PATTERN OF BRAIN ABNORMALITIES ON MAGNETIC RESONANCE IMAGING IN ADULTS WITH EPILEPSY AT MUHIMBILI NATIONAL HOSPITAL

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MMED (Radiology) Dissertation

Muhimbili University of Health and Allied Sciences

October, 2019

Muhimbili University of Health and Allied Sciences

Department of Radiology and Imaging

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By

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A Dissertation Submitted In Partial Fulfillment of the Requirement for the Degree of Master of Medicine (Radiology) of the

Muhimbili University of Health and Allied Sciences

October, 2019

CERTIFICATION

The undersigned certifies that she has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Science a dissertation entitled**, "Patterns of Brain Abnormalities On Magnetic Resonance Imaging In Adult patients With Epilepsy At Muhimbili National Hospital.",** in (partial) fulfillment of the requirements for the degree of Master of Medicine Radiology of Muhimbili University of Health and Allied Sciences.

_____

Dr. Mboka Jacob

Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I, **Roselyne A. Okello**, declare that, this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for similar or any other degree award.

Signature……..... Date…….

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ACKNOWLEDGEMENT

My uttermost gratitude to God Almighty for seeing me through this journey, the unwavering strength and grace in order for me to accomplish this work.

My sincere gratitude to the Radiology Department MUHAS and MNH, particularly my research supervisor, Dr. Mboka Jacob, for her guidance and support as we took up the study, research proposal, data collection till the end of the project.

I would also like to extend my gratitude to Dr. Magda (Radiologist (MOI), the neurology team at the Neurology clinic, the MRI department (MNH) for the assistance and support I received during data collection.

I wish to acknowledge the support that I have received from my classmates (Radiology MMED 2016) the encouragement and teamwork that we all had to put to realize a common goal.

The MUHASSO Stationery is uniquely appreciated for the assistance in the secretarial work from the development of dissertation proposal, questionnaires and finally to this report.

I would also like to appreciate the Director of Post graduate studies and the Director of Research who have relentlessly been available for students as they achieve what they came to do.

A very special gratitude to my parents who have been my backbone in prayers and motivation. My Siblings Catherine, Marie, Olga, Ann and Ricky. My nephew and nieces who have taught me love.

DEDICATION

To

My Parents

Mr. Felix Mkan Okello and Mrs. Jane Pamela Okello

Your prayers and support in me realizing my childhood dreams is what has kept me going.

ABSTRACT

Background

Epilepsy is a neurological disorder that presents with episodic seizures, some of which are amenable to treatment. Patients with Epilepsy have been reported to have underlying brain structural abnormalities, though little is known on magnitude and extent of these abnormalities in patients with epilepsy at our settings. The current study aimed at establishing neuroimaging findings in epilepsy that may be used to predict disease severity, prognosis and management outcome.

Objective

To determine the pattern of brain abnormalities on Magnetic Resonance Imaging (MRI) in adult patients with epilepsy referred to MRI unit at Muhimbili National Hospital (MNH).

Materials and methods

This was a prospective, cross-sectional, hospital-based study where 65 adult patients with epilepsy aged 18 years and above were consecutively enrolled after obtaining a written consent. The study was conducted for six months at Radiology and Imaging Department, MNH. Demographic and clinical information were obtained by interviewing patients and use of patients' medical records. Information was recorded using standardized questionnaires. Brain MRI was conducted in all patients on 1.5 Tesla scanner machine and reported by the Primary investigator and radiologist and final diagnosis was reached by consensus**.** Statistical analysis was done using Statistical package for Social Science (SPSS) version 23. Categorical and continuous variables were analyzed using two-tailed Chi-square test student t-test, and analysis of variance (ANOVA) respectively. A p-value of less than 0.05 was considered statistically significant.

Results

Sixty-five adult patients with epilepsy were included in this study. Twenty-seven (41.5%) were male and thirty-eight (58.5%) females. The mean age was 36.4 years, the age ranged from 18 to 65 years. Thirty (46.2 %) had underlying brain structural abnormalities on MRI. The observed brain abnormalities included: brain atrophy (10.8%) brain infarction (9.2%), white matter disease (6.2%), tumors (4.6%), focal cortical dysplasia (4.6%), mesial

temporal sclerosis (3.1%), atriovenous malformations (3.1%), intracerebral hemorrhage (3.1 %) and infection (1.5%). There was no relationship between age, sex and brain abnormalities on MRI. There was also no relationship between types and distribution of brain abnormalities on affected lobes. On Diffusion weighted; restriction was exhibited by infection, tumors, mesial temporal sclerosis, and brain infarction. Other types of lesions showed no restriction.

Conclusion

Underlying structural brain abnormalities are common in adult patients with epilepsy. The most common abnormalities are brain infarction and brain atrophy of the temporal and frontal lobes. Diffusion weighted Imaging could be useful in differentiating different types of brain abnormalities.

Recommendations

Brain MRI should be recommended to all adult patients with epilepsy, as some of the lesions are easily amenable to treatment. MRI is useful in differentiating types of abnormalities hence helps in making accurate and precise management. Studies using larger sample size should be carried out in order to have results that could be generalized to the community.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

1	1.5T	1.5 Tesla
2	3.0T	3.0 Tesla
3	3D	3 Dimension
4	CSF	Cerebrospinal fluid
5	CT	Computed Tomography
6	DNET	Dysembryoplastic Neuroepithelial tumors
7	DWI	Diffusion Weighted Images
8	FLAIR	Fluid Attenuated Inversion Recovery
9	GM	Grey Matter
10	ILAE	International League Against Epilepsy
11	MD	Doctor of Medicine
12	MMED	Master of Medicine
13	MNH	Muhimbili National Hospital
12	MRI	Magnetic Resonance Imaging
13	NICE	National Institute for health and Clinical Excellence
14	SE	Spin Echo
15	SPSS	Statistical Package for Social Services
16	STIR	Short Tau Inversion Recovery
17	T1	Longitudinal relaxation time
18	T2	Transverse relaxation time
19	TE	Echo time
20	TR	Repetition time
21	WHO	World Health Organization
22	WM	White Matter

CHAPER ONE

INTRODUCTION

1.1Background

Epilepsy is a debilitating neurological disorder. Its prevalence and incidence increase with age, severely interfering with a person's livelihood and status in the community. There is low rate of detection of brain abnormalities related to epilepsy in low and middle-income countries; this can be attributed to decreased awareness of causes, availability of experts and diagnostic facilities. Seizure episodes limit a patient on the type of professional activities they are willing or able to perform, hence dramatically slowing one's ability to achieve maximum potential as human. Activities such as driving, operating machines or even engaging in sports represent the restricted areas for a patient with epilepsy. Obtaining or maintaining employment for a patient with epilepsy is also difficult because employers may weigh the investments they are making on such an employee. This has a trickle-down effect as it affects family resources in case of a breadwinner.

There are a number of reported causes of epilepsy, which include genetic, structural, metabolic or unknown causes. While this classification is valid across different age categories, adult-onset epilepsy might stem from an acquired vascular, degenerative and neoplastic etiology (1).

Following the UK based National Institute for health and Clinical Excellence (NICE) guidelines on Epilepsy and the International League Against Epilepsy (ILAE) recommendation on diagnosis and treatment, clinicians are to encourage the use of MRI for early screening of epilepsy and detection of brain abnormalities for adequate treatment (2)(3).

MRI is used to identify structural abnormalities in the brain, differentiates the causes of epilepsy by detecting the epileptogenic lesions in order to improve patient management. The National Institute for health and Clinical Excellence (NICE) guidelines on epilepsy recommend use of epilepsy protocol in MRI for further diagnosis(2). Further, Kuzniecky et al reported that use of Epilepsy protocol in MRI will be more specific in determining epileptogenic lesions as they might be missed out on routine MRI protocols(4).

Whereas the MRI findings in epileptic patients seem not to be static and do not involve set diagnosis criteria, there is a need to study patterns of neuroimaging findings across geographical regions, with possibly differing etiologies and types of epilepsy.

This study aimed to assess the underlying brain abnormalities by using MRI in adults with epilepsy referred to the radiology department at the Muhimbili National Hospital.

1.2. LITERATURE REVIEW

A meta-analysis among US Medicare beneficiaries reported the annual prevalence of epilepsy in the US is 10.8/1000**(5)** . The prevalence was noted to be higher in the black Americans as compared to the Asians and Latin Americans and lower in white Americans (5). The study further notes that the incidence is higher in women and it increases with age irrespective of gender and race. The WHO has estimated that 50 million people in the globe are living with epilepsy and around 100 million people will have at least one seizure episode in their life, and most of the causes of epilepsy are amenable to treatment **(6).** The incidence disproportionately affects Africans; the incidence is 86- 156 per 100,000 in various countries in Africa, while in developed countries, it is estimated to have 40-70 per 100,000 new cases. The overall prevalence in Africa ranges from 2.2 to 58 per 1000(6).

The prevalence rate of epilepsy in both children and adults in Tanzania range from 2.9 per 1000 to 20/1000 (7). This study was performed in Hai Tanzania and showed higher prevalence in males as compared to females, though the difference was not significant. There was higher prevalence noted by age and sex in adolescents and young adults with the highest prevalence of 4.78/1000 among females of age group 20-24 years and males 7.63 /1000 of the same age group. This is compared to the lowest incidence in adults aged more than 60 years which was noted to be 0.85/ 1000 females and 1.56 /1000 males(7). This is however is not the case with other studies done in the Sub-Saharan Africa as another study done in northern Tanzania showed a slightly higher prevalence of epilepsy at 8.7/1000. It postulated a higher prevalence of 14.3/1000 and 8.4 /1000 among females and males respectively while the age specific prevalence were also higher among females as compared to males. The study further shows a concurring trend with the Hai study to note that there was higher prevalence of epilepsy in young adults and adolescents as compared to older population of more than 54 years(8).

MRI is best suited to detect underlying etiology of epilepsy. However, literature regarding the exact role of MRI in determining etiology of status epilepticus is sparse (9).Studies are continuously defining the role and need of MRI in evaluation of epilepsy. Kuzniecky et al

(4) delineated the role of MRI in epilepsy and stated that the patients with symptomatic generalized or focal seizures should have a structural neuroimaging study.

According to L Li et al, the use of high resolution MRI has increased significance in detecting structural abnormalities. Lesions seen in patients with epilepsy mostly include cortical dysgenesis and hippocampal asymmetry, which can either be associated with tumors, vascular malformations or infarcts (10). Most notable tumors are astrocytoma, dysembryoplastic neuroepithelial tumors, cavernomas, gangliogliomas, oligodendrocytoma, neurocytoma and angioma(10). Abnormalities such as mesial temporal sclerosis, previous infarcts, encephalomalacia, gliosis mainly in the frontal lobe, arachnoid cysts and brain atrophy, basal ganglia abnormalities, ventricular abnormalities, white matter abnormalities, have also been reported in these patients(10).

MRI helps localize structural abnormalities that are amenable to surgery. According to a prospective study done between Jan 2005 and Feb 2011 among 2000 patients with localization related epilepsy, 313 (15 %) of the patients had lesions amenable to surgery(11). Eight main categories of abnormalities were identified: arachnoid cyst, diffuse cortical atrophy, basal ganglia abnormalities, ventricular abnormalities, white matter abnormalities, reduced hippocampal volume, hippocampal lesions, focal gyral abnormality, gliotic lesions mostly on frontal lobes, and brain atrophy(12)**.** In patients with idiopathic generalized epilepsy, most findings are non-specific, However as not so many cases have been reported, Betting et al notes significant brain MRI abnormalities in these group of patients (12).

The temporal lobe has shown to be the most affected lobe in patients with epilepsy (10). Mostly patients have been noted to have temporal lobe gliosis, hippocampal asymmetry, tumors, vascular malformations and cortical dysgenesis in order of reducing frequency.
The Frontal lobe is also affected by tumors, vascular malformations, infarct and cortical dysgenesis (10).
Parietal lobe and occipital lobe are the least affected and most likely will present with cortical dysgenesis and vascular malformations(10).
Mesial temporal sclerosis is the most common epileptogenic pathology seen in patients with epilepsy. This can be associated with a second pathology. MRI features include

atrophy of the mesial temporal structures, increased T2 W and FLAIR signal, loss of inter digitations in the hippocampal head, enlargement of the CSF space in the temporal horn of the lateral ventricle and tilt of the hippocampal formation from the horizontal towards the horizontal or vertical plane(13). Although DWI increases scan time, it provides information regarding the functional connectivity of a given area and describing the spatial relation of the lesion and the white matter tract. This is due to the measurement of molecular motion of the water within the brain tissue. Data obtained in patients with temporal lobe epilepsy showed that there was decreased diffusivity of the hippocampus ictally and immediately post-ictal reflecting cytotoxic edema. While, in between seizures the mesial temporal diffusivity may be increased. These changes reflect the alterations in the histoarchitexture of the mesial structures.

Furthermore, hippocampal volume measurement and monitoring T2 relaxation techniques increases MRI sensitivity(10). Hippocampal volume and signal quantification can significantly improve detection of hippocampal sclerosis in an otherwise normal MRI by using epilepsy protocol. This can further help in lateralizing the seizure focus in patients(14).

Focal cortical dysplasia is a heterogeneous group of disorders of cortical formation and one of the most common causes of epilepsy. Focal cortical dysplasias are abnormal gyration patterns, which mostly demonstrate blurring of the grey-white matter junction and cortical signal abnormalities on MRI. T1 W sequence mostly show change in thickness of the cortical mantle, loss of grey – white matter differentiation with hyper intense signal relative to the normal cortex. T2 W and FLAIR sequences demonstrates radial hyper intensity in the white matter underlying the focal cortical dysplasia(10). They can be associated with hippocampal sclerosis and cortical glioneuronal neoplasms. In patients with focal cortical dysplasia epilepsy frequently presents in adulthood. R. Kuzniecky further states that focal cortical dysplasias are evidenced by areas of cortical thickening, loss of interface between white and gray matter, focal atrophy and hyper intense T2/FLAIR sequences. These are classified into three types, whereby, Type I may present with mild hyper intensity of white matter in T 2 and FLAIR sequences, mild focal increase in cortical thickness and loss of white matter differentiation. Type II hallmark is hyper intense T2 /FLAIR signal in the subcortical white matter with a wedge shape that extends to the ipsilateral ventricle ependymal surface. Type III is associated with other lesions(4).

Cavernomas are the most common vascular malformation seen in patients with epilepsy. MRI characteristically shows popcorn appearance with a core of mixed signal intensities and a hypo intense rim. Use of gradient echo sequence is used to increase the sensitivity of demonstrating punctate microheamorrhages(10).

Tumors associated with epilepsy include gangliogliomas, dysembryoplastic neuroepithelial tumors (DNET), astrocytoma and oligodendrogliomas(4). DNET tumors are thought to be epileptogenic and they are mostly benign as they don't demonstrate mass effect and are mostly associated with cortical dysplasia. They cause intractable partial seizures. Typically, these tumors are diagnosed in children or young adults. There is slight male predilection. These tumors are iso, hypo intense in T1W, hyper intense on T2W sequences. There's no grey –white matter differentiation with variable degree of enhancement with gadolinium(10). Kuzniecky et al, further emphasizes that these tumors are frequently located in the temporal lobe and maybe associated with FCDs. They are mostly limited to the cortex and are hypointense on T1 while demonstrate hyperintensity on T2 and FLAIR sequences. There is no associated peritumoral edema or mass effect and they demonstrate variable contrast enhancement(4). These tumors typically present with cystic alteration with or without calcifications on MRI. The Gangliogliomas are usually well defined, T1 hypo intense, T2 hyperintense with variable contrast enhancement (4).

Diffusion weighted imaging sequence has been proven to provide a vital role in the imaging of patients with epilepsy. Szabo et al, have described the role of DWI in establishing epileptogenic pathology in patients with complex partial status epilepticus. They noted hyperintensity DWI signal intensity in patients post ictal phase(15). Huber et al further emphasizes this role. They noted that there was increased diffusivity in patients after single episode of seizure in areas with pathology (16). Further, Foster et al, has described the role of DWI in differentiation of disorders affecting the hippocampus(17) .

Cortical and hippocampal volume deficits in temporal lobe epilepsy is a novel way of identifying epileptogenic structural pathologies. This is takes neuroimaging of epilepsy a notch higher. Laura et al demonstrated the differences in cortical and hippocampal volume deficits in patients with temporal lobe epilepsy (TLE) by quantitative MRI methods to examine the extent of volume abnormalities in the hippocampal and extra hippocampal brain regions. Using a 1.5 MRI scanner, multi echo, flow compensated, cardiac gated pulse sequences, and acquiring 22 contiguous 3 mm thick coronal MRI images oriented

perpendicular to the anterior commissure- posterior commissure line. While the Axial MRI sequences were used to acquire other intracranial lesions. This methods are specific an sensitive approach in localizing epileptogenic temporal lobe and hippocampal sclerosis(14) Patients with TLE have smaller cortical gray matter volumes bilaterally in the temporal lobes and fronto-parietal cortex, reduced white matter volumes in the temporal lobes, enlarged ventricle and right temporal sulcal volumes, while hippocampal volume deficits in TLE are ipsilateral to the epileptogenic temporal lobe. These findings have been replicated in multiple neuroimaging and neuropathological studies. Other abnormalities noted are nerve cell loss in the cerebral cortex, thalamus and cerebellum.(14)

1.3 PROBLEM STATEMENT.

WHO (2004) has estimated that 50 million people in the globe are living with epilepsy and around 100 million people will have at least one seizure episode in their life and most of the causes of epilepsy are amenable to treatment. The report also noted that the incidence amongst Africans is higher as it is around 86- 156 per 100,000 in various countries in Africa as compared to the developed world where it has been estimated to have 40-70 per 100,000 new cases. The prevalence in Africa range from 2.2 to 58 per 1000 (6)which again shows high incidence rate in Africa as compared to the United States. Various studies done in Tanzania show prevalence rate of epilepsy in both children and adults to be 2.9 per 1000 to 20/1000 (6)(7). Epilepsy interferes with people's daily activities this makes one afraid of indulging in certain duties and in essence reduces the choices one has to make in life in terms of career and family life. This leads to loss of self-esteem in character and eventually a person may not be open to social interactions, hence interfering with livelihood and community social status of an individual. Due to the seizure episodes, people with epilepsy are limited to the kinds of job they undertake. As such, employers are keen not to recruit them hence reducing the employment opportunities. Engaging in activities that need manpower such as driving and operating heavy machineries are limited in their realm of involvement. This has a domino effect in the income generation and livelihood of people living with epilepsy, making it harder for them to survive.

A number of patients clinically diagnosed with epilepsy in developing countries such as Tanzania, do not undergo brain examinations using neuroimaging techniques in spite of the

reported associated brain abnormalities in these patients. Not only that, but finding the accurate imaging diagnostic tool of epilepsy poses a challenge in its adequate management. Whereas literature has shown in the past the roles of the various modalities, scarce knowledge still exist around the contribution of Magnetic Resonance Imaging in diagnosing epilepsy and constitutes a rather secondary tool, after other imaging techniques. The study aimed at establishing the magnitude and pattern of brain structural abnormalities in adult patients with epilepsy.

1.4 RATIONALE

The role of imaging in determining the etiology of epilepsy in assessment of underlying structural brain abnormalities is of paramount importance for precise and accurate management and development of interventions for prevention. The NICE guidelines on Epilepsy suggest that all patients with epilepsy should be imaged regardless of pharmacology control(2). In this study MRI was used, as it is superior to other neuroimaging modalities, it has superior tissue contrast and non-ionizing radiation properties. MRI is better than CT scan in the detection of structural lesion and it's relatively safe.

Little is known on the magnitude and extent of structural brain abnormalities in adult patients with epilepsy hence this study aims at establishing neuroimaging findings in epilepsy that may be used to predict disease severity, prognosis and management outcome. Not only that, but the results of this study may shape the future of diagnosis and management of epilepsy in East Africa and this can be extrapolated to other African countries.

1.5 RESEARCH QUESTIONS

1. What is the proportion of patients with underlying brain structural abnormalities by age and sex among adult patients with epilepsy referred for brain MRI at Muhimbili National Hospital?

2. What are the common types of brain abnormalities in adult patients with epilepsy referred for brain MRI at Muhimbili National Hospital?

3. What diffusion characteristics are seen on the brain abnormalities in Diffusion weighted imaging MRI in patients with epilepsy**?**

1.6 OBJECTIVES

1.61 Broad Objective

- To determine pattern of brain abnormalities in adult patients with Epilepsy referred to MRI unit at Muhimbili National Hospital (MNH) from November 2018 – April 2019.

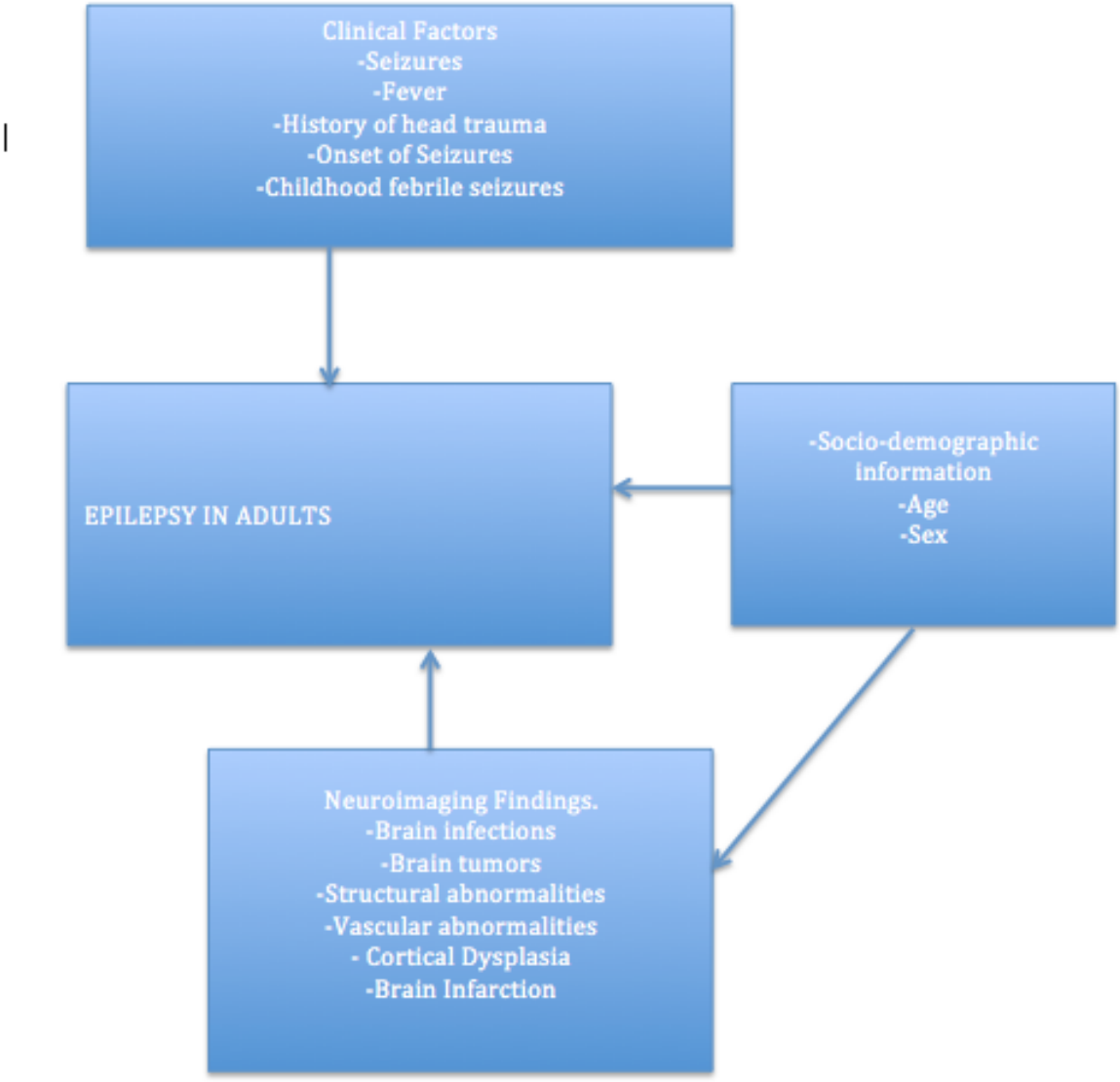
1.62 Specific Objectives

1. To determine proportion of patients with underlying brain abnormalities by age and sex among adult patients with epilepsy referred for brain MRI at Muhimbili National Hospital
2. To determine types of brain abnormalities by age among adult patients with epilepsy referred for brain MRI at Muhimbili National Hospital.
3. To determine diffusion characteristics of brain abnormalities on Diffusion weighted imaging among adult patients with epilepsy referred for brain MRI at Muhimbili National Hospital.

Conceptual Framework

The figure below, illustrates the conceptual framework that will be used to conduct the study. The study intends to establish the patterns of common brain abnormalities in adult patients with epilepsy in this population. The proportion of brain abnormalities in relation to age and sex, the presenting complaints ,the common brain lesions seen,the most common abnormalities seen and determine the diffusion weighted characteristics of the lesions**.**

Figure 1: Conceptual Framework



CHAPTER TWO

METHODOLOGY

2.1 Study design

This was a descriptive cross-sectional hospital-based study.

2.2 Study Population

Adult patients with epilepsy referred for brain MRI at Department of Radiology (MRI unit), Muhimbili National Hospital.

2.3 Period of the Study.

The study was conducted between November 2018 to April 2019.

2.4 Study setting.

Muhimbili National Hospital (MNH).

The study was done at Muhimbili National Hospital (MNH) located in Dar es Salaam city, the commercial capital of Tanzania. The city has five municipal councils (Kinondoni, Ubungo, Kigamboni, Temeke and Ilala) and is the largest and oldest city in Tanzania.

MNH is the largest tertiary care, government owned and run hospital in Tanzania, it serves as a national referral hospital and an instructional teaching hospital for Muhimbili University of health and Allied Sciences (MUHAS). The study extensively involved the Department of Radiology and Imaging (MRI UNIT).

2.5 Sample Size Calculation

Considering the study power of 95, a random error was estimated to be 0.5. Sample size of 65 was estimated. A prevalence of 0.384% was used. This was picked from a study that assessed the incidence of Epilepsy in adults patients in Tanzania(7).

.The sample size calculation from Fisher's formula;

- $N = z^2p\ (1\text{-}p) \div E^2$ Where by:
- N- Is the sample size
- Z – Is the point of normal distribution corresponding to the significance level of 1.96

- P – Prevalence is 0.384% (7)
- E- Error margin 0.05.

Sample

- From this formula the sample size was calculated as follows:
- $N = (1.96)^2 X\ 0.0384(1 – 0.0384) \div (0.05)^2 = 59$
- Sample Size = 59
- Adjusted sample size for non –response = 6
- 59+6= 65

2.6 Patient Recruitment

All patients who met the inclusion criteria were included into the study.

65 adult patients with epilepsy were consecutively included in the study until the sample size was reached for a period of 6 months.

In this study; Epilepsy was defined as:

- Two unprovoked seizures occurring more than 24 hours apart.
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (example, ≥60 percent) occurring over the next 10 years. This may be the case with remote structural lesions such as stroke, central nervous system infection, or certain types of traumatic brain injury (1).

2.7 Inclusion and Exclusion Criteria

A). **Inclusion criteria**

Adult patients age 18-65 years who were diagnosed with epilepsy according to ILAE definition.

All patients who consented to the study

B). **Exclusion criteria.**

- Study participant with contraindications to MRI investigation
- (Patients with Aneurysmal clips, cardiac pacemaker, Implanted cardiac defibrillator, neurostimulation system, spinal cord stimulator, cochlear, otology or

other ear implant, insulin or other infusion pump, prosthesis, heart valve prosthesis, artificial/prosthetic limb, metallic stent, shunt, wire mesh implant, tissue expander, surgical staples, clips or metallic sutures, IUCD, diaphragm, dentures/partial plates, body piercing jewelry and Claustrophobia)

2.8 Data Collection and Instruments

All information was recorded in a standardized questionnaire designed for this study (Appendix I).

The following information was collected:

I. Clinical information

II. Brain MRI findings.

2.8.1 Clinical information

A designed questionnaire specific for this study was used. The questionnaire had two parts. Part A (For recording demographic and clinical information) and Part B (for recording MRI findings).

The Principal Investigator interviewed consenting patients by using close-ended structured questionnaire.

Data collected included socio-demographics, clinical symptoms that included fever, seizure episodes, frequency and onset of the seizure episode, previous history of headache, trauma and loss of consciousness. Associated factors that are age and sex were assessed.

2.8.2 Magnetic Resonance Imaging (MRI)

A trained radiographer performed the imaging. Brain MRI was done using 1.5 T-scanner, (Phillips, Achiever, Best, Eindhoven, Netherlands). The matrix for sequences in this MRI protocol included the following whole-brain sequences: an axial turbo spin-echo (TSE) T2-weighted sequence (TR/TE of 3,000/120 ms; slice thickness, 5 mm), a coronal TSE T2-weighted sequence (3,000/120 ms; slice thickness, 5 mm), and an axial FLAIR sequence (TR/TE, 6000/120; inversion time, 2000 ms; slice thickness, 5 mm). 3D sagittal T1-weighted turbo field-echo (TFE) volume sequence (TR/TE, 6.9/3.2) with an isotropic

spatial resolution of 1mm and Diffusion weighted images included the matrix of each sequences.

1. Brain infection: (4)

   Cystic lesion that is isointense or mildly hyperintense to CSF on T1W, T2W, FLAIR with hypointense ring and surrounding ring enhancement.

   Surrounding mild edema

   DWI – **Restricted diffusion.**

2. Tumors; -(4)(10)

i. DNET

- Cystic alterations with or without calcifications
- Mural nodules with enhancement of gadolinium
- Hypointense on T1W and hyperintense on T2W.
- Limited to the cortex.
- Variable contrast enhancement pattern.

ii. Ganglioma

   Clear limits

   Hypointense on T1W and hyperintense in T2W

   Variable contrast enhancement pattern

   May present with annular pattern.

iii. Low grade astrocytoma

- Hypointense on T1W and hyperintense on T2W
- Variable contrast enhancement pattern.

3.Mesial temporal sclerosis:(4)

a. Brain atrophy
b. T2W hyperintense
c. T1W hypointense

4.Gliosis, encephalomalasia.brain atrophy (4)

5..Other abnormalities. 1. Brain infarction (4)

2.Non-traumatic intracerebral hemorrhage

3. Focal cortical dysplasia
4. Atriovenous malformations
5. White matter abnormalities

Visual assessment of ADC / DWI maps was done and graded as low ADC if hypointense and high ADC values if hyperintense.

2.9 Image Evaluation

Interpretation of the MR images was performed by two evaluators (Principal investigator and one Radiologist). The final diagnosis was reached by consensus.

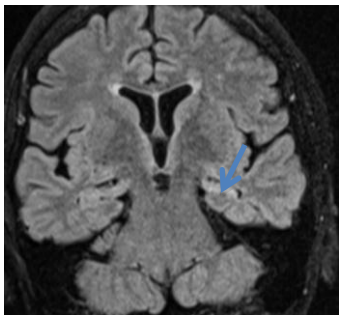


Figure 2: Mesial temporal sclerosis
in a 48 years old female with epilepsy referred for Brain MRI at Muhimbili National Hospital. Coronal FLAIR image showing hyperintense area on the left hippocampal temporal lobe.

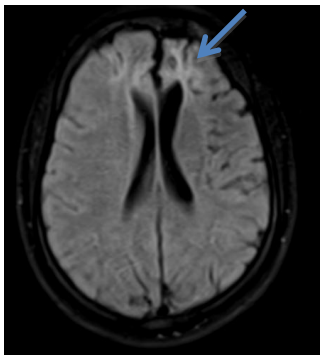


Figure 3: Focal brain atrophy
in a 22 years old male with epilepsy referred for Brain MRI at Muhimbili National Hospital. Axial FLAIR image showing hyperintense signal intensity seen on the left frontal lobe with focal prominent gyrus and sulcus and reduced volume as compared to the right side.

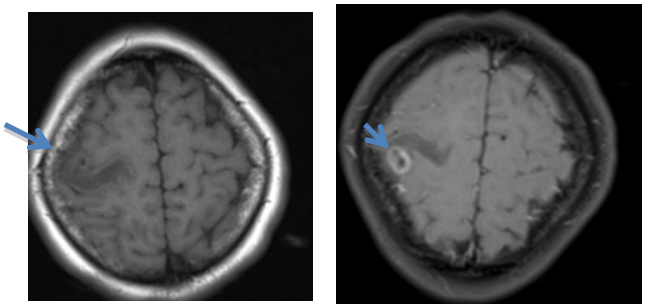


Figure 4: Brain Infection
Abscess in a 28 years old female with epilepsy referred for Brain MRI at Muhimbili National hospital . A) Axial T1W ;hypointense ring lesion with surrounding edema seen on the right parietal lobe B) T1W + C; the lesion shows ring enhancement on contrast study

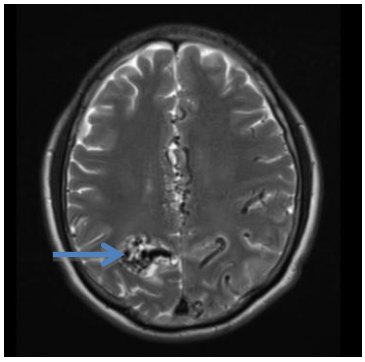


Figure 5: Atriovenous Malformation
Cerebral vascular malformations in a 43 years old female with epilepsy referred for Brain MRI at Muhimbili National Hospital. Axial T2 W image showing flow voids within the lesion seen on the right parietal lobe.

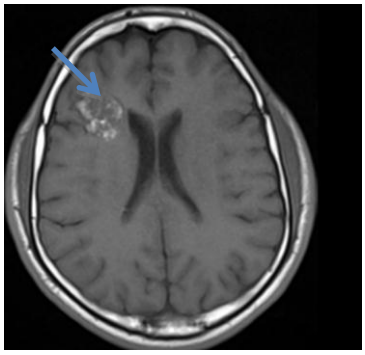


Figure 6: Intracerebral hemorrhage
in a 32 years old female with epilepsy referred for Brain MRI at Muhimbili National Hospital. Axial T1W Image showing hyperintese signal lesion on the right frontal lobe. The lesion exhibited flow voids on Susceptibility weighted imaging.

2.10 Data Management and Analysis

Data analysis was done using Statistical package for Social Science (SPSS) version 20. Data analysis compared different variables and different patterns of abnormalities. The outcome was adult patients with epilepsy and patterns of brain MRI. Categorical variables were sex, types of brain abnormalities, affected lobes and diffusion-weighted characteristics of the abnormal lesions. Continuous variable was age. Comparison between categorical variables was analyzed using two-tailed Chi-square test. Comparison between continuous and categorical variables was analyzed by using Student t-test for two groups comparison and analysis of variance (ANOVA) for multiple group comparison. P-value of <0.05 was considered to indicate statistically significant difference.

2.11 Ethical Considerations

Formal ethical approval was obtained from the Muhimbili university of Health and Allied Sciences Senate Research and Publications Committee. All ethical issues were adhered to as per Senate Research and Publications Committee criterion.

Permission to conduct the study at MNH Radiology department was obtained from MNH Authority.

The Researcher introduced herself to individual patients. The Investigator explained the purpose of the study before asking the patient to participate in the study. Only those patients who freely gave consent were included in the study. All patients' information was kept confidential. The Interview was conducted in a private room. Identification numbers were used on questionnaires and clinical forms instead of patient's name. Refusal to participate in this study did not in any way affect the patient's right to receive standard treatment

CHAPTER THREE

3 RESULTS

3.1 Profile of the study Participants

The study included 65 adults whose age ranged between 18 and 65 years. The females were 38(58.5%) and males 27(41.5 %). Most of patients were adolescents and young adults aged between 18-20 years (24.6 %) and between 21-30 years (20%) (Figure 7). The mean age was 36.4 ± 15.8 and most of our patients had adult onset epilepsy while seven had childhood onset of epilepsy.

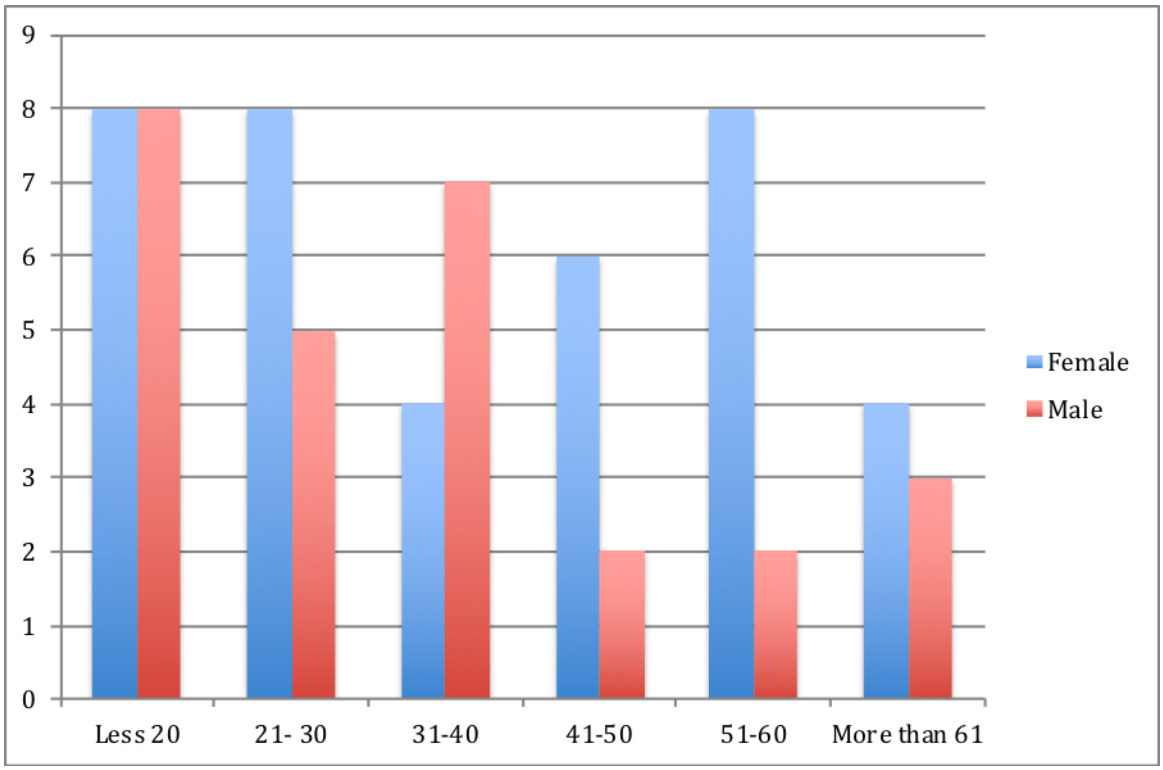


Figure 7: Frequency distribution graph of study participants by age and sex.

3.2 Proportion of patients with underlying brain abnormalities on MRI by age and sex.

Thirty (46.2 %) patients had brain abnormalities while 35 (53.8 %) had normal brain MRI findings. The most frequent observed abnormalities were brain atrophy (10.8%) followed by brain infarction (9.2%). Other abnormalities noted were white matter disease (6.2%), tumor (4.6%), focal cortical dysplasia (4.6%), mesial temporal sclerosis (3.1%), atriovenous malformations (3.1%), intracerebral hemorrhage (3.1 %), infection (1.5%). The proportions of brain abnormalities were higher in males (48.1%) as compared to female (44.7%). However, we note that highest number of patients with brain abnormalities were aged more than 60 years followed by young adults between 21-30 years and those who were less than 20 years. The mean age for patients who presented with normal MRI findings was 33 years while for the patients who presented with abnormal MR findings was 38 years (p= 0.913) (Table 1).

Table 1: Distribution of patients with brain abnormalities on MRI by Age and Sex

		MRI		**Total**
		Normal N=35	Abnormal N=30	
Age Group (%)	Less 20	10(62.50)	6(37.50)	16(100.00)
	21- 30	7(53.80)	6(46.20)	13(100.00)
	31-40	6(54.50)	5(45.50)	11(100.00)
	41-50	5(62.50)	3(37.50)	8(100.00)
	51-60	5(50.00)	5(50.00)	10(100.00)
	More 60	2(28.60)	5(71.40)	7(100.00)
	Total	35(53.80)	30(46.20)	65(100.00)
Sex (%)	Female	21(55.30)	17(44.7)	38(100.00)
	Male	14(51.9)	13 (48.10)	27(100.00)
	Total	35(53.80)	30(46.2)	65(100.00)

3.3 Types of Brain MRI abnormalities in adult patients with epilepsy.

Most common presenting abnormalities were brain infarction in which had both acute and chronic presentations and brain atrophy. White matter disease was seen in four patients. Focal cortical dysplasia was also seen in three patients, while intracranial hemorrhage, atriovenous malformation and mesial temporal sclerosis was seen in two patients each. Brain infection seen was brain abscess that was pyogenic in nature. We saw three patients who had tumors of which two were gangliogliomas noted by MRI and one had low-grade astrocytoma (Table 2)

3.4. Distribution of types of brain abnormalities on MRI by age and sex

There was no relationship between types of brain abnormalities and age or sex (table 2 &3)

Table 2: Frequency distribution of Brain MRI findings by sex.

Brain MRI findings	Sex		Total (%)	P (Value)
	Female (%)	Male (%)		
Normal	21(55.30)	14(51.90)	35(53.80)	
Infections	0(0.00)	1(3.70)	1(1.50)	
Tumors	1(2.60)	2(7.40)	3(4.60)	
Cerebral Infarction	3(7.90)	3(11.10)	6(9.20)	(0.816)
Intracranial Hemorrhage	2(5.30)	0(0.00)	2(3.10)	
Atriovenous Malformations	1(2.60)	1(3.70)	2(3.10)	
Brain Atrophy	5(13.20)	2(7.40)	7(10.80)	
Focal cortical Dysplasia	2(5.30)	1(3.70)	3(4.60)	
White Matter Disease	2(5.30)	2(7.40)	4(6.20)	
Mesial Temporal Sclerosis	1(2.60)	1(3.70)	2(3.10)	
Total	38(100.00)	27(100.00)	65(100.00)	

Table 3: Distribution of types of brain abnormalities on MRI by mean age

	N	Mean	P-value
Normal	35	33.69	
Infections	1	33	
Tumors	3	43.67	**1.015**
Cerebral Infarction	6	37	
Intracranial Heamorrhage	2	41.5	
Atriovenous Malformations	2	31.5	
Brain Atrophy	7	47.57	
Focal cortical Dysplasia	3	26	
White Matter Disease	4	37.75	
Mesial Temporal Sclerosis	2	35.5	
Total	65	36.06	

3.5 Location of brain abnormalities

Our study noted that the most common affected lobe was the parietal lobe. It was noted that cerebral infarction and deep white matter diseases were mostly seen at the parietal region. The frontal lobe was mostly affected by tumors and cortical dysplasia, while most brain atrophy was mostly localized at the temporal lobes. Mesial temporal sclerosis also was noted at the hippocampal area of the temporal lobe. The occipital lobe was the least affected lobe. There were no abnormalities seen at the cerebellum (P=0.094). There was no association between the affected lobe and the abnormalities seen (Table 4)

Table 4: Distribution of epileptogenic lesions by site (affected lobes).

Brain abnormalities	**Affected Lobes (%)**				**Total**
	Frontal Lobe	Temporal Lobe	Occipital lobe	Parietal lobe	
Infections	1(14.30)	0(0.00)	0(0.00)	0(0.00)	1(3.30)
Tumors	2(28.60)	0(0.00)	0(0.00)	1(7.70)	3(10.0)
Cerebral Infarction	0(0.00)	0(0.00)	2(50.00)	430.80	6(20.0)
Intracranial Hemorrhage	1(14.30)	0(0.00)	0(0.00)	1(7.70)	2(6.70)
Atriovenous Malformations	0(0.00)	0(0.00)	1(25.00)	1(7.70)	2(6.70)
Brain Atrophy	2(28.60)	3(50.00)	1(25.00)	1(7.70)	7(23.0)
Focal cortical Dysplasia	1(14.30)	1(16.70)	0(0.00)	1(7.70)	3(10.0)
White Matter Disease	1(0.00)	0(0.00)	0(0.00)	3(30.0)	4(13.0)
Mesial Temporal Sclerosis	0(0.00)	2(33.30)	0(0.00)	0(0.00)	2(6.70)
Total	8(100.00)	6(100.00)	4(100.00)	12(100.0)	30(100.00)

3.6 Patterns of diffusion weighted characteristics of brain lesions as seen on MRI.

Restricted diffusion was observed on tumors, infections, brain infarction and brain atrophy. Other brain lesions such as atriovenous malformations, focal cortical dysplasias and mesial temporal sclerosis exhibited (P=0.16). This shows there was no statistical significance between the brain abnormalities noted and the diffusion-weighted characteristics.

Table 5: Frequency distribution of brain abnormalities by diffusion weighted characteristics

Brain abnormalities	Diffusion restriction		Total
	Restricted Diffusion (%)	No restriction (%)	
Infections	1(6.30)	0(0.00)	1(3.30)
Tumors	3(18.80)	0(0.00)	3(10.00)
Cerebral Infarction	3(18.80)	3(21.40)	6(20.00)
Intracranial Hemorrhage	1(6.30)	1(7.10)	2(6.70)
Atriovenous Malformations	0(0.00)	2(14.30)	2(6.70)
Brain Atrophy	1(6.30)	6(42.90)	7(23.30)
Focal cortical Dysplasia	2(12.50)	1(7.10)	3(10.00)
White Matter Disease	3(18.80)	1(7.10)	4(13.30)
Mesial Temporal Sclerosis	2(12.50)	0(0.00)	2(6.70)
Total	16(100.00)	14(100.00)	30(100.00)

CHAPTER FOUR

4.1 DISCUSSION

Epilepsy is a debilitating neurological disorder that severely interferes with a person's livelihood and status in the community. The ILAE commission recommends neuroimaging in all patients with epilepsy to establish the underlying brain abnormalities(3). There is low rate of neuroimaging in patients with epilepsy in low and Middle-income countries; this can probably be attributed to decreased awareness of causes, availability of experts, and diagnostic facilities.

There are a number of studies that have been done locally and mostly in the rural regions of Tanzania where there is presumed high incidence of epilepsy. These studies show that epilepsy is more common in females and young adults or adolescents (7)(8).

In the current study we had sixty-five (65) adult patients with epilepsy were included; the proportion of females was higher at 58.5 % as compared to males. And the age groups that were mostly affected were young adults less than 20 years and 31-40 years at 24.6 % and 20.0 % respectively, these observations are in keeping with findings of other studies elsewhere (7)(8). Most of our patients had adult onset epilepsy while seven had childhood onset of epilepsy. We also included patients with previous stroke and head trauma as these have been noted to be secondary causes of epilepsy and are included in the practical definition of epilepsy and as it has been proposed by the International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE) (1)(18).

In this study we used 1.5 T MRI machines, where 46.2 % of patients had brain abnormalities and 53.8 % had normal brain MRI. Patients with brain abnormalities were older (mean age 38) as compared to those with normal brain MRI (mean age 33). In as much as we cannot quantify that these were the primary epileptogenic lesions we see that more studies done have indicated similar findings (19) (12). In the current study, the observed brain abnormalities included: brain atrophy was focal found in patients of a mean age of 47 years (10.8%) brain infarction (9.2%), white matter disease (6.2%), tumors (4.6%), focal cortical dysplasia (4.6%), mesial temporal sclerosis (3.1%), atriovenous malformations (3.1%), intracerebral hemorrhage (3.1 %) and infection (1.5%). These

findings are in concordance with the findings of previous studies by Kuzniecky et al(4) ,L Li et al(10)Winkle et al(19) and Betting et al(12). Our study indicated that most brain abnormalities seen were brain atrophy at (10.8%) and brain infarction at (9.2%), this is congruent with a study done by Winkler et al (19) in rural Tanzania on patients with epilepsy and nodding syndrome in an area endemic for onchocerciasis. In their study, brain atrophy was the most common abnormality (12/32), while 10/32 patients had normal findings on MRI (19). Though other studies done on neuroimaging of epilepsy have noted hippocampal sclerosis to be the commonest epileptogenic lesion (4)(10)(14), it was the second most common pathology seen (9/32) in the study done by Winkler et al(19) . While our study found out only 2 (6%) of patients had mesial temporal sclerosis. This study also noted the mean age of patients with brain atrophy was 47 years. Cortical atrophy has been noted to be present in patients with idiopathic generalized epilepsy as studied by Betting et al(12). Brain infarction was seen in patients who presented with acute stroke; they exhibited acute cerebral infarction, patients who had previous insult; exhibited chronic infarction the mean age of patients who presented with that was 37 years. Acute stroke has been studied to be a cause of epilepsy, this has been shown by Szabo et al in their study with use of DWI and perfusion MRI in patients who had stroke and presented with complex partial seizures(15). In the current study white matter abnormalities, atriovenous malformation and tumors were mostly seen in young adults this findings mirror study done by Betting et al(12) and Winkler et al(19). There was one case of a cerebral infection seen which was pyogenic. There are studies that have associated brain infection as a cause and risk factor for epilepsy as described by Vezzani et al(20). There was no statistically significant association between the age and the brain abnormalities or with sex and the brain abnormalities.

Previous studies done have indicated that temporal lobe is the most common site of epileptogenic lesions followed by frontal lobe(10). However, we found that the parietal lobe was the most affected lobe. The occipital lobe was the least affected lobe, while the frontal lobe and the temporal lobe had almost the same frequency of affliction. However there was no statistical significance between location of the epileptogenic lesion and sex or age.

Previous studies done show that restricted diffusion is seen in patients with epilepsy who had abnormalities like acute stroke, infection and mesial temporal sclerosis in the post ictal

phases (13,15,16,17). This is comparable to this study as it can postulate that restricted diffusion seen was due to a seizure episode in patients who presented with acute infarction. infection and mesial temporal sclerosis. However, there was no statistically significant difference in diffusion-weighted characteristics of different types of lesions.

CHAPTER FIVE

5.1 CONCLUSION

Underlying structural brain abnormalities on MRI are common in adult patients with epilepsy as almost half of the patients who were referred for Brain MRI had abnormal findings. The most common abnormalities are brain infarction and temporal lobe brain atrophy. Diffusion weighted Imaging is useful in differentiating different types of brain abnormalities. Epilepsy is a debilitating condition and as such it should be treated with urgency when it comes to neuroimaging diagnosis. MRI has been established to be a superior tool in imaging as it helps with better resolution and better diagnosis of structural abnormalities. More females were affected and higher incidence noted in adolescents and young adults. As such, when we subject our epilepsy patients to MRI it will help identify epileptogenic lesions that are amenable to treatment and surgery hence better and improved outcomes for our patients.

5.2 RECOMMENDATIONS.

Brain MRI should be recommended to all adult patients with epilepsy, as some of the lesions are easily amenable to treatment. Not only that but also MRI is useful at differentiating types of abnormalities hence helps in making accurate and precise management.

Larger population based and prospective studies are needed to establish the importance of MRI in epilepsy management.

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APPENDICES

Appendix I: Questionnaire

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE - DEPARTMENT OF RADIOLOGY

P.O.BOX 65001 MUHIMBILI

DAR ES SALAAM

TANZANIA

Circle the appropriate number

Identity number ;

DOB:…… Sex : 1. Female 2. Male

Age(Years)…….

Part 1

Presenting symptom & signs

Convulsions	1. Yes	2. No
○ Episodes		
○ Duration		
Fever	1.Yes	2.No
Head Trauma	1.Yes	2.No
Previous stroke	1.Yes	2. No
Childhood febrile seizures	1. Yes	2. No
Onset of epilepsy	1. In childhood	2. Adult

Part 2. Image findings

Infection	1. Present	2. Absent
Infection Type	1.Fungal	
	2. Bacterial	
	3. Parasitic	

	4. Viral	
Tumors	1. Yes	2. No.
	1. DNET	
	2. Ganglionoma	
	3. Astrocytoma	
	4. Oligodendrocytoma	
Lobes Affected	1. Yes	2. No
	1. Frontal lobe	
	2. Temporal lobe	
	3. Occipital lobe	
	4. Parietal	
	5. Cerebellum	
Mesial Temporal Sclerosis	1. Yes	2. No
DWI	`1. Restricted diffusion	
	2. No restricted diffusion	
Other abnormalities:	1.Brain infarction	
	2. Intracranial Hemorrhage	
	3. Arteriovenous malformations	
	4. Brain Atrophy	
	5. Focal Cortical Dysplasia	
	6. White matter disease	

Appendix II: Consent Form (English Version)

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

DIRECTORATE OF RESEARCH AND PUBLICATIONS, MUHAS

ID-NO…

Consent to Participate in a Study

My name is Dr. Roselyne Okello. I am conducting study on Patterns of Brain MRI among adult patients with epilepsy referred to Radiology department at MNH/ MUHAS for brain MRI.

Study Purpose

The study is conducted as partial fulfillment of the requirements for the degree of Master OF Medicine in Radiology at MUHAS. This study aims to establish the magnitude and extent of structural brain abnormalities by looking at the most common patterns by using MRI in patients with epilepsy at Muhimbili National Hospital. You are being asked to participate in this study because your information on symptoms and findings will help to establish the radiological pattern of these problems. Kindly be honest and true for accuracy of the results that could lead to better intervention and recommendations in future.

How to be involved

The Patients who agree to participate in this study will be required to sign the consent form, then interviewed after that.

Confidentiality

The information obtained from you will be confidential. No name will appear on any document of this study instead Identification numbers will be used.

Participation and Right to Withdraw

Involvement in this study is voluntary. You can participate or refuse to participate from this study. Refusal to participate from this study will not interfere with your management.

Benefits

The information that you provide will help us to correlate the MRI patterns of Epilepsy in adults and associated presenting symptoms. Thus the study outcomes will help to raise awareness and improve patients' management thus improve quality of life.

Contact Personally

If you ever have questions about this study, you should contact the Principal Investigator, **Dr. Roselyne A. Okello,** Muhimbili University of Health and Allied Sciences, P. O. Box 65001, Dar es Salaam. Tel. 0685679755**.**

In case you have questions about your rights of participation in this study, you may contact **Dr. Bruno F. Sunguya, Chairperson of the Senate Research and Publications Committee**, P. O. Box 65001 DSM. Telephone**:** +255 022 2152489 and **Dr. Mboka Jacob who is the supervisor of this study (Tel. +255 715 828 834)**

Participant agrees.

I ……. have read the contents in this form. My questions have been answered. I am willing to participate in this study.

Signature of participant ……Date…….……

Signature of Researcher ……..Date…….

Appendix III: Consent Form (Swahili Version)

CHUO KIKUU CHA SAYANSI ZA AFYA MUHIMBILI

KURUGENZI YA TAFITI NA UCHAPISHAJI

FOMU YA RIDHAA

Namba ya utambulisho ---

Ridhaa ya kushiriki kwenye utafiti

Habari! Jina langu ni Dr. Roselyne Okello nafanya utafiti wenye lengo la kujua kwa uhalisia ukubwa wa na kuangalia magonjwa ya ubongo kwenye MRI yanayo ambatana na kifafa kwa wagonjwa wanaofanyiwa MRI ya kichwa kwenye idara ya Radiologia katika Hopitali ya Taifa Muhimbili.

Madhumuni ya Utafiti huu ni pamoja na kutimiza sehemu ya matakwa ya shahada ya uzamili ya matibabu kitengo cha vipimo vya mionzi (Radiology) Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili. Hali kadhalika kupata vipimo ambavyo vinaweza kutumika kwenye matibabu ya Wagonjwa.

Jinsi ya kushiriki

Ukikubali kushiriki katika utafiti huu, utasailiwa alafu utatakiwa kujibu maswali kutoka kwenye dodoso lililoandaliwa alafu utaendelea na kipimo kama kawaida.

Usiri

Taarifa zote zitakazokusanywa kupitia dodoso hili zitakuwa ni siri. Jina lako halitatumika badala yake tutatumia namba ya utambulisho.

Uhuru wa kushiriki na haki ya kujitoa

Kushiriki kwenye utafiti huu ni hiari. Unaweza kushiriki au kukataa kushiriki na hii haitakuondolea haki ya kupata matibabu yako.

Nani wa kuwasiliana naye

Kama una maswali kuhusiana na utafiti huu, wasiliana na mtafiti mkuu, Dr. Roselyne Okello, Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili, S. L. P. 65001, Dar es Salaam. Simu 0685679755. **Dr. Bruno F.Sunguya, Mwenyekiti wa kamati ya Utafiti**

na Uchapishaji, **S.L.P 65001, Dar es Salaam. Simu +255 022 2152489au msimamizi wa utafiti huu Dr. Mboka Jacob.Simu 0715 828 834**

Kama umekubali kushiriki weka sahihi

Mshiriki nimekubali …….....Mimi**.....** nimesoma maelezo ya fomu hii nimeyaelewa na nimekubali kushiriki katika utafiti huu.

Sahihi ya mshiriki…… Tarehe ya kutia sahihi…….....

Sahihi ya mtafiti…… Tarehe ya kutia sahihi……