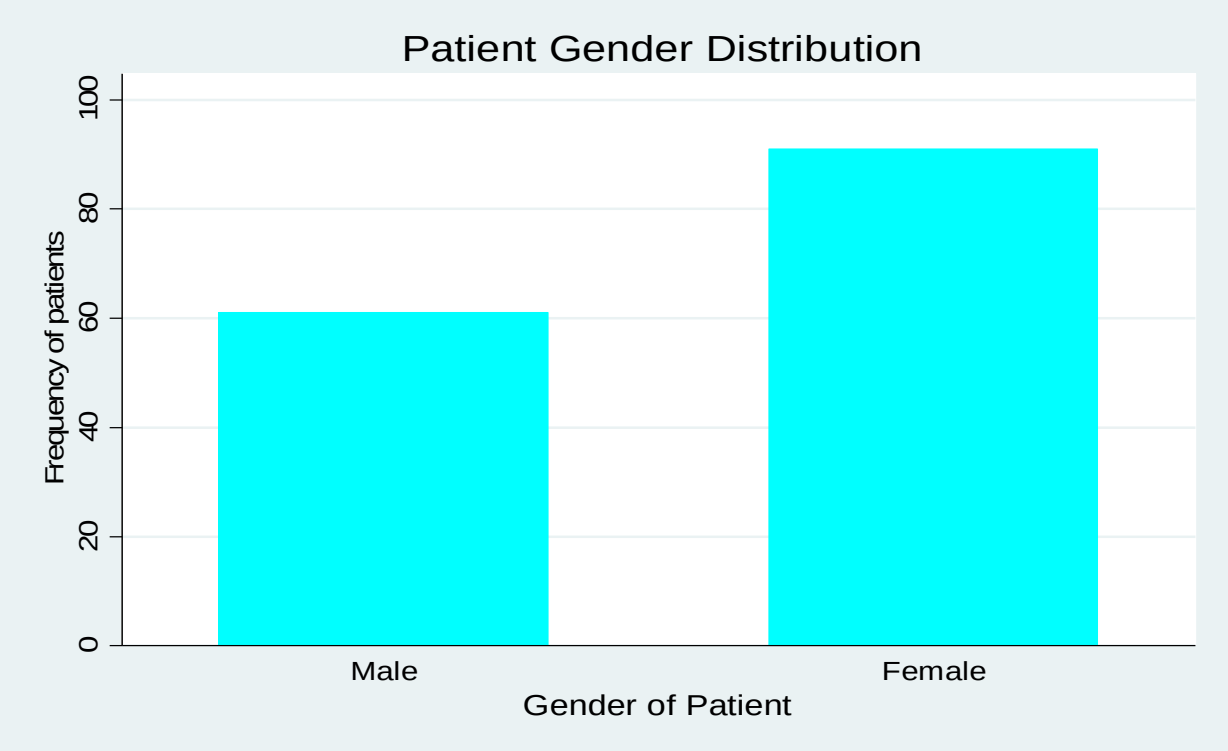


Figure 2: Bar chart of patient gender distribution

6.3 OCCUPATION DISTRIBUTION

Most of the patients were housewives, farmers, businessmen or students. Most of the farmers were female. The table below shows the respective distributions.

Table 2: Patient distribution by occupation

	Frequency	Percent	Mean Age	Male Percentages
Housewives	33	21.71	45.60	0%
Farmer	44	28.95	50.63	47.73%
Teacher	4	2.63	46.75	50%
Businessperson	26	17.11	39.38	46.15%
Student	24	15.79	16.63	62.50%
Casual worker	6	3.95	43.5	83.33%
Unemployed	7	4.61	35.57	28.57%
Driver	1	0.66	31	0%
Police officer	1	0.66	49	100%
Tailor	1	0.66	35	0%
Civil Servant	2	1.32	40	50%
Clerk	1	0.66	50	0%
Cook	2	1.32	39	100%
Total	**152**	**100**		

6.4 ETHNICITY

A majority of patients were Kikuyu with 53.29% (n= 81) with Kamba being 13.82% (n=21). These were followed by the Ameru, Kisii and the Luo ethnic communities. The distribution is shown in table 4 below.

Table 3: Patient distribution by ethnicity

	Frequency	Percent
Kikuyu	81	53.29
Luhya	4	2.63
Luo	10	6.58
Kalenjin	3	1.97
Kamba	21	13.82
Kisii	12	7.89
Maasai	3	1.97
Ameru	13	8.55
Mijikenda	1	0.66
Embu	2	1.32
Mbeere	1	0.66
Taita	1	0.66
Total	**152**	**100**

6.5 CLINICAL PRESENTATION OF BRAIN TUMOURS

An overwhelming majority patients experienced headache or vomiting 96.05 %(n= 146). Only 6 patients did not experience any headache or vomiting. A detailed breakdown of all the symptoms is shown in table 4.

Table 4: Patient distribution by symptoms and signs

Symptom	Frequency(Percentage) N=152
Headache and vomiting	146(96.05%)
Seizures	41(26.97%)
Speech deficit	23(15.13%)
Visual deficit	114(75.00%)
Cranial nerve deficits	32(21.05%)
Motor deficits	70(46.05%)
Sensory deficits	33(21.71%)
Cerebellar signs	27(17.76%)
Confusion	55(36.18%)
Cognitive deficits	40(26.32%)
Incontinence	18(11.84%)
Hormone imbalance	19(12.50%)

Other common brain tumour signs and symptoms were visual deficits (75%, n= 114), motor deficits (46.5%, n= 70), confusion (36.18%, n=55), seizures (26.97%, n=41) and cognitive deficits (26.32%, n=40).

6.6 HISTORY OF BRAIN OR ANY OTHER TUMOUR IN THE FAMILY

An overwhelming majority patients did not have any previous history of brain tumour 98.68 % (n= 150). Only 2 patients had any previous history of a brain tumour representing 1.31%. Similarly, all patients had no previous history off any other tumour.

Table 5: Patient distribution by history of brain tumour

	Frequency	Percent
Yes	2	1.31
No	150	98.68
Total	**152**	**100**

Only 1.31% of all the brain tumours presenting at KNH had a previous brain tumour or any other tumour reported in the family.

6.7 GLASGOW COMA SCALE EVALUATION

The patients had a median Glasgow coma scale (GCS) of 15. The least GCS recorded was 5 while the highest was 15. The least GCS recorded for male patients was 7 while that for female patients was 5. Both genders had a GCS of 15 recorded as the highest.

6.8 TYPE OF IMAGING DONE FOR DIAGNOSIS

In most of the patients both MRI brain and CT head scans were conducted with a proportion of 58.55% (n= 89). CT scans were done in 34.87% (n= 53) patients while the rest had only MRI brain scans done.

Table 6: Patient distribution by type of imaging done for diagnosis

	Frequency	Percent
MRI	10	6.58
CT Scan	53	34.87
MRI and CT scan	89	58.55
Total	**152**	**100**

6.9 RADIOLOGICAL LOCATION OF TUMOUR

With regards to the type of the radiology, a large proportion of the tumours were supratentorial at 80.26% (n=122) with the infratentorial compartment accounting for 19.74%. Infratentorial tumours occurred at a younger age compared to supratentorial tumours.

Table 7: Patient distribution by radiological location of tumour

	Frequency	Percent	Mean age	Male mean proportion
Supratentorial	122	80.26	42.13	39.34(48)
Infratentorial	30	19.74	34.53	43.33(13)
Total	**152**	**100**		

6.10 HISTOPATHOLOGY TYPE OF THE TUMOUR

Meningiomas (41.4%, n=63) and gliomas (26.3%, n=40) accounted for the majority of the brain tumours at 67.7%. A detailed distribution of the histopathology tumour type is shown in the table below. Fifteen of the 152 tumours were pituitary adenomas comprising 9.86% of all the tumours analyzed, a classification not considered by the WHO classification of primary brain tumours and will be analyzed separately.

Of the 15 pituitary adenoma patients, 7 (46.67%) were male while 8 (53.33%) were female. These pituitary adenomas had a GCS of 15.

Table 8: Patient distribution by histopathology

	Frequency	Percent
Pilocytic astrocytoma	3	2.19
PXA	1	0.73
Diffuse fibrillary astrocytoma	4	2.92
Anaplastic astrocytoma	4	2.92
Glioblastoma	22	16.06
Oligodendroglioma	2	1.46
Ependymal tumours	3	2.19
Choroid plexus tumours	1	0.73
Pineacytoma	1	0.73
Desmoplastic/nodular medulloblastoma	5	3.65
Menigothelial	25	18.25
Fibroblastic	12	8.76
Transitional	20	14.60
Psammomatous	4	2.92
Atypical	2	1.46
Germinoma	1	0.73
Craniopharyngioma	9	6.57
Schwanomma	4	2.92
Metastatic tumour	7	5.11
Ganglioglioma	1	0.73
Central neurocytoma	3	2.19
Hemanglioblastoma	3	2.19
Total	**137**	**100**

	Mean age(SD)	Male Proportions (n)
Pilocytic astrocytoma	21.67(7.23)	100%(3)
PXA	15(-)	100%(1)
Diffuse fibrillary astrocytoma	22.25(11.59)	25%(1)
Anaplastic astrocytoma	40.5(18.79)	0%(0)
Glioblastoma	48.36(13.19)	63.64%(14)
Oligodendroglioma	46.5(0.70)	50%(1)
Ependymal tumours	18.33(5.77)	66.67%(2)
Choroid plexus tumours	64(-)	0%(0)
Pineacytoma	24(-)	0%(0)
Desmoplastic/nodular medulloblastoma	19.4(6.27)	60%(3)
Menigothelial	41.88(12.30)	20%(5)
Fibroblastic	49.58(9.58)	33.33%(4)
Transitional	46.5(13.73)	20%(4)
Psammomatous	31(10.68)	100%(4)
Atypical	37(25.46)	100%(2)
Germinoma	45(-)	0%(0)
Craniopharyngioma	28.44(16.14)	66.67%(6)
Schwanomma	44.25(16.96)	25%(1)
Metastatic tumour	48.71(12.16)	57.14%(4)
Ganglioglioma	43(-)	100%(1)
Central neurocytoma	26.67(8.33)	33.33%(1)
Hemanglioblastoma	40.33(13.32)	33.33%(1)

Glioblastomas comprised of 55% (n=22) of all neuroepithelial tumours. It was followed by the pilocytic astrocytoma (n=3) and ependymal tumours (n=3) at 7.5%. PXA (pleomorphic astrocytoma) and ganglioglioma were the least analyzed neuroepithelial tumours at 2.5 %(n=1) of all neuroepithelial tumours.

Amongst the 63 meningiomas analyzed, the meningothelial variety was the most common at 39.68 %(n=25) followed by the transitional variety at 31.74 %(n=20). These were followed by the fibroblastic type at 19.04 %(n=12) and psammomatous variety at 6.34 %(n=4). The atypical meningiomas were the least seen meningiomas at 3.17 %(n=2).

Other tumours that were analyzed were the craniopharyngiomas at 5.92% (n=9), metastatic lesions at 4.6% (n=7), medulloblastomas at 3.28% (n=5) and Schwannomas at 4.63 %(n=4).

6.11 MENINGIOMA EVALUATION

Sixty three patients had meningiomas. Of these, 48 (76.19%) patients were female while 15 (23.81%) were male with a male to female (M: F) ratio of 1:3.2. Additionally, these patients had a mean age of 43.97 +/-13.07 whilst ranging from 16 to 69 years. The median GCS at presentation in our study for meningiomas was 15/15.

In terms of radiological location of the meningiomas, the most common site were the sphenoid wing meningiomas (8.55%, n=13) followed by the convexity meningiomas (7.24%, n=11) with the planum sphenoidale (0.66%, n=1) been the rarest subtype of meningioma seen.

Table 9: Patient distribution by meningioma evaluation

	Frequency	Percent
No meningioma	89	58.55
Convexity	11	17.46
Sphenoid wing	13	20.63
Tuberculum sellae	4	6.35
Parasaggital	5	7.94
Tentorial	4	6.35
Foramen magnum	2	3.17
Petroclival	4	6.35
Parafalcine	7	11.11
Intraventricular	3	4.76
Cavernous	2	3.17
Clinoidal	2	3.17

Planum sphenoidale	1	1.58
Olfactory groove	2	3.17
CPA meningioma	3	4.76
Total	**152**	**100**

6.12 GLIOMAS

Forty patients had gliomas. Of these, 23 (57.50%) patients were male while 17 (42.50%) were female with a male to female ratio (M: F) of 1.35:1. Furthermore, they recorded a median GCS of 15/15.Additionally, these patients had a mean age of 39.65 +/-16.96 whilst ranging from 13 to 70 years.

Gliomas tended to most commonly occur in the frontal lobe (32.5%, n=13) followed by the temporal region (22.5%, n=9) and were least commonly found in the brainstem, cerebellum and intraventricular region at 7.5%.

Table 10: Patient distribution by glioma type

	Frequency	**Percent**
No Glioma	112	73.68
Frontal	13	32.5
Parietal	5	12.5
Temporal	9	22.5
Brainstem	3	7.5
Basal Ganglia	4	10
Cerebellar	3	7.5
Intraventricular	3	7.5
Total	**152**	**100**

6.13 MEASURES OF ASSOCIATION

In this analysis, chi-square test was to done to analyze the relationships between the different variables. In this test, a 95% confidence level was assumed.

Age and Meningioma

There was a statistically significant relationship between age and the occurrence of a meningioma with a p-value of 0.007 and a Pearson Chi-Square value of 12.0803(3 degree of freedom).

Table 11: contingency table on age and meningioma

	Meningioma		
Age group	No	Yes	Total
13 - <25	21	6	27
25- <40	31	17	48
40- < 55	17	27	44
55- <70	20	13	33
Total	89	63	152

Age and Glioma

Age had no statistically significant relationship with the occurrence of a glioma. A chi-square test yielded a value of 0.7285 (3 degree of freedom) and p-value of 0.859.

Table 12: Contingency table on age and glioma

	Glioma		
Age group	No	Yes	Total
13 - <25	19	8	27
25- <40	36	12	48
40- < 55	34	10	44
55- <70	23	10	33
Total	112	40	152

Gender and meningioma

There was a statistically significant relationship between the gender of the patient and the occurrence of a meningioma. A p-value of 0.001 was yielded by the chi-square test and a Pearson Chi-Square value of 11.9305(1 degree of freedom).

Table 13: Contingency table on sex and meningioma

	Meningioma		
Gender	No	Yes	Total
Male	46	15	61
Female	43	48	91
Total	89	63	152

Gender and glioma

There was a statistically significant relationship between the gender of the patient and the occurrence of a glioma. A p-value of 0.009 was yielded by the chi-square test and a Pearson Chi-Square value of 6.8159(1 degree of freedom).

Table 14: Contingency table on sex and glioma

	Glioma		
Gender	No	Yes	Total
Male	38	23	61
Female	74	17	91
Total	112	40	152

CHAPTER SEVEN: DISCUSSION

Incidence of brain tumours is related to age, with the highest incidence rates overall being in older men and women according various published neuroepidemiological studies. In contrast to most tumour types, however, brain tumours occur relatively frequently across all age groups, including children, teenagers and young adults. In our study which was done in patients aged 13 years and above, the mean age of occurrence of brain tumours was 40.63 years with a standard deviation of 15.36. The age range was from 13-70 years. This is in contrast to one published study which found an average age of presentation of brain tumours of 59 years overall.[5]

There was a statistically significant relationship between age and the occurrence of a meningioma with a p-value of 0.007 and a Pearson Chi-Square value of 12.0803 (3 degree of freedom). These findings are consistent with published literature where age is a known risk factor of meningioma due to the summation of other risk factors including radiation exposure and environmental agents that interact with inherent genetic factors leading to meningioma formation.[5]

Age had no statistically significant relationship with the occurrence of a glioma. A chi-square test yielded a value of 0.7285 (3 degree of freedom) and p-value of 0.859. This finding in our study could be attributed to the high crossover of childhood gliomas, which are the commonest tumours in childhood, into our study population. From our study it was noted that meningiomas occurred at a mean age of 43.97 years while gliomas at 39.65 years. According to one western study, they quoted a mean age of 64 years and 65 years for glioblastoma and meningiomas respectively.[5]

From the histogram it was noted that there was a larger peak at 40 years of age with three smaller peaks at 20 years, 50 years and 60 years. These figures generally depict a younger age of occurrence of brain tumours from our study when compared to data obtained from the Australian Institute of Health and Welfare[26] where it was found that the average age of brain cancer diagnosis was 58.7 years in Australia.

In our local set up, the prevalence and incidence of brain tumours seems to be more common in younger age groups. Overall, from other studies done in the Western world the median age of onset for brain tumours is 59 yrs, and the median ages of onset for glioblastoma and meningioma are 64 and 65, respectively from published literature.[5] As with other types of cancer, the increased incidence of most types of brain tumours with increasing age has been postulated in literature to be due to length of exposure required for neoplastic transformation, the need for genetic alterations to take effect prior to onset of clinical disease, or due to diminished immune surveillance.[20] Interestingly, there has been noted in literature to be a decline in the incidence of glioblastoma and astrocytoma among those patients aged 85 and older.[21] Oligodendrogliomas and ependymomas have been found to peak in middle age in one study.[21]In our study, oligodendroglioma mean age was 46.5 years, ependymoma at 18.33 years, metastatic tumours at 48.71 years and GBM at 48.36 years. These findings thus show that metastatic and GBM tend to occur at a slightly younger age group in our setup as compared to Western world published studies as indicated above while ependymomas occur at a younger age group in comparison to those studies. Oligodendroglioma tend to occur at 46.5 years which is consistent with published literature quoted above.

In our study we found a total of 61 male adults (40.13%) and 91 female adults (59.87%) presenting with brain tumours in KNH between January 2012 and December 2014. This figures represented an M: F ratio of 1:1.49 across all types of adult brain tumours. It is well documented in literature that primary malignant brain tumours and gliomas are more common in men while meningiomas are more common in women with a 2:1ratio from a local study done by Kanja and Mwang'ombe on meningiomas in KNH. In our study, the M:F ratio for gliomas was 1.35:1 with an age range of 13-70 years whereas for meningiomas was M:F ratio of 1:3.2 with an age range of 16-69 years showing gliomas were more common in men and meningiomas more common in women. Meningiomas constituted 45.99% of all the brain tumours analyzed in our study and this might explain the higher percentage of females presenting with brain tumours overall in our study. Males were more affected by gliomas with a male to female ratio of 1.4:1 in the Mwang'ombe et al. study in 2005[3] whose findings are replicated in our study.

Farmers (28.95%, n=44) and housewives (21.71%, n=33) comprised the most common occupation to present with brain tumours during the study period. Agriculture is the backbone of

the Kenyan economy. Nairobi County, where KNH the main referral hospital in Kenya is located is surrounded by rich agricultural lands. Most of the inhabitants are farmers and the reason more of them are seen is because of accessibility to KNH and the ability to pay for the neurosurgical services. The high number of housewives seen could be the spouses of these farmers from the surrounding rich agricultural areas whose husbands can be able to pay for the services and also ease of accessibility to Nairobi by road. K Ohta and colleagues (2005) studied the importance of geographical proximity and an efficient road system as a key predictor of prompt and efficient access to specialized neurosurgical services in a Japanese population.[28] It could also be postulated that neurosurgical patients who come from far flung areas generally seek help from local doctors or herbalists and are unable to travel to Nairobi due to financial constraints that are compounded by lack of efficient transport or road network. Also the other referral hospital in Kenya situated in Eldoret County is taking up the bulk of cases from the western region and this could explain the low rates of ethnic communities from that region presenting in KNH for neurosurgical care. The main concern are where patients from the coastal communities and the northern frontier districts are seeking neurosurgical services due to the very low numbers been seen in KNH which should be the their nearest referral centre geographically.

Global age-standardized mortality rate for PMBT is 2.8 for males and 2.0 for females per 100,000, and estimated mortality is higher in developed countries than in less developed countries[5]. This could be attributed to a variety of factors including late diagnosis of brain tumours, poor access to quality neurosurgical services for diagnosis and few neurosurgical specialists available in the developing countries. This can also explain why particular ethnic groups who are not farmers inhabiting the arid and semi-arid regions plus the coastal communities were seen less in KNH as compared to more affluent ethnic groups who practice commercial farming in nearby geographical regions or counties. Thus the socioeconomic status of the populace combined with ease of access to the neurosurgical referral centres has a direct effect on the overall management of brain tumours.

In our study the majority of patients analyzed were Kikuyu with 53.29% (n= 81) with Kamba being 13.82% (n=21). The higher rates of ethnic Kikuyu could be attributed to the fact that they are mainly farmers and come from richer agricultural lands surrounding Nairobi where KNH is located. The Kamba ethnic community come from hotter and drier areas also surrounding

Nairobi County which are less affluent and thus the patients with brain tumours in those areas might not afford to travel to KNH for neurosurgical care. Kisii (7.89%, n=12) and the Ameru (8.55%, 13) people were also seen more frequently with brain tumours in KNH and they are known to be commercial farmers and business people with the ability to access neurosurgical care although they come from far off regions from Nairobi County.

It has also been reported in other studies that regions with the highest reported rates of malignant brain tumours e.g. Northern Europe, the US white population, and Israel with rates of 11 to 20 per 100,000 people, generally have more accessible and developed medical care and access to specialized neurosurgical services than areas with the lower rates e.g. India and the Philippines with rates of 2-4 per 100,000 people[7]. However, some of the variations seen may suggest ethnic differences in inherited susceptibility or cultural or geographic differences in risk factors.[8, 9] Among the most consistent findings in literature on the epidemiology of brain tumours is the difference in incidence rates between genders; gliomas are more common in men and meningiomas more common in women[10] and this finding was also replicated in our study as was shown above.

In terms of clinical presentation, headache, nausea and vomiting (96.5%, n=146) was the most common clinical symptom finding. This is associated with mass effect attributed to the brain tumour that necessitates the patient to be referred to KNH for specialised neurosurgical care. Other common presentations were visual deficits (75%, n=114), motor deficits (46.5%, 70), confusion (36.18%, n=55), seizures (26.97%, 41) and cognitive deficits (26.32%, n=40). This could be attributed to direct effect on critical brain areas by the tumour, mass effect, leptomeningeal spread and compromise of vascular flow to these areas. The known and published fact is that lower-grade glial tumours and most meningiomas have a more indolent course that may persist over years, whereas the more aggressive tumours (e.g., anaplastic oligodendrogliomas, anaplastic astrocytomas, glioblastoma multiforme) may have a rapid onset of neurologic decline.

Only 1.13% of all the brain tumours presenting at KNH in our current brain tumour study had a previous brain tumour or any other tumour reported in the family. About 5% of brain tumours may be linked to hereditary genetic factors or conditions, including Li-Fraumeni syndrome, neurofibromatosis, nevoid basal cell carcinoma syndrome, tuberous sclerosis, Turcot

syndrome, and von Hippel-Lindau disease from various international studies. Scientists have also found “clusters” of brain tumours within some families without a link to these known hereditary conditions and research is underway to determine the cause. In particular, optic pathway gliomas have been linked to in NF1.[13] Studies of various syndromes, familial aggregation and linkage and mutagen sensitivity in adults suggest genetic susceptibility to gliomas although the mechanisms are not clear.[13] People with certain mutations in the NF2 gene have a substantial risk of developing schwannoma, ependymomas and meningiomas. High dose ionizing radiation is an established risk factor for meningiomas. However, brain tumours aggregate in families and this may be as a result of multifactorial inheritance where genetic factors determine the degree of risk from exposure to exogenous environmental factors such as irradiation.[13]

In our study sixty three patients had meningiomas. Of these, 48 (76.19%) patients were female while 15 (23.81%) were male with a male to female (M: F) ratio of 1:3.2. Additionally, these patients in our study had a mean age of 43.97 +/-13.07 whilst ranging from 16 to 69 years. In a local study done by Kanja and Mwang’ombe on the histology and clinical pattern of meningiomas at KNH, they found a mean age for meningiomas at 42.6 years and an M: F ratio of 1:2. In our study there was a statistically significant relationship between the gender of the patient and the occurrence of a meningioma. A p-value of 0.001 was yielded by the chi-square test and a Pearson Chi-Square value of 11.9305(1 degree of freedom). This finding is in keeping with most international studies including our own local study by Kanja and Mwang’ombe that found an M: F ratio of 1:2 for meningiomas at KNH.

In terms of radiological location of the meningiomas, the most common site were the sphenoid wing meningiomas (8.55%, n=13) followed by the convexity meningiomas (7.24%, n=11) with the planum sphenoidale (0.66%, n=1) been the rarest subtype of meningioma seen. There was a high percentage of patients in our study presenting with visual symptoms which could be attributed to the high occurrence of anterior skull base meningiomas at 38.09 %(n=24), sellar suprasellar lesions 6.57 %(n=9) and pituitary adenomas at 9.86 %(n=15). This can have a big implication in terms of post operative quality of life with a considerable number of patients not regaining their sight.

In our study forty patients had gliomas. Of these, 23 (57.50%) patients were male while 17 (42.50%) were female with a male to female ratio (M: F) of 1.35:1. Additionally, these patients

had a mean age of 39.65 +/-16.96 whilst ranging from 13 to 70 years. Generally, gliomas tended to occur at a younger age than meningiomas in our setup. This was however postulated to be due to the higher rates of crossover of childhood gliomas into our study population.

There was a statistically significant relationship between the gender of the patient and the occurrence of a glioma. A p-value of 0.009 was yielded by the chi-square test and a Pearson Chi-Square value of 6.8159(1 degree of freedom). Gliomas tend to occur more commonly in males than females according to most published studies as discussed earlier.

Gliomas tended to most commonly occur in the frontal lobe (32.5%, n=13) followed by the temporal region (22.5%, n=9) and were least commonly found in the brainstem, cerebellum and intraventricular region at 7.5%. This is consistent with most international studies whereby the frontal lobe is the commonest location due to its higher brain matter volume according to Suuvi L et al 2007 where he found that 87% of adult gliomas were in the cerebral lobes and the frontal lobe was the most common site at 40% followed by the temporal lobe at 29% and the parietal lobe at 14%. In our study we got a higher percentage of cerebellar astrocytoma compared to the Suuvi et al study at 7.5% versus 1.5% respectively.

Meningiomas (41.44%, n=63) and gliomas (26.31%, n=40) accounted for the majority of the brain tumours at 67.7%. Fifteen of the 152 tumours were pituitary adenoma comprising 9.86% of all the tumours analyzed, a classification not considered by the WHO classification of primary brain tumours 2007 version and will be analyzed separately. In the United States, 70,000 new cases of primary malignant and benign brain and CNS tumours are diagnosed each year; 31% of these tumours are gliomas and 37% are meningiomas.[1] In a local study by Boore et al[18] they found a percentage 40.8% to be meningiomas and gliomas at 26.8%. Our findings strongly correlated with this local Boore et al study. In the Mwang'ombe et al[17, 19] study done retrospectively from 1983-1994, they found a meningioma rate of 34.4% and a glioma rate of 45.8% which did not correlate with our current study.

Glioblastomas comprised of 55% (n=22) of all neuroepithelial tumours which is consistent with most local and international studies. It was followed by the pilocytic astrocytoma (n=3) and ependymal tumours (n=3) at 7.5%. PXA (pleomorphic astrocytoma) and ganglioglioma were the least prevalent neuroepithelial tumours at 2.5 %(n=1) in our study. In the Mwang'ombe et al

study done in 2005[3], metastatic lesions accounted for 2.8% of all brain tumours whereas in our study it accounts for 2.8% showing a greater degree of metastatic brain lesion diagnosis and operation. These patients with metastatic brain tumours are been diagnosed early enough thereby facilitating early intervention surgically for tumours that were previously not amenable to surgery due to amongst other things a low performance score in the earlier years.

Amongst the 63 meningiomas analyzed, the meningothelial variety was the most common at 39.68 %(n=25) followed by the transitional variety at 31.74 %(n=20). These were followed by the fibroblastic type at 19.04 %(n=12) and psammomatous variety at 6.34 %(n=4). The atypical meningiomas were the least seen meningiomas at 3.17 %(n=2). Other tumours that were analyzed were the craniopharyngiomas at 5.92% (n=9), metastatic lesions at 4.6% (n=7), medulloblastomas at 3.28% (n=5) and Schwanomma at 4.63 %(n=4).

The Central Brain Tumour Registry of the United States, CBTRUS, in its report for the period 2005-2009 reported an overall incidence rate of 26.81 per 100,000 adults aged above 20 years. The distribution of these primary brain tumours by site was reported to be 35.2% in the meninges, 15.3% sellar-suprasellar region, 8.9% in the frontal lobes, 6.6% temporal lobe, 4.3% parietal lobe, 1.2% occipital lobe, 1.2% intraventricular, 1.6% brainstem, 6.9% involving the cranial nerves, 2.8% cerebellum, 0.4% pineal region and 9.7% other brain[4].

In the USA, according to the CBTRUS 2005, the distribution of tumours by histology was gliomas at 29%, meningiomas 35.5%, pituitary tumours at 14.1%, craniopharyngiomas at 0.9%, and lymphomas at 2.2% and germ cell tumours at 0.5%. Notably, glioblastomas accounted for 54% of all gliomas followed by diffuse astrocytomas at 9.5%. Our local study figures for glioblastoma, meningioma and glioma correlated with this CBTRUS data available. We had lower rates for diffuse astrocytomas at 2.92% as compared with 9.5% according to the CBTRUS 2005 data available to the general public-.

In a retrospective study performed at the Kenyatta National Hospital between 1983 and 1994, gliomas were found to be the commonest intracranial tumours (45.8%).[17] Meningiomas were the next common tumours (34.4%). In another study conducted at the same hospital by Boore et al., meningiomas were the most frequently diagnosed, accounting for 40.8% (29) of cases, followed by astrocytomas at 26.8%.[18] The difference in findings between these two studies could be

attributed to the fact that, at that particular time period, meningiomas were the most frequent tumours operated on in KNH and the study used intraoperative cytological smear as study specimens. Males were most affected by gliomas with a male to female ratio of 1.4:1[3] in the Mwang'ombe et al study in 2005 which was consistent with our current findings

Of the 15 pituitary adenoma patients, 7 (46.67%) were male while 8 (53.33%) were female. These pituitary adenomas had a presenting GCS of 15 and the most common symptoms were headache, visual symptoms, endocrine abnormalities and hydrocephalus. M: F ratio was 1:1.14 which is consistent with most international studies. In the CBTRUS 2005, pituitary adenomas had a prevalence of 14.1% compared to our current study at 9.86%.

With regards to the type of the radiology, a large proportion of the tumours were supratentorial at 80.26% (n=122) with a mean age of 42.13 years with the infratentorial compartment accounting for 19.74% with a mean age of 34.53 years. This finding is consistent with other published literature findings that supratentorial brain tumours are commoner in adults than infratentorial tumours[28]. Only 15-20% of all intra-axial masses in adults are infratentorial and among them the most common are the metastatic lesions, hemangioblastomas and the meningiomas of the skull base[28]. Infratentorial tumours also tended to occur at a lower age group due to cross over of childhood tumours into our study population. Up to 20% of all intracranial mets seen in adults are in the posterior fossa[29].

The average GCS of patients operated on for brain tumours over the three year period under consideration was 15/15. This information indicates that on average patients with a good performance scale were operated on and this has been shown to directly contribute to better outcomes post op.

Another important finding is that most patients at 58.55% had both an MRI brain and a CT scan head done compared to 34.87% of the patients who had only a CT head done prior to surgery. MRI brain has been found to be useful for better characterization of the brain tumour and critical for surgical planning. CT scan head is used for screening of patients presenting with signs and symptoms of brain tumours and only in certain exceptional circumstances for example due to cost or in an emergency setup is CT scan used alone to plan for surgery.

CHAPTER EIGHT: CONCLUSION

Brain tumours are been seen at a younger age in KNH with a peak at about 40 years of age for all brain tumours compared from other western studies depicted above. Gliomas are presenting at a younger age on average when compared to meningiomas in our local setup at KNH. This is likely due to spill over of paediatric astrocytic lesions into our minimum age of consideration in this study at 13 years which is lower than the minimum age that the CBTRUS use of 20 years.

The western world have high life expectancy rates of more than 70 years and thus have a larger pool of elderly patients presenting with brain tumours when compared to our pool of elderly patients which is greatly diminished due to low life expectancy rates. This will have an effect where the patients presenting with brain tumours in our local setup will be younger compared to the western world

Gliomas are more common in males and meningiomas are more common in females with an overall ratio of 1:1.49.Meningiomas are the most common tumour overall at 41.44% compared with 26.31% for gliomas which is consistent with the Boore et al study locally and CBTRUS 2005-2009.Glioblastoma is the most common astrocytic tumour at 55%. It is a WHO grade IV lesion with known grave prognosis.

Factors such as geographical proximity to KNH and availability of a source of income from commercial farming and business people are clearly evident, on further evaluation of the ethnic and occupational pattern, as a key determinant of ready access to specialized neurosurgical treatment which has a direct effect on prognosis.

Headache, visual deficits, motor deficits and confusion are the four most common tumour presentations. Familial brain tumour syndromes are uncommon in our setup at 2.6% compared with a worldwide average of 5%.

Meningiomas prevalence still high in our study with a male to female ratio of 1: 3.2 Meningiomas are been seen at an older age group when compared to gliomas with a mean age of 43.97 yrs and 39.65 years respectively. This however could be due to a heavy crossover of childhood gliomas into our study population making the mean age to be lower for gliomas compared to meningiomas. Supratentorial brain tumours are more common in the adults than infratentorial tumours as clearly shown in our study.

A higher rate of metastatic tumours are now been seen more at 5.11% compared to the Mwang'ombe et al study done in 2005 at 2.8%. This could be attributed to these patients presenting early with a good performance score and good primary tumour control.

Gliomas are commonly located in the frontal lobe then the temporal and then the parietal lobes and this is consistent with most international studies and this can be attributed to the large brain mass in the frontal lobe Sphenoid wing and convexity meningiomas are the most common location types for meningiomas

Most patients are having an MRI brain done before operation due to the superior imaging quality and better lesion characterisation compared to CT scan alone. CT scan is been done commonly for screening and then an MRI brain is requested for better tumour characterization and surgical planning.

Also patients with a good performance score are more likely to be operated on due to the direct effect on good outcomes as was shown with an average GCS of 15/15 for the brain tumours on average preoperatively.

CHAPTER NINE: RECOMMENDATIONS

Due to the earlier presentations in brain tumours, doctors and other care givers need to have a high index of suspicion in order to pick these lesions up early to enable prompt treatment. This knowledge should be disseminated early in training school.

A larger prospective study needs to be done so as to eliminate any undue errors or missing record and to better characterise and device better ways of managing brain tumours. This study should ideally consider increasing the minimum age for adult tumours to 20 years to avoid the crossover of childhood tumours that are analyzed. This will provide a clearer picture of the patterns of adult brain tumours to aid in management.

Any unexplained secondary headaches should be investigated promptly by imaging especially when associated with vomiting. Screening should be done with a CT head with contrast and in case of any suspicion an MRI brain should be ordered to aid in further management.

Local studies to be done to clearly outline the reason gliomas are more common in males consistently in several studies whilst females dominate in meningioma occurrence. This should include genetic study to better advance the current notion of targeted therapy for brain tumours.

The government should aim to improve the socioeconomic status of Kenyans and decentralize neurosurgical care to enable better access to health care in general and neurosurgical care.

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APPENDICES

APPENDIX 1: DATA COLLECTION TOOL

Clinical presentation

Please tick yes or no in the space provided. Do not leave any section blank.

Hospital IP Number	
Study ID	
Age (years)	
Sex (Male or Female)	
Residence (County)	
Occupation	
Ethnicity	

A: Symptoms and signs

	Yes	No
Seizures		
Headache, nausea or vomiting		
Speech deficits (e.g. aphasia)		
Visual disturbance (e.g. double vision or blurred vision)		
Cranial nerve deficits (e.g. dysphagia, strabismus)		

Motor deficits		
Sensory deficits (e.g. loss of two point discrimination, stereoagnosia)		
Cerebellar signs (e.g. intention tremors, gait ataxia)		
Abnormal behaviour or confusion		
Cognitive deficits (e.g. amnesia)		
Stool or urinary incontinence		
Hormone imbalance (e.g. amenorrhea, obesity, galactorrhea)		
Period in weeks from the start of the symptoms to presentation in KNH		

Section B: History

Is there anyone in the family who has been sick with or died of?

Brain tumour	Yes	No	If yes who?
Any other tumour	Yes	No	If yes who and which tumour if known?

Section C: Examination findings:

Glasgow coma scale	
ENTER THE TOTAL GLASGOW COMA SCALE OF THE PATIENT HERE ON ADMISSION (out of 15)	

Radiological presentation

Type of imaging (MRI, CT scan or both)	
Size of lesion (mm) if present	

Location: Meningiomas

Select the main area: Convexity, sphenoid wing, tuberculum sellae, diaphragm sellae, parasagittal; or tentorial or foramen magnum, or petroclival or parafalcine or intraventricular
Other (describe, and also say if in multiple regions)

Location: Gliomas

Select the main area: Frontal, parietal, temporal, occipital, brain stem, basal ganglia, cerebellar or bilateral
Other (describe, and also say if in multiple regions)

All other tumours

	YES	NO
Metastatic		
Intraventricular		
Sellar or Suprasellar		
Pituitary		
Other (describe)		

Histology

Tumour type
WHO grading

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/188

23rd April, 2015

KENYATTA NATIONAL HOSPITAL APPROVED 23 APR 2015 KNH/UoN-ERC P.O. Box 20723-00202 Nairobi

Dr. Solomon Muriithi Wahome
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Solomon

Research Proposal : Pattern of brain tumours in Kenyatta National Hospital: A 3 year cross-sectional study (P153/03/2015)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 23rd April 2015 to 22nd April 2016.

This approval is subject to compliance with the following requirements:

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

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chair, KNH/UoN-ERC
The Dean, School of Medicine, UoN
The Chair, Dept. of Surgery, UoN
Supervisors: Dr. J. Kiboi, Prof. Nimrod J. Mwangombe