Anatomical and histological spectra of intracranial meningiomas seen in KNH; a retrospective and prospective study.

A DISSERTATION SUBMITTED IN PART FULFILMENT FOR THE AWARD OF DEGREE OF MASTER OF MEDICINE IN NEUROSURGERY AT THE UNIVERSITY OF NAIROBI.

By

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I certify that this dissertation is my original work and has not been presented for a degree in any other university.

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Last but not least my appreciation goes to all those friends who assisted at various stages making this study possible.
DEDICATION

This work is dedicated to:

My wife Lucy for her patience and support throughout the study.

My parents Mr. and Mrs. Kaguri who taught me discipline of patience and hard work.
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<tr>
<td>KNH</td>
<td>Kenyatta National Hospital</td>
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<td>CBTRUS</td>
<td>Central Brain Tumor Registry of the United States</td>
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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>RNA</td>
<td>Ribonucleic acid</td>
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<td>NF</td>
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<td>Karnofsky Performance Scale</td>
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<td>CT scan</td>
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<td>MRI</td>
<td>Magnetic Resonance Image</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>CSF</td>
<td>Cerebral Spinal Fluid</td>
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<td>NECT</td>
<td>Non-enhanced CT scan</td>
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<td>H&amp;E</td>
<td>Haematoxylin and Eosin</td>
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SUMMARY

Introduction:
Meningiomas are usually benign, slow-growing tumors, originating from the arachnoid cap cells. They account for approximately 20% of all primary intracranial tumors and they are the second commonest brain tumor. The incidence seems to be higher in Africa, at 24-38 per cent. Approximately 90% of the intracranial meningiomas are supratentorial. The anterior half is involved far more frequently than the posterior half. The most common sites are the convexity, parasagittal, falx, and sphenoid ridge, together making up 60% of intracranial meningiomas.

Objectives:
The aim of this study was to determine the clinical, radiological and histological pattern of intracranial meningiomas at KNH. The specific objectives were to determine the socio-demographic characteristics and clinical presentation and correlate this to the clinical patterns of intracranial meningiomas, to determine the intracranial anatomical locations of meningiomas and to document the WHO histological grades of meningiomas operated at KNH.

Material and Methods:
A two years retrospective and prospective study was carried out at KNH. Fifty patients managed between April 2009 and August 2010 were recruited in the retrospective arm. Their medical records and imaging studies were reviewed. The histology blocks were retrieved and examined. In the prospective arm a total of 28 patients with clinical and radiological findings suggestive of meningioma were recruited between September 2010 and April 2011. Histological examination of their biopsy was also done.

Results:
A total of 78 patients managed at KNH for intracranial meningiomas were sampled and included in the study. Females (69.2%) were more affected than males (30.8%). Meningiomas occurred in supratentorial compartment (85.9%) more frequently than infratentorial compartment (14.1%). Anterior cranial base was the commonest location comprising of 51.5% (Tuberculum sella 5.9%, olfactory groove 20.6% and Sphenoid wing 25%). Commonest location of meningiomas in the posterior fossa was the tentorium 60% and the petrous region 30%.
According to WHO classification, the benign form (grade I) was the commonest at 94.7%. Grade II (atypical) and grade III (malignant) represented 4% and 1.3% respectively. The commonest cellular subtype in grade I tumours were fibroblastic 25.4%, transitional (mixed) 25.4% and meningothelial (syncitial) at 22.5%.

Conclusion:
Meningiomas occurred more frequently in females than in males with a female to male ratio of 2.1. Young adults were more affected than their elderly counterparts. The mean age was 42.6. Patients presented late with majority having large tumours and significant visual impairment. There is significant decline in operative mortality reflecting improvement in neurosurgical care. Most intracranial meningiomas occur in the supratentorial compartment with anterior cranial base contributing over fifty percent. Majority of meningioma are histologically benign and hence curable by surgical resection.
Introduction

Meningiomas are usually benign, slow-growing tumors, originating from the arachnoid cap cells. They account for approximately 20% of all primary intracranial tumors and they are the second commonest brain tumor. The incidence seems to be higher in Africa, at 24-38 per cent. Approximately 90% of the intracranial meningiomas are supratentorial. The anterior half is involved far more frequently than the posterior half. The most common sites are the convexity, parasagittal, falk, and sphenoid ridge, together making up 60% of intracranial meningiomas.

In 1980 Awori and Otsyula reviewed 52 cases of meningiomas operated on at Kenyatta National Hospital (KNH) from 1974 to 1979 and concluded that meningiomas occurred in Africans as frequently as elsewhere. A male preponderance was noted in this series. (1)

Another study in the same institution by Mwang’ombe and Ombachi in 1993 on brain tumors showed that gliomas were the commonest intracranial tumors (45.8%) followed by meningiomas (34.6%). (2) A more recent study by Mwang’ombe and Boore on touch smear cytology as a diagnostic tool in central nervous system (CNS) tumors showed that meningiomas were the most frequently diagnosed tumors (42.3%) followed by gliomas (34.4%). (3) These statistics indicated that meningiomas constitute a large proportion of neurosurgical work at KNH.

The aim of this study was to determine the clinical, radiological and histological pattern of intracranial meningiomas at KNH. The specific objectives were to determine the socio-demographic characteristics and clinical presentation and correlate this to the clinical patterns of intracranial meningiomas, to determine the intracranial anatomical locations of meningiomas and to document the WHO histological grades of meningiomas operated at KNH.
LITERATURE REVIEW

Historical perspective:

Meningiomas probably have affected humans since prehistoric times. They are suspected to have been present in pre-Columbian Incas from the Peruvian Andes whose skulls have shown the hyperostosis that can occur with these tumors. Anatomists and pathologists were the first to describe the condition in detail, with one of the best early works being the description by Felix Plater in 1614.

The first documented report that dealt specifically with meningiomas was published in 1774 by a French surgeon Antoine Louis who called them *Fungus durae matrix*. Various descriptions and terms followed. In 1831 and 1834 they were depicted by Bright and Cruveilhier respectively in Lithographs for pathology atlases. In 1847 they were named *psammomas* (sandlike) by Virchows who was the first to note the presence of granules. In 1864 Bourchard named them *epitheliomas* and 1869 Golgi named them *endotheliomas*. Harvey Cushing proposed the term *meningotheliomas* in an effort to describe these tumors according to a tissue name. Later, Cushing opted for the term meningioma to refer to these tumors.

In the 18th and 19th centuries meningiomas were diagnosed during a patient’s life only if they caused changes in the overlying skull that could be appreciated through inspection or palpation. Only a few attempts were made to remove these lesions surgically, and a few of these were beneficial to the patient. Of 13 such operations performed between 1780 and 1896 whose outcome was specified, nine ended in patient’s death. In 1864, John Cleland, a professor of anatomy in Glasgow, reported on two tumours he had found during dissection, one of them arising from cribriform plate and the other from right frontal region adjacent to the superior longitudinal sinus. He noted that they originated from arachnoid rather than the dura. He also observed that they resembled the paccionian granulations. In 1915 Cushings and Weed reasserted Cleland’s opinion that meningioma originated from arachnoid cell cluster. In 1938, Cushing and Eisenhardt published a monograph on meningiomas. They reported in details on 313 patients encountered between 1903 and 1932.
Epidemiology

Hospital-based brain tumour series indicated that the incidence is approximately 20% of all intracranial tumours, a figure derived from several large series. The percentage ranges from 13.4% in the report by Cushing in 1932 to 27.3% in the report by Zimmerman et al. in 1969. The highest incidence of meningiomas was noted by Percy et al. in a population based study that reviewed records from 1935 to 1958. In this study meningiomas accounted for 38% of primary intracranial tumours.

In a population based clinical study performed in Manitoba from 1980 to 1985, 22% of primary intracranial tumours were meningiomas, with an overall incidence of 2.3/100,000. One large study of the distribution of intracranial tumours in a population in Australia between 1982 and 1990 showed the median ages for meningioma were 58.7 and 59.3 for men and women, respectively. The same report noted that meningioma is the only tumour with a significant female excess (sex ratio = 0.48) and that the excess is greatest between ages 45 and 70. Rohinger et al. noted that the incidence peaked for males in the seventh decade at 6.0/100,000 and for females in the eighth decade at 7.5/100,000. According to the Central Brain Tumor Registry of the United States (CBTRUS) 2001 statistics, Meningiomas, are the most common brain tumor. They are estimated to constitute 26% of all primary CNS tumors with annual incidence rate approximately 6 per 100,000 populations.

In children there is a tendency towards more aggressive forms and a male predominance. In middle-aged group, a predilection to female population can be reflected by female-to-male ratio of 3:2 or even 2:1, with tumor enlargement being observed during pregnancy and a moderate elevation of risk in breast carcinoma patients. Meningiomas in children are rare (1-2% of all primary brain tumors) and differ from those in adults and other childhood tumours in several respects, including: A male preponderance (71%), More frequent incidence of intraventricular (17%) and posterior fossa (19%) meningiomas than in adults. Mean age of 10.9 years (versus the peak 5.5 years for other childhood brain tumours. Significantly higher incidence (32%) of tumour calcification than that reported in adults (10%). Sarcomatous elements rendering them less favourable for surgical removal, and a high recurrence rate.
In 1993, Molleston et al. reported a case of a meningioma with malignant histologic features in a 6-month-old child and provided a review of the literature. Meningiomas in infants show a male preponderance, a greater frequency of convexity meningiomas (38% versus 13.4% in adults and 17% in children), absence of dural attachment, and fewer incidences of seizure (23% compared with 29% and 31% in adults and children, respectively). Several studies indicate that the incidence also is increasing with time, but as with other primary and metastatic intracranial tumors, these increased rates may reflect improved imaging capabilities and extended life-spans of the population in general (6-17).

Etiology

Several factors have been identified, among the most prominent of which are ionizing radiation and head injury. Others are hormone and other receptor binding sites, genetic factors and viruses.

Ionizing radiation

As early as 1953, a link was suggested between ionizing radiation and intracranial meningiomas (6). A very strong case for this link is the study of radiation therapy given for tinea capitis (ringworm of the scalp) to children in Israel between 1948 and 1960. The children in this population and their incidences of meningiomas were compared with those of control subjects from the general population and from siblings who were not treated. Results showed that 89% of the meningiomas found in the exposed subjects could be attributed to the radiation therapy they had received in childhood. Radiation doses of only 1-2 Gy were found to increase the risk of neural tumors, including meningiomas. A 1974 retrospective review of these children revealed that the incidence of meningiomas occurring in the irradiated group was four times that of the non-irradiated group (4/10,000 vs. 1/10,000, respectively). The latent period between irradiation and diagnosis of meningioma ranged from 16 to 21 years (6,19). The dose of radiation found to affect the children in the above study has another common usage, namely dental radiographs, which, since the advent of antifungal medication for treating tinea capitis, are the most common source of exposure of the head to ionizing radiation.
Head trauma

Head trauma has for some time been considered a possible risk factor for meningioma. As early as 1922, Cushing noted the prevalence of tumors at the exact "situation where a stunning blow had been received on the skull years before" and that such prevalence constituted more than mere coincidence. His conclusions followed a specific incidence involving Major General Leonard Wood, Chief of Staff of the Army and a powerful military leader, who, after striking his head on a low chandelier, began to notice a small growth in the bone at the site of the injury. For several years he experienced weakness in the left side of his body and then began having seizures.

He was brought to Cushing's attention in 1910 and underwent a craniotomy, which was Cushing's first successful operation on a meningioma. Subsequently, Cushing and Eisenhardt reviewed the histories of 295 patients who had a history of head trauma and found that 94 (30%) of the injuries were thought to have been related to the development of meningiomas.10

In another study, Rachlin and Rosenblum noted that patients with meningiomas showed an increased recollection of trauma.20 Likewise, Preston-Martin reported in 1989 that a large case-control study of 189 women with meningioma revealed a significantly higher incidence of recall of prior trauma requiring medical attention than occurred in either of the control groups.18 Numerous case studies and small series also have reported patients with various types of head injuries prior to diagnosis of meningioma. Contrary, other larger studies do not support a link between head injury and later occurrence of a meningioma. A study at the Mayo Clinic of 3587 residents of Olmstead County revealed individuals who had sustained head trauma with loss of consciousness, posttraumatic amnesia, or skull fracture compared with expected rates for the community showed no significant increased risk of meningioma in a 30,000 person-years of follow-up after injury. These studies appear to circumvent the recall bias of smaller case-control studies.21
Several factors have prompted studies of estrogens and progestogens as risk factors for meningiomas, among which are the 2:1 predominance in women, a possible connection between breast cancer and meningiomas, the presence of estrogen and progesterone receptors on some meningiomas and the indication that meningiomas change size during pregnancy and the menstrual cycle. Since Donnell et al first described in 1979 the presence of an estrogen-receptor protein in 4 of 6 meningiomas (22), numerous efforts have been made to describe an association between meningiomas and estrogen receptors, progesterone receptors, and androgen receptors. Attempts to explain the meaning of the sex hormone binding status of meningiomas vary. One review showed that approximately 30% of 330 meningiomas had evidence of estrogen receptors and approximately 70% of 264 tumors had progesterone receptors. The association of meningiomas with breast cancer remains controversial. A review of a Connecticut population-based tumor registry showed a prevalence of meningiomas among patients with breast cancer that appeared to have been more than coincidental, of 130 cases in which at least one tumor involved the CNS, 8 had a combination of breast cancer and meningioma (p < 0.05). Similarly, Helseth et al. (23) found in searching the Norwegian Cancer Registry 21 patients who had registered with breast cancer and later developed a meningioma, a figure that significantly differed from the anticipated 11 cases. They also noted an increased incidence of developing breast cancer in patients with meningiomas who were 50 to 64 years of age (p = 0.042). Another study of patients with breast cancer showed that of 41 patients with breast cancer and intracranial tumors, 15 patients had meningiomas, but 10 of these were diagnosed only at autopsy and were deemed clinically insignificant (24).
An inherited predisposition for developing a meningioma also has been suggested. Aggregations of meningiomas have been reported in several families\(^{26, 27}\), as has the occurrence of multiple meningiomas in two monozygotic twins.\(^{28}\) Another phenomenon involves the chromosomal abnormalities that have been identified in meningiomas by cytogenetic studies, the most frequent of which is the loss of one copy of chromosome 22. The monosomy of chromosome 22 has been confirmed by a study using molecular genetics techniques on primary tumor tissue, which also showed a greater proportion of terminal deletions of the long arm of chromosome 22. The study showed that the minimal deletion common to 81 meningiomas was distal to the myoglobin locus of the long arm of chromosome 22, which corresponds to the region 22q12.3-qter. The same genetic abnormalities are found in all common histological types of meningiomas.\(^{29}\) To date, loss of DNA on chromosome 22 has been demonstrated in only 40% of meningiomas, but the likelihood that the other 60% of meningiomas have alterations of chromosome 22 that are too small to demonstrate is probable.\(^{30}\) Neurofibromatosis (NF) is one of the most common autosomal dominant disorders; two types are recognized: the classic von Recklinghausen's neurofibromatosis (Type I) and bilateral acoustic neurofibromatosis (Type II). The genetic anomalies responsible for each have been elucidated. Meningiomas have been found to occur with either form of neurofibromatosis, but more commonly with Type II. Meningiomas are also known to occur sporadically. One theory regarding the sporadic form is that two rare events must occur, namely a mutation to form a recessive oncogene on chromosome 22 and a loss of the dominant allele from the second copy of chromosome 22. In cases of NF Type II, the probability that the recessive oncogene on chromosome 22 is inherited requires that only the loss of a tumor suppressor gene from the second copy of chromosome 22 would be needed to form a tumor.\(^{31}\)
Sites of Origin:

Approximately 90% per cent of the intracranial meningiomas are supratentorial. The anterior half is involved far more frequently than the posterior half. The most common sites are the convexity, parasagittal, falx, and sphenoid ridge, together making up 60% per cent of intracranial meningiomas. 

In Cushing and Eisenhardt series of 1938, the intracranial distribution was as follows:
- Parasagittal 22%, free convexity 18%, Sphenoid ridge 18%, Olfactory groove 9.8%.
- Suprasellar 9.5%, Posterior fossa 7.8%, Peritiorcular 4.7%, Temporal fossa 2.7%, Falx 2.4%.
- Choroidal 2.0%, Gasserian 1.7%, Multiple 0.7%, Intraorbital 0.7%, Combined with neuromas 0.7%.

DeMonte and Al-Mefty summarized the overall intracranial distribution of meningiomas by combining several large reported series, and concluded the following:
- Parasagittal/falcine 25%, Convexity 19%, Sphenoid ridge 17%, Suprasellar (Tuberculum) 9%, Posterior fossa 8%.
- Olfactory groove 8%, Middle fossa/Meckel’s cave 4%, Tentorial 3%, Peri-torial 3%, Lateral ventricle 1–2%, Foramen magnum 1–2%, Orbit/Op. ic nerve sheath 1–2%.
Clinical Presentation

The clinical symptoms of a meningioma are determined by its anatomic site. Meningiomas are extra-axial and occur where arachnoid cells are most numerous, especially within the arachnoid villi along the dural venous sinuses. Eighty-five to ninety percent of meningiomas are located supratentorially. The most common locations include convexity, sphenoid ridge, and planum sphenoidale. Meningiomas are rare in children and, when they occur, are more often aggressive and located either in the posterior fossa or intraventricularly.

The most common presenting symptoms of meningiomas are headache (36%), change in normal examination (27%), and memory impairment (16.5%).

Parasagittal meningiomas occur anywhere along the anterior or posterior course of the falx, with symptoms dependent on the location. Anterior parasagittal tumors produce headaches, memory loss, and personality changes. Tumors located in the middle of the falx produce motor and sensory deficit, and those located posteriorly produce homonymous hemianopsia.

Anterior tumors may obstruct cerebrospinal fluid outflow at the foramen of Monro, and obstruction of the sagittal sinus by posterior tumors can produce a sagittal sinus syndrome.

The symptoms of sphenoid ridge meningiomas depend on the medial to lateral location along the sphenoid ridge. The medial tumors originate from near the anterior clinoid process, with early unilateral visual loss. They invade the cavernous sinus, with attendant cranial nerve deficits. The lateral tumors displace the frontal and temporal lobes while growing in the Sylvian fissure, and produce headache, seizures, and motor and speech deficits.
Radiological features

The radiological appearance of meningiomas on CT scan has been well described. Meningiomas are typically isodense on CT before contrast and homogeneously hyperdense following intravenous iodinated contrast. CT offers the advantages of determining the extent of hyperostosis and the degree of tumor calcification both of which add to the diagnostic accuracy and help the surgeon with surgical planning.\(^{(14)}\)

MRI with and without gadolinium contrast is necessary to precisely delineate the full extent of the tumor, particularly in the case of skull base tumors that can involve critical neurovascular structures. On T1-weighted MRI, the majority of meningiomas are isointense, while the remainder is slightly hyperintense to grey matter. Contrast-enhanced T1-weighted images reveal dramatic and usually homogeneous enhancement of meningiomas and, often, their associated “dural-tail”. On T2-weighted sequences, nearly 50% of all meningiomas are hyperintense, while the other half are isointense to grey matter. T2-weighted sequence is also highly sensitive in delineating the extent of peritumoral edema. Furthermore, utilization of MRI allows the opportunity to obtain MR-angiography (MRA) and/or MR-venography (MRV) in order to better visualize the extent of vascular involvement, particularly the patency of dural sinuses and the encasement of major arteries.\(^{(14)}\)

Management options

In general, management options include observation, surgery, and radiation alone, or as an adjuvant therapy following surgery. Treatment plans must be individualized for each patient based on the age, overall condition of the patient, tumor location and size, neurological symptoms and deficits caused by the tumor, and the patient’s personal wish after a thorough discussion of all available options.\(^{(12,14)}\)

Observation

Surgery is not necessary for every patient with a meningioma. Observation alone, with periodic (usually yearly) follow-up by neurological and MRI evaluations, is indicated for elderly patients, especially if they have minimal or no symptoms caused by the tumor. In addition, observation may be an appropriate option for the following people regardless of their age: (1) patients with certain skull base meningiomas with minimal or no symptoms (e.g. cavernous sinus meningioma causing mild facial tingling or numbness), (2) patients with incidental small tumors with no surrounding edema, and (3) patients who insist on non-intervention after a thorough discussion of all treatment options.\(^{(12)}\)
Surgical management

The objective of the operation is total removal of the meningioma including the dural attachment and bone that is involved with the tumor. The completeness of the surgical removal is the single most important prognostic factor. However, this goal must always be tempered by surgical judgement, recognizing that the first priority is to try to preserve or improve neurological function. For patients in whom total removal of the tumor carries significant risk of morbidity, it is better to leave some tumor and plan to observe the patient. In some patients the tumor may remain stable indefinitely. In others reoperation at a future date or radiation therapy is indicated. The key considerations in tumor removal include:

1. Careful positioning of the patient and a well planned incision to give adequate exposure.
2. Early interruption of the blood supply to the tumor.
3. Internal decompression of the tumor using the cavitron, cautery loops, and/or bipolar coagulation.
4. Careful dissection of the tumor capsule, gradually displacing it into the area of decompression, dividing vascular and arachnoid attachments as they are encountered and minimizing retraction on the surrounding brain tissue.
5. Removal of the involved dura and bone when possible.
6. Reconstruction of dural defects, when indicated, with a free graft of pericranial tissue or fascia. (32, 34)


**WHO Classification**

The WHO classification 2000 was developed based on a 1999 international consensus conference of neuropathologists. It gives additional information pertaining the grading and likelihood of recurrence and aggressive behavior of the tumor. Using the grading system, meningiomas could be classified into three groups with increasing aggressiveness.

**WHO Grade I**

Tumors under this category are meningothelial, fibroblastic, mixed, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte-rich and metaplastic meningiomas. The most common being meningothelial, fibroblastic and mixed, while angiomatous and secretory type carry the worst prognosis.

**WHO Grade II — Atypical Meningiomas**

This group contains atypical meningiomas, clear cell meningioma and chordoid meningioma. Atypical meningiomas are meningiomas with increased mitotic activity (4 or more mitoses per 10 high-power fields) or three or more of the following: increased cellularity, small cells with high nucleus cytoplasmic ratio, prominent nucleoli, uninterrupted patternless or sheet-like growth, and foci of ‘spontaneous’ or ‘geographic necrosis’.

**WHO Grade III — Anaplastic (malignant) meningioma**

This group represents frank malignant tumors, with two other rare variants: papillary and rhabdoid meningioma. Histological features include either prominent malignant cytology or a high mitotic index. Prognosis is grave, with median survival less than 2 years. 

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(35)
STUDY JUSTIFICATION

Meningiomas constitute approximately 20-26% of all intracranial tumors. This constitutes a large proportion of neurosurgical work worldwide. The surgical morbidity and mortality associated with meningiomas have steadily improved with time mainly because of the earlier detection and partly because of improvement in surgical and anaesthetic technique.

The clinical patterns, imaging findings, and histology in our set up have not been documented. There is a knowledge gap of this condition in our set-up and, therefore, this study will act as a baseline for other studies in this topic. Describing the burden of disease and related patient variables in our setup will aid in providing useful data that can generate other entry points into studying this condition. The results of this study will help in improving patient management.

STUDY OBJECTIVES

Broad objective

The broad objective was to determine the clinical, radiological and histological patterns of meningiomas, managed at KNH.

SPECIFIC OBJECTIVES

The specific objectives were:

1) To determine the socio-demographic characteristics and clinical presentation and correlate this to the clinical patterns of intracranial meningiomas at KNH.
2) To determine the intracranial anatomical locations of meningiomas at KNH.
3) To document the WHO histological grades of meningiomas operated at KNH.
MATERIALS AND METHODS

STUDY AREA

The study was carried out at Kenyatta National Hospital, the country's main referral and the teaching hospital for the University of Nairobi.

STUDY POPULATION

The study population comprised of all patients who were diagnosed and managed for intracranial meningiomas at KNH ward 4C and private wing from April 2009 to April 2011. A total of 78 patients were included.

STUDY DESIGN

A two years retrospective and prospective study was carried out. Fifty patients managed between April 2009 and August 2010 were recruited in the retrospective arm. Their medical records and imaging studies were reviewed. The histology blocks were retrieved and examined by a senior pathologist for both histological type and WHO grade. In the prospective arm, a total of 28 patients with clinical and radiological findings suggestive of meningioma were recruited between September 2010 and April 2011. Histological examination of their biopsy was also done.

INCLUSION AND EXCLUSION CRITERIA

All patients admitted in ward 4C and private wing with clinical and radiological diagnosis of meningioma which were confirmed histologically were included. Patients with extracranial meningiomas and those who declined to give consent were excluded.
SAMPLE SIZE DETERMINATION

Sample size was determined using Yamanes' s formula Reference population based on
Previous study by Farzana et al at KNH between 2002-2004.

\[
n = \frac{N}{1 + N(e)^2}
\]

Where

- \(n\) = required sample size
- \(N\) = Reference population set at 96 based on previous study \(^{14}\)
- \(e\) = Error margin, set at ± 5%

Substituting the above in the formulae we get; \(n = 69\) subjects

Minimal sample size will be 69 patients.

DATA COLLECTION AND CLINICAL METHODS

The principal investigator reviewed all patients admitted with clinical and radiological
features suggestive of a meningioma. CT scan and MRI findings suggestive of a meningioma
include an extra axial lesion with a broad dural attachment and dural tail sign. There may be
hyperostosis of the overlying bone and calcification of the lesion. The lesion is isodense to
hypodense on non-enhanced CT scan (NECT) and enhances avidly on giving contrast.

Thorough medical history was taken and physical examination performed. The patients who
met inclusion criteria were selected and consecutively sampled for the study. The imaging
studies were reviewed and the intracranial location of meningioma determined. The
sociodemographic data and clinical data was collected by means of a questionnaire.
LABORATORY METHODS

The biopsy was taken to the histopathology section of the department of medicine where tissue sections were prepared and stained using routine Haematoxylin and Eosin (H&E) stains. The sections were then examined by the pathologist for the following histological features of meningioma:

a) Proliferation of meningothelial cells
b) Formation of whorling pattern.
c) Presence of calcific bodies.

The WHO histology grade was determined based on WHO classification -2000 system.

DATA ANALYSIS

Analysis was done in consultation with a statistician using the statistical package for social sciences (SPSS) version 19.

Descriptive statistics such as frequencies, proportions, measures of central location and variation (mean, mode, ranges and standard deviation) were used for most variables (age, gender, WHO histology grading among others). The above data was presented in tables, pie charts or bar graphs. The intracranial anatomical distribution of meningiomas was expressed as a proportion in percentage (No. of meningiomas at specific location / total no of meningiomas).

STUDY FEASIBILITY

The study was carried out in KNH. This is the main teaching and referral hospital in Kenya. KNH receives patient from within Kenya and also from the neighbouring east and central African countries. There is adequate infrastructure which includes a neurosurgical unit which caters for all neurosurgical patients, a radiology department equipped with computed tomography (CT) and magnetic resonance images (MRI) scanners which provides imaging services and pathology department from the University of Nairobi. The patient’s records are well kept with an efficient retrieval system.
ETHICAL CONSIDERATIONS

1. Permission to carry out the study was sought from the Kenyatta National Hospital Scientific and Ethical Research Committee.
2. Patients were enrolled into the study only after giving informed consent.
3. The usual care and evaluation of procedures was followed.
4. Those that decline to give consent were not discriminated.
5. Confidentiality with each client was maintained.
6. There was no harm for patients who participated in this study.

STUDY LIMITATIONS

1. Being a hospital based study the results cannot be generalised to population.
2. Time limitations will not enable long term follow up to determine the recurrence rate.
3. The asymptomatic meningiomas are unlikely to be captured.
A total of 78 patients managed at KNH for intracranial meningiomas were sampled and included in the study. Females (69.2%) were more affected than males (30.8%). Meningiomas occurred in supratentorial compartment (85.9%) more frequently than infratentorial compartment (14.1%). Anterior cranial base is the commonest location comprising of 51.5% (Tuberculum sellar 5.9%, olfactory groove 20.6% and Sphenoid wing 29%). Commonest location of meningiomas in the posterior fossa was the tentorium 60% and the petrous region 30%.

According to WHO classification, the benign form (grade I) was the commonest at 94.7%. Grade II (atypical) and grade III (malignant) represented 4% and 1.3% respectively. The commonest cellular subtype in grade I tumours were fibroblastic 25.4%, transitional (mixed) 25.4% and meningothelial (syncitial) at 22.5%.

**RESULTS**

**DEMOGRAPHIC DATA**

Figure 1: Distribution of intracranial meningiomas according to gender.

Distribution according to gender was determined in 78 patients with intracranial meningiomas. Majority of the patients were females 54 representing 69.2% while males were 24 representing 30.8%. Females were more affected than males with a female: male ratio of 2:1.
Table 1: Descriptive statistics on the age of the patients.

<table>
<thead>
<tr>
<th>Age</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-24</td>
<td>5</td>
<td>6.6</td>
</tr>
<tr>
<td>25-36</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>37-48</td>
<td>30</td>
<td>39.5</td>
</tr>
<tr>
<td>49-60</td>
<td>16</td>
<td>21.1</td>
</tr>
<tr>
<td>61-72</td>
<td>4</td>
<td>5.3</td>
</tr>
<tr>
<td>&gt;72</td>
<td>2</td>
<td>2.6</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>100</td>
</tr>
</tbody>
</table>

Distribution of meningiomas according to age was determined in 76 out of 78 patients. The minimum age was 13 years while the maximum age was 83 years. The average age was 42.82 with a standard deviation of 13.815, and a median of 40. The grouping interval was determined using the formula; \[ \text{Highest value - Lowest value} = \frac{11}{1+3.322 \log (N)} \]

Figure 2: Distribution of intracranial meningiomas according to age.

Majority of the patients (39.5%) were aged 37-48 years, while 25% were aged 25-36 years and 21.1% were aged 49-60 year. Only 6.6% were aged 13-24 years, 5.3% between 61-72 years and 2.6% above 72 years. No patient was below the age of 13 or above the age of 83.
Table 2: Age and sex distribution of intracranial meningiomas.

<table>
<thead>
<tr>
<th></th>
<th>13-24</th>
<th>25-36</th>
<th>37-48</th>
<th>49-60</th>
<th>61-72</th>
<th>above 72</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>female</td>
<td>1</td>
<td>12</td>
<td>25</td>
<td>13</td>
<td>1</td>
<td>1</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>19</td>
<td>30</td>
<td>16</td>
<td>4</td>
<td>2</td>
<td>76</td>
</tr>
</tbody>
</table>

Figure 3: Age and sex distribution of intracranial meningiomas.

Age and sex distribution of meningiomas was compared by cross tabulation. Majority of females (47%) affected were aged between 37-48 years, while majority of the males (30.4%) affected were aged between 25-36 years.
Table 3: presenting symptoms.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headaches</td>
<td>69</td>
<td>43.7</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>31</td>
<td>19.6</td>
</tr>
<tr>
<td>Seizures</td>
<td>29</td>
<td>18.4</td>
</tr>
<tr>
<td>Motor deficit</td>
<td>13</td>
<td>8.2</td>
</tr>
<tr>
<td>Mental changes</td>
<td>7</td>
<td>4.4</td>
</tr>
<tr>
<td>Gait disturbances</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Speech impairment</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Anosmia</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>others</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>Syncope</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Exophthalmose</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Figure 4: presenting symptoms.

Headache (43.7%), visual impairment (19.6%) and seizures (18.4%) were the most prevalent symptoms. Other symptoms were motor deficit (8.2%), mental changes (4.4%) and gait disturbances (1.3%).
Duration of symptoms was determined in 77 out of 78 patients. In 32.5% the symptoms had lasted 6-12 months, 28.6% less than 6 months, 22.1% 13-24 months, while 16.9% had symptoms that had lasted more than 24 months.
Table 5: Clinical signs found on examination.

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual loss</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>Papilledema</td>
<td>19</td>
<td>21.8</td>
</tr>
<tr>
<td>Partial aphasia</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Unilateral facial palsy</td>
<td>5</td>
<td>5.7</td>
</tr>
<tr>
<td>Mild hemiplegia</td>
<td>21</td>
<td>24.1</td>
</tr>
<tr>
<td>No signs</td>
<td>9</td>
<td>10.3</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>87</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

The commonest clinical sign found on examination was visual loss at 30%, followed by mild hemiplegia 24.1%, papilledema 21.8%. 10.3% had no signs, 8% had partial aphasia while 5.7% had unilateral facial palsy.
The Karnofsky performance scale (KPS) was 70-100% in 55.8%, 50-70% in 42.9%, and less than 50% in 1.3% of the patients.
Imaging study performed was determined in 78 patients. In 91.4% of the patients CT scan of the brain was done, while 7.4% had MRI scan done. Only 1.2% had other imaging study performed which included 4 vessel angiogram.

Tumour size was determined in 76 out of 78 patients. Majority of the patients (67.1%) had tumours measuring 21-40mm, 25% had tumours measuring 41-60mm, while 7.9% had tumours measuring more than 60mm. No patient had tumour measuring 20mm or less.
Majority of the patients (85.9%) had supratentorial meningiomas, while only 14.1% had posterior fossa meningiomas.

Table 7: Distribution of the supratentorial meningiomas.

<table>
<thead>
<tr>
<th>Site</th>
<th>Frequency</th>
<th>Valid Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>convexity</td>
<td>13</td>
<td>19.1</td>
</tr>
<tr>
<td>parasagittal</td>
<td>15</td>
<td>22.1</td>
</tr>
<tr>
<td>sphenoid wing</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>tuberculum sellae</td>
<td>4</td>
<td>5.9</td>
</tr>
<tr>
<td>tentorium</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>olfactory groove</td>
<td>14</td>
<td>20.6</td>
</tr>
<tr>
<td>multiple meningioma</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>petrous meningioma</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>68</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
The supratentorial meningiomas were distributed as follows: Sphenoid ridge (23.5%), parasagittal (22.1%), olfactory groove (20.6%), Convexity (19.1%), tuberculum sellae (5.9%), Tentorium (2.9%) and another 2.9% were located in multiple sites.

Of the patients who had tumours located in the parasagittal area, 42.9% were anterior and 42.9% were in middle third. Only 14.3% were located in the posterior third.
Of the patients who had tumours in the sphenoid area, 57.9% were located in the outer third (pterional), 26.3% in the middle third (alar), while 15.8% were located in the inner third (clinoidal).

Figure 13: Indicates the distribution of posterior fossa meningioma.

Of the patients who had posterior fossa meningiomas, 60% were located in the tentorium, 30% in other areas such as the left pterous apex, while 10% were located in the clivus. None was located in the fourth ventricle, cerebellar convexity or in the foramen magnum.

29
Surgical treatment was employed in 96.1% of patients who were treated surgically, while 3.9% were treated conservatively. There was no any other method of treatment employed other than the two.

Of the patients who were treated conservatively, majority, 50% the indication was that they were asymptomatic, and 50% had other reasons such as relatives refusing surgery. None of the patients was treated conservatively because of being elderly or medically unfit for surgery.
Of the patients who had surgical treatment, majority (59.5%) had a good state at discharge, 31.1% had a very good state, while 5.4% had a fair state. There was mortality of 4.1%.

Table 8: Histology grade according to WHO classification.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>grade I</td>
<td>71</td>
<td>94.7</td>
</tr>
<tr>
<td>grade II</td>
<td>3</td>
<td>4.0</td>
</tr>
<tr>
<td>grade III</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Of the 78 patients, 75 were graded as per WHO classification. Majority (94.7%) were grade I, 4% grade II, and 1.3% grade III.
Table 9: The cellular type for WHO grade I.

<table>
<thead>
<tr>
<th>Cellular Type</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningothelial</td>
<td>16</td>
<td>22.5</td>
</tr>
<tr>
<td>Fibroblastic</td>
<td>18</td>
<td>25.4</td>
</tr>
<tr>
<td>Mixed</td>
<td>18</td>
<td>25.4</td>
</tr>
<tr>
<td>Psammomatous</td>
<td>5</td>
<td>7.0</td>
</tr>
<tr>
<td>Angiomatous</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Microcystic</td>
<td>12</td>
<td>16.9</td>
</tr>
<tr>
<td>Secretory</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Lymphoplasmocyte-rich</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Metaplastic</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Figure 18: The cellular types for WHO grade I tumours.

Among the WHO grade I tumours, fibroblastic (25.4%) and mixed cellular types (25.4%) were the commonest followed by meningothelial (22.5%), microcystic (16.9%), psammomatous (7%) and angiomatous (2.8%).
Majority (11.8%) of patients with visual loss had the tumour in the olfactory groove region. Mild hemiplegia occurred in 10.5% of the patients with parasagittal meningiomas and 9.2% of the patients with sphenoid ridge meningiomas. Papilledema was common in convexity meningiomas (6.6%), while 3.9% with partial aphasia had tumours in the sphenoid ridge.
Most (18.2%) tumours measuring 21-40mm were found in the sphenoid ridge, followed by parasagittal (16.7%), convexity (13.6%), and olfactory groove (6.1%). Majority (9.1%) of tumours measuring 41-60mm were found in the olfactory groove, followed by sphenoid ridge (6.1%), parasagittal (4.5%) and convexity (3%). Majority (6.1%) of tumours measuring >60mm were found in the olfactory groove, while convexity and parasagittal areas accounted for 1.5% each. No patient had a tumour measuring 20mm or less.
In patients who had symptoms lasting less than 6 months, tumours were mostly found in sphenoid ridge (11.9%), parasagittal (7.5%), convexity (6%) and olfactory groove (4.5%). Patients who had symptoms lasting 6-12 months, tumours were mostly located in the sphenoid ridge (11.9%), convexity (6%), parasagittal (4.5%), while olfactory groove and tuberculum sellae each had 3%. In patients who had symptoms lasting 13-24 months, tumours were located in the olfactory groove (10.4%), convexity (4.5%), while sphenoid ridge and parasagittal were 3% each. In patients with symptoms lasting more than 24 months, tumours were mostly found in the parasagittal area (7.5%), convexity (3%), while sphenoid ridge, tuberculum sellae, olfactory groove and multiple each had 1.5%.
Figure 22: Correlation between functional status of the patient as per KPS and the tumour size.

Fourty three percent of patients with tumour size 20-40mm. scored 70-100\% on KPS while 23\% scored 50-70\%. Patients with smaller tumours had a better score.

Table 10: Pearson Correlations between tumour size and preoperative functional status

<table>
<thead>
<tr>
<th>Tumour size in millimeters</th>
<th>Pearson Correlation</th>
<th>Sig. (2-tailed)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.222</td>
<td>76</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.056</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>75</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pearson correlation is 0.222 while p value is 0.056. indicating a statistically significant correlation. The r value is positive indicating that as the tumour size increases, disability as per KPS increases.
Twenty two percent of patients with KPS of 70-100% had symptoms that had lasted 6-12 months, followed by less than 6 months (17%). Most (14%) patients with moderate or severe disability (KPS 50-70%) had had symptoms for 13-24 months. Patients with prolonged duration of symptoms scored poorly.

Table 11: Pearson Correlations between duration of symptoms and preoperative functional status (KPS).

<table>
<thead>
<tr>
<th>Duration in months of the symptoms</th>
<th>Pearson Correlation</th>
<th>Sig. (2-tailed)</th>
<th>N</th>
<th>Preoperative functional status. (KPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration in months of the symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pearson Correlation</td>
<td>1</td>
<td>.081</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td></td>
<td>.481</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>77</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative functional status. (KPS)</td>
<td>Pearson Correlation</td>
<td>.081</td>
<td>77</td>
<td>1</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.481</td>
<td></td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>77</td>
<td>77</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A positive pearson correlation (r) of 0.081. As the tumour size increases, disability level as per KPS increases. P=0.481 which is greater than the set p of 0.05. The relationship is statistically not significant between the two variables.
Table 12: Pearson Correlations between duration of symptoms and tumour size.

<table>
<thead>
<tr>
<th></th>
<th>Duration in months of the symptoms</th>
<th>Tumour in millimeters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of the symptoms</td>
<td>Pearson Correlation 1.213</td>
<td>0.213</td>
</tr>
<tr>
<td></td>
<td>Sig. (2-tailed) 0.067</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td>N 77</td>
<td>75</td>
</tr>
<tr>
<td>Size of the tumour in</td>
<td>Pearson Correlation 0.213</td>
<td>1</td>
</tr>
<tr>
<td>millimeters</td>
<td>Sig. (2-tailed) 0.067</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td>N 75</td>
<td>76</td>
</tr>
</tbody>
</table>

Pearson correlation of 0.213, while $p=0.067$, thereby showing that there is a statistically significant relationship between the two variables. Pearson correlation of 0.213 being positive, it signifies that as the duration of symptoms increases, the tumour size increases.

Figure 24: Correlation between functional status of the patient as per KPS and location of the tumour.

Patients with KPS 70-100% had most tumours in the convexity (13%) followed by parasagittal (12%) and sphenoid ridge (10%). Patients with KPS 50-70% had most tumours in the sphenoid ridge (13%) followed by parasagittal and olfactory groove at 10% each, then convexity (6%). Patients with sphenoid ridge and olfactory groove tumours scored poorly.
Hematoxylin and eosin preparation of different meningioma cellular types. Magnification ×40

Photomicrograph 1

Meningothelial meningioma marked by cells arranged predominantly in whorling pattern.

Photomicrograph 2

 Transitional (mixed) meningioma demonstrating meningothehial cells in whorling pattern and fibrous cells.
Hematoxylin and eosin preparation of different meningioma cellular types. Magnification ×40

Photomicrograph 3

Meningothelial meningioma marked by sheets of cells forming syncytium

Photomicrograph 4

Transitional or mixed meningioma, marked by both syncytial and fibrous patterns. Magnification ×40
Hematoxylin and eosin preparation of different meningioma cellular types. Magnification ×40

**Photomicrograph 5**

Fibroblastic meningioma characterized by spindled cells arranged in interlacing bundles. Magnification ×40

**Photomicrograph 6**

The microcystic meningioma pattern, characterized by a loose, mucinous-type stroma. Magnification ×40
Hematoxylin and eosin preparation Atypical meningioma, WHO grade II

Photomicrograph 7

Magnification ×20

Photomicrograph 8

Atypical meningioma marked by a disordered cellular architecture, large bizarre cells with inclusion bodies. Magnification ×40
Discussion

The predominance of meningiomas in females is well documented in literature. In this study meningioma occurred more commonly in females (60.9%) than in males (30.8%) with a female-to-male ratio of 2.2:1. This contrasts with the previous finding by Awori et al., who reported male predominance in a previous study reviewing 56 cases of meningiomas operated at Kenyatta National Hospital between 1974 and 1979.\(^1\) However, it compares well with other studies which report female predominance. In Cushing's series of 1938 comprising 313 patients, women were 191 (61%) and men were 122 (39%) giving a ratio of 1.5:1 \(^10\) In a more recent series of 733 patients by Black et al., women were 502 (71%) and men were 231 (28%). Female to Male ratio was 2.5:1. \(^15\)

Meningiomas affected young adults aged 25-48 years more frequently (64.5%) than their elderly counterparts (7.9% above age 60 years). The median age was 40 years with a mean of 42.6, nearly two decades lower than what has been reported elsewhere. This finding contrasts with other studies. Preston-Martin et al. reported a median age of 58.7 for males 59.3 for females.\(^14\) In Cushing's series the mean was 46.6\(^10\) while in Black's series the mean was 38.\(^17\) Rohringer et al. noted that the incidence peaked for males in the seventh decade and for females in the eighth decade.\(^15\) The peak age was 37-48 years for females and 25-36 for males. Males were affected a decade earlier compared to the females just as observed by Rohringer.\(^15\). There was no patient under the age of 13 years reported. Awori et al. had noted even a lower peak age at presentation of 21-30 years.\(^1\) Meningiomas seem to affect a much younger age group in our setup compared to the western population. These differences could be due to the dynamics of the population, with African population being younger than the western population. Considering that the study was done in a single institution over a two years period, further evaluation in a large series is necessary.

Majority of patients (32.5%) presented to Kenyatta National Hospital within 6-12 months after the onset of symptoms. Only 28.6% presented within less than 6 months while in 22.1% and 16.9% symptoms had lasted for 13-24 months and more than 24 months respectively. Approximately 50% of patients presented to the hospital one year since the onset of symptoms. This compares to a study done by Mascarenhas et al. in Portugal. \(^19\)
In Mascarenhas series. 39% of patients had symptoms lasting less than 6 months. 15% had symptoms for 6-12 months. 13% had symptoms for 12-24 and 33% had symptoms for over 2 years. (39) An association between size of the tumour and the duration of symptom was observed. Prolonged duration of symptoms positively correlated to the tumour size (r=0.213 and p =0.56) The commonest clinical symptoms of meningiomas were headaches (43.7%) and visual impairment. (19.6%) These are non specific symptoms and reflect increased intracranial pressure. Seizures occurred in 18.4% of the patients. In Mascarenhas series, headache was reported in 44% of patients. seizures in 13%, and motor impairment in 11%. Only 7% of patients had visual impairment. (38) Loss of vision was the commonest clinical sign found on examination. with 30% of patients having various degree of visual loss. This was followed by hemiparesis. 24.1% and papiloedema. 21.8%.

Besides the non specific symptoms, patients with olfactory groove meningiomas had visual loss as the most common (11.8%) finding and mild hemiplegia (2.6%) Majority (9.1%) of tumours in this location were large, measuring 41-60mm and 6.1%, measuring >60mm. By virtue of their subfrontal location, olfactory groove meningiomas may become very large prior to producing symptoms. In the series described by Turazzi, et al., (39) 23 of 37 tumours were greater than 6 cm. This is because frontal lobes are non eloquent areas and tumours in this region attain large size before they elicit symptoms.

Patients with sphenoid ridge meningioma had hemiplegia (9.2%) and aphasia (6.6%) as the most common finding. This is due to compression to the motor and speech cortex respectively. Tumours in this location were measuring 21-40mm in 18.2% and 41-60mm in 6.1% of patients. The association found between size and location might have to do with the fact that certain locations do not admit great volumes for anatomical reasons. As a lesion grows, its probability of interfering with functionally important areas obviously increases, as well as the probability of the nervous system’s mechanisms of adaptation and recovery running out. This may account for the association between abnormal physical examination and larger lesions.

The functional status, as per karnofsky performance scale (KPS) was 70 -100% in 55 8% and 50-70% in 42.9%. Only 13% scored below 50%. Among the patients with small tumours (21-40mm), functional status, as per (KPS) was 70 -100% in 43% and 50-70% in 23%. This score was better compared to patients with large tumours (41-60mm) who scored 50-70% in 16% and 70-100% in 9% of patients. The tumour size is significant determinant of the functional status.
The functional status was better (70-100%) in majority of patients who had most tumours in the convexity 13%, followed by parasagittal 12%, and sphenoid ridge 10%.

Majority of patients who had moderate or severe disability (50-70%) had most tumours in the sphenoid ridge 13%, followed by parasagittal and olfactory groove at 10% each.

Tumours located in the sphenoid ridge and olfactory groove were also noted to be large and correlated with low KPS (50-70%).

CT scan of the brain was imaging study performed in 91.4% of the patients. MRI scan was done in 7.4% of the patients. CT scan has become widely available and affordable compared to MRI. MRI with angiography and venography was done only in complex tumours where vascular anatomy was considered important in planning surgery. Four-vessel angiogram was performed in only 1.2%. Tumour size measured 21-40mm in 67.1%, 41-60mm in 25% and more than 60mm in 7.9% of the patients. No patient had tumour measuring 20mm or less.

Meningiomas occurred in the supratentorial compartment (85.9%) more frequently than in the infratentorial compartment (14.1%). Anterior cranial base was the commonest location of the tumours comprising of 51.5% (Tuberculum sellar 5.9%, olfactory groove 20.6% and Sphenoid wing 25%). Commonest location of meningiomas in the posterior fossa was the tentorium (60%) and the petrous region (30%). The olfactory groove (20.6%) and sphenoid wing (25%) meningiomas were more common in this study than study done elsewhere.
Table 13: Intracranial distribution of meningiomas in different series.

<table>
<thead>
<tr>
<th>Site</th>
<th>Cushing and Eisenhardt (1938) (%)</th>
<th>Traub, 1961 (%)</th>
<th>Naidich et al, 1996 (%)</th>
<th>DeMonte and Al-Mefty (1991)</th>
<th>This series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasagittal / Ifalx</td>
<td>22.4</td>
<td>46.5</td>
<td>25.7</td>
<td>25</td>
<td>22.1</td>
</tr>
<tr>
<td>Free convexity</td>
<td>18.3</td>
<td>32.5</td>
<td>17.6</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Sphenoidal ridge</td>
<td>18</td>
<td>18.1</td>
<td>12.5</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>Olfactory groove</td>
<td>9.8</td>
<td>7.6</td>
<td>5.1</td>
<td>8</td>
<td>20.6</td>
</tr>
<tr>
<td>Suprasellar</td>
<td>9.5</td>
<td>2.3</td>
<td>9.6</td>
<td>9</td>
<td>5.9</td>
</tr>
<tr>
<td>Posterior fossa</td>
<td>7.8</td>
<td>7.6</td>
<td>16.2</td>
<td>8</td>
<td>14.1</td>
</tr>
<tr>
<td>Choroidal</td>
<td>2.0</td>
<td>2.3</td>
<td>3.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>0.7</td>
<td></td>
<td>1.5</td>
<td></td>
<td>2.9</td>
</tr>
</tbody>
</table>

Two patients (2.9%) presented with multiple meningiomas. None of them had clinical features to suggest neurofibromatosis type II. In one patient the locations were sphenoid ridge and parasagittal.

The mortality rate was 4.1%, which compares to other studies in the west. Cushing’s (5.3%) and Black’s (0.4%) There was a significant improvement from 39% reported by Awori et al in 1970s. This is a reflection of development of neurosurgical care in Kenya. These developments include improvement in neurodiagnosis due to widespread availability of CT scans in the country and MRI Scan in KNH, introduction of microsurgery and improvement in neuroanaesthesia and ICU care. There are also several experienced neurosurgeon and neuroanaesthetist.

One of the patients who died, one had undergone a staged surgery for olfactory groove meningioma due to bleeding. Surgery was completed one week later but she developed sepsis and died. Another patient had olfactory groove meningioma and was HIV positive with KPS below 50%. Of the patients who had surgical treatment, 31.1% had fully recovered at the time of discharge and 59.5% were in good status.
The histological distribution of meningiomas was as follows. Grade I, 94.7%, grade II, 4%, and grade III, 1.3%. This compared well with WHO classification which incorporates several staging studies using advanced labelling techniques. Grade I (90-94%), grade II (5-7%), and grade III (1-5%). In Black’s series, 89% of meningiomas were Grade I, 8.5% were Grade 2, and 2.5% were Grade 3. Among the grade I tumours, the commonest cellular sub types were meningotheial (22.5%), fibroblastic (25.4%), transitional (25.4%) and microcystic (16.9%).

Conclusions

1. Meningiomas were twice as common in females compared to males just as reported in other series in the west.

2. Meningiomas affects young adults in our setting compared to the western world, with an age difference of nearly two decades. This could be due to differences in the two populations, with our population being much younger than the western population.

3. Features of increased intracranial pressure were the commonest mode of presentation.

4. Patients presented late with majority having large tumours and significant visual impairment.

5. There is significant decline in operative mortality reflecting improvement in neurosurgical care.

6. Most intracranial meningiomas occur in the supratentorial compartment with anterior cranial base contributing over fifty percent.

7. Majority of meningioma are histologically benign and hence curable by surgical resection.
1. Early diagnosis and treatment to prevent visual loss. Patients complaining of persistent headache or blurred vision should be investigated early and referred appropriately.

2. There is need to conduct a large prospective study to evaluate the age difference noted between our population and the western population and to document operative morbidity and recurrence rate of these tumours.

3. Further development of neurosurgical care is necessary. There is need to train cranial base neurosurgeons since majority of these tumours occur in this region.
References:


8. L. Mascarenhas, M. Fonseca, M. Honavar; H. Romão, M. Resende and A. Rocha Vaz Analysis of the influence of the variable size on the characteristics and behavior of Meningiomas, 2005.
GENERAL PATIENT INFORMATION AND CONSENT FORM

Introduction
Participation in this study is voluntary. We aim to find out the clinical patterns of meningiomas at K N H.

What is meningioma?
It is a growth that arises from the coverings of the brain within the cranial cavity. It normally causes increased pressure within the head and this manifest with headache, vomiting, and poor vision among other symptoms.

What is involved in this study?
Once you consent for your participation, we will take a medical history, examine you and then follow you up as you undergo the treatment.

Are there any risks involved?
There are no risks involved. You will receive the normal standard treatment for this disease and then you will be examined at regular interval to assess the progress.

Will I be penalized for not participating?
No, you will receive the same attention and treatment as those who choose to participate.

What benefits will I get if I participate?
If you are found to have any other neurological disease, we will treat accordingly.

What about confidentiality?
All the information we obtain will be kept confidential.

How much will it cost me?
No extra cost will be incurred.
What are my rights as a participant?

Participation in the study is voluntary. Once inducted in the study, you can choose to discontinue at any time. This will not cause discrimination.

What do you do with the information you get?

This information will help us understand the disease better. Like any other scientific information, we will seek to share our findings with other doctors in Kenya and the rest of the world.

Are you satisfied with the information given?

If yes, fill in and sign the consent below.

CONSENT FOR THE STUDY

ID No: ___________________________ Of: ___________________________ or

Parent/guardian of: ___________________________ study no: ___________________________

I hereby consent for myself/my child to be included in this study. The nature of the study has been fully explained to me by Dr. ___________________________. I have not been promised any material gain to participate.

Signed: ___________________________ (Parent/guardian)

Date: ___________________________
APPENDIX II:

STAINING TECHNIQUES

1. Dewax the section in two changes of xylene

2. Hydrate the tissue in descending of alcohol. Absolute, 95%, 70%, 50% upto water

3. Stain in haematoxyline for 7-15 minutes

4. Rinse in water.

5. Differentiate in 1% acid alcohol - 10 dips.

6. Rinse in water.

7. Blue in scott’s tap water - 10 dips

8. Rinse in water.

9. Counter stain in 1% Eosin

10. Dehydrate in ascending manner - 50%, 70%, 95%, absolute alcohol.

11. Clear in 3 changes of xylene.

12. Mount on the slide ready for examination.
APPENDIX III:

PATIENT PROFORMA

STUDY NO: _______________________
PRNO: _______________________

1. Demographic data
(Tick as appropriate)

11. Gender: [ ] Male
   [ ] Female

12. Date of birth (dd-mm-yyyy) _______________________

13. Age (years) _______________________

14. What is highest education level you have completed?
   [ ] None
   [ ] Secondary
   [ ] College

2. Clinical Data

21. What are the main presenting symptoms?
   [ ] Headache
   [ ] Gait disturbances
   [ ] Seizures
   [ ] Syncope
   [ ] Motor deficit
   [ ] Speech impairment
   [ ] Visual impairment
   [ ] Anosmia
   [ ] Mental changes
   [ ] Asymptomatic
   [ ] Exophthalmose
   [ ] Others (specify)
2. What is the duration in months of the symptoms mentioned above (2.1)?

[ ] < 6
[ ] 6 - 12
[ ] 13 - 24
[ ] > 24

3. What are clinical signs found on examination?

[ ] Visual loss
[ ] Unilateral facial palsy
[ ] Papilledema
[ ] Mild hemiplegia
[ ] Partial aphasia
[ ] No signs

4. Indicate preoperative functional status of the patient

Karnofsky performance Scale (KPS)

[ ] Normal/ or minimal symptoms & working 70-100
[ ] Moderate or severe disability 50-70
[ ] Dependent/ not working <50

5. Indicate the imaging study performed

[ ] CT scan
[ ] MRI scan
[ ] Others (specify)

6. What is size of the tumor in millimeter?

[ ] ≤ 20
[ ] 21 - 40
[ ] 41 - 60
[ ] > 60

6(a) If supratentorial meningiomas, please indicate the site.

[ ] Supratentorial meningiomas
[ ] Posterior fossa meningiomas
<table>
<thead>
<tr>
<th>Convexity</th>
<th>Lateral ventricle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasagittal</td>
<td>Tentorium</td>
</tr>
<tr>
<td>Sphenoid ridge</td>
<td>Cerebellar convexity</td>
</tr>
<tr>
<td>Tuberculum sellae</td>
<td>Intraorbital</td>
</tr>
<tr>
<td>Others (specify)</td>
<td></td>
</tr>
</tbody>
</table>

6a (i) If parasagittal, specify

| Anterior third | |
| Middle third | |
| Posterior third | |

6a (ii) If Sphenoid ridge indicate the site

| Outer third (pterional) | |
| Middle third (Alar) | |
| Inner third (clinoidal) | |

6(b) If posterior Fossa Meningiomas, indicate site

| Cerebellar convexity | |
| Tentorium | |
| Fourth ventricular | |
| Foramen magnum | |
| Clivus | |
| Others (specify) | |
Indicate the treatment method employed

- [ ] 7.1 Conservative
- [ ] 7.2 Surgical
- [ ] Others (specify)

7.1 If conservative treatment, please state the indication.
- [ ] Asymptomatic
- [ ] Medically unfit for surgery
- [ ] Age (elderly)
- [ ] Others (specify)

7.2 If surgical treatment, please indicate the state of patient at discharge.
- [ ] Very good
- [ ] Poor
- [ ] Good
- [ ] Mortality
- [ ] Fair
Histology grade according to WHO classification.

- Grade I
- Grade II
- Grade III

If WHO grade I, indicate the cellular type

- Meningothelial
- Fibroblastic
- Mixed
- Psammomatous
- Angiomatous
- Microcystic
- Secretory
- Lymphoplasmacyte-rich
- Metaplastic
- Others (specify)
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P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP*, Nairobi.
Email: KNHplan@Ken.Healthnet.org

8th December 2010

Kaguri S. Kanja
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Kanja

Research proposal: “Anatomical and histological spectra of intracranial meningiomas seen in
KNH: a retrospective and prospective study” (P308/09/2010)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed
and approved your above revised research proposal for the period 8th December 2010 –

8th December 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond
the deadline given. Clearance for export of biological specimens must also be obtained from
KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of
the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing
related research study so as to minimize chances of study duplication.

Yours sincerely,

PROF N. GUANTAI
SECRETARY, KNH/UON-ERC

cc. The Deputy Director CS, KNH
The HOD, Records, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Surgery, UON
Supervisors: Prof. N. J. Mwang’ombe, Dept. of Neurosurgery, UON
Dr. Gichuru Mwangi, Dept. of Surgery, KNH,
Dr. A. K. Gachie, Dept. of Pathology, UON

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