COMPARISON OF MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGICAL FINDINGS OF ADULT PATIENTS WITH PRIMARY BRAIN TUMORS AT MOI TEACHING AND REFERRAL HOSPITAL

BY

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THIS THESIS IS SUBMITTED TO THE SCHOOL OF MEDICINE, MOI UNIVERSITY IN PARTIAL FULFILLMENT OF THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN RADIOLOGY AND IMAGING OF MOI UNIVERSITY.

DECLARATION

Student's Declaration

I declare that this thesis is my original work, and that it has not been presented elsewhere for academic purposes or otherwise to the best of my knowledge. The research work was carried out while pursuing my Master of Medicine in Radiology and Imaging course at the Moi University, School of Medicine. No part of this work may be reproduced without permission of the author and/ or Moi University.

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DEDICATION

I dedicate this thesis to my loving husband Terer Erick for his support and encouragement in writing this thesis and to my children Ian, Ryan and Ethan, for their support and motivation. I also dedicate this work to my mother Mrs. Sivilina Kipsang, for her encouragement and constant inspiration in my life.

ACKNOWLEDGEMENT

I wish to thank the Almighty God for giving me the chance to undertake this study. I want to thank Moi University and specifically the School of Medicine for this opportunity to do this study. I sincerely wish to thank my Supervisors for their guidance and support during writing of this thesis. To all the lecturers in the Department of Radiology and Imaging and other Departments for their invaluable input during this process, my colleagues and everyone else for their invaluable guidance and support during the development of these thesis.

LIST OF ABBREVIATIONS

CSS	Cancer-Specific Survival
CT	Computerized tomography scans
FLAIR	Fluid Attenuation Inversion Recovery
IREC	Institutional Research and Ethics Committee
KNH	Kenyatta National Hospital
LGGs	Low grade gliomas
MES	Managed Equipment Services
MRI	Magnetic Resonance Imaging
UHC	Universal Health Coverage
WHO	World Health Organization

OPERATIONAL OF TERMS

Suspected Adult	A person aged 18 years and above who can give informed consent, who is clinically suspected by the healthcare worker as having brain tumor
Brain tumor	Abnormal cells that form within the brain and central nervous system. They can either be benign (non-cancerous) or malignant (cancerous).
Primary brain tumor	Tumors arising from the cells and tissues of the brain and the central nervous system. Primary tumors are categorized as glial (composed of glial cells) or non-glial (developed on or in the structures of the brain and benign or malignant.
Benign	This is a tumor that does not invade nearby tissues or other parts of the body.
Malignant	This is a tumor characterized by rapid abnormal cell growth, invasiveness and metastasis
Sensitivity	It is the ability of a test (MRI) to correctly classify an individual as diseased as compared with the goal standard (histopathology)
Specificity	The ability of a test to correctly classify an individual as disease free.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Brain tumors are common and fatal, therefore requiring medical providers to have a basic understanding of their diagnosis and management. The management of patients with brain tumors depends on the imaging finding. Magnetic Resonance Imaging (MRI) is one of the imaging modalities while histopathology diagnosis is the gold standard in the diagnosis of brain tumors. Histopathology services are limited to referral hospitals, private laboratories and institutions.

Objective: To describe and compare the radiological findings and histopathological diagnosis of primary brain tumors in adults at Moi Teaching and Referral Hospital (MTRH).

Methods: This was a cross-sectional study design conducted from April 2019 to March 2020 at the MTRH Eldoret-Kenya. A total of 79 patients were enrolled into the study. Data was collected using interviewer administered questionnaire where the MRI findings of the respondents were analyzed and recorded. Histopathological diagnosis was followed up and recorded. Continuous variables, means and categorical variables were summarized in frequency, percentages and bar graphs. The comparison between the MRI and histopathology diagnosis of primary brain tumors in adult patients at MTRH was done using sensitivity and specificity. This was calculated using two-by-two (2X2) tables.

Results: The age of the participants ranged from 18 to 85 years with a mean age of 46 years. The commonest clinical presentations were headache 71(80.68%), seizures 26(29.55%), vomiting 24(27.2%) and blurred vision 16(18.18%). The MRI diagnosis of brain tumors was meningioma 29(36.36%), glioblastoma, 24(30.68%) pituitary adenomas 12(13.64%) and diffuse astrocytoma 7(9.09%). There was a significant statistical association between tumor margins and type of tumor (p-value=0.044, Fisher Exact test). The presence of perilesional edema was significantly associated with the histopathological diagnosis (p-value=0.049, Fisher Exact test). The sensitivity of MRI in the diagnosis of meningioma, glioblastoma, pituitary adenoma and diffuse astrocytoma were 96.7%, 88.5%, 90.9% and 66.7 % respectively. The specificity ranged from 92.5-98.6 %. The overall diagnostic agreement between MRI and histopathology in the diagnosis of adult primary brain tumors in this study was 86.1%.

Conclusion: The most common brain tumors in our study were meningiomas, glioblastoma, pituitary adenoma and diffuse astrocytoma in both radiological and histopathological diagnosis. The sensitivity and specificity of MRI in diagnosis of brain tumors ranged from 66.7%-96.8% and 92.5%-98.6% respectively.

Recommendation: Use of MRI in the diagnosis of primary brain tumors in adults and guiding management is recommended.

CHAPTER ONE: INTRODUCTION

1.0 Introduction

This chapter contains the background of the study, the statement of the problem, the study objectives and the justifications of the study.

1.2 Background of the study

A brain tumor is an abnormal tissue in which cells divide and grow uncontrollably, unchecked by the control mechanism. Primary brain tumors arise from the normal constituents of the brain or brains' immediate surrounding. These are the abnormal tissue within the brain, meninges, cranial nerves, skull, pituitary gland and pineal gland (Louis et al., 2007). They can be benign or malignant.

They are also categorized as glial or non-glial. Glial tumors are composed of glial cells while nonglial develop on or in the structures of the brain, including nerves, blood vessels and glands. Primary glial tumors include diffuse astrocytoma, glioblastoma, oligodendrogliomas, ependymomas and anaplastic astrocytoma. Non-glial tumors include meningiomas and pituitary adenomas.

Meningiomas are the most common benign intracranial tumors and account for 36.6 % of all primary brain tumors and the incidence increase with advance in age (Buerki et al., 2018). Histopathology is the basis on which WHO has classified meningiomas. The WHO classification of meningioma is based on the histopathology and grades into three categories. The overall classifications are benign (Grade I), atypical (Grade II) and malignant/anaplastic (Grade III) (Louis et al., 2016).

Globally, primary brain tumors account for about 2 % of all malignancies in adult population (Jemal, Siegel, Xu, & Ward, 2010).

In Africa, meningiomas is the most common intracranial tumor (Ibebuike, Ouma, & Gopal, 2013), other neoplasms include gliomas, pituitary tumors and metastatic tumors.

In Kenya however, brain cancer accounts for 2.1 % of all cancers in males and 1. 9 % in the females (Korir, Okerosi, Ronoh, Mutuma, & Parkin, 2015). Gliomas formed 45 % of all intracranial tumors seen in Kenyatta National Hospital (KNH) with astrocytoma, ependymoma and oligodendroglioma subtypes being noted (Mwang'ombe N. J. M. & Mwago, 2000). In a study conducted in Eldoret by Mwita C et al (2018) the most common histopathological subtypes were glioblastoma (GBM)(71%) and diffuse astrocytoma (22.6%) (Mwita et al., 2018a).

According to the WHO, grading of brain tumors, and all other tumors is based on the histopathological characteristics such as cellularity , mitotic activity, pleomorphism, necrosis and endothelial proliferation (Komori, 2017). In this system, which is used in the clinical setting to decide on the type of therapy, there are four grades. Grade I and II are of low proliferation while Grade III and IV are malignant and aggressive types (Louis et al., 2016).

Grade I occur predominantly in children and young adults. They are stable or slow growing. Histopathologically, they have monomorphism bipolar cells and angiocentric growth patterns. These tumors can be cured following surgical resection alone. Examples of this grade include pilocytic astrocytoma and angiocentric glioma.

Grade II brain tumors show atypical cells that are generally infiltrating in nature. They have low mitotic activity. They often recure following local therapy and some may progress to higher grades. Examples of grade II brain tumors include chordoid glioma of the third ventricle and low-grade diffuse astrocytoma.

Grade III lesion show evidence of malignancy. These include nuclear atypia and increased mitotic activity. They also have infiltrative capacity and require aggressive radiotherapy and chemotherapy. Examples of grade III tumors include anaplastic astrocytoma, anaplastic oligoastrocytoma and anaplastic pleomorphic xanthoastrocytoma.

Grade IV have high mitotic activity and necrosis. They develop neovascularity and infiltrates surrounding tissues. Often, they have a rapid postoperative progression and fatal outcomes. Examples of grade IV tumors include glioblastoma (GBM) and diffuse midline glioma

The various histopathological classification of brain tumors varies in magnitude and prevalence. According to the Central Brain Tumor Registry of the United States in a descending order, the tumors occurs as follows: glioblastoma, lymphoma, non-specific astrocytoma, glioma, anaplastic astrocytoma and meningioma. ("Central Brain Tumor Registry of the United States," 2018.).

Meningiomas forms the majority (16-20%) of brains tumors. It's the most common non-glial tumors of the central nervous system (Toh et al., 2008). They are slow growing and often benign in nature. They affect the outer covering of the brains and often found in the cerebral hemisphere. Radiologically, both typical and atypical features can be seen. They present in either a spherical well circumscribed mass or a flat infiltrating lesion. MRI features include capping cyst of similar intensity to CSF. There is isointense signal intensity on T1 and T2, and homogenous enhancement with gadolinium contrast. A notable radiological feature of meningioma is the Dural tail sign (DTS). This is a linear contrast enhancing dural tail extending from the tumor

along the dural mater. However, this feature can also be seen in Schwannoma and in metastatic lesions (Sotoudeh, 2010).

There is a female preponderance with a male to female ratio of 1:2. Meningiomas have varied clinical presentation depending on the type, location and size of the tumor. Tumors that are less than 2cm are often found incidentally during autopsy while larger tumors may cause severe mass effect like midline shift and ventricular obstruction. WHO grading of meningiomas are into three criteria; grade I, II and III. Grade I meningiomas are benign, grade II tumors are atypical meningioma while grade III are the malignant/anaplastic meningioma. Each of the grade has various subtypes. The diagnosis of meningioma is initially by MRI and CT scans. Confirmatory test is by the use of Histopathology.

Gliomas represent 40 % of all brain tumors. Gliomas can either be astrocytoma or oligodendroglioma, glioblastoma and diffuse glioma. Glioblastoma (GBM) is the most common of these subtypes. Astrocytoma arises from the astrocytes and occur in the cerebrum. The clinical presentation of gliomas varies depending on the stage and location of the tumor. The most common presentation is headache, pressure effect and manifest as seizures and changes in the personality. Oligodendrogliomas arise from the supporting cells of the brain. They occur in the cerebral hemispheres and causes seizures, headaches and changes in the behavior. Seizures occurs in over 25% of the patients (Schiff et al., 2015). Gliomas affect more males than female with a male to female ratio of 1.4:1(Chen et al., 2013).

Despite majority of brain tumors being generally benign (some are malignant), their location within the central nervous system can cause serious morbidity and mortality to the individual patient and burden to the health care system. Neuroimaging is

necessary for the diagnosis, treatment and clinical management of any brain tumors (Arbizu et al., 2011).

Neuroimaging of brain tumors is an ever-evolving field with various technologies being established. Magnetic Resonance Imaging (MRI) is one of the specialist imaging modalities for patients with suspected brain tumor in addition to Computerized tomography scans (CT).

It is the standard imaging modality to precisely determine the tumor location and to describe it anatomical relationship with surrounding brain structures (Pope & Brandal, 2018). In addition, MRI is widely available, it has superior tissue contrast and has no ionizing radiation. MRI is better to other imaging modalities like CT scan since it can view in several planes. (Yan et al., 2016).

Conventional structural Magnetic Resonance Imaging remains the standard care of imaging method for neuro-imaging practice. Standardized protocols that can be performed on a minimum 0.3 tesla MRI system include 3 dimensional T1, Axial Fluid-Attenuated Inversion Recovery (FLAIR), and gadolinium contrast enhanced T1 (Villanueva-Meyer, Mabray, & Cha, 2017).

MRI scans may identify asymptomatic brain tumors and can help monitor growth overtime; thereby providing an essential tool to survey tumor burden at various stages in the course of treatment of brain tumors (Neugut et al., 2019).

The availability and accessibility of MRI services across the counties in Kenya has been enhanced by the national government project of Managed Equipment Services (MES) launched in 2013 and the Universal Health Coverage (UHC) under the Big Four Agenda (MOH, 2013). This is an agreement between the national government and the county government where 6 global medical firms were contracted to supply,

install, train user and offer maintenance and repair of diagnostic medical equipment. This will enable MRI to be used as one of the primary imaging modalities for suspected brain pathologies in the peripheral facilities at the county level (Mabray, Barajas, & Cha, 2015). Through this program the devolved health services are supported by the national government by equipping 2 hospitals in each county and 4 national referral hospitals with outsourced specialized medical equipment (MOH, 2016).

The MES project is aimed at relieving the counties the burden of purchasing medical equipment and ultimately ensure that those seeking specialized health care do not incur exorbitant cost for medical care (Mutua & Wamalwa, 2020). This move was aimed to reduce the cost of seeking neurosurgical and histopathological services at the main referral centers. The neurosurgical services for brain tumors are expensive, invasive and associated with morbidity and mortality(Senders et al., 2018).

Moi Teaching and Referral Hospital is the main referral center in North Rift and Western Kenya (MTRH, 2020). It has a catchment population of approximately 18 million. It is located in Eldoret Town in Uasin Gishu County in the Rift valley region of Kenya. It has a bed capacity of approximately 800 beds.

1.3 Statement of the problem

Brain tumors in adults are common and they cause great morbidity and mortality. The burden of brain tumors in Kenya is rising as in other parts of the world (Fitzmaurice et al., 2017).

Neuroimaging using MRI is one of the noninvasive diagnostic tool with no ionizing radiation (Mabray et al., 2015). However, the gold standard for the diagnosis of brain tumors is histopathological examination of tissue biopsy. These procedures are

expensive, invasive and associated with morbidities and mortalities (Senders et al., 2018). Moreover, the number of neurosurgical services and the availability of histopathological laboratories is limited to the referral hospitals and major private hospitals (K. Patel et al., 2016). This causes delays in the definitive management of such patients.

Magnetic resonance imaging (MRI) allows for the characterization of patterns, diagnosis and grading of brain tumors in adults and assessment of treatment response ((Pope & Brandal, 2018). It is the standard imaging modality for determining precisely tumor location and its anatomical relationship with surrounding brain structures (Arbizu et al., 2011). With the installation of MRI centers in all the county referral hospital in Kenya, through the MES program, this will be one of the imaging modalities for all brain pathologies especially suspected brain tumours. The Managed Equipment Services (MES) enabled MRI decentralization in the counties across Kenya leading to improved access and reduced cost of health care.

However, there is underutilization of these radiological services (Mutua & Wamalwa, 2020). Training of radiologists by the county governments has also ensured availability of skilled health workforce (Miseda, Were, Murianki, Mutuku, & Mutwiwa, 2017). The use of telemedicine in remote areas reduces the need for patients to travel long distances to get their radiological reports(Fraser & McGrath, 2000; Odhiambo & Mars, 2018; Seto, Smith, Jacques, & Morita, 2019). This study therefore, intend to compare MRI characteristics with histopathological findings of suspected brain tumors among adults in MTRH. The information from this study will be used to recommend the use of MRI in peripheral facilities without histopathology services to guide management patients as they wait for surgery or other management using MRI findings.

1.4 Justification

Brain cancer is the leading cause of morbidity and mortality in the developing countries (Kanavos,et al. 2006). Globally, primary brain tumors account for about 2 % of all malignancies in adult population (Jemal et al., 2010). Brain tumors specifically are common and fatal, and therefore requiring general medical providers to have a basic understanding of their diagnosis and management (Khodamoradi, F. 2017). There is need to know more about primary brain tumors with regard to comparison of MRI features and histopathological diagnosis so as to better manage patients who present to us.

Accurate diagnosis of suspected brain tumors is critical in ensuring prompt and adequate management. Though histopathology is the gold standard for the diagnosis of brain tumor, it is done much later after MRI studies. Moreover, the procedure of histopathological examination of tissue biopsy is limited to tertiary health facilities, is expensive and is associated with poor prognosis (Ray, Bonafede, & Mohile, 2014).

MRI provides detailed information about the brain tumors anatomy, cellular structure, makes it a very important tool for the effective diagnosis, treatment and monitoring of brain tumors. (Gao & Jiang, 2013). MRI has more accuracy for diagnosis brain tumors and biopsy correlation (Hohenfeld, Werner, & Reetz, 2018).

Congruency between MRI findings and histopathological diagnosis of primary brain tumors will enable timely patient management and improve the survival rates.

Furthermore, this will decongest the referral hospital, reduce the waiting time before diagnosis and reduce the cost of imaging and treatment to the patients with brain tumors. Moreover, it is relatively cheaper and safe compared to surgery and

histopathological examination. Tissue biopsy and brain surgery is associated with hemorrhage and other complications.

Currently, there is limited published information in the region of the comparison of MRI findings of brain tumors and the histopathological findings in MTRH. Local studies on the correlation between radiological findings and the histopathological findings of the various histopathological subtypes of meningioma was last done in 2013(Onyinkwa M. et al, 2013). Despite the lack of data in the region, findings in France by Marcos et al (2012) noted that there was no association between MRI findings and Histopathology with regard to diffuse glioma (Dellaretti et al., 2012). .

The data from this study, when available, will have the potential of being used as guide and evidence on policy development with regard to the care and management of patients with brain tumors in MTRH and in Kenya as a whole.

1.5 Research question

This study aimed to answer the following question:

1. What are the MRI findings and histopathological diagnosis of suspected brain tumors in adults at MTRH?
2. What are the findings when comparison made between the MRI findings and histopathological diagnosis of brain tumors in adults at MTRH?

1.6 Objectives

1.6.1 Broad objectives

To describe and compare the MRI findings and histopathological diagnosis of suspected brain tumors in adults at MTRH.

1.6.2 Specific objectives

1. To describe the common Magnetic Resonance Imaging findings of adult patients with suspected brain tumors in MTRH.
2. To describe the histopathological findings of common brain tumors in adult patients with primary brain tumors in MTRH.
3. To compare the MRI findings and the histopathological diagnosis among adult patients with primary brain tumors in MTRH.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology and classification of Brain tumors

Intracranial tumors can either be primary or secondary. Primary brain tumors comprise a diverse group of pathologic types derived from the various cells that compose the central nervous system (CNS). Brain tumors are the abnormal tissue within the brain, meninges, cranial nerves, skull, pituitary gland and pineal gland (Louis et al., 2007). According to the WHO, grading of tumors is based on the histopathological characteristics. In this system, which is used in the clinical setting to decide on the type of therapy, there are four grades. Grade I and II are of low proliferation while Grade III and IV are malignant and aggressive types. Primary brain tumors vary depending on the histopathological types. (Hussaini, M. 2013). On the other hand, secondary brain tumors arise from metastasis from systemic cancers e.g. lung cancer, melanoma and breast (Owonikoko et al., 2014).

Primary brain tumors account for about 2 % of all malignancies in adult population (Jemal et al., 2010). In Kenya, however, brain cancer accounts for 2.1 % of all cancers in adult males and 1. 9 % in the females (Korir et al., 2015). The burden of brain tumors has been on the rise in Kenya (Muriithi S. 2015) and across the world (A. P. Patel et al., 2019). This has led to increased attention due to its poor prognosis. Several other studies have indicated an increasing trend in the incidence of this cancer (Inskip, Hoover, & Devesa, 2010).

The various histopathological classification of brain tumors shows variation in magnitude. According to the Central Brain Tumor Registry of the United States (“Central Brain Tumor Registry of the United States,” 2019) in a descending order,

the tumors occurs as follows: glioblastoma, lymphoma, non-specific astrocytoma, glioma, anaplastic astrocytoma and meningioma.

Meningiomas forms the majority (16-20%) of brains tumors. It's the most common non-glial tumors of the central nervous system (Toh et al., 2008). They are slow growing and often benign in nature. They affect the outer covering of the brains and are often found in the cerebral hemisphere. Radiologically, both typical and atypical features can be seen.

Gliomas can either be astrocytoma or oligodendroglioma. Astrocytoma arises from the astrocytes and occurs in the cerebrum. The most common presentation is pressure effect and manifest as seizures and changes in the personality. Oligodendrogliomas arise from the supporting cells of the brain. They occur in the cerebral hemispheres and causes seizures, headaches and changes in the behavior. The World Health Organization (WHO) classification system of central nervous system tumors, revised in 2000 and 2007, categorizes gliomas from grade 1 (lowest grade) through grade 4 (highest grade). This classification relies on histopathological features, including cellularity, nuclear/cytological atypia, mitotic activity, vascularity, and necrosis, microvascular proliferation as observed on light microscopy with the aid of immunohistochemistry.

There is geographic variation in the distribution of primary brain tumors. In the United States, the most prevalent brain tumors are intracranial metastases from systemic cancers, meningiomas, and gliomas, specifically, glioblastoma (McFaline-Figueroa & Lee, 2018). In Africa, meningiomas is the most common intracranial tumor (Ibebuike et al., 2013), other neoplasms include gliomas, pituitary tumors and metastatic tumors. In the urban centers and among the HIV infected individuals,

gliomas is the most common. (Jokonya et al., 2018; Olasode, Shokunbi, & Aghadiuno, 2000; Wambalaba, Son, Wambalaba, Nyong'o, & Nyong'o, 2019).

In Kenya however, brain cancer accounts for 2.1 % of all cancers in males and 1. 9 % in the females (Korir et al., 2015). Of all the brain tumors in adult high grade gliomas is the most common ((N. J. M. Mwang'ombe & Mwago, 2000). From the same study, metastatic tumors accounted for 2.8% of all brain tumors. The second most common brain tumors was meningioma and then astrocytoma. The burden of brain tumors has been on the rise in Kenya (Muriithi, S. et al., 2015) and across the world (Patel A. P.et al., 2019). This has led to increased attention due to its poor prognosis.

Local studies in Eldoret showed that among the meningiomas, grade I were the most common including meningothelial, fibroblastic and transitional (Onyinkwa M et al, 2013).

The burden of brain tumors in western Kenya is largely unknown. The Moi Teaching and referral hospital remains the main center for neurosurgery in western and as a result majority of the patients with brain tumors continue to present at the hospital.

The incidence of brain tumors varies with age. The most common brain tumor for patients aged 34-74 years is meningioma followed by glioblastoma multiforme.

Hereditary factors contribute to 5% of all the primary brain tumors. Some of the associated diseases include p53 defects, tuberous sclerosis, von Hippel-Lindau disease, Turcot's syndrome and familial polyposis. These conditions have been shown to increase the risk of primary brain tumors. Neurofibromatosis 1(NF 1) has been linked to optic pathway glioma (Campen & Gutmann, 2018).

Patients with brain tumors, according to ("Overview of the clinical features and diagnosis of brain tumors in adults - UpToDate," 2019) presents with a myriad of

signs and symptoms. The tumors produce these symptoms by local brain invasion, compression of adjacent structures or by increased intracranial pressure (ICP).

These symptoms can either be physical or behavioral depending on the localization of the tumor in the brain. The physical symptoms include focal signs, fatigue and headaches while the behavioral signs include hallucinations, depressions, and anxiety among other mood signs (Adams, Sullivan, & Vitaz, 2015). The general symptoms of headache and seizures are caused by the increased intracranial pressure (Grant R, 2004). Some tumors present with language deficits like difficulty reading or writing. The symptoms may present depending on the type of tumors though according to (Comelli, Lippi, Campana, Servadei, & Cervellin, 2017) the information may not be precise to the brain tumor concerned. Focal signs of unilateral weakness or personality changes are brought about by tissue destruction (Perkins, 2016).

Headache is the most common symptoms of intra cranial tumors. It is best described as severe, worse in the morning and is associated with nausea and vomiting (Perkins, 2016) . Some of the patients may report tension type headache, which according to (Adams et al., 2015) is usually bifrontal.

The presentation of brain tumors varies with age. There is striking difference in the clinical presentation between brain tumors in children and in adults. This epidemiologic property determines the age of onset and the prognosis after standard therapy.

Advance in age is associated with decrease in some brain tumor types like medulloblastoma, pilocytic astrocytoma and ependymoma.

The embryonal tumors are the most frequent tumors, in order of increasing age. Medulloblastoma followed by pilocytic astrocytoma in children aged 0–4 years;

pilocytic astrocytoma followed by embryonal tumors in children aged 5–9 years; malignant glioma in children aged 10–14 years; pituitary tumors in children aged 5–19 years. Pituitary tumors followed by meningioma in adults aged 20–34 years, and meningioma followed by glioblastoma multiforme in adults aged 34–74 years (Merchant, Pollack, & Loeffler, 2010).

According to the United states Central brain tumors registry, majority (58%) of the all brain tumors were reported in the females (Ostrom et al., 2019) , however, malignant tumors occurred more in males (55%) and 64% of non-malignant tumors in female. Sex hormones has a role in the development and prognosis of glioblastoma multiforme. Females showed a better 1-3- and 5-year cancer-specific survival (CSS) compared to the male patients after surgery (Tian et al., 2018).

Tumors in the brain causes increase in the intracranial pressure. The subsequent swelling of the brain and blockage of cerebrospinal fluid will lead to development of the myriad of symptoms that are seen in brain tumors. The headache gets worse over time as the tumor size increases and disease progresses.

Depending on the location of the tumors in the brain, there could be a characteristic headache that the patient will complain of. For example, tumors in the posterior fossa will worsen at night or early morning and in recumbency and improves with vomiting. In addition, there can be associated behavioral and mental changes. (Fawzy, Almassry, & Ismail, 2016)

2.2 Neuroimaging

Advances in neuro imaging has improved the diagnosis of intracranial pathologies. The main purpose of neuroimaging is threefold: initial diagnosis, preoperative planning and in monitoring of disease progression. According to (Lavra, Scartozzi, Zaccagna, Cartocci, & Saba, 2017), tumor imaging during the initial diagnosis helps to differentiate between tumors and other non-neoplastic lesions like ischemia and extra-axial neoplasm and metastasis. Furthermore, preoperative planning is facilitated through tumors grades, guiding the biopsies and local ablative therapy. In the monitoring of disease progress and therapeutic response, imaging can pick recurrent tumors from delayed radiation necrosis.

Magnetic resonance imaging (MRI) provides detailed information about the brain tumors anatomy, cellular structure and vascular supply. This, according to (Gao & Jiang, 2013), makes it a very important tool for the effective diagnosis, treatment and monitoring of brain tumors. (Hohenfeld et al., 2018) further describes MRI as an important diagnostic tool for not only brain cancer, but also inflammatory and neurodegenerative disorders. (Zahir, Md, Sadrabadi M Md, & Md, 2011.) observed that MRI has more accuracy than CT scan for diagnosis brain tumors and biopsy correlation.

In patients with suspected brain tumors, MRI is able to be utilized to describe the anatomy of the tumor. In addition, compared to the PET and CT scans, which use x-ray based medical diagnostic techniques MRI does not employ ionizing radiation but uses radiofrequency (RF) fields (Ng, Ahmad, Nizam, & Abdullah, 2003)). These non-ionizing techniques gives a safety component to the patients.

The MRI sequencing used include T1, T_2 and Fluid Attenuation Inversion Recovery (FLAIR) and T1 with contrast. The use of MRI in the evaluation of brain tumors aims to:

1. To determining the location of the lesion (i.e., intra-axial vs. extra-axial),
2. To establishing the specific location within the brain for treatment/biopsy planning,
3. To evaluating mass effect on the brain, ventricular system, and vasculature,
4. Along with physiologic MRI sequences suggesting a possible diagnosis.

Extra-axial tumors include meningiomas, schwannomas, and skull base tumors. They can be differentiated from intra-axial tumors based on associated interposition of cerebrospinal fluid, vessels, or dura between the mass and cortex (Mabray et al., 2015).

The number of lesions in the MRI imaging is important when considering metastatic disease. There will be more lesions in metastatic disease, demyelination, inflammation and infections. Other conditions that may present with solitary lesions include hematoma, abscess and infarct (Smirniotopoulos & Jäger, 2020).

Most primary brain tumors cross the midline and may infiltrate the white matter tracts of the corpus callosum. Mass effect can interfere with the brain itself, the ventricular system or the vascular system.

MRI provides soft tissue contrast that allow better visualization of infiltrates and disrupted parenchyma. It provides mainly structural information such as tumors size, site and morphological appearance. It however does not provide information on the tumor grade, aggressiveness or its histopathological criteria. Parenchymal enhancement is achieved by the use of intravenous gadolinium-based contrast that

reduces T1 relaxation time and increase tissue contrast. This is by accentuating areas of leakages in the blood brain barrier (Ibrahim & Dublin, 2018). These contrasts increase the information content of the diagnostic images, and also they improve sensitivity and specificity of diagnostic images.

The patterns of contrast enhancement by the tumors helps in the identification of suggested diagnosis. Ring enhancement by the lesions indicates area of central necrosis. This may also be seen in organized abscess as well as neoplasm and inflammatory conditions. MRI images are used to assess the main patterns of CNS enhancement and are therefore useful for the correct radiological diagnosis.

2.3 MRI features

MRI exploits differences in relaxation times (T1 and T2) between nuclei that have an odd number of nucleons (protons and neutrons) – usually hydrogen protons from water molecules present in bodily tissues. Variable resonance signals are generated when the nuclei are subjected to magnetic field. An equilibrium state is restored upon stimulation by radiofrequency. Images are generated from the difference in the relaxation rates due to the tissues under the view. This has allowed detection of lesions of the central nervous system ((Huk & Gademann, 1984)(Yang, He, Li, & Yang, 2019).

T1-weighted images contain dark appearance of Cerebrospinal fluid (CSF). Gray matter (GM) is darker than white matter (WM). T1 gives better result in the case of brain structure images and fat appears brighter in this type. Time of Excitation (TE) and Time of relaxation (TR) time is short to produce the images (uses longitudinal relaxation). The Clinical use of T1 is to evaluate tissue architecture. Both pre contrast and post contrast sequences can be done. Pre contrast high intensity identifies blood

products, fat, melanin and mineralization. Post contrast enhancement shows nonspecific breakdown of the blood brain barrier.

T2-weighted images which contain higher signal intensity of CSF and fluid as compared to tissue and for that reason it appears bright. T2 used long time for TE and TR to produce images (traverse relaxation). T2 is brighter for water and fluid, ideal for the edema tissue.

FLAIR is just like to T2 but it has attenuated CSF fluid but abnormalities remain bright. It is good for imaging the cerebral edema. It uses very long TE and TR time for producing images.

The figure below represents the difference between these types of sequence in MRI image.

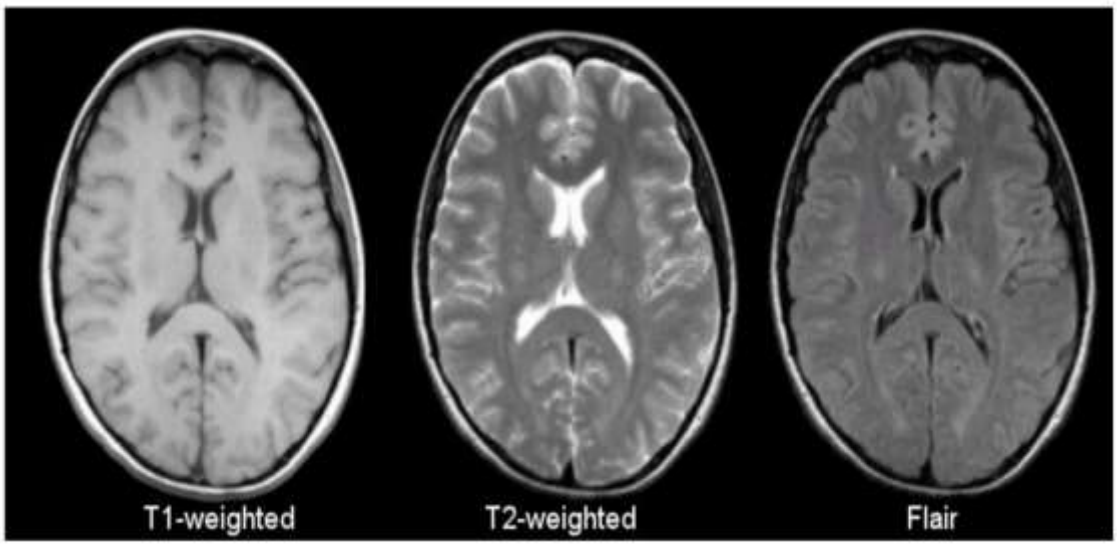


Figure 1: Types of MRI image sequences

Gadolinium-enhanced magnetic resonance imaging is the preferred modality in the imaging of brain tumors. This is because of its resolution and the enhancement with the contrast agent. The conventional anatomic MRI T1-weighted imaging, fluid

attenuated inversion recovery T2-weighed imaging, and gadolinium-enhanced T1-weighted imaging (Rovira, Auger, & Alonso, 2013).

Other advanced techniques of MRI of brain tumors include; diffuse-weighted imaging, perfusion-weighted imaging, dynamics contrast- enhanced T1 permeability imaging, diffusion-tensor imaging and magnetic resonance spectroscopy (Young, 2007). They are used to improve the specificity by differentiating between different tumor subtypes and in identifying signs of higher malignancy (Sadeghi, 2017).

The location of a brain tumor is essential in differentiating between various tumors. Brian tumors can either be extra-axial or intra-axial. Extra-axial tumors include meningiomas, schwannomas, and skull base tumors. They can be differentiated from intra-axial tumors based on associated interposition of cerebrospinal fluid, vessels, or dura between the mass and cortex (Mabray et al., 2015).

It is important to consider the number of lesions seen on the imaging scan. Multiples lesions suggest either a metastatic disease. It can also suggest a non-neoplastic disease like demyelination, infections or inflammations.

Several imaging characteristics suggest tumor subtypes. A cyst and solid nodule within a tumor suggest that the brain tumors such as ganglioglioma, pilocytic astrocytoma, pleomorphic xanthoastrocytoma, and, in the posterior fossa, hemangioblastoma. Some other features such as calcifications can be seen in oligodendrogliomas, ependymomas, and pineal tumors. Necrosis and hemorrhage is seen on high grade gliomas, certain metastases, and rarely central nervous system (CNS) lymphoma in immunocompromised patients (Rudresha et al., 2017).

The presence of brain edema is associated with brain tumors, in both primary and metastatic tumors. There is leakage of plasma across the vessel wall into the parenchyma after a break in the blood brain barrier. The presentation of a patient with brain edema depends on the location and extent of the edema. Increased intracranial pressure may lead to neuronal dysfunction and even fatal herniation(Esquenazi, Lo, & Lee, 2017). Malignant gliomas and other aggressive tumors have been associated with causing brain edema. Similarly, malignant tumors produce brain edema. Brain edema can be vasogenic or infiltrative in nature. Vasogenic edema occurs when there is a reactive increase in extracellular water due to leakage of plasma fluid from altered tumor capillaries. This is common with metastatic tumors and in non-infiltrative tumors like meningioma. Infiltrative edema on the other hand occurs more commonly with gliomas. It represents infiltrative tumors cells and vasogenic edema that disrupt the white matter but not the blood brain barrier. They are also referred to as non-enhancing tumors (Esquenazi et al., 2017; Stummer, 2007).

Low grade gliomas (LGGs) appear homogeneous on conventional magnetic resonance imaging (MRI). However, it appears homogeneous with low signal intensity on T1-weighted sequences and hyperintensity on T2-weighted and Fluid-Attenuated Inversion Recovery (FLAIR) sequences. The figure below shows the images of LGG. (Nelson, 2011) noted that gliomas infiltrate the surrounding parenchyma despite apparent radiographic margins observed on T2/FLAIR sequences.

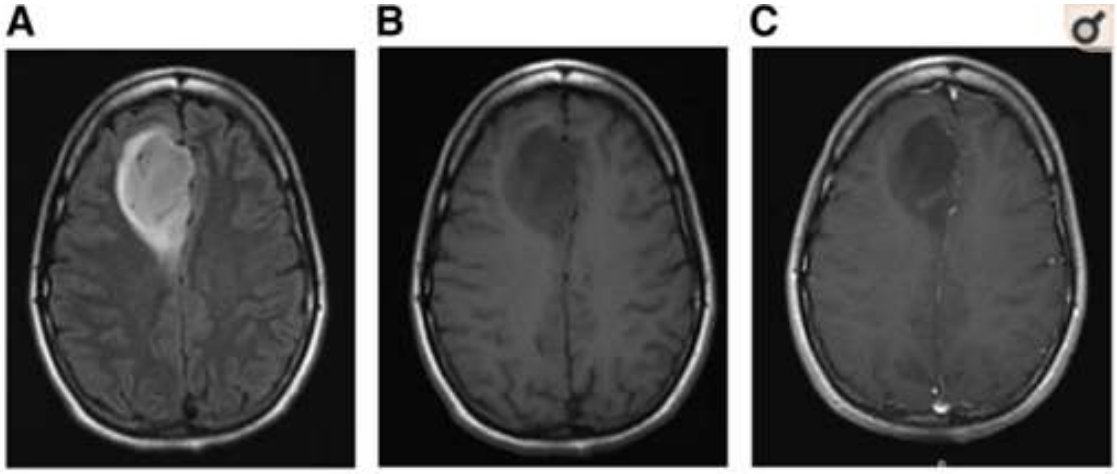


Figure 2: Imaging features of low-grade glioma

The grade 2 oligoastrocytomas shown in Figure 2 appears as relatively homogenous regions of high signal intensity on T2/FLAIR weighted images in A. it also shows low signal intensity on T1 pre-contrast images in B. the figure C shows faint contrast enhancement on T1 post contrast image.

With regards to meningioma, specific preoperative MRI features associated with high grade meningioma. These features includes patients age, tumor-brain interface ,capsular enhancement and tumor enhancement. (Lin et al., 2014). On MRI meningioma present with isointense signal intensity on T1 and T2 weighted series. On gadolinium contrast, meningiomas will have a strong homogeneous enhancement. Histopathologically, meningiomas will have nuclear pseudo inclusions, pseudo-syncytial growth and formation of concentric calcifications. (Gupta & Dwivedi, 2017; Louis et al., 2007; Thambi et al., 2017).

Meningiomas are slow growing tumors that arise from the meningothelial cells around the arachnoid. The various histopathological grading is based on the WHO classification. (Gupta & Dwivedi, 2017; Louis et al., 2007).

Metastatic brain lesions will have a mixed picture of hypointensity under T1 and hyperintensity under T2 and FLAIR signal intensities. A similar picture is seen in rapidly growing primary brain tumors like glioblastoma multiforme and anaplastic astrocytoma.

Meningiomas account for 20-32% of all intracranial tumors. According to WHO classification, there are three histopathological grades with 15 subtypes. They present with benign, well defined and slow growing tumors and may have uneventful clinical course. The use of MRI features in the diagnosis of meningioma enables differentiation between intra-and extra-axial lesions.

Typical meningioma has characteristic MRI features that can be used to predict the WHO grades. However, several other benign and malignant pathologies may mimic these features. Majority of lesions are WHO grade I and they include meningothelial, psammomata's, secretory, fibroblastic, transitional and microcytic subtypes. WHO grade II and III are identified by the number of mitoses, cellularity and nuclear-to-cytoplasmic ratio.

The imaging characteristics of meningioma include lobular, extra-axial masses with well circumscribed margins. Meningiomas have hypointense to slight hypointensity relative to grey matter on the T1-weighted sequence. On T2 sequence, they are isointense to hyperintense.

When contrast is administered, meningiomas demonstrates avid, homogenous enhancement.

Glioma infiltrates diffusely into the surrounding brain tissues. This is appreciated in MRI imaging where infiltrative, heterogeneous ring enhancive lesion with central necrosis will be noted. There is also peritumoral edema (Alexander & Cloughesy, 2017; Rapalino, Batchelor, & González, 2016).

In a study in Ghana, similar findings were noted where gliomas were the most common brain tumors (38%) followed by meningiomas(36%) (Ekpene et al., 2018).

In a study done in Kenya by Mwang'ombe, 45.8% of the intracranial tumors were gliomas while meningiomas were 34.4 %(N. Mwang'ombe & Kitunguu, 2013).

The appearance of the tumors of MRI imaging can be solid or cystic. Hematogenic dissemination of infections and metastatic neoplasm present with solid nodular with ring enhancing lesions. Combination of solid and cystic nodules within the tumor may suggest ganglioma, pilocytic astrocytoma or hemangioblastoma. Calcification of the tumors in MRI imaging is seen in some brain tumors. These include oligodendrogliomas, ependymoma and pineal tumors.

Necrosis and hemorrhage is seen in high grade gliomas and certain metastatic tumors. However, there is usually similar conventional MRI features between a recurrent tumor and radiation necrosis causing a diagnostic dilemma. They both depict contrast-enhancing with mass effect (Soliman, ElBeheiry, Abdel-Kerim, Farhoud, & Reda, 2018).

Extra-axial tumors such as meningioma can be differentiated from intra-axial tumors based on associated interposition of cerebrospinal fluid, vessels and dura. They will displace the brain away from the skull. Diffuse gliomas will infiltrate the white-matter and tracts leading to enhancement of ventricles and sulci.

Furthermore, intra-axial tumors can be primary or secondary brain neoplasm. These lesions according to Otto presents with characteristic imaging findings (Rapalino, Batchelor, & González, 2016b).

They represent a wide range of primary and secondary brain neoplasm. These are tumors within the brain parenchyma. This is in contrast with extra axial tumors which are outside the brain.

2.4 Histopathological assessment of the brain tumor

Histopathological diagnosis is the gold standard for the classification of all tumors.

Brain biopsy is obtained using either needle biopsy, stereotactic biopsy or open biopsy(Schuette, Taub, Hadjipanayis, & Olson, 2010). Needle biopsy is performed by drilling into the incision and extracting the abnormal tumor or tissue.

Stereotactic biopsy is a procedure where 3-dimension imaging using a combination of CT scan and MRI is used to obtain the tissues from the brain. This procedure is applicable to brain lesions that cannot be excised or when there is evidence of infiltration (Dellaretti et al., 2012). Other conditions that makes surgical resection difficult including multiple lesions, deep seated cerebral lesions makes it necessary to perform stereotactic biopsy (Mizobuchi et al., 2019). However, the commonest complications associated with this procedure is bleeding (Akshulakov et al., 2019) Open biopsy is done by performing a craniotomy to exposed the brain tumor and obtain the samples. This is the most performed yet it is the riskiest and associated with more morbidity. Pathological classification of brain tumors is the corner stone upon which the management plan and treatment strategy depends (Louis et al., 2007). An adequate microscopic diagnosis carries important prognostic information and forms the basis for further patient management.

The use of Hematoxylin and Eosin (H&E) stained slide is an invaluable means in the diagnosis, classification and stratification of brain tumors. Both primary and metastatic tumors can be identified using this stain. The interpretation of the slide should consider the age of the patient as well as the clinical presentation. Other advanced histopathological procedures include immunocytochemistry.

In order to demonstrate the antigens expressed by the tumor's cells, the use of immunocytochemistry methods is used. This will assist to further classify the tumors (Painter, Clayton, & Herbert, 2010).

The neuroimaging findings complements the histopathological findings in arriving at the final diagnosis. Specific neuroimaging parameters to consider include:

The location - supratentorial, infratentorial, intra-ventricular,

Growth pattern- circumscribed versus infiltrative, solid versus cystic,

Enhancement pattern-non-enhancing versus enhancing, and

The presence or absence of edema, necrosis, calcification etc.

On the other hand, histopathological analysis reveals the amount of necrosis, proliferative regions, collagen and vascularity within the tumors area (Gonzalez-Segura et al., 2011).

Tumors of the central nervous system often have a wide morphological spectrum and classification is dependent on the recognition of areas with the characteristic histopathology. The WHO classification of Tumors of 2007 and revised in 2016 (Louis et al., 2007, 2016).

Primary brain tumors (PBT) are classified histopathologically as (WHO grade is shown in brackets):

4.1.1.1. Astrocytic tumors:

4.1.1.1.1. Pilocytic astrocytoma (grade I);

4.1.1.1.2. SEGA (grade I);

4.1.1.1.3. Diffuse astrocytoma (grade II);

4.1.1.1.4. Anaplastic astrocytoma (grade III);

4.1.1.1.5. Glioblastoma (grade IV)

4.1.1.2. Oligodendroglial tumours:

4.1.1.2.1. Oligodendrogliomas (grade II);

4.1.1.2.2. Anaplastic oligodendrogliomas (grade III)

4.1.1.3. Mixed gliomas:

4.1.1.3.1. Oligoastrocytoma (grade II);

4.1.1.3.2. Anaplastic oligoastrocytoma (grade III)

4.1.1.4. Ependymal tumours

4.1.1.5. Choroid plexus tumours

4.1.1.6. Pineal parenchymal tumours

4.1.1.7. Embryonal tumors`:

4.1.1.7.1. Medulloblastoma

4.1.1.7.2. Primitive neuroectodermal tumors

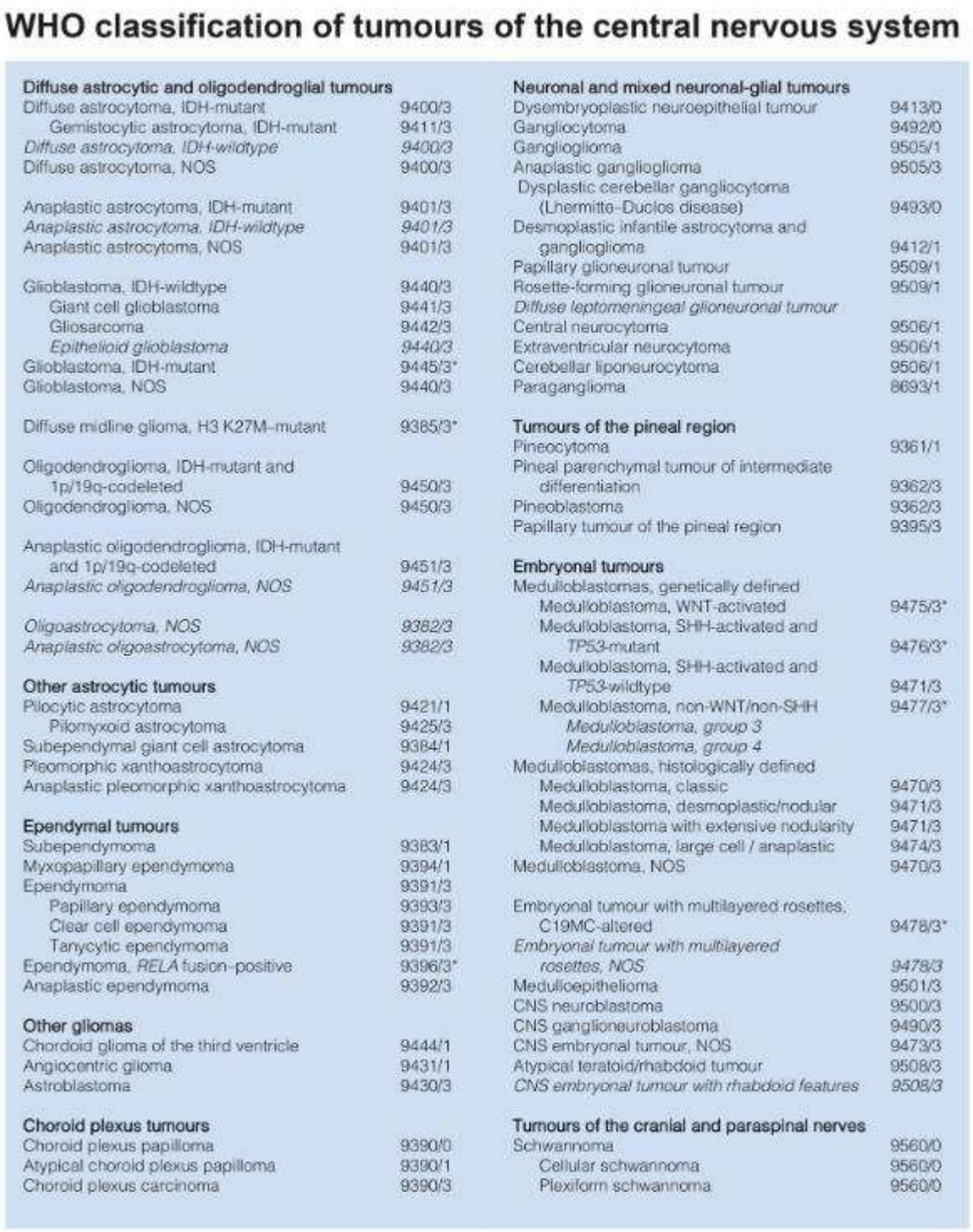
4.1.1.8. Meningeal tumors:

4.1.1.8.1. Meningioma

4.1.1.9. Primary CNS lymphoma

4.1.1.10. Germ-cell tumors

4.1.1.11. Tumors of the sellar region



WHO classification of tumours of the central nervous system

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

Figure 3: WHO 2016 classification of tumors of the central nervous system

Low grade glioma histopathologically, diffuse astrocytoma consists of well-differentiated fibrillary or gemistocytic neoplastic astrocytes on a loose matrix. Oligoastrocytomas are diffusely infiltrating tumors with a mixture of oligodendroglial

and astrocytic cell types (Louis et al., 2007). Oligodendrogliomas are infiltrating tumors containing cells with uniform-appearing nuclei and perinuclear clearing, often described as having a “fried egg” appearance.

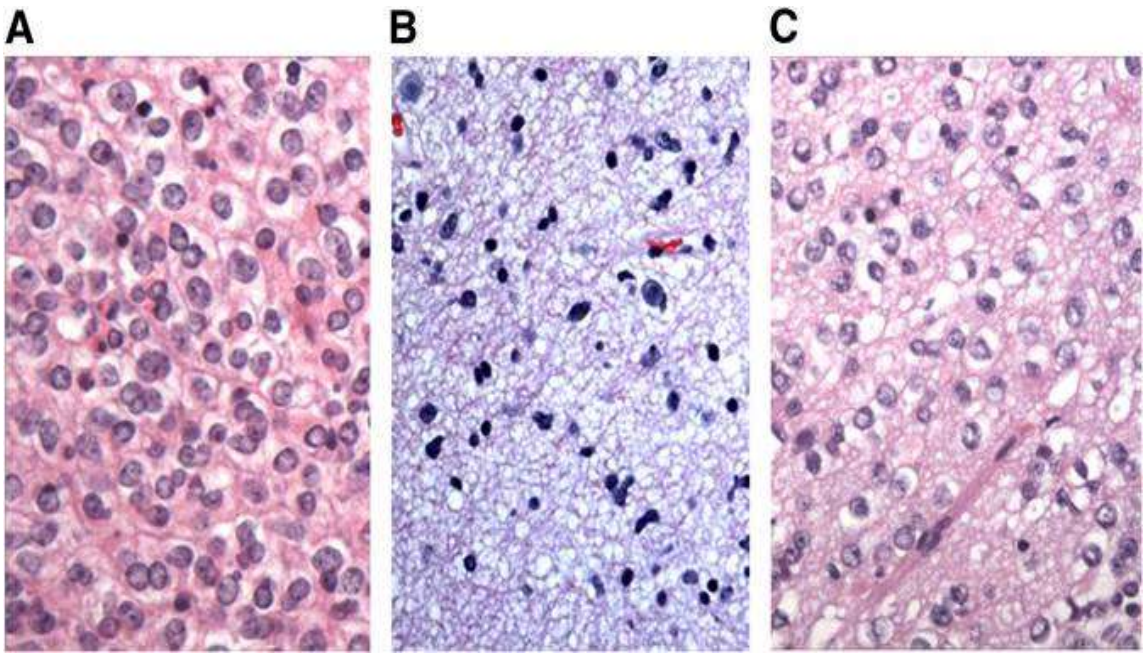


Figure 4: Histopathological features of Low-grade glioma

Histopathologic features of low-grade glioma.

(A): Oligodendrogliomas showing uniform-appearing, infiltrating cells with perinuclear clearing in a honeycomb pattern.

(B): Astrocytoma, consisting of fibrillary neoplastic astrocytes on a loose tumor matrix background.

(C): Oligoastrocytoma, containing a mixture of both tumor cell types.

All the images Hematoxylin and eosin stain. Magnification, 400×.

2.5 Sensitivity and specificity

The sensitivity and specificity of a screening or diagnostic test is the accuracy relative to a reference standard. It indicates the concordance of a test with respect to a chosen referent/gold standard. The gold standard is the preferred method of diagnosis or a benchmark that is available under reasonable conditions. (Cardoso, Pereira, Iversen, & Ramos, 2014; Franco & Di Napoli, 2016)

The use of sensitivity and specificity provides the validity of the diagnostic test. These can be obtained by comparing the diagnostic test with the gold standard in a two-by-two table. The diagnostic test is compared with the gold standard with regard to the ability to identify the disease or not.

Table 1: Table showing 2*2 (two-by-two) table

	Gold standard disease present	Gold standard disease absent	
Test Positive	True Positive (a)	False Positive (b)	Total test Positive (a+b)
Test Negative	False Negative (c)	True Negative (d)	Total Negative (c+d)
	Total disease(a+c)	Total Normal (b+d)	Total Population (a+b+c+d)

Sensitivity =a/a+c

=a (true positive)/a+c (true positive +false negative)

Specificity = d/b+d

=d (true negative)/b+d (true negative false positive)

Sensitivity is the probability of the test being positive when the disease is present. Specificity is the probability of testing negative when the disease is absent (Molinaro, 2015).

An ideal diagnostic test presents with a sensitivity of 100% with respect to identifying the pathology and a specificity of 100% in pointing out absence of a disease. In practice there is no gold standard instead diagnostic methods with highest sensitivity and specificity.

CHAPTER THREE: METHODOLOGY

This chapter outlines the methods that were used in conducting the study in terms of study design, study site, study population, sampling technique, eligibility criteria, sample size and data management and analysis.

3.1 Study design

The study was a hospital based cross sectional study that was carried out between April 2019 and March 2020.

3.2 Study site

The study was conducted at the Radiology and Imaging department, Neurosurgical department and at the Histopathology departments of the Moi Teaching Referral Hospital (MTRH) situated in Eldoret town Kenya. The hospital is the national referral for Western Kenya, parts of Eastern Uganda and South Sudan. It has a catchment population of over 13 million residents. It has a bed capacity of over 816. The MRI center of the MTRH will form the specific study area (MTRH, 2020). The hospital uses 0.36T MagSense 360 (Mindray, China) open MRI. It is approximately 320 kilometers Northwest of the capital city Nairobi and lies 0° 31´N 35° 17´E. Uasin-Gishu county has a cosmopolitan population and agriculture is its main socioeconomic activity.

3.3 Study population

The study population was all patients aged 18 years and above undergoing MRI scan for suspected brain tumors at the MRI center of MTRH.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

a. All adult patients presenting at MTRH MRI unit for MRI examination who had suspected brain tumors and consented for the study
b. All adult patients who had histopathological examination of tissue biopsy and with conclusive histopathology diagnosis.

3.4.2 Exclusion criteria

a. Patient with confirmed diagnosis of brain tumors on treatment and follow- up.
b. Patients with a known, other non-brain primary tumor.
c. Patient on post-operative period following brain surgery.

3.5 Study period

The study was conducted for a period of 12 months between the month of April 2019 and March 2020.

3.6 Sample size Determination

Our main aim of the study was to compare the MRI findings and histopathological findings of brain tumors. A similar study done in Ethiopia by Tesfay et al., (2013) found prevalence of meningioma to be 39% and sensitivity and specificity of MRI in diagnosing meningioma to be 98% and 97% respectively. The sample size was calculated using Buderer's (1996) formula.

$$n = \frac{Z^2{}_{\alpha/2}(S_N)(1-S_N)}{L^2 \times prevalence)}$$

Where;

S_N = the anticipated sensitivity

1-α = size of the critical region (confidence level)

$Z^2_{\alpha/2}$ = standard normal deviation corresponding to the critical region α

L^2 = absolute precision desired on either side (5%)

Substituting for the above figures by Tesfay et al., (2013), the minimum sample size required was 79.

3.7 Sampling technique

Consecutive sampling method was used in this study until the desired sample size was obtained. This was due to the small number of patients who presented with suspected brain tumors and had histopathologic examination done in the past one year. According to past records at the hospital, the number of patients who underwent 0.36T MRI and had subsequent histopathological results in 2017 was 86. We therefore set out to recruit all patients with suspected brain tumors for a period of one year.

3.8 Study procedure

The staff and technicians at the MRI center were sensitized prior to the study.

All adult patients at the MRI center who presented with a clinical diagnosis of suspected brain tumors were informed about the study and MRI was done according to the MTRH protocol (Appendix II).

The MRI image findings were reported by the principal investigator and the findings verified by two independent consultant radiologists. Patients who met the eligibility criteria and those who consented were recruited in the study. A structured interviewer administered questionnaire was used to collect the study variables. The patients were followed by the principal investigator or the research assistant in the neurosurgery department where surgery and biopsy were done. Specimens were taken immediately

after debulking or surgical resection to the pathology laboratory for histopathology examination. The histopathology technician fixed the samples with 10% formalin, processed and sectioned. These sectioned were then stained using Hematoxylin and Eosin stains. If indicated, immunohistochemistry was done. The histopathology results were availed after two weeks.

A review and recording of the histopathology diagnosis from the pathology laboratory for the same patients was done upon agreement by the consultant pathologist. The histopathological diagnosis was followed up by the researcher. The final histopathological diagnosis for those with conclusive report was then be compared with the initial radiological diagnosis using sensitivity and specificity.

3.9 Study recruitment schema

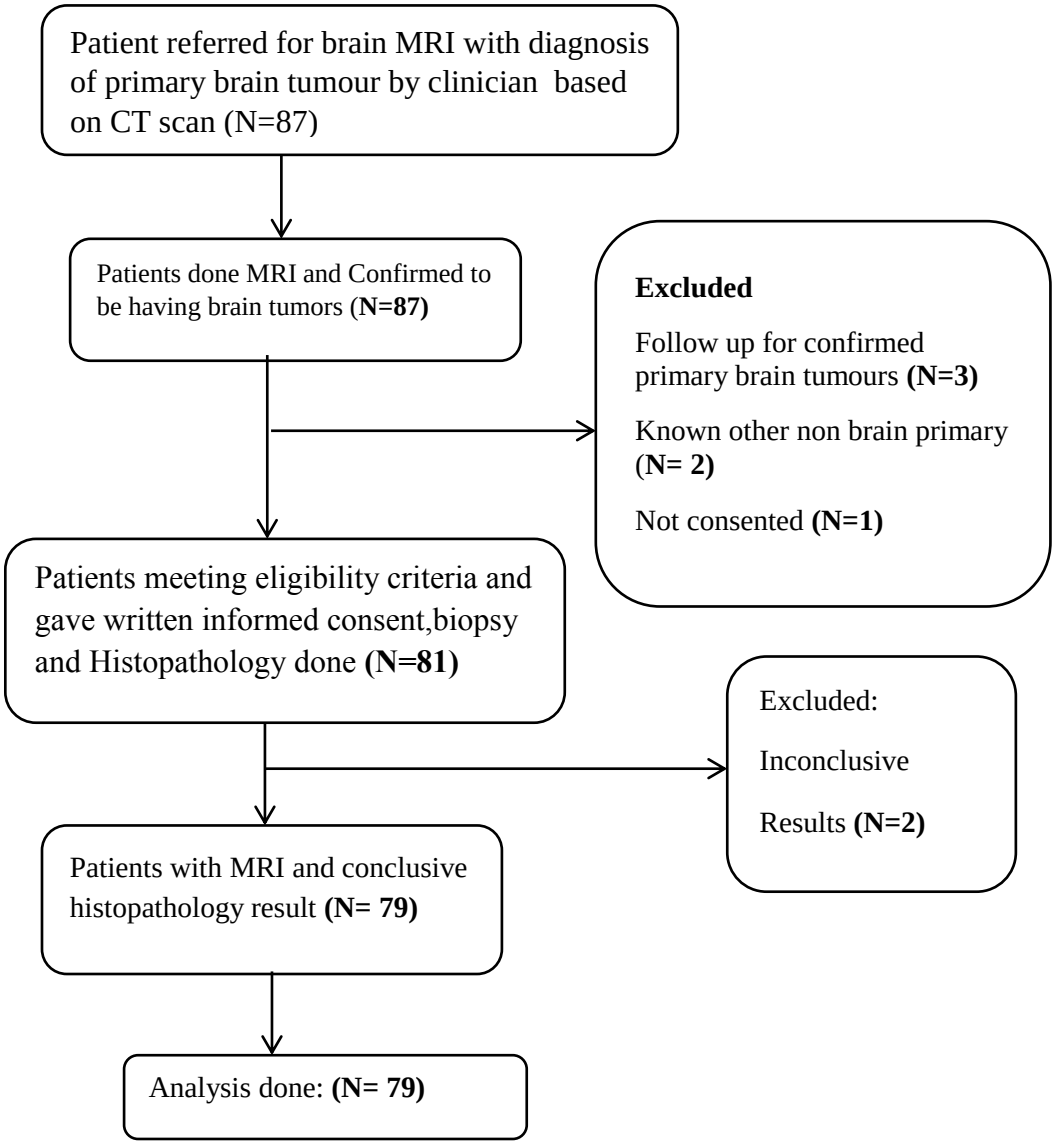


Figure 5: Study procedure

3.10 Data collection and management

3.10.1 Data collection

Data was collected between April 2019 and March 2020 using as structured interviewer administered questionnaires (**Appendix II**). The first section was a closed ended questionnaire in which the patients' bio data was established. This was done during an interview lasting 5-10 minutes with each study participant. The second part comprised filling in the patient's MRI brain features as reported by the principal investigator and at least two consultants' radiologists. The third part of the questionnaire entailed filling in the histopathology diagnosis, agreed upon by at least two pathologists, of the corresponding study participant.

3.10.2 Quality control and security

Data was double entered into a computer for purposes of validation. The computers were password protected and access allowed only for authorized persons. Databases obtained was stored electronically, copies of filled questionnaire were stored in locked cabinets located in the principal investigators residence.

3.10.3 Data processing

Data was entered into an electronic database in preparation for analysis. The Epi Info database was used. Double data entry was done to check for any errors. During entry the data was de-identified to ensure confidentiality of the information and protect the participants. Completeness and consistencies were checked regularly. After entry and cleaning was complete the questionnaires were kept in a safe cabinet under a lock and key kept by the investigator. The database was encrypted to prevent any unauthorized access. Backups for the database was created in remote disks and flash drives that was kept in different safe locations to guard against loss of information. After data entry,

data was imported into STATA/MP version 13 where coding, cleaning, data manipulation and analysis was done.

3.10.4 Data analysis and presentation

The common Magnetic Resonance Imaging findings were described through frequencies and proportions same as the description of histopathological diagnosis of common brain tumors. Continuous variable such as age, were summarized using means and categorical variables such as gender, MRI features and histopathological results, were summarized in frequency, percentages and bar graphs. The comparison between the MRI and histopathology diagnosis of primary brain tumors in adult patients at MTRH was done using sensitivity and specificity. The MRI sensitivity and specificity for diagnosing primary brain tumors was established for the most common primary brain tumors, that is Diffuse astrocytoma, Meningioma, pituitary adenoma and glioblastoma.

The validity of the MRI scans in the diagnosis of brain tumors was measured using sensitivity and specificity. All statistical test performed at 0.05 α level of significance.

3.11Study limitation:

This study was a hospital-based study and only symptomatic patients presenting at the MRI center were recruited therefore this was not a representation of the general population.

3.12 Ethical considerations

Approval to carry out the study was sought from the MTRH **(Appendix V)** and Moi University Institutional Research and Ethics Committee (IREC) **(Appendix IV)**.

Patients to the study participants was informed about the study. No incentives were used to convince the patients for consent to participate in the study. The data collection tool did not contain the names of the participants. Confidentiality was maintained throughout the study. Medical attention was given as necessary irrespective of their consenting to participate in the study.

The raw data collected was stored in a locked cabinet throughout the study period while the data in the computer software and programs was in a password protected file. The results will be presented in the university thesis defense and will be availed for reference at the College of Science Resource Centre and the Moi University Repository. The results of this study will be availed for publication in a reputable journal for access and use by the scientific and general population in the improvement of patient management.

CHAPTER FOUR: RESULTS

4.0 INTRODUCTION

The findings are based on 79 patients aged 18 years and above who underwent MRI scan for suspected brain tumors at the MRI center of MTRH between the month of April 2019 and March, 2020.

4.1 DEMOGRAPHICS AND CLINICAL PRESENTATION

Table 2: Demographics characteristics (N=79)

Variables	Category	Frequency(N=79)	Percentage
Age	Mean (SD)	46.03(12.9)	
Gender	Male	33	41.77
	Female	46	58.2

The mean age of the respondents was 46 years. Majority of the respondents n= 46(58.2%) were female.

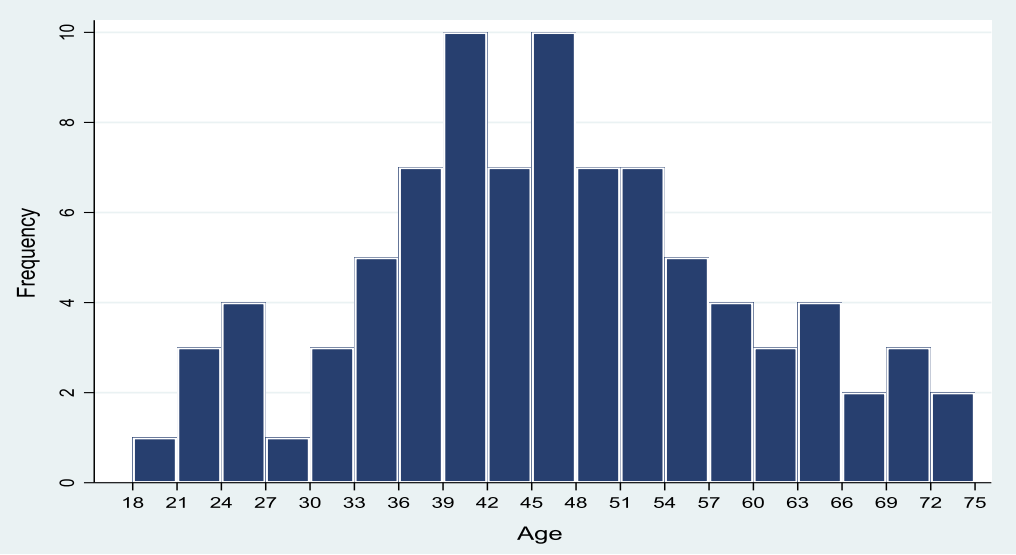


Figure 6: Age distribution

The distribution of age was normally distributed with a mean age of 46 years and ranged between 18 years and 75yrs.

Table 3: Table showing the Clinical presentation of respondents

Clinical presentation	Frequency	Percentage
Headache	71	80.68
Seizures	26	29.55
Blurred vision	16	18.18
Vomiting	24	27.27
Hemiplegia	11	12.50
Confusion	2	2.27
Hemiparesis	1	1.14
Slurred speech	1	1.14

The clinical presentation documented the presenting complain that the respondents reported as the chief complain that made them seek medical attention. Majority 71(80.68%) presented with headache. Twenty nine percent complained of seizures. Hemiparesis and slurred speech was least reported (1.14%) complain. Vomiting was reported in n=24(27.27%) of the respondents.

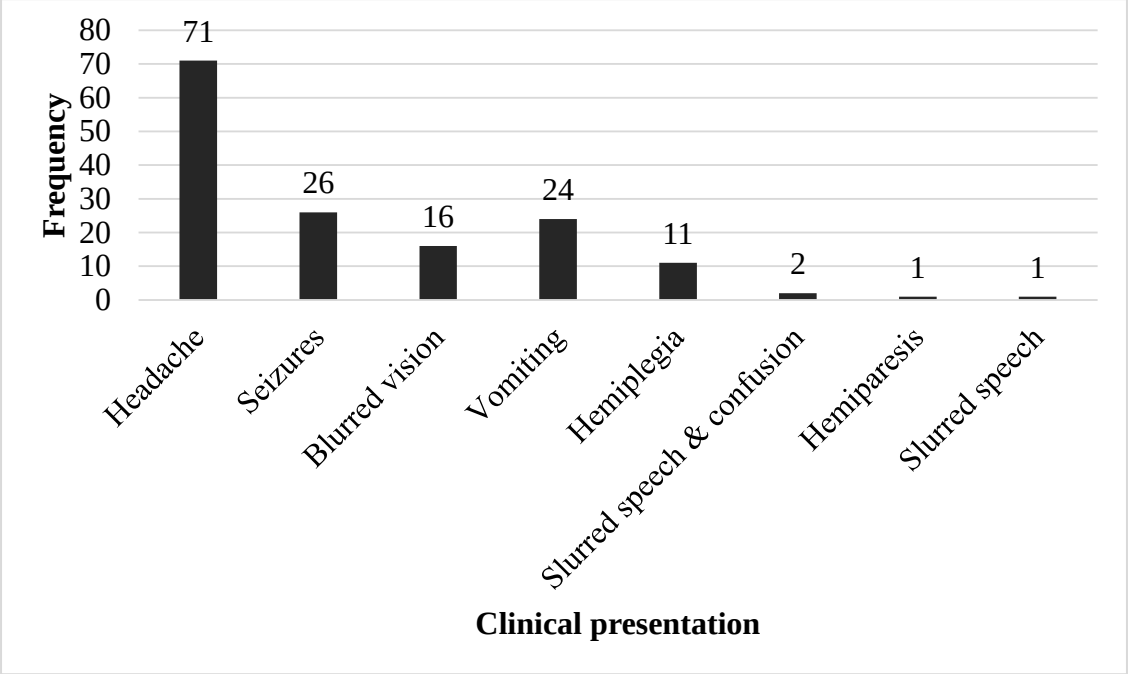


Figure 7: Graph showing the Clinical presentation of respondents

Objective One: To describe the common Magnetic Resonance Imaging findings of adult patients with suspected brain tumors in MTRH

4.2 MAGNETIC RESONANCE IMAGING FINDINGS

Table 4: Table showing Radiological features of primary brain tumors.

Variables	Category	Frequency	Percentage
Location (N=79)	Intra axial	36	45.57
	Extra axial	29	36.71
	Sellar/suprasellar	12	15.19
	Intraventricular	2	2.53
Number of lesions (N=79)	1	78	98.80
	>1	1	1.20
Size of lesion (in cm) N=79	<1.5	9	10.23
	1.5 – 3.0	34	38.64
	>3.0	45	51.14
Shape of lesion (n=79)	En plaque	1	1.15
	Mass	78	98.85
Tumor margins (n=79)	Distinct	41	52.9
	Indistinct	8	10.13
	Others- broad base	30	38.97
Presence of perilesional oedema N=79	Nil	10	12.50
	Mild	15	19.32
	Moderate	32	40.91
	Extensive	22	27.27
Appearance (n=79)	Cystic	1	1.15
	Solid	64	81.61
	Both	14	17.24
Mass effect (n=79)	Midline shift	55	69.62
	Sulci Effacement	21	26.58
	Others (Herniation,) Ventricular Obstruction	3	3.80

The description of the radiologic features of the tumor lesion was based on the location, shape and number of lesions among other features.

Majority of the tumor lesion n=45(51.1%) were more than 3 cm in size with almost all n=78 (98.85%) being masses compared to en plaque shape.

The tumor margins were distinct in most n=68(86.05%) of the lesions observed. The presence of edema in the radiological examination was noted. Forty percent of the lesions studied had moderate edema while n=22(27.27%) had extensive edema.

Most of the lesions n=64(82%) had solid appearance while others had either cystic or both.

Table 5: Table showing Signal intensity on MRI

Variables	**Category**	**Frequency**	**Percentage**
Signal intensity T1	Hypointense	69	87.50
N=79	Hyperintense	3	3.41
	Heterogeneous	7	9.09
Signal intensity T2	Hypointense	13	15.91
N=79	Hyperintense	43	54.55
	Heterogeneous	23	29.55
Signal intensity FLAIR	Nully/hypointense	24	29.89
(n=79)	None Nully/hyperintense	51	64.37
	Heterogeneous	5	5.75
Signal intensity T1	Nil	3	3.8
with contrast	Homogenous	10	12.7
N=79	Heterogenous	39	49.37
	Others(Ring Enhancing)	27	34.18

The MRI signal intensity using T1-weighted showed majority of the tumors having hypointense 69(87.5%) signal and n=7(9.09%) being heterogeneous.

Majority n=43(54.55%) had hyperintense signal intensity on T2-weighted MRI scans while n=23(29.55%) had hypointense image signals.

Fifty-one (64.37%) of the cases were hyperintense on the FLAIR signal intensity. There was heterogenous FLAIR signal intensity in n=5(5.75%) of the responses.

Contrast enhancement was seen in n=75(95%) of the suspected brain tumors images when gadolinium contrast was used followed by no enhancement in n=3(3.8%) of the cases.

4.3 RADIOLOGICAL DIAGNOSIS OF BRAIN TUMORS

Table 6: Table showing Radiological diagnosis of brain tumors (n=79)

Diagnosis	**Frequency**	**Percent**
Meningioma	29	36.36
Glioblastoma	24	30.68
Pituitary Adenoma	12	13.64
Diffuse Astrocytoma	7	9.09
Craniopharyngioma	2	2.27
Ependymoma	2	2.27
High grade astrocytoma	1	1.14
Central neurocytoma	2	2.27
Totals	79	100

The radiological diagnosis of the suspected tumors was made based on the various MRI imaging features. The most common brain tumors radiologically were meningioma n=29(36.36%), followed by glioblastoma n=24(30.68%), pituitary adenomas n=11(13.64%) and diffuse astrocytoma n=7(9.09%). Diagnosis of ependymoma, central neurocytoma, epidermoid cyst and craniopharyngioma were rare.

Objective two: To describe the histopathological findings of common brain tumors in adult patients with primary brain tumors in MTRH.

4.4 HISTOPATHOGICAL DIGNOSIS OF BRAIN TUMORS

Table 7: Table showing the Final Histopathology diagnosis of brain tumors **(n=79)**

Diagnosis	**Frequency**	**Percent**
Meningioma	31	39.24
Glioblastoma	26	32.91
Pituitary Adenoma	11	13.92
Diffuse astrocytoma	6	7.59
Tuberculoma	1	1.27
Craniopharyngioma	1	1.27
Ependymoma	1	1.27
Abscess	1	1.27
Anaplastic astrocytoma	1	1.27
Totals	79	100

According to the histopathological diagnosis, the most common brain tumor was meningioma 31(39.24%), followed by glioblastoma 26(32.91%), and then pituitary adenoma 11(13.92%) and then diffuse astrocytoma 6(7.59%).

Objective three: To Compare the MRI Findings and the Histopathological Diagnosis among Adult Patients with Primary Brain Tumors in MTRH.

4.5 COMPARISON BETWEEN RADIOLOGICAL DIAGNOSIS AND HISTOPATHOLOGICAL DIAGNOSIS

The study set to analyze the relationship between the various MRI features and the final histopathological diagnosis of the brain tumors.

Table 8: **Table showing comparison between tumor size and the mass effect**

	Size of lesion			
Mass effect	**<1.5**	**1.5 – 3.0**	**>3.0**	**p-value**
Midline shift	4 (8%)	22 (42%)	26 (50%)	
Sulci effacement	5 (28%)	5(28%)	8 (44%)	0.230
Ventricular obstruction	0	1 (25%)	3 (75%)	

Association between mass effect and size of the lesion was not statistically significant (p=0.230), However 75% of those with ventricular obstruction had tumor size >3.0. Sulci effacement mass effect were almost equally distributed among all the classification of lesion sizes.

Table 9: Table showing association between tumor location and histopathology diagnosis

	Tumor location				
Histopathology Diagnosis	**Sella /suprasellar**	**Intraaxial**	**Extraaxial**	**Intraventricular**	**Total**
Meningioma	2 (6.4 %)	0	29 (93.5 %)	0	31
Glioblastoma	0	26(100%)	0	0	26
Pituitary Adenoma	11 (100%)	0	0	0	11
Diffuse astrocytoma	0	6 (100 %)	0	0	6
Brain abscess	0	1 (100%)	0	0	1
Craniopharyngioma	1 (100%)	0	0	0	1
Ependymoma	0	0	0	1(100%)	1
Tuberculoma	0	1 (100%)	0	0	1
Anaplastic astrocytoma	0	1 (100%)	0	0	1
Totals	14	35	29	1	79

Most meningioma were extra-axial in location 29(93.5%).

Table 10: Table showing the association between perilesional edema and the histopathologic diagnosis of brain tumor.

	Perilesional Edema				
Histopathology Diagnosis	**Nil**	**Mild**	**Moderate**	**Extensive**	**Total**
Meningioma	0	5(16%)	17(55%)	9(29%)	31
Glioblastoma	0	5(19%)	10(42%)	11(39%)	26
Pituitary Adenoma	7(64%)	3(27%)	1(9%)	0	11
Diffuse astrocytoma	0	2(33%)	2(33%)	2(33%)	6
Brain abscess	0	1(100%)	0	0	1
Craniopharyngioma	0	0	1(100%)	0	1
Ependymoma	1(100%)	0	0	0	1
Tuberculoma	0	0	1(100%)	0	1
Anaplastic astrocytoma	0	0	0	1(100%)	1
Totals	8	16	32	23	79

Perilesional edema was extensive in respondents with glioblastoma 11(39%) and in n=9(29%) of those with meningioma. Moderate edema was seen in 10(42%) of patients with glioblastoma. Minimal or no edema was found in 7(64%) of those patients with a histopathological diagnosis of pituitary adenoma.

Table 11: Table showing comparison between tumor type and MRI radiological features.

For the purpose of analysis, benign tumors in this study included meningiomas, pituitary adenoma, ependyma, oligodendroglioma while malignant tumor were anaplastic astrocytoma and glioblastoma.

	Tumor type		
Radiological findings	**Benign**	**Malignant**	**p-value**
Tumor margins			
Distinct	42 (64%)	24 (37%)	0.044
Indistinct	3 (27%)	8 (73%)	
Appearance			
Cystic	0	1 (100%)	
Solid	40 (63%)	23 (37%)	0.173
Both	6 (43%)	8 (57%)	
Edema			
Nil	8 (100%)	0	
Mild	9 (56%)	7 (44%)	0.049
Moderate	20 (61%)	13 (39%)	
Extensive	10 (45%)	12 (55%)	

There is a significant (p=0.044) association between tumor margins and type of tumor where indistinct tumor margins were associated with malignant tumors more (73%) than distinct margin features (37%). There was significant association between edema and tumor type. All (100%) patients with no edema had benign tumors, while mild and moderate edema was associated more with benign tumors compared to extensive edema which was associated more with malignant tumors.

Table 12: Table showing Association of MRI signal intensity T1 with contrast and histopathology diagnosis

	Signal intensity (T1 with contrast)				
Histopathology Diagnosis	**None**	**Homogeneous**	**Heterogeneous**	**Ring enhancing**	**Total**
Meningioma	0	9(29%)	22(71%)	0	31
Glioblastoma	0	0	1 (3.8%)	25 (96.2%)	26
Pituitary Adenoma	0	1(9.1%)	8(81.8%)	0	9
Diffuse astrocytoma	1(16.7%)	0	5(83.3)	0	6
Brain abscess	0	0	0	1(100%)	1
Craniopharyngioma	0	0	1(100%)	0	1
Ependymoma	0	0	1(100%)	0	1
Tuberculoma	1(100%)	0	0	0	1
Anaplastic astrocytoma	0	0	1(100%)	0	1
Totals	3	10	40	26	79

Meningioma had both homogeneous and heterogenous signal intensity on T1 with contrast imaging at 29% and 71%, respectively. Most of the pituitary adenoma n=8(81.8%) had heterogeneous while most of the glioblastoma had ring enhancing n=25(96.2%).

Table 13: Table showing the MRI findings against Histopathological diagnosis (Gold standard) in diagnosis of Glioblastoma.

	Histopathology diagnosis		
Radiological Diagnosis	**Glioblastoma**	**Not glioblastoma**	**Total**
Glioblastoma	23	4	27
Not glioblastoma	3	49	52
Total	26	53	79

Chi Square test $p<0.001$

As the MRI test, the true positive were 23(85.2%), true negative were 49(94%), false negative were 3(5.8%) and false positive were 4(14.8%). Sensitivity 88.46%. Specificity 92.45%

Table 14: Table showing the MRI findings against Histopathological diagnosis (Gold standard) in diagnosis of Meningioma.

	Histopathology diagnosis		
Radiological Diagnosis	**Meningioma**	**Not meningioma**	**Total**
Meningioma	30	1	31
Not meningioma	1	47	48
Total	31	48	79

Chi Square test $p<0.001$, Total row agreement of 97.47%. Sensitivity 96.77%. Specificity 97.92%

Table 15: Table showing the MRI findings against Histopathological diagnosis (Gold standard) in diagnosis of Pituitary Adenoma.

	Histopathology diagnosis		
Radiological Diagnosis	**Pituitary Adenoma**	**Not pituitary adenoma**	**Total**
Pituitary Adenoma	10	2	12
Not adenoma	1	66	67
Total	11	68	79

The Sensitivity of MRI is the diagnosis of pituitary adenoma was 90.91% and specificity of 97.06% (Fisher's Exact test $p<0.001$).

Table 16: Table showing the MRI findings against Histopathological diagnosis (Gold standard) in diagnosis of Diffuse Astrocytoma.

	Histopathology diagnosis		
Radiological Diagnosis	**Diffuse Astrocytoma**	**Not Diffuse astrocytoma**	**Total**
Diffuse Astrocytoma	4	1	5
Not astrocytoma	2	72	74
Total	6	73	79

The sensitivity of MRI in diagnosing diffuse astrocytoma was 66.67% with a specificity of 98.63%. Fisher's Exact test ($p<0.001$).

Table 17: Table showing accuracy of MRI findings against Histopathological (Gold standard) in diagnosis of primary brain tumors.

	TP	TN	FP	FN	Sn	Sp
Glioblastoma	85%	94.2%	14.8%	5.8%	88.5%	92.5%
Meningioma	96.8%	97.9%	3.2%	2.1%	96.8%	97.9%
Pituitary Adenoma	83.3%	98.6%	16.7%	1.5%	90.9%	97.06%
Astrocytoma	80%	97.3%	20%	2.7%	66.7%	98.6%

TP – True positive, TN – True negative, FP – False positive, FN – False negative, Sn – Sensitivity

Sp – Specificity

The overall diagnostic agreement between MRI and histopathology in diagnosing brain tumor was 86.1%.

4.6 MRI SAMPLE IMAGES

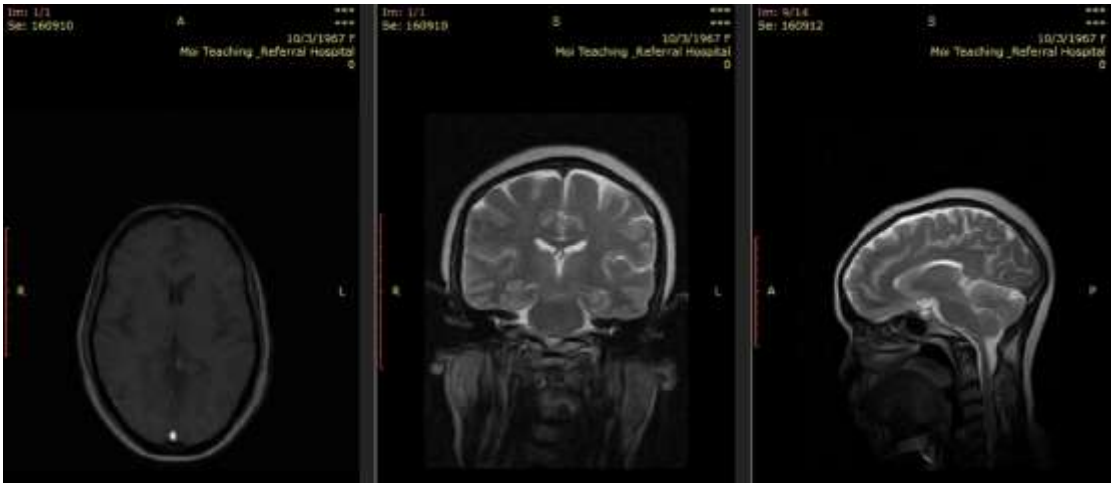


Figure 8: Brain MRI of a 52-year-old female showing normal imaging features in all the sequences. Diagnosis: Normal MRI brain findings.

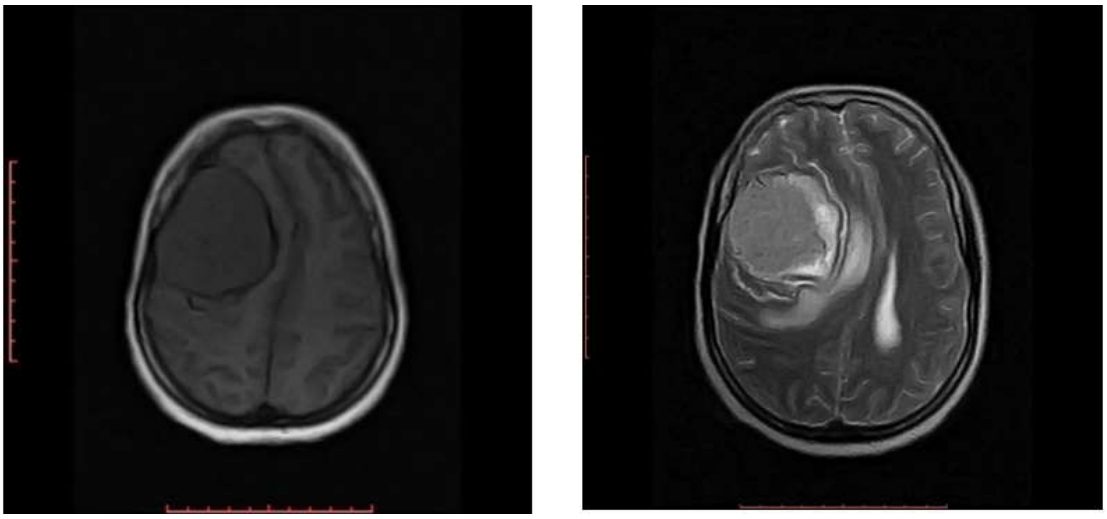


Figure 9: Brain MRI of 42-year-old Female who presented with headache. It showed a well-defined left parietal extra axial mass which was hypointense on T1 and hyperintense onT2. It also had perilesional edema, midline shift and compression of Right Lateral ventricle. This was confirmed to be Meningioma.

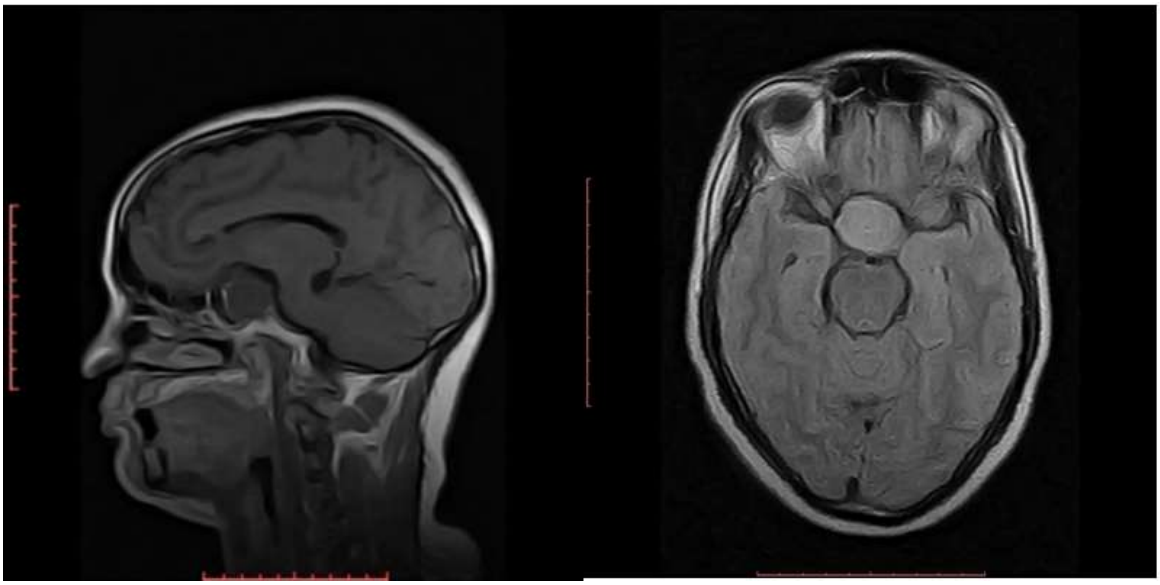


Figure 10: MRI of the brain of a 49-year-old male who presented with blurred vision. T1 Sagittal and Axial FLAIR, showed a well defined supra-sellar mass measuring 3.2 cm in diameter. It was hypointense to Gray Matter on T1 and hyperintense on FLAIR with expansion of the sellar. Diagnosis-Pituitary macroadenoma

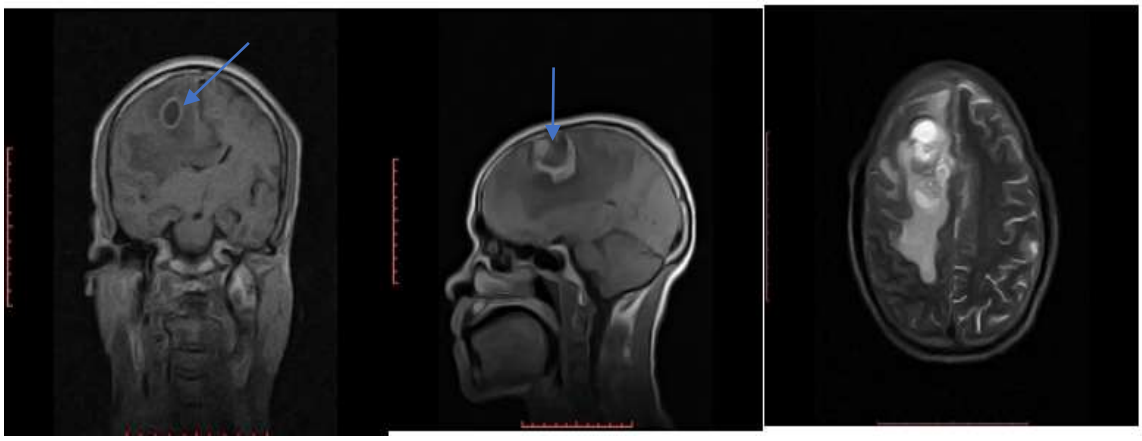


Figure 11: MRI brain T1 and T2 imaging, Coronal, axial and sagittal images of a 54-Year-old Male showing frontoparietal lesion which is heterogenous in all the sequences and ring enhancing past T1 with gadolinium contrast with perilesional edema. This was conformed to be glioblastoma.

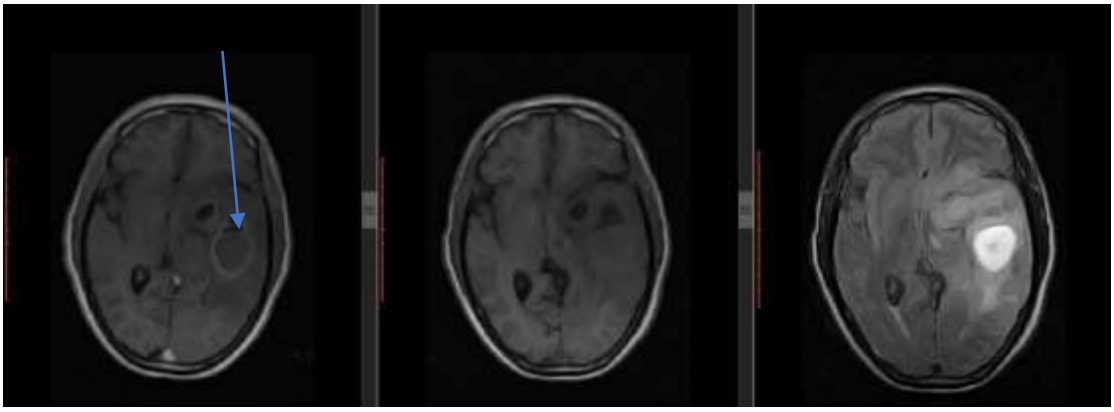


Figure 12: MRI brain of a 55-year-old male showing a left temporal lobe mass which is heterogeneous in all sequence and ring enhancing in T1 with contrast. This was confirmed to be glioblastoma.

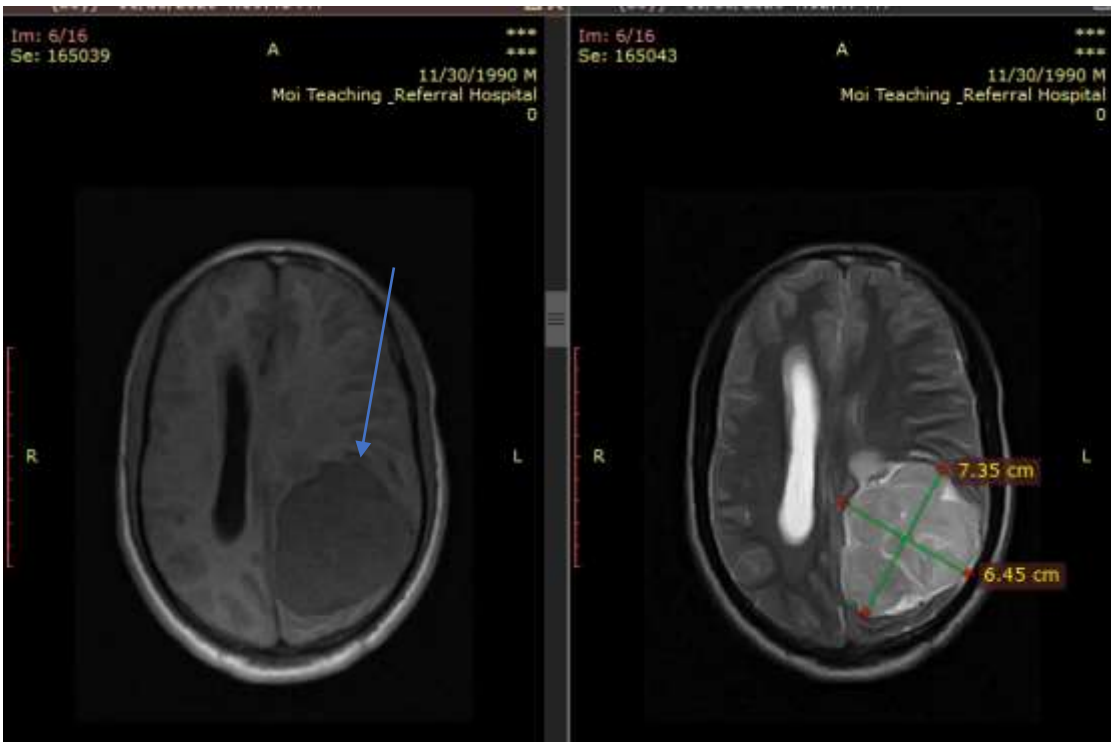


Figure 13: MRI brain of a 30-year-old male T1 and T2 axial images showing an extra axial left parietal mass which is hypointense on T1 and hyperintense on T2, with perilesional edema and noncommunicating hydrocephalus. This was confirmed to be meningioma.

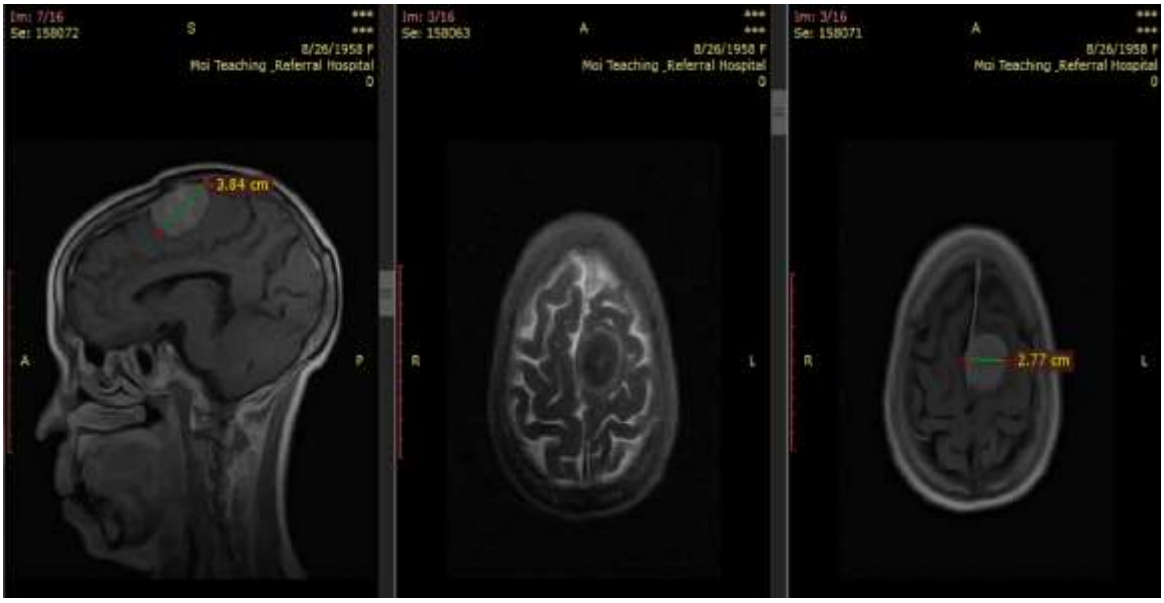


Figure 14: MRI brain of a 62 year old female. Sagittal and axial images showing a well defined left frontoparietal extra axial lesion which is isointense on T1 and hypointense on T2 measuring 3.8 cm with a dural tail. This was confirmed to be meningioma.

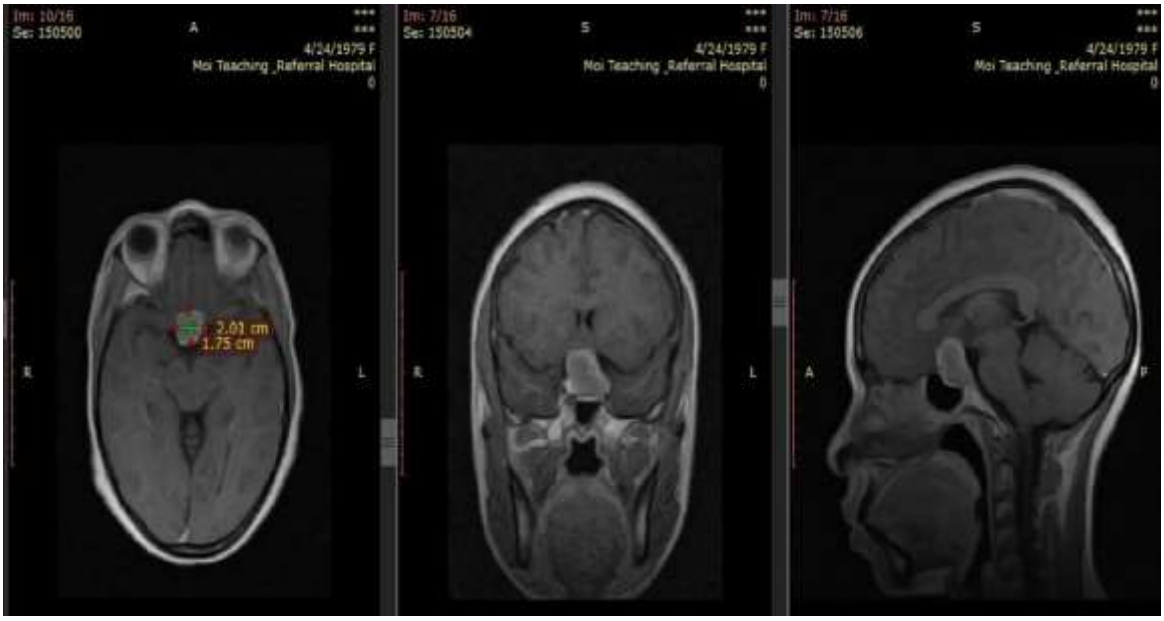


Figure 15: MRI brain images of a 40-year-old female. Axial and Sagittal images showing well defined sellar/suprasellar mass measuring 2.0 by 1.75 cm. It is heterogenous in all sequences. Confirmed to be pituitary adenoma.

CHAPTER FIVE: DISCUSSION

5.1 Demographic characteristic

From this study the mean age of the respondents was 46 years. These findings were similar to one study which was undertaken in South Africa which showed the median age of intracranial neoplasm as 46 years and a mean of 43 years (Ibebuike et al., 2013). This could be due to the similar geographical settings of the study area, both being in Africa. The race of participants in both studies were more likely to be the same.

This was in contrast with a study in the United Arab Emirates which showed the mean age of diagnosis was 33 years (Khan, Kambris, & AlShamsi, 2020). In another study in Finland, the occurrence of malignant glioma was greatest at the age group 60-69 years, with the highest age-specific incidence rate being at 70-79 years. From the same study, however, the incidence increased with age at an average of 37.6% increment per each decade of age (Natukka, Raitanen, Haapasalo, & Auvinen, 2019). This variation could be attributed to the different economic development and the different age pyramids in these two study areas.

Females were the most affected gender in this study n=46(57.95 %). This finding is similar to a study in South Africa by Ibebuike which found out that 55% of the study population were female (Ibebuike et al., 2013). Females were more affected by tuberculoma according to a study done in Nairobi (Mwang'ombe N. J. M. & Mwago, 2000). In contrast, males were affected more in other studies in the United Arab Emirates. Diffuse astrocytoma and oligodendroglia tumors affected more males than females in a study in the United Arab Emirate(UAE) by Khan (Khan et al., 2020). This could have been due to the fact that the study focused on expatriates working in the UAE. Another study done in Finland by Natukka and others found out that

gliomas were more common in male (52%) than female (Natukka et al., 2019). The male preponderance in this study in Finland could be due to the higher male to female ration in the general population of Finland.

Headache and seizures were the most reported clinical presentation in this study representing N=71(80.68% and N=26(29.55 % respectively. This findings were similar to a study in Saudi Arabia by Elwtidy that found out that intraventricular tumors present with headache in 70 % of the patients (Elwatidy, Albakr, Al Towim, & Malik, 2017).

These findings were contrary to one done in Italy by Comelli et al, that found that headache was only found in 14.6% of the study population of patients presenting in the emergency department (Comelli, et al., 2017). In this study however, focal signs were the leading clinical presentation among patients with brain tumors. The difference in these findings could be due to the varying setting of the study. Patients in the ED would present differently from those presenting in the radiology department.

The second most common presentation was seizures which was recorded in N=26(29.5 %) of the respondents. This is in congruency with a study in Turkey by Ertürk that found that the range of epilepsy in brain tumors ranged from 30 to 100 % depending on the tumor type. The types of seizures depend on the location of the tumors. It could be the only symptom in some tumors. Seizures are among the most common presentation of brain tumors (Ertürk Çetin, İşler, Uzan, & Özkara, 2017). According to this study, the occurrence of epilepsy in brain tumors are mainly focal with or without generalization.

In a study done by Maschio, the rate of epilepsy among patient with brain tumors was 20-40 % at the onset of the disease, and 20-45% as the disease progresses (Maschio, 2012; van Breemen, Wilms, & Vecht, 2007).

A contrary findings were noted by Lynam et.al, in the United states where seizures occurred in over 38% of those with primary brain neoplasm (Lynam et al., 2007). Another study with contradicting findings was done in Riyadh, Saudi Arabia by Elwatidy involving 42 patients with intraventricular tumors. In that study seizures were only found to occur in 17% of patients with interventricular tumors (Elwatidy et al., 2017). The difference could be attributed to the methodology used in this study. The study was retrospective while our study was cross sectional.

5.2 Radiological features

For this study, structural sequences T_2-weighted, FLAIR, pre- and post-contrast T_1-weighted were used to provide the examination findings. When used in the initial brain tumor evaluation, it provides information on the location of the lesion, extent of tissue involvement and resultant mass effect upon the brain. The location and rate of growth rate of the tumor affects the clinical symptoms that the tumors will present with.

Extra-axial tumors represented N=29(32%) of the brain tumors in this study. These was contrary to the findings in Ghana by Ekpene that had majority as intra-axial (77.5%) (Ekpene et al., 2018).

Intra-axial tumors formed N=36(46%) of the lesions in this study. Examples of intra-axial lesions include glioblastoma, diffuse astrocytoma, primary CNS lymphoma, ganglioglioma and oligodendroglioma.

Majority of the tumors in this study were solitary lesions N=78(98.8%). This was contrary to the findings by Schwartz in the United States who found that 40% of the lesions had solitary lesions (Schwartz, Erickson, & Lucchinetti, 2006). This could have been due to the fact that the study included metastatic lesions unlike our study focused on primary brain tumors.

In this study N=24(27%) of the image's studies had extensive brain edema. This was in keeping with a study in Egypt done by Abdelzaher that found out that perifocal edema was found in 27.7 % of the study participants (Abdelzaher, El Deeb, Gowil, & Yehya, 2013). This was contrary to the findings of Tobias Mattei in Brazil who found out 14% of the study population had extensive edema (Mattei et al., 2005). These differences could be due to the focus on specific tumor subset and difference in the sample size with the Brazil study having 55 participants. Extensive edema was found in glioblastoma (39%) as compared to meningioma (29%). There was statistically significant association between extent of edema and the histopathological diagnosis (p=0.049). This findings were similar to a study in Brail by Mattei that showed statistical significant association between histological features and extent of perilesional brain edema(p=0.0089) (Mattei et al., 2005). The findings contrasted a study in Westermil, Australia by Kizana which found out no association between perilesional edema and the final diagnosis (Kizana, 1996). This was probably due to the use of higher tesla MRI (0.5 T) and the focus was on benign tumors only which could have less edema.

Sixty-four (81.61%) of the tumors in this study had a solid appearance as compared to 14(17.24%) that had both solid and cystic appearance. The lesions with cystic appearance were n=1(1.15%). This was contrary to the findings of a study in India by Ramachandra et

al. that found out that 20% of the lesions had cystic components (Ramachandra, Neil Mekala, Mataparthy, & Chandra, 2020).

Most of the tumor's lesions seen in this study were more than 3cm in size N=45(51%). This findings was similar to a study in China done by Wu et al that found out that the median tumor size was 5.0cm (range 2.3-9.9 cm)(Wu et al., 2015). Contrary findings were reported by Liouta in Athens, Greece that found that 55.5% of the lesions were more than 4 cm in diameter (Liouta, Koutsarnakis, Liakos, & Stranjalis, 2016). The differences could be attributed to the different methodology used.

The noticeable mass effect of the tumors in this study was midline shift that was in n=55(72.37%) and sulci effacement in n=21(27.63%). Mass effect of tumors is determined by the midline shift and the tumor volume. A midline shift of more than 5mm is considered significant especially in primary tumors (Baris, Celik, Gezer, & Ada, 2016). Contrary findings were in a study in KNH by Mwangombe who found that only 38% of the lesions had mass effect (Mwang'ombe N. J. M. & Mwago, 2000). This could be attributed to the fact that the study focused on ring enhancing lesions and majority were tuberculoma which studies have shown to have little or no mass effect. The tumor size and mass effect were analyzed to assess the comparison. The association between mass effect and size of the lesion was not statistically significant (p=0.230).

However, 75% of those with ventricular obstruction had tumor size >3.0 cm. Sulci effacement mass effect were almost equally distributed among all the classification of lesion sizes. This was contrary to a study by Baris who found that there was statistical significance between midline shift and tumor volume ($p<0.0001$) (Baris et al., 2016).

Tumor margins were distinct in n=41(52.9%) of the cases in this study. This was similar to Ahmad in a study done in Delhi, India, that had 46.67% of the lesions with well-defined margins. (Ahmad, Anjum, Singh, Singh, & D G, 2014). This findings were contrary to Dellaretti in Brazil who found 68% of the tumors had diffuse indistinct margins (Dellaretti et al., 2012). The difference could be attributed to the fact that the study focused on brainstem lesions which are mostly diffuse brainstem glioma. Furthermore, there was a larger sample size of 96 participants.

There is a significant (p=0.044) association between tumor margins and type of tumor where indistinct tumor margins were associated with malignant tumors more (73%) than distinct margin features (37%). There was significant association between edema and tumor type. All (100%) patients with no edema had benign tumors, while mild and moderate edema was associated more with benign tumors compared to extensive edema which was associated more with malignant tumors.

In this study (95.3%) of the lesions were ring enhancing on contrast T1 signal intensity. The ring enhancing lesions vary in size and usually varying amount of perifocal vasogenic edema. Ring enhancing lesions located in the deep matter is associated with mass effect and surrounding edema is often due to primary brain tumors or abscesses.

When using T1 signal intensity, N=69(87.5%) of the study images were hypointense. This findings were similar to a study by Onyikwa in Eldoret that showed 61% of the lesions were hypointense (Onyinkwa M,et al., 2013). This was in contrast with a study done in India that showed 95% of the cases having hypointense signal intensity (Ramachandra V, Neil Mekala, Mataparthy, & Chandra, 2020). In the same study, the cases with hyperintense signal intensity were 73.5% and this was also contrary to our

study that had 3.4 % of the cases having hyperintense signal intensity. Majority of the meningiomas (71%) had heterogenous signal intensity in T1 with contrast. There were similar findings in a study by Watts in Australia (Watts et al., 2014). Ninety two percent of the glioblastoma had ring enhancing signal intensity on T1 with contrast. This was similar to the findings of Schwartz in the USA (Schwartz et al., 2006).

From this study N=13(15.91%) of the cases were hypointense on T2 signal intensity. This was in contrast with other studies in the USA by Schwartz which showed a higher rate of 67% (Schwartz et al., 2006). This could be attributed to the advance in technology in the USA compared to our local set up.

Forty-three (54.55%) of the cases showed hyperintense signal intensity on T2 weighted. This was contrary to the findings in India by Ramachandra which showed 73% of the lesion had hyperintense signal intensity while 25 % had hypointense signal intensity on T2 (Ramachandra V et al., 2020). The study had lower number of participants (30) and focused on ring enhancing lesions.

5.3 Radiological diagnosis of brain tumors in adults at MTRH

MRI scans were assessed by the researcher and confirmation made by two independent radiologists. T1-weighted, post gadolinium T1 weighted and FLAIR were analyzed. The various radiological features of the brain tumors as seen in MRI images were evaluated.

MRI diagnosis of brain tumors in this study had the following in order of decreasing order of frequency: meningioma N=31(39.24%), glioblastoma N=27(30.68%), pituitary adenoma N=12(13.64) and diffuse astrocytoma N=8(9.09%).

Meningiomas accounted for N=31(39.24%) of the respondent in this study. This finding is similar to other studies that noted meningioma to be the most common

intracranial tumors. In a study in South Africa by Ibebuile k et.al(2013), the most common intracranial tumor was meningioma at 31.8% (Ibebuike et al., 2013). This findings was also similar to a study by Das in Singapore that showed that the most common CNS tumor was meningioma accounting for 35.1% (Das, Chapman, & Yap, 2000). A local study done in Nairobi by Mwangombe found out that meningioma formed 34.4% of the brain tumors (Mwang'ombe N. J. M.& Mwago, 2000). This similarity could be due to the similar geographical setup of these two studies.

In contrary a study done by Comelli I. et al (2017) in Italy that found out that among patients presenting with brain tumors in the emergency department, gliomas were the most frequent at 46.3%, followed by meningiomas at 21.9% (Comelli et al., 2017). Another contradicting study was done in Ghana by Ekpene et al, this found out gliomas (77%) were the most frequent followed by meningioma (46%) (Ekpene et al., 2018). The difference could be attributed to the fact that the Italy study was in the emergency department and there is a likelihood of underreporting of benign tumors.

The second most common tumor in this study was glioblastoma accounting for 30.6% of the respondents. This finding is similar with other studies in America and Africa. In the United states, it is noted that glioma was the most common form of central nervous system neoplasms that arise from glial cells, affecting six per 100,000 people every year (Mesfin & Al-Dhahir, 2018). In a study conducted by Mwangombe in Nairobi Kenya, gliomas formed 45.8% of brain tumors (Mwang'ombe N. J. M.& Mwago, 2000).

On the contrary, in a study by Das(2000) in Singapore, glioblastoma formed only 9.3% of the histopathological confirmed tumors (Das et al., 2000). These findings

were also contrary to a study done in South Africa by Kelly, that found that high grade glioma were 22% of that study population (Kelly & Moodley, 2020).

The differences in the findings of these studies could be attributed to the varying genetic and environmental factors in the settings of the studies.

The third common radiological diagnosis of brain tumors in this study was pituitary adenoma accounting for N=12(13.64%) of the respondents. This was similar to other studies in Canada with Ezzat that found an overall prevalence of pituitary adenoma at 16.7%.

This was contrary to a study in Benin, that showed pituitary adenoma formed 27% of all brain tumors (Gandaho et al., 2016). The difference could be due to the longer duration of the study(5years), different study design (retrospective study) and the fact that not all patients underwent histopathological biopsy examination and some diagnoses were based on radiology only.

Diffuse astrocytoma accounted for N=7(9.09%) of all the intracranial tumors in this study. This findings compares with one done in Morocco by Karkouri who found that 12% of the tumors were diffuse astrocytoma (Karkouri et al., 2010). Another study with similar findings was conducted by Kapoor in India and they found out 12% of the tumors were astrocytoma (Kapoor & Kulkarni, 2020). Similar geographical conditions could have contributed to the congruent findings. Contrary findings were documented by Mwita et al(2018) in a study in Eldoret Kenya, that found out that 22.6 % of the tumors were diffuse astrocytoma (Mwita et al., 2018b). The variations was due to higher sample size of patients with astrocytoma, the study was done in three hospitals and the study focused on clinical clinicopathological characteristics.

5.4 Histopathological diagnosis of brain tumors in adults at MTRH

The histopathological diagnosis for each suspected brain tumors was done by following up the histopathological biopsy results after neurosurgery. The diagnosis was made using the current WHO guidelines. The slides were reviewed to assess the growth pattern and cellularity of the tumor margins. The final histopathological diagnosis was made in 79 of the cases that underwent surgical removal/biopsy of the brain tumors.

From this study the leading histopathological diagnosis of brain tumor was meningioma N=31(39.24%) followed by glioblastoma N=26(32.9%), pituitary adenoma N=11(13.92%) and diffuse astrocytoma N=6(7.59%).

These findings were in agreement with a study by Thambi R. et. al., (2017) in India which showed that the most common histopathology type of brain tumor was meningioma (38%) with a female predominance (Thambi R. et al., 2017).

This finding is contrary to the one done by Mwita in Eldoret which showed the most common histopathological type in intracranial brain tumor was glioblastoma at 70% (Mwita et al., 2018b). Similar findings were also noted in Ghana (Ekpene et al., 2018) and in Nigeria (Olasode et al., 2000).

5.5 Comparison between radiological and histopathological diagnosis

The study aimed to determine the comparison between the radiological/MRI features seen on MRI examination and the histopathological diagnosis among adult patients with suspected brain tumors in MTRH.

In order to determine the comparison between the radiological/MRI features seen and the histopathological diagnosis, the study analyzed the sensitivity and specificity between these two observations. These provided a statistic that will take into account the comparison of the MRI scan features against the histopathological diagnosis

which is the gold standard. Furthermore, it represents the extent to which the data represents the variables being studied.

The sensitivity of MRI in diagnosis of Glioblastoma in this study was 88.46% while the specificity was 92.45% ($p<0.05$). This was similar to a study in the Pakistan by Amin which found a sensitivity of 90.7% and specificity of 94.4% in the diagnosis of glioblastoma. Contrary findings were noted by Wang in China that had sensitivity of 80.0% and specificity of 78.46%(Wang et al., 2014). This could be due to the difference in the study methodology. The study in china was a metanalysis.

The sensitivity and specificity of MRI scanning in diagnosis of meningioma was 96.77% and 97.92% ($p<0.05$) respectively. These findings were similar to a study in China by Yan F et. al, that had a sensitivity of 96.9% in the diagnosis of meningiomas (Yan et al., 2016). This finding contrasts Bridson L. et al in Liverpool/UK which found the sensitivity of 89% and specificity of 95%. The difference could be due to the small sample size (18) and the fact that the participants were both those who underwent surgical operation and those who did not.

The sensitivity of MRI in the diagnosis of diffuse astrocytoma in this study was 66.67%. the specificity was 98.63%. Similar findings were found in the study in Dhaka, Bangladesh by Munshi et al, that showed a sensitivity of 60% for grade I astrocytoma. In the same study, the specificity of MRI in the diagnosis of astrocytoma was 97.7% (Munshi et al., 2019).There was low sensitivity of MRI imaging in the diagnosis of diffuse astrocytoma could be due to the diverse range of features of conventional imaging that often require advance techniques in their diagnosis.

The sensitivity and specificity of MRI scanning in the diagnosis of pituitary adenoma in this study was 90.91% and 97.06 % respectively. This findings were similar to

study in China by Yan that had a MRI sensitivity of 96.7% in the diagnosis of pituitary adenoma (Yan et al., 2016). The similarity could be due to the similar study setting involving evaluation of MRI reports of patients who underwent surgical procedure for the suspected brain tumor. This was contrary to findings of Hossain et al, in Bangladesh that showed MRI was 86% sensitive (Hossain M.I et al, 2017). This could be due to a large sample size and the longer duration of the study.

The overall diagnostic accuracy of MRI in the diagnosis of brain tumors was 86.1% ($p<0.05$). This was similar to findings of Yan et al. in China who found the overall sensitivity in all the tumor population was 82.2(72-90.7%) (Yan et al., 2016).

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This chapter covers the conclusions drawn from the study and the recommendation thought appropriate as a result.

1. The most common primary brain tumors on MRI in our study were meningiomas (39.2%).
2. On histopathological diagnosis meningiomas were the most common tumors. Tumor margins, perilesional edema and signal intensity enhancement patterns had a significant association with the final histopathological diagnosis of primary brain tumors.
3. On the comparison of radiological (MRI) and histopathology diagnosis of brain tumors, the sensitivity and specificity of MRI in diagnosis of brain tumors ranged from 66.7%-96.8% and 92.5%-98.6% respectively, and overall diagnostic accuracy of 86.1%.

6.2 Recommendations

We recommend the use of conventional MRI in the diagnosis of primary brain tumors and guiding management in adults in resource limited settings. This is applicable in the peripheral health facilities in Kenya with MRI services but with limited histopathological and neuro surgical services.

Further studies should be conducted in other similar settings to compare the use of MRI in the diagnosis of primary brain tumors.

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APPENDICES

Appendix I: Consent forms
Investigator's profile

My name is Everlyne Kipsang, a student pursuing masters in Radiology and Imaging at the Moi university. I am a qualified medical officer. I would like to recruit you into my research study entitled: "**Comparison of MRI findings and histopathological diagnosis of brain tumors in MTRH".**

The purpose of this study is to seek understanding of the relationship of these two findings and help improve patient care.

Procedure: All the patients in the MRI center with suspected brain tumors will be guided by the researcher to fill the informed consent and details entered into a questionnaire. The radiological features and the histopathological diagnosis after surgery will be analyzed to seek their comparison.

Benefits: There will be no direct benefit to the participant in this study. You will be awarded same level of quality care like other patients.

Risks: There is no anticipated risks associated with participating in this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person

Rights to Refuse: Participation in this study is voluntary, there is freedom to decline to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Participant informed consent

I Mr/Mrs/Miss/Guardian…….hereby give informed consent to Everlyne Kipsang to include in the proposed study entitled 'Comparison of MRI features and histopathological diagnosis of adult brain tumors in MTRH'. I have read the information concerning this study, and I fully understand the purpose and my requirement. I also understand that my withdrawal from the study will not affect the care that I require for my condition.

Signature…….Date…….

KISWAHILI VERSION

Mpelelezi : Jina langu ni Dr. Everlyne Kipsang. Mimi ni daktari aliyefuzu nakusajiliwa na bodi ya madaktari ya Kenya (Kenya Medical practitioners and dentist board). Mimi ni msomi wa shahada ya uzamili katika Radiology katita chuo kikuu cha Moi. Ningependa kukusajili ujiunge na uchunguzi ninaofanya kujua kama picha za ubongo zinazofanywa za saratani ubongo zinaambatana na aina ya histologia.

Kusudi: Utafiti huu utatafuta kuelezea kama kuna uhusiano kati ya matoke ya MRI na ya histologia ya wagonjwa waliona saratani ya ubongo

Utaratibu: Watu wenye umri wa miaka kumi na nane na juu wataelekezwa na mtafiti kujaza fomu za utafiti baada ya kubali kufanyiwa utafiti. Matokeo ya MRI na za histologia itatumika kuchunguza uhusiano kati yao.

Faida: Hakutakuwa na manufaa ya moja kwa moja ya kushiriki katika utafiti huu. Masomo ya kujifunza yatapewa ubora wa usimamizi kama masomo yasiyo ya kujifunza

Hatari: Hakuna hatari inayotarajiwa kwa washiriki inayotokana na utafiti huu.

Usiri: Taarifa zote zilizopatikana katika somo hili zitatambuliwa kwa usiri mkubwa na hazitafunuliwa kwa mtu yeyote asiyeidhinishwa

Haki za Kuepuka: Kushiriki katika utafiti huu ni kwa hiari, kuna uhuru wa kupungua kushiriki au kuondoka kwa wakati wowote. Utafiti huu umekubalika na Kamati ya Utafiti na Maadili ya Taasisi (IREC) ya Chuo Kikuu cha Moi / Chuo cha Mafunzo na Hospitali ya Moi.

Kusaini au kufanya alama unakubalikushiriki katika utafiti

Mgonjwa……

Mpelelezi…….

Tarehe……

Appendix II: Questionnaire/Data Collection Tools
Section A: Sociodemographic

Date …….. Serial number……

Age…….

Gender □ MALE□ FEMALE

County of Residence……..

Section B: Presentation: What was the clinical presentation of the patient with suspected brain tumor?

□Headache

□Seizures

□ Blurred vision

□Vomiting

□Hemiplegia

Others (specify)……

Section C: MRI Imaging (Radiological Features): What MRI features were present on the MRI images?

1. Location of the lesions:

   □ Intra Axial □ extra axial □Sphenoidal ridge

   □ intra ventricular □ Dural □supra tentorial - □ temporal

   □frontal □occipital □ parietal □

   Others(specify)…….

2. Number of the lesions □ One □ Two □ More than two (Specify Number) ……..
3. Size of the lesions □ <1.5cm □ 1.5-3.0cm □ >3.0cm
4. Shape of the lesions □Mass □ En plaque
5. Tumor margins □Distinct □ Indistinct □ Cleaved
6. Presence of Oedema □Nil □ Moderate □Mild □ Extensive
7. Appearance of the lesion □cystic □ solid □ both solid and cystic □ others (specify)……
8. Mass effect present □midline shift □ herniation

   □ventricular obstruction

9. Signal intensity of the lesion

   a. T1 □ hypointense/isointense □hyperintense □heterogeneous
   b. T2 □ hypointense/isointense □hyperintense □ heterogeneous
   c. FLAIR □ hypointense, □ hyperintense □heterogeneous
   d. T1 with contrast □ enhancing □nil □ moderate □ mild

      □ heterogenous

Final MRI diagnosis

Primary brain tumor…….

Section D: Histopathological examination

Histopathological findings

Diagnosis……..

1. Grade 1□
2. Grade 2□
3. Grade 3 □
4. Grade 4 □
5. Others

   (specify)……..

Final histopathological diagnosis…….

Appendix III: Moi Teaching and Referral Hospital Brain Magnetic Resonance Imaging Protocol

Magnetic resonance imaging of the brain was performed using 0.36 tesla Magsence 360 machine (Mindray, China) at the MTRH MRI department. The patient lied supine on the MRI couch and cushions were used to immobilize the head within the head and neck coil. Other cushions was placed under the legs for extra comfort. Laser beam localizer was centered over the glabella.

Using the volume array coil, sagittal and axial T1-weighted turbo spin echo (repetition time/echo time of 400-600/15-25ms) and T2-weighted turbo spin echo (repetition time/echo time of 3,000-4000/100-120ms) images were acquired. A slice thickness of 5.0 mm, a field of view between 230-250mm and a matrix of 256 by 256 were used.

3-plane T1weighted low resolution scan localizer was used for planning. Sagittal slices were planned on coronal plane using the position block placed parallel to the midline of the brain. Axial images were planned on sagittal plane with position block parallel to the genu and splenium of the corpus callosum. Slices were sufficient to cover the whole brain from the vertex to the line of the foramen magnum. T2 FLAIR axial were planed on the axial plane with position block parallel to the genu and splenium of the corpus callosum. T1 weighted images with contrast axial and coronal were used after administration of IV gadolinium DTPA 0.1 mmol/kg. injection. The soft copy images were printed onto laser film hard copies and stored directly as DICOM (Digital Imaging and Communications in Medicine) files in the workstation and in CD-ROMs.

Appendix IV: IREC approval

MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2018/264
Approval Number: 0003291

3rd April, 2019

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
03 APR 2019
APPROVED
P. O. Box 4606-30100 ELDORET

Dr. Kipsang Jepkogei Everlyne,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Kipsang,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Comparison of Magnetic Resonance Imaging and Histopathological Findings of Adult Patients with Suspected Brain Tumors at Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3291*** on 3rd April, 2019. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 2nd March, 2020. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix V: Hospital approval

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

8th April, 2019

Dr. Kipsang Jepkogei Everlyne,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Comparison of Magnetic Resonance Imaging and Histopathological Findings of Adult Patients with Suspected Brain Tumors at Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - Senior Director, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM