PREVALENCE AND PATTERN OF WHITE MATTER ABNORMALITIES IN ADULT PATIENTS REFERRED FOR BRAIN MAGNETIC RESONANCE IMAGING AT MUHIMBILI NATIONAL HOSPITAL

Doreen Muola, MD

MMed (Radiology) Dissertation
Muhimbili University of Health and Allied Sciences
October, 2017

Muhimbili University of Health and Allied Sciences

Department of Radiology and Imaging

PREVALENCE AND PATTERN OF WHITE MATTER ABNORMALITIES IN ADULT PATIENTS REFERRED FOR BRAIN MAGNETIC RESONANCE IMAGING AT MUHIMBILI NATIONAL HOSPITAL

By

Doreen Muola

A Dissertation Submitted in (partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Radiology and Imaging) of

Muhimbili University of Health and Allied Sciences
October, 2017

CERTIFICATION

The undersigned certifies that she has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Science a dissertation entitled**, "Prevalence and Patterns of White Matter Abnormalities in Adult Patients Referred for Brain Magnetic Resonance Imaging 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, **Doreen N. Muola**, 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**…….

ACKNOWLEDGEMENT

Ultimate gratitude is extended to God the Almighty for His amazing grace throughout the completion of this dissertation.

I am grateful to my lecturers, particularly my research supervisor, Dr. Mboka Jacob, for her unwavering guidance since the development of the research proposal until the writing of this report, along with the whole team of Radiology department at MUHAS.

I appreciate the assistance and support I received from MNH through EMD and radiology departments, for permission to collect data in the facilities and supporting me during the process

My colleagues have always stood by me, their constant reminders and corrections have contributed to the refining of this work

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.

To my Dad and siblings, Thank you for always believing in me and cheering me on.

A very special thanks to my husband, Dr. Aggrey M. Manani, for his love, unwavering support, patience all through, for listening and discussing ideas about this dissertation with me on many occasions, and my daughter Ella N. Manani, for motivating me to push myself beyond my limits.

DEDICATED

To

Memories of My Mother

Petronanda N. Muola (1962 -2004)

Your interest in my education, as in all my ventures was never less than my own. Forever in my heart.

ABSTRACT

Background: White matter Abnormalities are a worldwide problem. They are regularly encountered at health care facilities. Their occurrence varies globally with different rates based on age and sex. Women are generally affected more and with increasing age. White matter abnormalities are associated with an increased risk of stroke, cognitive decline, dementia and death hence affecting the quality of life of the affected individual.

MRI is widely used to diagnose white matter abnormalities which are brought about by a variety of causes. Little is known on MRI patterns of White matter abnormalities in our set up hence this study is aiming at determining the prevalence and pattern of white matter abnormalities using MRI in adult patients referred for brain MRI at Muhimbili National hospital.

Objective: To determine the prevalence and pattern of white matter abnormalities by using Magnetic Resonance Imaging in adult patients referred for brain MRI at Muhimbili National Hospital.

Materials and Methods: This was a descriptive cross sectional study which was conducted at radiology department, Muhimbili National Hospital from June to December 2016. Adults referred for brain Magnetic Resonance Imaging were included in this study. Consenting patients from 18 years of age were consecutively included in the research. Structured questionnaires were used for recording patients' demographics, clinical information and imaging findings obtained from brain MRI images. Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 20. Statistical Association were done by using cross tabulations and Chi-square test was used to compare proportions. P value of < 0.05 was considered statistically significant.

Results: This study included 144 adults aged from 18 to 84 years referred to the radiology department for brain Magnetic Resonance Imaging. The prevalence of White matter abnormalities was 47.9%. The proportion of adults with white matter abnormalities according to sex was 29(46.8%) for male and 40(48.8%) for female and it was increasing with age. The

most frequent pattern of white matter abnormalities was periventricular (41.4%). The research showed significant correlation between hypertension and white matter abnormalities (P value =0.0001). There was also significant correlation between impaired cognitive function, depression and dementia and white matter abnormalities.

Conclusion: Almost half of the studied individuals had white matter abnormalities. Majority of whom were patients aged 60 years and above. Female patients appear to be more affected than males by white matter abnormalities though this was not statistically significant in our study. Hypertension was a significant risk factor. Impaired cognitive function, depression and dementia are significantly related to white matter abnormality.

Recommendations: Large population based prospective studies should be carried out in order to be able to have results that could be generalized to the community. Not only that but also further studies are needed to explore various risk factors including genetic factors to underpin the development of white matter abnormalities in affected individuals. MRI is recommended to adult patients with impaired cognitive function to estimate the severity and monitor disease progress.

TABLE OF CONTENTS

CERTIFICATION i
DECLARATION ANDCOPYRIGHT ii
ACKNOWLEDGEMENT iii
DEDICATED iv
LIST OF TABLES ix
LIST OF FIGURES x
LIST OF ABBREVIATION xi
CHAPTER ONE 1
1.0 INTRODUCTION 1
1.1 BACK GROUND 1
1.2 Literature Review 2
1.3 Problem Statement 5
1.4 Rationale 5
1.5 Research Question 6
1.6 Objectives 6
1.6.1 Broad Objective 6
1.6.2 Specific Objectives 6
CHAPTER TWO 7
2.0 RESEARCH METHODOLOGY 7
2.1 Study Design 7
2.2 Study Population 7
2.3 Study Area / Study Period 7
2.4 Sample Size Estimation 7
2.5 Sampling Technique 8
2.6 Inclusion Criteria 8
2.7 Exclusion Criteria 8
2.8 Data Collection 8
2.9 Imaging and Evaluation 9

2.9.1 MR Imaging 9
2.11 Data Management and Analysis 11
2.12 Ethical Considerations 11
CHAPTER THREE 12
3.0 RESULTS 12
3.1 Profile of the study Participants 12
3.2 Prevalence of white matter abnormalities according to age and sex in adult patients referred for brain MRI at Muhimbili National Hospital. 13
3.3 Pattern of white matter abnormalities (N=69) 14
3.4 Factors associated with white matter abnormalities. 17
3.5 Symptomatology of patients with white matter abnormalities 19
3.6 The comparison of pattern of white matter abnormalities and presenting symptoms 20
CHAPTER FOUR 26
4.0 DISCUSSION 26
CHAPTER FIVE 29
5.0 CONCLUSION AND RECOMMENDATION 29
5.1 Conclusion 29
5.2 Recommendation 29
APPENDICES 34
Appendix I: Questionnaire 34
Appendix II: Consent Form(English Version) 37
Appendix III: Consent Form (Swahili Version) 39

LIST OF TABLES

Table 1: Percentage Distribution of study participants by demographic characteristics in adult patients referred for brain MRI at Muhimbili National Hospital …….…….12

Table 2: Frequency distribution of adult patients with white matter abnormalities referred for brain MRI at Muhimbili National Hospital by Sex.……...13

Table 3: Percentage Frequency distribution of Periventricular White matter abnormalities by adjacent ventricles in adult patients' referred for brain MRI at Muhimbili National Hospital**.**……15

Table 4: Risk factors in adult patients with white matter abnormalities referred for brain MRI at Muhimbili National Hospital**.**……...…….....17

Table 5: The adult patient's symptomologies with white matter abnormalities in adult patients' referred for brain MRI at Muhimbili National Hospital ……..18

Table 6: Cognitive decline associated with white matter abnormities by location in adult patients' referred for brain MRI at Muhimbili National Hospital……19

Table 7: Dementia associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital……..20

Table 8: Depression associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital…….…….21

Table 9: Impairment of upper extremity functions associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital…….22

Table 10: Impairment of gait associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital…….……...…...……23

Table 11: Urinary dysfunction associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital…..……...…...…….24

LIST OF FIGURES

Figure 1: Brain MRI images from different patients, FLAIR axial images.....…….10

Figure 2: Frequency distribution of adult patients with white matter abnormalities referred for brain MRI at Muhimbili National Hospital by age ……...13

Figure 3: The MRI pattern of the periventricular white matter abnormalities according to size in adult patients' referred for brain MRI at Muhimbili National Hospital…….……..14

Figure 4: The adult patients with subcortical white matter abnormalities according to size in adult patients' referred for brain MRI at Muhimbili National Hospital....…… ……...15

Figure 5: The subcortical patterns for the adult patients with subcortical white matter abnormalities according to location referred for brain MRI at Muhimbili National Hospital....……..…… …16

LIST OF ABBREVIATION

ADC	Apparent diffusion coefficient
CSF	Cerebrospinal fluid
Fig.	Figure
FLAIR	Fluid - attenuated inversion recovery
DM	Diabetes Mellitus
HIV	Human Immunodeficiency Virus
HTN	Hypertension
MNH	Muhimbili National Hospital
MRI	Magnetic resonance imaging
SCWMA	Subcortical white matter abnormalities
SPSS	Statistical Package for the Social Sciences
PVWMA	Periventricular white matter abnormalities
WM	White matter
WMA	White matter abnormalities
Tsh	Tanzanian shillings

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

White matter abnormalities are a worldwide problem. They are regularly encountered at health care facilities. Their occurrence varies globally with different rates based on age and sex. Women are generally affected more than the males and with increasing age (1)(2).

White matter consists of glial cells and myelinated axons that transmit signals from one region of the cerebrum to another and between the cerebrum and the lower brain centers. It lies below the cortical surface and comprises approximately 40-50 of total volume of the healthy young adult human brain (3). Both white and grey matter is of equal importance as the cortical areas cannot fulfill their functions without the white matter connections. There is therefore importance in knowing the white matter connections as they are susceptible to certain diseases such as cerebrovascular diseases, infection, multiple sclerosis and etc.

Conventional neuroimaging identifies normal white matter tracts which appear homogenous. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) in the detection of white matter abnormalities of the brain (4). Abnormal signals in cerebral white matter are increased in prevalence and severity in association with aging and cerebrovascular risk factors among older individuals (5)(6)(7). They are frequently observed on T2 weighted magnetic resonance imaging (T2W MRI) of the brain. They are alternatively referred to as lesions or hyperintensities, which is because of their white appearance on T2W MRI (8). On CT scan they are hypodense. They are usually caused by demyelination (9), arteriosclerosis, and perivascular space dilatation (10), gliosis, loss of axons and oligodendroglial cells and blood vessels stenosis.

White matter abnormalities are associated with an increased risk of stroke, cognitive decline, dementia and death (8). The aim of this study is to determine the prevalence and MRI patterns of white matter abnormalities in Tanzania as little is known.

1.2 Literature Review

White matter abnormalities prevalence varies considerably among several MRI studies depending on study design, study population and rating scales. Estimates vary from as low as 5 up to 95(1)(8). White matter abnormalities increase in prevalence and severity in association with aging and cerebrovascular risk factors among older individuals (5)(6)(7). In a study conducted by Park. H et al (2) the prevalence of White matter abnormalities increases with age: the prevalence was 2.4, 9 and 32 for subjects in their 50s, 60s and 70s respectively.

In Africa, data on white matter abnormalities has huge holes. Little is known about the epidemiology and frequent MRI patterns of white matter abnormalities in Africa. The Aric study (11), studied the association between ethnicity and white matter lesions. It found that white matter lesions odds are higher in African Americans than in European Americans and this is attributed to higher mean systolic and diastolic pressures in the African Americans (11)(12).

Women are also found to have a higher degree of white matter abnormalities than men.(1)Other risk factors for WM disease are Hypertension and presence of cardiovascular disease (atherosclerosis), Diabetes Mellitus, Smoking and Low income earners (2)(13)(14). Most of this risk factors occur much earlier in life, when the prevalence of white matter abnormalities is still low.

Unlike the West where multiple sclerosis is the commonest white matter abnormality encountered, in the Tropics infectious and post infectious disorders(Human immunodeficiency virus (HIV), tuberculosis, cytomegalovirus) probably account for a majority of the white matter abnormalities (15)(16). The Hawaii Aging with HIV Cohort describes a 48 prevalence of moderate WM abnormalities among HIV+ patients without neurological disease (17). In another by Lewis J. et al, the prevalence of WM abnormalities is 63.4 in HIV+ patients (18).

White matter abnormalities caused by different disease have a non-specific imaging appearance. However, the white matter abnormalities are categorized based on their appearance on cross sectional imaging. Various patterns are Multifocal disease, confluent

disease or diffuse disease and selective white matter disease in which there is a geographic predilection for involvement of a specific white matter distribution (19).

MRI studies have a high contrast resolution for depiction of white matter abnormalities. Different sequences are used to study the white matter. Most commonly used are T1W MRI, T2W MRI, FLAIR and diffusion weighted MRI. Most studies classify WMAs based on T2W MRI as they appear hyperintense (20–22).

There are various approaches used to assess pattern of WM abnormalities. The commonest are Fazekas et al (20) , Rotterdam (21) and Ki Woong et al (22). Fazekas et al classified white matter abnormalities into periventricular (a strip of white matter adjacent to the lateral ventricles) and or deep subcortical (the white matter just underneath the gray matter) changes.
According to Rotterdam et al (21) W/M abnormalities classification involves a semi quantitative approach whereby presence, severity and location are noted. Ki Woong et al (22) classified according to etiology, WMA are sub classified into Ischemic and non-ischemic. Ischemic abnormalities are further divided into Periventricular white matter abnormalities (range 3-13mm from ventricular surface), Juxtacortical white matter (within 4mm from corticomedullary junction) and deep white matter abnormalities (located between the previous two). Non-ischemic WMAs are usually within 3mm from ventricular surface(juxta ventricular WM) and likely from CSF leakage (22).

Diffusion weighted imaging (DWI) has also been used to study WM abnormalities, provides functional information at the cellular level and explores the random Brownian motion of water molecules. The normal or abnormal diffusion properties of a tissue can be quantified by using the apparent diffusion coefficient (ADC). The ADC measures the magnitude of diffusion of water molecules within a tissue thus serving as a biomarker of tissue response(to ischemia, infection, tumors) (23).
Diffusion weighted images are based on a T2W background image attenuated by the rate of apparent diffusion gradient. Increased water diffusion will present as hyposignal and decreased water diffusion present as hypersignal (24). In a study done by Denis Le Bihan et al (25) showed that, the differences in ADC measured in different biologic tissues could be used

to distinguish between normal and pathologic tissues. Highest ADC values, in a normal brain, are usually in newborns and usually decrease with age due to myelination. In adults above 40 years of age high ADC values were found in cerebral white matter with increasing age. White matter abnormality lesions show high ADC values and with no restricted diffusion. (26)

White matter abnormalities could be asymptomatic or could be associated with an increased risk of stroke, cognitive decline, dementia, impairment of upper extremity functions and gait, urinary dysfunction and death (2)(8)((14)(27)(28). Periventricular white matter abnormalities are related to cognitive decline (1,21). Subcortical white matter abnormalities are related to late on-set depression (29).

White matter abnormalities are a worldwide problem. They are regularly encountered at health care facilities. Their occurrence vary globally. The aim of this study is to determine the prevalence and MRI patterns of white matter abnormalities in Tanzania as less is known.

1.3 Problem Statement

White matter abnormalities increase in prevalence and severity in association with aging and cerebrovascular risk factors among older individuals (5)(6)(7). The prevalence of white matter abnormalities varies considerably among several MRI studies and estimates vary from as low as 5 up to 95 (1)(8).

Risk factors for WM disease are Age, Female Sex, Hypertension and presence of cardiovascular disease(atherosclerosis), Diabetes Mellitus, Smoking and Low income earners (1)(2)(13)(14). If the risk factors are identified and causal factors controlled early then the risk of WMA in later stages of life could be reduced (28).

WMA are associated with significant impact on one's personal life, family life and the society. Cognitive function is affected and physical function reduced leading to dependence on relatives. Early identification and treatment of WMA reduces the fast progress of the disease improving the prognosis (30).

The aim of this study is to establish the magnitude of the white matter abnormalities in relation to prevalence of the abnormalities in Tanzania as little is known. The study will also establish the common white matter abnormality patterns using MRI in adult patients referred for brain MRI at Muhimbili National hospital. We will also be able to establish white matter abnormalities and associated risk factors.

1.4 Rationale

White matter Abnormalities are common with aging have complications such as cognitive function decline, dementia, decline in physical function and death. Little is known in Tanzania with regards to the prevalence and MRI findings of White matter abnormalities. Therefore the aim of this study is to determine prevalence, MRI findings of white matter abnormalities and determine relationship with presenting symptoms and risk factors and the association between these findings and the presenting symptoms. The study is going to establish baseline data to be used in future white matter neuroimaging studies.

1.5 Research Question

1. What is the prevalence of White matter abnormalities in adult patients sent for brain MRI at Muhimbili National Hospital?
2. What are the MRI patterns of white matter abnormalities in adult patients sent for brain MRI at Muhimbili National Hospital?
3. What is the relationship between White matter abnormalities on MRI and associated risk factors and symptoms?

1.6 Objectives

1.6.1 Broad Objective

To determine the prevalence and pattern of white matter abnormalities by using Magnetic resonance imaging in adult patients referred for brain MRI at Muhimbili National Hospital..

1.6.2 Specific Objectives

1. To determine the **prevalence** of adults with white matter abnormalities according to age and sex.
2. To determine the MRI pattern of white matter abnormalities.
3. To determine factors associated with white matter abnormalities
4. To determine the symptomatology of patients with White matter abnormalities.
5. To compare the pattern of white matter abnormalities and presenting symptoms

CHAPTER TWO

2.0 RESEARCH METHODOLOGY

2.1 Study Design

This study was descriptive cross sectional hospital based research

2.2 Study Population

This included adult patients referred to the radiology department for brain Magnetic Resonance Imaging at Muhimbili National Hospital from June to December 2016.

2.3 Study Area / Study Period

This study was conducted at Muhimbili National Hospital Radiology department. The study was conducted over a period of six months from June 2016 to December 2016.Muhimbili is the national and a teaching hospital in Tanzania. It is located in Dar- es salaam and acts as the main referral center for the 45 million Tanzanian population.

2.4 Sample Size Estimation

Considering the study power of 95, a random error was estimated to be 0.5. Sample size of 144 patients was estimated. The prevalence of white matter abnormalities varies considerably among several MRI studies and estimates vary from as low as 5 up to 95 (1)(8)(31). 10 was used.

The sample size calculated 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 of WMA used was 10 (31).

E- Error margin 0.05.

From this formula the sample size was calculated as follows:

$N = (1.96)^2 \text{ X } 0.10(1 - 0.10) \div (0.05)^2 \approx 138$

We will sample an extra 6 to account for possible non-response

n=138 + 6 (5 of 138)

Thus the sample size in this study is 144 Adults.

2.5 Sampling Technique

Convenience sampling method was used where patients referred for brain MRI were requested to participate.

2.6 Inclusion Criteria

Adults aged 18 and over referred for Brain MRI.

2.7 Exclusion Criteria

Adults with significant lesions impairing the assessment of white matter abnormalities.

216 adults' patients were referred for brain MRI during the study period. 144 patients who fulfilled the criteria were included for the study. Excluded 75 patients (24 brain tumours, 18 brain infarctions, 10 brain infection, 13 brain atrophy, 5 cerebral haemorrhage, 2 posterior fossa abnormalities)

2.8 Data Collection

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

Consenting patients were interviewed by a Principal Investigator by using a close ended structured questionnaire. Data collected also included socio-demographics, clinical symptoms which were cognitive decline, dementia, impairment of upper extremity functions and gait, urinary dysfunction. Risk factors assessed were age, sex, hypertension, diabetes mellitus and history of smoking.

For assessment of risk factors history of the following were enquired; history of high blood pressure, history and of DM, history of cigarette smoking. Patient HIV status, DM and Hypertension were obtained from patient records.

2.9 Imaging and Evaluation

2.9.1 MR Imaging

Imaging was performed by a trained Radiographer. Brain MRI was done using 1.5 T-scanner, (Phillips, Achiever, Best, Eindhoven, Netherlands). The scans consisted of axial T1W (TR/TE) of 400/8 ms), T2W (TR/TE of 3,000/120 ms), Fluid attenuated Inversion Recovery (FLAIR) and Diffusion weighted images included the **matrix** of each sequences to be used.
The slice thickness of 5mm thickness was used. The interslice gap of 224 × 168mm matrix and a field of view of 200 mm was used.

The presence of white matter hyperintensities on T2W Images were regarded as white matter abnormality. Fazeka et al (20) and Rotterdam scan study (21)classifications were used to classify the white matter abnormalities.

1. Fazeka Classification (20) classifies white matter abnormalities into periventricular (a strip of white matter adjacent to the lateral ventricles) and or deep subcortical (the white matter just underneath the gray matter) changes.

2. Using the Rotterdam scan study standardized scale, Periventricular WMA were rated semiquantitively as 0(none), 1(pencil-thin lining), 2(smooth halo) or 3(large confluent) for three separate regions; adjacent to frontal horns (frontal caps) adjacent to the wall of the lateral ventricles (bands) and adjacent to occipital horns (occipital caps). Subcortical WMAs were categorized according to their maximum diameter as small(1-3mm), medium (3-10mm) or large (>10mm) and rated in size per category for Frontal, parietal, occipital and temporal lobes.(21)

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

2.10 Image Evaluation

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

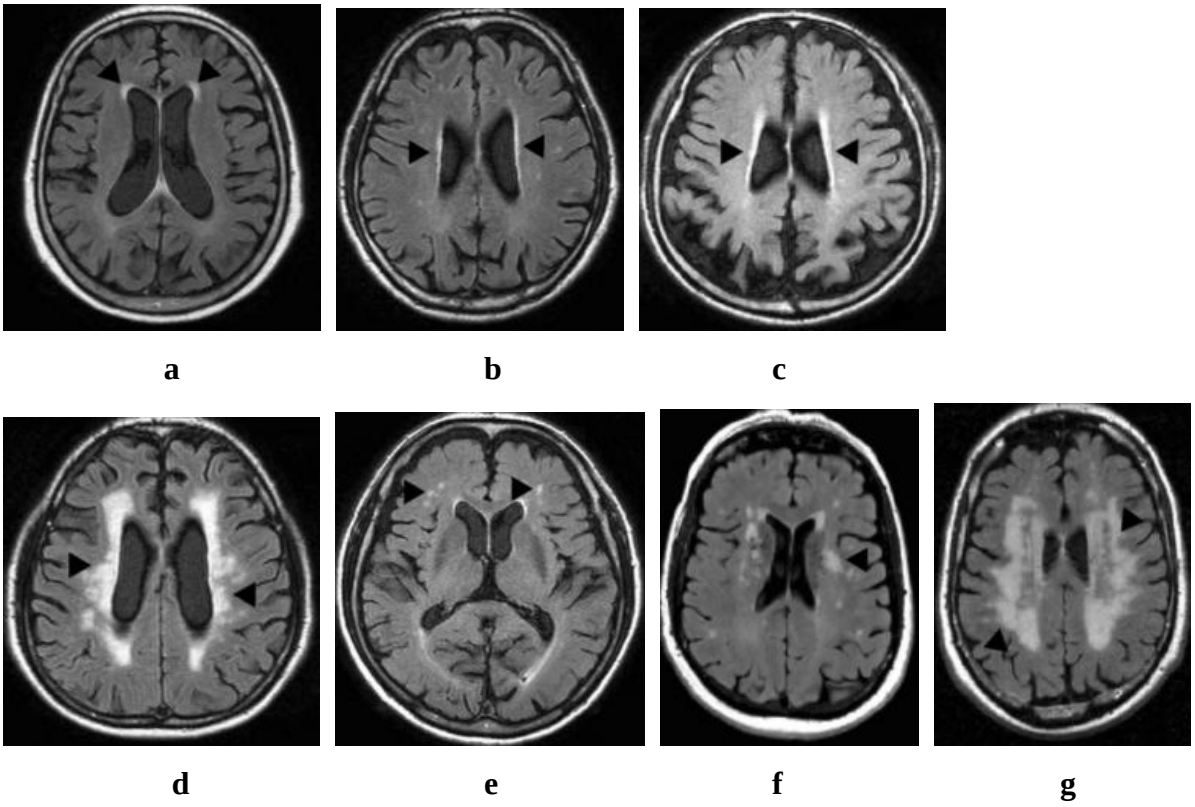

Figure 1. Brain MRI images from different patients, FLAIR axial images (a-g), showing forms of white matter abnormalities (WMA) a). Frontal caps**, b).** Pencil-Thin Lining PVWMA**, c).** Smooth Halo PVWMA**, d).** Irregular PVWMA**, e).** Small size SCWMA**, f).** Medium size/Beginning Confluent SCWMA**, g).** Deep Confluent SCWMA

2.11 Data Management and Analysis

Data analysis was done using SPSS version 20. Data quality check was done by running frequencies daily. Data transformation by recording, counting and cross tabulation was performed and obtained information processed using Pearson chi-square and Fisher's exact test to compare MRI findings and patient demographic and presenting symptoms. Fisher's exact test was used on cells with values less than 5. P-value of <0.05 was considered to indicate statistically significant difference.

Data analysis examined correlations between different variables and White Matter Abnormalities. The outcome was White Matter Abnormalities and the baseline independent variables included age, gender, hypertension, diabetes mellitus, HIV status and smoking status.

2.12 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

3.0 RESULTS

3.1 Profile of the study Participants

The study included 144 adults whose age ranged between 18 and 84 years. The females were 83(57.6) and males 62(42.4). Most of them were aged between 31-40 (23.6) and above 61 (20.1) years. The youngest age category, 18–20, had the smallest number of patients (4.9) followed by the 21-30 category (13.2). The mean age was 46.1 years and a standard deviation of 16.36. (Table 1).

Table 1: **Percentage Distribution of study participants by demographic characteristics in adult patients referred for brain MRI at Muhimbili National Hospital. N=144**

Demographic factors		Number of Participants	Percentage ()
Gender	Male	61	42.4
	Female	83	57.6
	Total	**144**	**100**
Age group (years)	18-20	7	4.9
	21-30	19	13.2
	31-40	34	23.6
	41-50	27	18.8
	51-60	28	19.4
	61+	29	20.1
	Total	**144**	**100**

3.2 Prevalence of white matter abnormalities according to age and sex in adult patients referred for brain MRI at Muhimbili National Hospital.

The observed prevalence of white matter abnormalities was 47.9%. The proportion of adults with white matter abnormalities according to sex was 29(46.8%) for male and 40(48.8%) for female (P = 0.811). [Table 2].

The proportion of white matter abnormalities increased with age and this was statistically significant (p = 0.0001). The above 61 years age group had the highest proportion of adults with White matter abnormalities 85.7% [figure 1]

Table 2: Frequency distribution of adult patients with white matter abnormalities referred for brain MRI at Muhimbili National by Sex. N=144

		White Matter Abnormality			P value(Pearson's X^2)
		Yes (%)	**No (%)**	**Total (%)**	**at 95CI**
Gender	Male	29 (46.8)	33 (53.2)	**62 (100)**	**0.811**
	Female	40 (48.8)	42 (51.2)	**82 (100)**	
	Total	**69 (47.9)**	**75 (52.1)**	**144 (100)**	

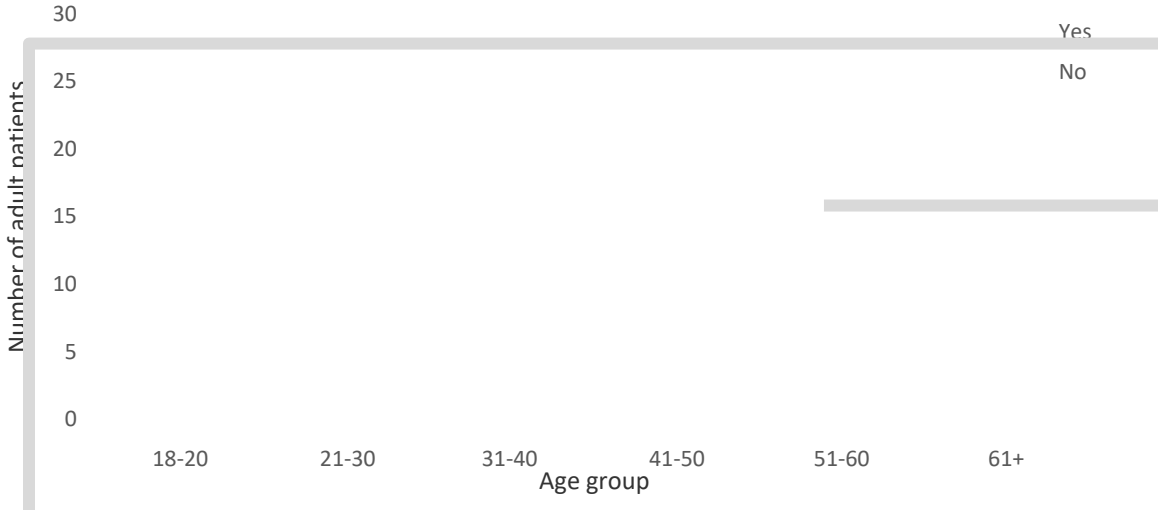

Figure 2: Frequency distribution of adult patients with white matter abnormalities referred for brain MRI at Muhimbili National Hospital by age. N=144.

3.3 Pattern of white matter abnormalities (N=69)

Of all the patients with white matter abnormalities, 41.4% had the periventricular pattern and 38.6% had the subcortical pattern. Among the periventricular white matter size, pencil thin lining WMA 27(39) was the leading size followed by smooth halo WMA 24(35) as shown in the Figure 2 below. Among those with WMA, 13 did not have any of the periventricular pattern of WMA

According to the location of the PVWMA, it was noted that, the WMA adjacent to lateral ventricular walls 58(40.3) were highest followed by WMA adjacent to frontal horns 49(34) [Table 3].

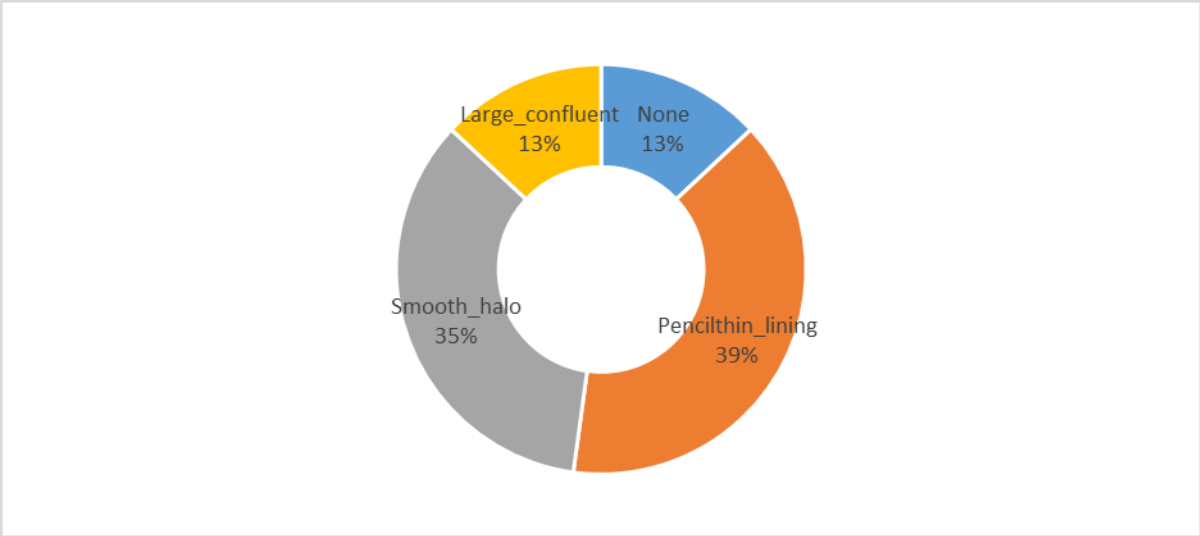

Figure 3: The MRI pattern of the periventricular white matter abnormalities according to size in adult patients' referred for brain MRI at Muhimbili National Hospital. N=69.

Table 3: Percentage Frequency distribution of Periventricular White matter abnormalities by adjacent ventricles in adult patients' referred for brain MRI at Muhimbili National Hospital. n=69)

Location of Periventricular White Matter Abnormality	Frequency	Percentage
Adjacent to frontal horns	49	34.0
adjacent to lateral ventricular walls	58	40.3
adjacent to occipital horns	24	16.7
adjacent to temporal horns	20	13.9

The subcortical white matter abnormalities differed according to size significantly. Most adult patients had small size subcortical white matter abnormality 33(48) followed by medium size 21(30) as shown in the figure 3 below.

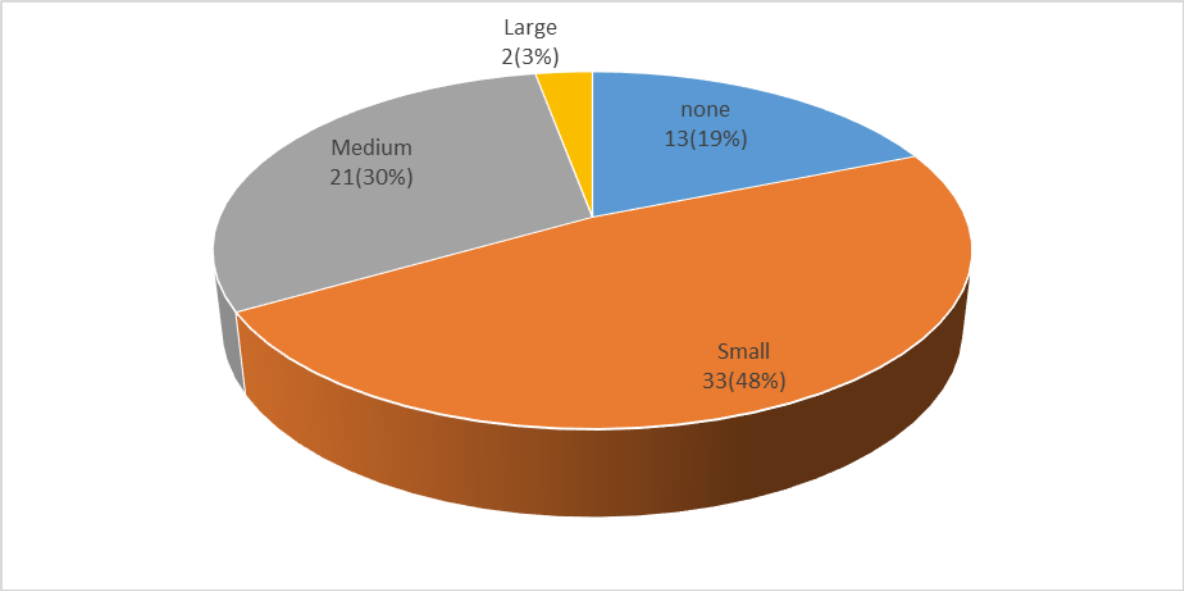

Figure 4: The adult patients with subcortical white matter abnormalities according to size in adult patients' referred for brain MRI at Muhimbili National Hospital. (N=69).

The frontal lobe 56(38.9) was the most affected by the subcortical white matter abnormalities followed by the parietal lobe 43(29.9) and the least affected being the temporal lobe which was 10(6.9) as depicted in the figure 4 below.

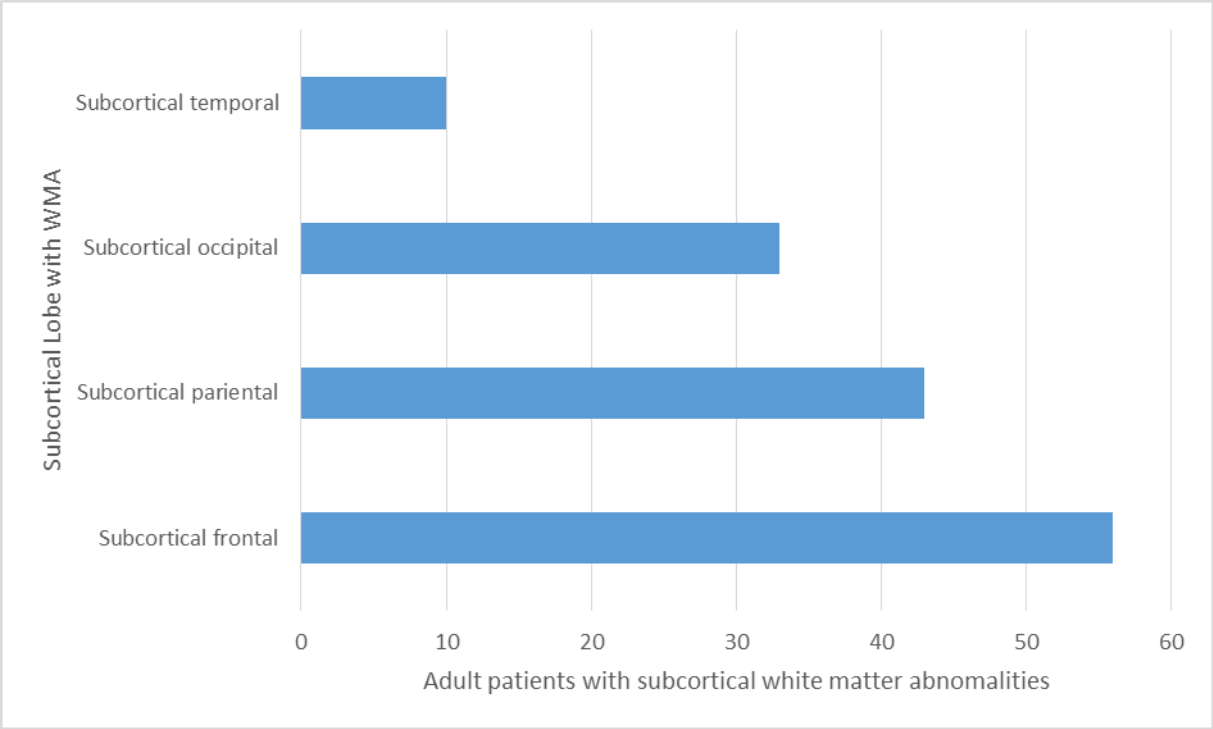

Figure 5: The subcortical patterns for the adult patients with subcortical white matter abnormalities according to location referred for brain MRI at Muhimbili National Hospital. N=69.

ADC MAPS

The results showed that all patients with white matter abnormalities had high ADC values i.e. appeared hyperintense **with no restricted diffusion**.

3.4 Factors associated with white matter abnormalities.

The frequency of WMA was high in patients with hypertension (P= 0.0001) than those with Diabetes Mellitus, HIV and smoking cigarettes (52.2, 14.5, 11.6 and 7.2 respectively). [Table 4]

Table 4: Risk factors in adult patients with white matter abnormalities referred for brain MRI at Muhimbili National Hospital. N=144.

Risk factors		White Matter Abnormality			P value(Pearson's X^2) at 95CI
		Yes (%)	**No (%)**	**Total (%)**	
Hypertension	Yes	36 (52.2)	18 (24)	**54 (37.5)**	**0.0001**
	No	33 (47.8)	57 (76)	**90 (62.5)**	
	Total	**69 (100)**	**75 (100)**	**144 (100.0)**	
Diabetes Mellitus	Yes	10 (14.5)	6 (8)	**16 (11.1)**	0.216
	No	59 (85.5)	69 (92)	**128 (88.9)**	
	Total	**69 (100)**	**75 (100)**	**144 (100.0)**	
HIV	Yes	8 (11.6)	9 (12)	**17 (11.8)**	0.94
	No	61 (88.4)	66 (88)	**127 (88.2)**	
	Total	**69 (100)**	**75 (100)**	**144 (100.0)**	
Cigarette smoking	Yes	5 (7.2)	3 (4)	**8 (5.6)**	0.396
	No	64 (92.8)	72 (96)	**136 (94.4)**	
	Total	**69 (100)**	**75 (100)**	**144 (100.0)**	

3.5 Symptomatology of patients with white matter abnormalities

Cognitive decline, Dementia, Depression, Impaired upper extremity function were all most frequent in patients with white matter disease as compared to those without WMD and these observations were statistically significant. [Table 5].

Table 5: The adult patient's symptomologies with white matter abnormalities in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		White Matter Abnormality			P value(Pearson's X^2) at 95CI
		Yes (%)	**No (%)**	**Total (%)**	
Cognitive decline	Yes	27 (39.1)	2 (2.7)	**29 (20.1)**	**0.0001**
	No	42 (60.9)	73 (97.3)	**115 (79.9)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	
Dementia	Yes	33 (47.8)	3 (4)	**36 (25)**	**0.0001**
	No	36 (52.2)	72 (96)	**108 (75)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	
Depression	Yes	33 (47.8)	5 (6.7)	**38 (26.4)**	**0.0001**
	No	36 (52.2)	70 (93.3)	**106 (73.6)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	
Impairment upper extremity functions	Yes	24 (34.8)	4 (5.3)	**28 (19.4)**	**0.0001**
	No	45 (65.2)	71 (94.7)	**116 (80.6)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	
Gait impairment	Yes	35 (50.7)	9 (12.0)	**44 (30.6)**	**0.0001**
	No	34 (49.3)	66 (88.0)	**100 (69.4)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	
Urinary dysfunction	Yes	9 (13.0)	1 (1.3)	**10 (6.9)**	**0.006**
	No	60 (87)	74 (98.7)	**134 (93.1)**	
	Total	**69 (100)**	**75 (100)**	**144 (100)**	

3.6 The comparison of pattern of white matter abnormalities and presenting symptoms

a) Cognitive decline

The results revealed that cognitive decline was strongly significantly associated with both periventricular and subcortical white matter abnormality patterns. [P=0.00] [Table 6]

Table 6: Cognitive decline association with white matter abnormities by location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		Cognitive decline			P value (Pearson's X^2) at 95%CI
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent to frontal horns	Yes	22 (75.9)	27 (23.5)	**49 (34)**	0.0001
PVWMA adjacent to lateral ventricular walls	Yes	23 (79.3)	35 (30.4)	**58 (40.3)**	0.0001
PVWMA adjacent to occipital horns	Yes	18 (62.1)	6 (5.2)	**24 (16.7)**	0.001
PVWMA adjacent to temporal horns	Yes	15 (51.7)	5 (4.3)	**20 (13.9)**	0.0001
SCWMA frontal lobe	Yes	20 (69)	36 (31.3)	**56 (38.9)**	0.0001
SCWMA occipital lobe	Yes	13 (44.8)	20 (17.4)	**33 (22.9)**	0.002
SCWMA temporal lobe	Yes	5 (17.2)	5 (4.3)	**10 (6.9)**	0.015

b) Dementia

Dementia also had a strongly significant relationship with both periventricular and subcortical white matter abnormality patterns. [P=0.00] [Table 7]

Table 7: Dementia associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		Dementia			P value (Pearson's X^2) at 95%CI
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent to frontal horns	Yes	23 (63.9)	26 (24.1)	**49 (34.0)**	0.0001
PVWMA adjacent to lateral ventricular walls	Yes	27 (75)	31 (28.7)	**58 (40.3)**	0.0001
PVWMA adjacent to occipital horns	Yes	16 (44.4)	8 (7.4)	**24 (16.7)**	0.0001
PVWMA adjacent to temporal horns	Yes	12 (33.3)	8 (7.4)	**20 (13.9)**	0.0001
SCWMA frontal lobe	Yes	26 (72.2)	30 (27.8)	**56 (38.9)**	0.0001
SCWMA parietal lobe	Yes	19 (52.8)	24 (22.2)	**43 (29.9)**	0.001
SCWMA occipital lobe	Yes	17 (47.2)	16 (14.8)	**33 (22.9)**	0.0001
SCWMA temporal lobe	Yes	6 (16.7)	4 (3.7)	**10 (6.9)**	0.008

c) Depression

The results showed that depression had a strongly significant relationship with all white matter abnormality patterns except subcortical WMA affecting the temporal lobe [P=0.079] [Table 8]

Table 8: **Depression associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.**

		Depression			**P value (Pearson's X^2) at 95%CI**
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent frontal horns	Yes	27 (71.1)	22 (20.8)	**49 (34)**	0.0001
PVWMA adjacent to lateral ventricular walls	Yes	30 (78.9)	28 (26.4)	**58 (40.3)**	0.0001
PVWMA adjacent occipital horns	Yes	15 (39.5)	9 (8.5)	**24 (16.7)**	0.0001
PVWMA adjacent temporal horns	Yes	14 (36.8)	6 (5.7)	**20 (13.9)**	0.0001
SCWMA frontal lobe	Yes	26 (68.4)	30 (28.3)	**56 (38.9)**	0.079
SCWMA parietal lobe	Yes	21 (55.3)	22 (20.8)	**43 (29.9)**	0.0001
SCWMA occipital lobe	Yes	17 (44.7)	16 (15.1)	**33 (22.9)**	0.0001
SCWMA temporal lobe	Yes	5 (13.2)	5 (4.7)	**10 (6.9)**	0.0001

d) Impairment of upper extremity functions

Upper extremity function impairment also had a strongly significant relationship with all white matter abnormality patterns except subcortical WMA affecting the temporal lobe [P=0.089] [Table 9]

Table 9: Impairment of upper extremity functions associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		Impairment of upper extremity functions			P value (Pearson's X^2) at 95%CI
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent frontal horns	Yes	21 (75)	28 (24.1)	**49 (34)**	0.0001
PVWMA adjacent lateral ventricles walls	Yes	22 (78.6)	36 (31)	**58 (40.3)**	0.0001
PVWMA adjacent occipital horns	Yes	11 (39.3)	13 (11.2)	**24 (16.7)**	0.0001
PVWMA adjacent temporal horns	Yes	10 (35.7)	10 (8.6)	**20 (13.9)**	0.0001
SCWMA frontal lobe	Yes	21 (75)	35 (30.2)	**56 (38.9)**	0.0001
SCWMA parietal lobe	Yes	17 (60.7)	26 (22.4)	**43 (29.9)**	0.0001
SCWMA occipital lobe	Yes	12 (42.9)	21 (18.1)	**33 (22.9)**	0.005
SCWMA temporal lobe	Yes	4 (14.3)	6 (5.2)	**10 (6.9)**	0.089

e) Impairment of gait

Our results revealed that the Impairment of gait had a strongly significant relationship with all white matter abnormality patterns [Table 10]

Table 10: Impairment of gait associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		Impairment of gait			P value (Pearson's X^2) at 95%CI
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent frontal horns	Yes	26 (59.1)	23 (23)	**49 (34)**	0.0001
PVWMA adjacent lateral ventricles walls	Yes	30 (68.2)	28 (28)	**58 (40.3)**	0.0001
PVWMA adjacent occipital horns	Yes	14 (31.8)	10 (10)	**24 (16.7)**	0.001
PVWMA adjacent temporal horns	Yes	10 (29.4)	10 (10)	**20 (13.9)**	0.042
SCWMA frontal lobe	Yes	31 (70.5)	25 (25)	**56 (38.9)**	0.0001
SCWMA parietal lobe	Yes	22 (50)	21 (21)	**43 (29.9)**	0.0001
SCWMA occipital lobe	Yes	17 (38.6)	16 (16)	**33 (22.9)**	0.003
SCWMA temporal lobe	Yes	7 (15.9)	3 (3)	**10 (6.9)**	0.005

f) Urinary dysfunction

Urinary dysfunction also had a strong significant relationship with all white matter abnormality patterns [Table 11]

Table 11: Urinary dysfunction associated with white matter abnormality location in adult patients' referred for brain MRI at Muhimbili National Hospital. N=144.

		Urinary dysfunction			P value (Pearson's X^2) at 95%CI
Location of WMA		**Yes %**	**No %**	**Total %**	
PVWMA adjacent frontal horns	Yes	7 (70)	42 (31.3)	**49 (34)**	0.013
PVWMA adjacent lateral ventricles walls	Yes	8 (80)	50 (37.3)	**58 (40.3)**	0.008
PVWMA adjacent occipital horns	Yes	7 (70)	17 (12.7)	**24 (16.7)**	0.0001
PVWMA adjacent temporal horns	Yes	5 (50)	15 (11.2)	**20 (13.9)**	0.001
SCWMA frontal lobe	Yes	7 (70)	49 (36.6)	**56 (38.9)**	0.036
SCWMA parietal lobe	Yes	7 (70)	36 (26.9)	**43 (29.9)**	0.004
SCWMA occipital lobe	Yes	6 (60)	27 (20.1)	**33 (22.9)**	0.004
SCWMA temporal lobe	Yes	4 (40)	6 (4.5)	**10 (6.9)**	0.0001

CHAPTER FOUR

4.0 DISCUSSION

White matter Abnormalities are a worldwide problem. They are regularly encountered at health care facilities. Their occurrence varies globally with different rates based on age and sex. Women are generally affected more and with increasing age. White matter abnormalities are associated with an increased risk of stroke, cognitive decline, dementia and death hence affecting the quality of life of the affected individual.

In this study, White Matter Abnormalities were diagnosed in 47.9% adult patients based on brain MRI. Other Studies have reported prevalence of white matter abnormalities among adults ranging from as low as 5 up to 95 ((1)(8). The difference in prevalence could be accounted for by study design, study population and rating scales. The population in this study was 100% of African descent, who according to studies have higher odds than European Americans to have brain white matter lesions(11)(12).

There was a significant increase in prevalence of white matter abnormalities with increasing age. Patients aged 61 years and above had the highest prevalence of WMA at 85.7% which is similar to the prevalence in the ARIC study of patients with a mean age of 62 years(11). Park. H et al (2) also showed that the prevalence of White matter abnormalities increases with age.

Women appeared to be more affected by white matter abnormalities 48.8 than men 46.8. This is similar to studies carried out by Leeuw F De et al (1). The difference according to sex was not statistically significant ($p = 0.811$).

Hypertension has been found to be a significant risk factor in patients with white matter abnormalities (2)(14). This was similar to what was observed by the current study 52.2% ($p= 0.0001$). The ARIC study revealed that patients with hypertension had more than twice as often more severe white matter abnormalities and even worse in patients with longer duration of hypertension(11). Previous studies have shown that hypertension is a risk factor of developing white matter abnormalities, but the exact mechanism is not known

(10)(11)(14)(20). Hypertension is vital in the pathogenesis of atherosclerosis and small vessel disease which occur more in the elderly patients and therefore increase in white matter abnormalities in these patients (33).

Diabetes Mellitus, HIV and cigarette smoking were other risk factors associated with White matter abnormalities studied. They were not found to be significant risk factors in our research each with a P value of > 0.05 (DM - 0.216, HIV – 0.94, cigarette smoking – 0.396). These results were different from the results from various previous researches that had previously been carried out(2)(13)(14)(15)(16)(17)(18). This could be due to the fact that previous studies were purely based on diabetic patients (13) and HIV patients (17)(18). The Rotterdam study found no significant relationship between smoking and white matter abnormalities(1). Self-reporting of cigarette smoking may have been inaccurate, which may have led to incorrectly including or excluding patients within this study.

Periventricular white matter abnormality was the most encountered pattern of white matter abnormality at 41.4% and 38.6% of patients with WMA had subcortical white matter abnormality. The Helsinki Aging study (34) had lower proportion as compared to our findings 39% and 22% periventricular and subcortical respectively. The higher proportion in the current study could be due to the wide age range (from 18 to 84 years) as compared to the age range of 55- 85 years used in Helsinki Aging study. This shows that white matter abnormalities are not uncommon in individuals below 55 years. Our results contrast previous studies by F-E de Leeuw et al (1) which showed that subcortical WMA were more common than periventricular WMA. Many studies do not distinguish the different locations and patterns of white matter abnormalities. Most studies sum up the volume of the WMA regardless of location and patterns (22,31).

Among the periventricular pattern, pencil-thin lining was the most common pattern (39%) smooth halo (35%) and large confluent the least common (13%). In the Helsinki Aging study, the pencil thin lining was the most common in patients younger than 75 years and the large confluent was the most common pattern in patients older than 75 years (34). WMA adjacent to the lateral ventricular walls was most common (40.3%) followed by WMA adjacent to frontal

horns (34%). This contradicts findings in previous studies which found that PVWMA along the frontal horns are most common and present first as these are the areas where draining of interstitial water is greatest (20,34,35).

Among the subcortical white matter abnormalities, the small size was the most common (48%) followed by the medium size (30%) with the frontal lobe being the most common affected lobe. In the Helsinki Aging study, small and medium size SCWMA was equivocal and the most common in the under 75 years while medium size was more common in the above 75 years cohort. The Frontal lobe was similarly more affected as seen in our study (34,36).

These WMA lesions showed high ADC values and appeared hyperintense in T2W and FLAIR sequences, hypointense on TIW with no restricted diffusion. These findings are similar to those of other studies (26). The high ADC values with no restriction on DWI are related to significant tissue destruction probably due to axonal loss (37).

White matter abnormalities were significantly associated with increased risk in cognitive decline, dementia, depression, impairment of upper extremity functions and gait and urinary dysfunction, this is similar to various previous conducted researches (8)(2)(14)(27)(28). The various symptoms were significantly associated with each brain lobe except impairment of upper extremity which was not strongly associated with white matter abnormality of the temporal lobes. Previous research showed that, Periventricular white matter abnormalities are related to cognitive decline (1,21). Subcortical white matter abnormalities are related to late on-set depression (29). This was not so in our research as both periventricular and subcortical white matter abnormalities were significantly associated with both cognitive decline and depression (each had a $p = 0.0001$)

Limitations of our study included that causal relationships cannot be assessed due to its cross-sectional design. Because the majority of our subjects were women (57.2%) and patients had been referred for brain MRI for various reasons, these study findings may not be generalizable to the public.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATION

5.1 Conclusion

White matter abnormalities are a common condition affecting almost one half of the study population. Prevalence of white matter abnormalities (WMA) increases with age. Women appear to be more affected by white matter abnormalities than men but this was not statistically significant. The most affected white matter fibers are the periventricular. Although several risk factors seem to be associated with WMA in previous studies, hypertension has been reported to play a significant role in the development of white matter abnormalities.

There is a statistical significant relationship between the various patterns of white matter abnormalities and the presenting symptoms.

5.2 Recommendation

Larger population based and prospective studies are needed to establish the etiology and risk factors of white matter abnormalities. These studies could also be used to establish long term outcome and the role of early intervention such lifestyle modification i.e. exercise, low calorie but balanced diet and early treatment.

MRI of the brain is the recommended modality and should be encouraged for diagnosis and follow-up of these patients. To yield unbiased results on prevalence, incidence and outcome, a uniform rating scale should be established in order to enable comparison of results between studies. This rating scale could also be reliably used to follow up patients in order to monitor progression or stagnation of white matter abnormalities.

REFERENCES

1. Leeuw F De, Groot JC De, Achten E, Oudkerk M, Ramos LMP, Heijboer R, et al. Prevalence of cerebral white matter lesions in elderly people : a population based magnetic resonance imaging study . The Rotterdam Scan Study. 2001;9–14.

2. Park H, Jo J, Cheong J, Chang H, Lee H, Suk S. Prevalence and risk factors of cerebral white matter changes and silent infarcts on brain computed tomography scans among community-dwelling healthy adults : The PRESENT project. 2014;19(4):351–6.

3. Guttmann CR, Jolesz F a, Kikinis R, Killiany RJ, Moss MB, Sandor T, et al. White matter changes with normal aging. Neurology. 1998;50(4):972–8.

4. Erkinjuntti T, Ketonen L, Sulkava R, Sipponen J, Vuorialho M, Iivanainen M. Do white matter changes on MRI and CT differentiate vascular dementia from Alzheimer ' s disease? 1987;5:37–42.

5. Nyberg L, Adolfsson R, Launer LJ, Program B. SPECIAL ISSUE HIGH PREVALENCE OF WHITE MATTER HYPERINTENSITIES IN NORMAL AGING: RELATION TO. 2003;1093–105.

6. Xiong YY, Mok V. Age-Related White Matter Changes. 2011;2011.

7. Hâncu A, Irene R, Butoi G. White Matter Changes in Cerebrovascular Disease : Leukoaraiosis. 2009;

8. Markus HS. The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and. 2009;1–9.

9. Fazekas F, Kleinert R, Offenbacher H, Payer F, Schmidt R, Kleinert G, et al. The morphologic correlate of incidental punctate white matter hyperintensities on MR images. Am J Roentgenol. 1991;157(6):1317–23.

10. Awad IA, Johnson PC, Spetzler RF, Hodak JA. Incidental subcortical lesions identified on magnetic resonance imaging in the elderly. II. Postmortem pathological correlations. Stroke [Internet]. 2009;17(6):1090–7.

11. Liao D, Cooper L, Cai J, Toole JF, Bryan NR, Hutchinson RG, et al. Presence and severity of cerebral white matter lesions and hypertension, its treatment, and its control. The ARIC Study. Atherosclerosis Risk in Communities Study. Stroke [Internet]. 1996;27(12):2262–70.

12. Yanek R, Moy TF, Becker LC, Cuzzocreo J. NIH Public Access. 2015;37(4):244–50.

13. Researchreviews M, Takata T, Saiseikai O, Hospital N. Cognitive dysfunction associates with white matter hyperintensities and subcortical atrophy on magnetic resonance imaging of the elderly diabetes mellitus Japanese elderly diabetes ... Cognitive dysfunction associates with white matter hyperintensities an. 2015;(December).

14. Longstreth WT, Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA, et al. Clinical Correlates of White Matter Findings on Cranial Magnetic Resonance Imaging of 3301 Elderly People: The Cardiovascular Health Study. Stroke [Internet]. 1996;27(8):1274–82.

15. Pandit L. Differential diagnosis of white matter diseases in the tropics: An overview.

16. Howlett WP, Howlett W. Part ii – Neurological Disorders CHAPTER 8 NEUROLOGICAL ILLNESS IN HIV DISEASE. 2012;

17. Neuroaids H, Neuroscience S. NIH Public Access. 2006;63(5):822–7.

18. Magnetic B, Imaging R, Haddow LJ, Dudau C, Chandrashekar H, Cartledge JD, et al. Cross-Sectional Study of Unexplained White Matter Lesions. 2014;28(7):341–9.

19. Johnson BA. A Practical Approach to White Matter Disease. :1–4.

20. Fazekas F, Chawluk JB, Hurtig HI, Zimmerman RA. MR Signal Abnormalities at 1 . 5 T in Alzheimer ' s Dementia and Normal Aging. 1987;(June):421–6.

21. Groot JC De, Leeuw F De, Oudkerk M, Gijn J Van. Cerebral White Matter Lesions and Cognitive Function : The Rotterdam Scan Study. 2000;145–51.

22. Manuscript A. NIH Public Access. 2009;64(4):273–80.

23. Schaefer PW, Grant PE, Gonzalez RG. State of the Art. :331–45.

24. Patay Z. Diffusion-weighted MR imaging in leukodystrophies. 2005;2284–303.

25. Breton E. L: 0. :401–7.

26. Scherer A, Rassek M, Witsack HJ, Mo U. Imaging in the Brain in ChildrenFindings in the Normal Brain and in the Brain with White Matter Diseases 1. 2002;(2).

27. Sachdev PS, Wen W, Christensen H, Jorm AF. White matter hyperintensities are related to physical disability and poor motor function. 2005;362–7.

28. Zheng JJJ, Delbaere K, Close JCT, Sachdev PS, Lord SR. Impact of white matter lesions on physical functioning and fall risk in older people: a systematic review. Stroke. 2011;42(7):2086–90.

29. Barber R, Scheltens P, Gholkar A, Ballard C, Mckeith I, Ince P, et al. White matter lesions on magnetic resonance imaging in dementia with Lewy bodies , Alzheimer ' s disease , vascular dementia , and normal aging. 1999;66–72.

30. Govender R, Wilmshurst JM, Wieselthaler N, Town C, Town C. Acquired Demyelinating Disorders of the CNS in Children. 2007;

31. Determinants of cerebral white matter lesions.

32. McEwen BS, Alves SE, Bulloch K, Weiland NG. Ovarian steroids and the brain:

implications for cognition and aging. Neurology. 1997;

33. Fazekas F, Kleinert R, Offenbacher H, Schmidt R, Kleinert G, Payer F, et al. Pathologic correlates of incidental MRI white matter signal hyperintensities. Neurology. 1993;

34. Ylikoski A, Erkinjuntti T, Raininko R, Sarna S, Sulkava R, Tilvis R. White matter hyperintensities on MRI in the neurologically nondiseased elderly. Analysis of cohorts of consecutive subjects aged 55 to 85 years living at home. Stroke. 1995;

35. Zimmerman RD, Fleming CA, Lee BCP. Periventricular hyperintensity as seen by magnetic resonance: Prevalence and significance. Am J Neuroradiol. 1986;7(1):13–20.

36. Juva K, Sulkava R, Erkinjuntti T, Valvanne J, Tilvis R. Prevalence of dementia in the city of Helsinki. Acta Neurol Scand. 1993;

37. Scanderbeg AC, Tomaiuolo F, Sabatini U, Nocentini U, Grasso MG, Caltagirone C. Demyelinating plaques in relapsing-remitting and secondary-progressive multiple sclerosis: Assessment with diffusion MR imaging. Am J Neuroradiol. 2000;

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

Identity number ……. Age …… Sex F/M

Part 1

Presenting symptom & signs

- Cognitive decline 1. Yes 2. No
- Dementia 1.Yes 2.No
- Depression 1.Yes 2.No
- Impairment of upper extremity functions 1.Yes 2.No
- Impairment of gait 1.Yes 2.No
- Urinary dysfunction 1.Yes 2.No

Risk factors

- Hypertension 1.Yes 2.No

Duration 1. >5years 2. <5years

Diabetes Mellitus 1.Yes 2.No

Duration 1. >5years 2. <5years

HIV 1.Yes 2.No

Smoking 1.Yes 2.No

Duration 1. <5years 2. >5years

Number of cigars per day 1. <5 2. <10 3. One packet

Part 2. Image findings

White Matter Abnormality 1. Present 2. Absent

Periventricular WMA 0. None \

1. Pencil-thin lining

2. Smooth halo

3. Large confluent

Adjacent to 1. Frontal Horns

2. Wall of lateral ventricles (bands)

3. Occipital Horns

Subcortical WMA 1. Small (1-3mm)

2. Medium (3-10mm)

3. Large (>10mm)

1. Frontal Lobe
2. Parietal Lobe

3. Temporal Lobe

4. Occipital Lobe

ADC maps	`1. Low ADC values- Hypointense
	2. High ADC values- Hyperintense
Other abnormalities:	1.Brain infarction
	2. Brain tumors
	3. Brain infection
	4. Intracranial Hemorrhage

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. Doreen Muola; I am conducting study on the prevalence and MRI patterns of white matter diseases among adult patients referred to Radiology department at MNH 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 is aiming to establish the prevalence, signs and symptoms and MRI patterns of White Matter abnormalities 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 White matter abnormalities in adults and associated risk factors and 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. Doreen Muola, Muhimbili University of Health and Allied Sciences, P. O. Box 65001, Dar es Salaam. Tel. 0686612304**.**

In case you have questions about your rights of participation in this study, you may contact **Prof Said Aboud, 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. Doreen Muola nafanya utafiti wenye lengo la kujua kwa uhalisia ukubwa wa na kuangalia MRI pattern of White matter abnormalities kwa wagonjwa wanaofanyiwa MRI ya kichwa kwenye idara ya vipimo vya mionzi 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 TibaMuhimbili. 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.Doreen Muola, Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili, S. L. P. 65001, Dar es Salaam. Simu 0686612304. **Prof Said Aboud, 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……