BRAIN MRI FINDINGS IN HIV/AIDS PATIENTS WITH NEUROLOGICAL SYMPTOMS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

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By,

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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences the dissertation entitled **"*Brain MRI findings in HIV/AIDS patients with neurological symptoms at Muhimbili National Hospital, Dar es salaam, Tanzania*"** in (partial) fulfillment for the Degree of Masters of Radiology and Imaging at Muhimbili University of Health and Allied Sciences.

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Dr. Ramadhan Kazema

Supervisor

Date _____

DECLARATION AND COPYRIGHT

I**, Haika F. Maro,** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any university for similar or any other degree award.

Signature: _____Date: _____

DEDICATION

This work is dedicated to my lovely parents and siblings

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LIST OF ABBREVIATIONS

ADC	Apparent Diffusion Coefficient
AIDS	Acquired Immunodeficiency Syndrome
ARV	Anti-Retroviral Drugs
CMV	Cytomegalovirus
CNS	Central Nervous System
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CVA	Cerebrovascular accident
DWI	Diffusion Weighted Image
FLAIR:	Fluid Attenuation Inversion Recovery
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
HIVE	HIV encephalopathy
MAMC	Muhimbili Academic Medical Center
MNH	Muhimbili National Hospital
MRI	Magnetic Resonance Imaging
MUHAS	Muhimbili University of Health and Allied Sciences
PCNSL	Primary central nervous system lymphoma
PET	Positron Emission Tomography
PML	Persistent Multifocal leukoencephalopathy
T1W	T1 weighted sequence
T2W	T2 weighted sequence
UNAIDS	Joint United Nations Programme on HIV/AIDS
UWMH	Unexplained white matter hyper-intensities
WHO	World Health Organisation

DEFINITION OF TERMS

MRI sequence: a number of radio-frequency pulses and gradients that result in a set of images with particular appearance.

ACKNOWLEDGEMENT:

First and foremost, I would like to thank the almighty God for seeing me through my research. I would also like to convey my deep gratitude to my research supervisor, Dr Ramadhani Kazema who put his efforts and time in directing and mentoring me throughout the preparation of this research. Lastly, many thanks go to the staff members of Radiology departments at MUHAS and MNH, my mentors and colleagues for their support and guidance.

ABSTRACT

Background: HIV/AIDS is a pandemic infectious disease affecting about 36.7 million people globally, with 22 million out of these residing in the Sub-Saharan Africa. In Tanzania the prevalence of HIV/AIDS is 5.1% with an estimated population of 1.4 million living with the disease. Approximately 40%-90% of patients with AIDS will develop CNS manifestations during the course of their illness.

We studied brain MRI scans among HIV/AIDS patients who presented with clinical neurological manifestations at MNH.

Methods: A cross sectional hospital based study was conducted for duration of six months among adult HIV/AIDS patients undergoing MRI brain imaging for neurological complaints attending Radiology and Internal medicine departments at Muhimbili National Hospital (MNH), Dar es Salaam. The interpretation of the MRI brain scans were done by the Principal Investigator and Radiologist and reported findings were stored in a data sheet along with recent CD4 counts, viral load ,ARV status and socio-demographic information retrieved from hospital records.

Descriptive analyses were performed to summarize the data collected. To assess different associations, *t*-test or Wilcoxon test was used for continuous variables as appropriate while for categorical variables, a Chi-square test or Fisher exact test was used accordingly. Lastly, a multivariate logistic regression was used to assess association of abnormal brain MRI findings with different predictors with results presented as odds ratios and plotted in a coefficient plot. All analyses were performed in Stata software version 13.1 (Stata Corporation, College Station, Texas, USA).

Results: The mean age of participants was 44 years (age range from 18-66years), with females accounting for the higher proportion (74.3**%**) amongst the 101 enrolled participants. Most participants were from Dar es Salaam, predominantly from Ilala district.

Out of 101 brain MRI scans of the study population, 67% had abnormal findings predominantly among patients with CD4 cell count below 200cells/μL and viral load above 50 copies/mL. Infarct, diffuse global abnormalities (defined as cerebral atrophy with/without symmetrical white matter hyperintensities) and focal mass lesions with mass effect accounted for more than half

(62%) of the abnormal brain MRI findings. In a multivariate logistic regression adjusted for viral load and CD4 cell counts, patients with viral loads above 50 copies/mL had twice the odds of abnormal MRI as compared to those with less than 50 copies/mL (i.e., aOR 2.06, 95% CI 0.48-8.82) while those whose CD4 cell counts are above 200 cells/µL had 67% decrease in the odds of having abnormal MRI findings (aOR 0.33, 95% CI 0.07-1.5). Participants with seizure disorder had a 83% increase in the odds of having abnormal MRI finding as compared to patients without seizure disorders (aOR 1.83, 95% CI 0.33-10.4).

Conclusion: Neuro-imaging is a crucial component in the management of HIV/AIDS patients presenting with neurological symptoms especially those with low CD4 counts (≤200 cells/µL) and viral load above 50copies/mL. Due to higher sensitivity and soft tissue resolution, MRI of the brain is a useful aid in the diagnosis and treatment response assessment of HIV/AIDS patients with neurological manifestations.

CHAPTER ONE

1. Introduction

1.1 Background

HIV/AIDS is an infectious disease caused by the Human Immunodeficiency Retrovirus. Since the onset of the HIV epidemic, it is estimated that about 70million people have been infected, and 35 million died of HIV (1). The Sub-Saharan Africa which accounts for 13 percent of the world-wide population harbors the greatest population (70%) of people living with HIV/AIDS. According to the 2008 UNAIDS Report on the Global AIDS Epidemic, approximately 22 million (67%) of the estimated 33 million adults and children living with HIV globally, reside in sub-Saharan Africa (2). It is estimated that 1 in every 25 adults (4.4%) in Sub-Saharan Africa is HIV infected (1). By the end of 2015, an estimated 36.7 million [34.0–39.8 million] people were living with HIV globally (1, 2, 3). In Tanzania, based on the 2011-12 National HIV/AIDS and Malaria Indicator Survey, overall 5.1% of Tanzanians aged 15-49 are HIV-positive. HIV prevalence is higher among women (6.2%) than men (3.8%) with those living in urban areas being more likely to be HIV-positive than those living in rural areas (7.2% versus 4.3%) (4).

Involvement of the central nervous system (CNS) in HIV/AIDS patients is associated with significant morbidity and mortality. About a third of the AIDS-defining illnesses affect the nervous system (5). It is estimated that approximately 40 -90% of HIV infected persons will develop neurological manifestations during the course of their illness (6, 7, 8).

Direct effect of the human immunodeficiency virus, opportunistic infections, HIV/AIDS associated malignancies; cerebrovascular complications as well as side effects of the highly active antiretroviral therapy (HAART) are the possible pathological explanations causing CNS manifestations in an HIV individual (9).

Neuro-imaging is therefore crucial for these patients, where specific characterization of the lesions not only aid in the detection, diagnosis, and initiation of treatment but also verifies response to therapy.

There are several neuro-imaging modalities such as computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI) which can be used to diagnose a variety of CNS lesions. MRI has a better soft tissue resolution and detail, allows acquisition of images in multiple planes, with sensitivity superior to that of CT and thus it has become the "gold standard" choice in neuro-imaging (10).

This study thus aims at identifying the brain MRI findings amongst HIV/AIDS patients with neurological complaints, as well as determine the relation of the MRI findings to ART and immune status with its findings used in the provision of improved individualized evidence-based care and management as well as provide a groundwork for future researches.

1.2 Literature Review

HIV/AIDS and Neurology

'Neuro-AIDS' is a term coined to describe the vast number of neurological manifestations/sequelae of the HIV/AIDS disease (11). Clinical features suggestive of neurological manifestations include headache, meningism, and altered mental status, implying change in consciousness or cognition. Also included are focal neurological deficits such as visual or speech disturbance, motor, sensory and cranial nerve deficits (12). Approximately 40-90% of HIV patients will succumb to neurological manifestations of HIV/AIDS during their disease process. The brain may be affected by a variety of abnormalities in association with HIV infection. These clinical neuropathological manifestations of HIV/AIDS can be categorized as direct neurological effects of HIV, opportunistic CNS infections and HIV/AIDS associated neoplasms. Other manifestations include cerebrovascular complications of HIV and CNS effects of highly active retroviral therapy (HAART) (9).

HIV/AIDS Neuro-Imaging Patterns

According to Irwin Walot et al the imaging findings (patterns) of CNS abnormalities in HIV patients can be broadly classified into four categories: focal lesions with mass effect; focal lesions without significant mass effect; diffuse global CNS abnormalities; and ventriculitis, meningitis, and infarcts (10). Although there is a considerable overlap in the imaging characteristics of different entities, some findings are still found to be very suggestive of a particular disease. Imaging modalities, mainly magnetic resonance imaging (MRI), thus play an important role in the diagnosis and follow up of AIDS patients with neurological disorders (13).

Stroke as well as CNS opportunistic infections (OIs) such as tuberculosis (meningitis, tuberculoma), cryptococcal meningitis, toxoplasmosis, neurocystercercosis, neurosyphilis, primary CNS lymphoma (Epstein-Barr virus), progressive multifocal leukoencephalopathy (JC virus), cytomegalovirus, remain the most commonly described HIV-associated CNS diseases. Dementia and psychological perturbations and other cognitive dysfunctions unrelated to opportunistic infections above have also been described (14).

MRI Neuroimaging Patterns and HIV/AIDS associated Diagnoses

A: Focal mass lesions with mass effect

Focal brain lesions occur in 15-20% of AIDS patients. The most common focal mass lesions encountered in HIV have enhancement and surrounding edema. Their contrast enhancement patterns and severity of surrounding edema depends on the vascularity, integrity of the blood brain barrier and immune response (10). Lesions in this category include:

Toxoplasmosis is the most common CNS opportunistic infection in HIV/AIDS patients caused by a protozoa, Toxoplasmosis gondii (7,8). Toxoplasmosis lesions appear as small nodular and/or ring enhancing lesions with surrounding edema. They are often multiple, located at the basal ganglia or the cerebral hemispheres. On MRI, they are hypointense on T1W and moderately hyperintense to the brain parenchyma on T2W. Small punctuate hemorrhages may also be present and suggest its diagnosis (10,15-17).

Lymphoma is the most common CNS malignancy in AIDS patients (7,8,10). They are often multifocal but can also be solitary. They appear as solid mass lesion with solid or ring enhancement and surrounding edema. Lesions are often located in the basal ganglia, corpus callosum and periventricular white matter with tendency of subependymal spread (ventricular encasement). They are hypointense on T1W while their signal on T2W can vary from hypointense to hyperintense (10,17-20).

Cryptococcosis, is a fungal infection that is caused by Cryptococcosis neoformans. It a common fungal infection in AIDS patients with about 5% presenting as cerebral cryptococcosis. It spreads to the CNS from the initial site of infection, probably pulmonary and results in a spectra of CNS neuroimaging findings. It may present as meningitis (most common presentation) or focal encephalitis which may progress to form cerebral abscess or mass which appear hypointense on T1W and hyperintense on T2W with nodular or ring enhancement and various degrees of surrounding edema. Cerebral cryptococcosis may also present as gelatinous pseudocysts which are hypointense on T1W and hyper intense on T2W on MRI(similar to CSF signal) and have a predilection for the basal ganglia (10, 21-23).

Neuro-Tuberculosis is a form of extra pulmonary tuberuculosis that spreads to the CNS. The incidence of neuro-tuberculosis is documented to be still low, despite the increase in incidence of pulmonary tuberculosis in HIV/AIDS patients (24,25). It may present as meningitis or focal-parenchymal lesion. The focal parenchymal lesions may vary from cerebritis, granuloma to tuberculous abscess. Granulomas are often multiple with nodular or irregular ring enhancement while tuberculous abscess are often solitary with thin ring enhancement making differentiation from pyogenic abscess challenging. Both granuloma and tuberculous abscess are hypointense on T1W and hyperintense on T2W. Contrary to granuloma which may have little edema and little to no mass effect, tuberculous abscess are associated with significant edema and mass effect. Tuberculous meningitis appear as thickened basal lepto-meningeal enhancement (26-28).

Neuro-syphilis is diagnosed more frequently in AIDS than the general population. It is postulated that the HIV/AIDS alters the natural disease history of syphilis because HIV patients are more prone to progress to neuro-syphilis and have shorter latent period to develop neurological symptoms(29). Ischemic infarcts is the most common imaging presentation due to arteritis mainly of the basilar lenticulostriate vessels, perforators of the brainstem or large vessel of the middle cerebral territory. Less likely, syphilitic gummas may occur which appear as peripherally located nodular lesions in the cortex or dural that are isointense on T1W and hyperintense on T2W with nodular enhancement post contrast. The lesions have associated mass effect and edema (5, 30).

B: Focal lesions without significant mass effect

Lesions within this subset often involve only the white matter and cause no mass effect or enhancement. On MRI imaging, they appear hypointense on T1W and hyperintense on T2W (10).

Progressive Multifocal Leukoencephalopathy (PML) is a serious CNS infection caused by the JC virus that cause focal lesions without significant mass effect (31). Secondary to a weakened immune system, the reactivated JC virus infect and destroy the oligodendrocytes causing white matter demyelination. The lesions are multifocal and primarily located in the white matter including the U-fibers. Multiple sites can be involved including the periventricular white matter, posterior fossa, brain stem, spinal cord and basal ganglia with predominance of the parietal lobes.

On MRI, the lesions are hypointense on T1W and hyperintense on T2W.

They have little or no mass effect or enhancement (10).

C: Diffuse global CNS abnormalities

AIDS Dementia Complex(ADC) is a result of subacute encephalitis caused by the HIV virus which is neurotropic. This results in global reduced brain volume which manifest as widened subarachnoid spaces, sulci and basal cisterns with ventriculomegaly that is dispropriationate to patients's age. It may be associated with ill defined confluent symmetrical periventricular white matter altered MRI signal characteristics which are hypointense on T1W and hyperintense onT2W (10, 32).

D:Ventriculitis, meningitis, and infarcts

CMV infection is a late manifestation of AIDS, caused by the cytomegalovirus and may manifest as subacute encephalitis and encephalopathy similar to ADC or ventriculo-encephalitis where the infection begins at the ependymal or subependymal region and spread to the brain parenchyma.
It may also occur in conjunction with infection at other sites such as CMV retinitis. On MRI imaging, CMV ventriculo-encephalitis appear as ventriculomegaly and periventricular white matter T2W hyperintensities. On post contrast images, linear ependymal and ill defined periventricular enhancement can be seen. Occasionally, CMV meningitis may appear as dural enhancement (32-34).

Meningitis, especially basilar meningitis, with hydrocephalus is secondary to neuro-tuberculosis which occasionally may be associated with infarcts due to vascular stenosis or occlusion (28). Other causes of meningitis may include bacterial infection, CMV and cryptococcosis. On imaging, it appear as meningeal thickening with enhancement post contrast.

Infarcts is one of the HIV/AIDS related complications which are associated with poor outcome. Arterial ischemic stroke is the most common documented cerebrovascular accident (CVA) in HIV/AIDS patients. Various mechanisms which cause CVA have been documented, some of which include: opportunistic infection such as neuro-syphilis and tuberculous meningitis, HIV vasculopathy, coagulopathy and cardio-thromboembolism. HAART is also postulated to increase the risk of CVA(35-38).

Immune Suppression and Neurological Manifestation

Most of the neurological manifestations are attributed to the declining CD4 count levels. As a result of a weakened defense system, opportunistic infections and neoplasms arise, often from reactivation of previously acquired organisms. Such mechanism applies to agents such as Toxoplasma gondii and Epstein-Barr virus (EBV); the latter is strongly associated with CNS lymphoma (39). The clinical stage of HIV infection as reflected by viral load and CD4counts depicts the severity of the immune suppression and is related to the likelihood of developing a particular neurologic syndrome (39). A decrease in the CD4 receptor–positive T lymphocytes is the best predictor of the potential development of opportunistic infections. Patients are most vulnerable when the CD4 count falls below 200 cells/μL (40). In a study done by Graham CB et al, reported all cases that were positive for mass lesions or white matter lesions among the positive CT brain scans in HIV/AIDS patients with headache, occurred in patients with CD4 counts less than 200 cells/microL (P = .04) (41).

HAART and Neurological manifestation

HAART is a combination of drugs which suppress the human immunodeficiency virus and allow restoration of the immune system. In the era before use of HAART, 10%–20% of patients presented with neurologic disease as the first manifestation of symptomatic HIV infection (8, 42). However, in the advent of HAART, there has been a decline in the neurological manifestations in HIV patients especially those caused by opportunistic infection (43,44). In a few of these patients, partial restoration of specific immunity may worsen a preexisting disease; resulting in a condition referred to as immune reconstitution inflammatory syndrome (IRIS). IRIS occurs in the initial months after the onset of HAART and is thought to be related to recovery of the immune system. It presents with paradoxical worsening of clinical condition with raising CD4 count, declining viral load and radiologic manifestations of opportunistic infection after initiating drug therapy. IRIS thus impacts the neuro-imaging findings associated with the various infectious causative agents that affect the CNS in HIV-infected people.

More over in countries where HAART is available, the majority of cases of HIV-related neurologic disorders are cognitive dysfunction and peripheral neuropathies caused directly by HIV (45).

CSF and Neurological manifestation

Analysis of CSF in HIV infected patients with neurological manifestations can also assist in detecting and diagnosing the causative culprit. Abnormal CSF biochemistry, cytology and microbiology such as toxoplasmosis, and cryptococcal antigens, fungal, bacterial or parasites cultured from CSF are adjuvants in the diagnostic process in neuro HIV/AIDS. In a study by Caroline Charlier et al which assessed the cryptococcal neuro-radiological lesions in HIV positive patients found that, the presence compared to absence of cryptococcosis-related lesions in neuro-imaging was significantly associated with high serum (78% vs. 42%, P=0.008) and CSF (81% vs. 50%, P=0.024) antigen titers, independently of neurological abnormalities (46).

1.3 Problem Statement

HIV/AIDS pandemic is a global as well as a national burden. In Tanzania the prevalence is 5.1%; with the disease affecting mainly the workforce of the nation aged 15 to 49years (4).

Based on literature, a third of the AIDS defining illnesses manifest as neurological disease and it is estimated that in the course of the HIV/AIDS disease 40-90% of the HIV patients will succumb to neurological manifestation of the disease (10). HIV is a neurotropic virus (47) . Involvement of the CNS is associated with significant morbidity and mortality. About 20% of the emergency department visits by HIV patients is attributed to CNS complaints (48).

Problems with understanding of HIV-associated CNS disease in sub-Saharan Africa is largely due to limited data on these conditions, in part due to the paucity of neurologists, neurosurgeons and neuro-radiologists managing HIV-infected patients. In addition, due to limited imaging facilities, and limited diagnostic capabilities, confidently confirming diagnoses is difficult (14).

1.4 Rationale

Neurological manifestations constitute the next common clinical complaint after pulmonary disease among HIV patients. Short of prompt diagnosis and appropriate treatment, these clinicopathological entities invariably lead to significant morbidity or death. Provided that a majority of the central nervous system (CNS) disorders related to HIV and AIDS are treatable, prompt and

accurate diagnosis as well as longitudinal therapeutic monitoring forms an essential component of the management of these HIV/AIDS patients (49).

Currently, with the introduction of MRI scan machines in the Tanzanian health care system, there are limited studies conducted within Tanzania to assess the correlation of the neurological manifestations with the documented neuro-imaging MRI findings in HIV/AIDS patients. Although imaging of the neurological system is a pivotal and crucial entity in providing adequate multidisciplinary management to HIV/AIDS patients, the utility of valuable data obtained from such imaging studies can be profoundly masked by unfamiliarity of the correlation between the clinico-pathological entities and documented neuro-imaging MRI findings among diverse professionals taking care of HIV/AIDS patients. This study aimed to explore such relationship and hence inform health care practitioners and lay down a foundation for further studies.

Radiological identification of the local common causes of CNS manifestations in HIV/AIDS patients, their frequency of occurrence and correlation with the CD4 levels, and ARV status will not only aid in the proper detection and diagnosis of the disease entities but also provide evidence based local data to guide appropriate therapy through analyzing responses to therapeutic interventions.

1.6 Research Question

1: What are the radiological findings in HIV/AIDS adult patients who present with neurological manifestations?

2: What is the relationship between positive radiological findings, their ARV status and CD4 level findings?

1.7 Objective

1.7.1 Broad Objectives

The broad objective of this study was to assess MRI brain imaging findings in adults HIV/AIDS patients presenting with neurological symptoms at Muhimbili National Hospital (MNH), Dar es Salaam from September 2017 to March 2018.

1.7.2 Specific Objectives

i. To determine the proportion of positive MRI brain findings among HIV/AIDS patients presenting with clinical neurological complaints at MNH from September 2017 to March 2018;
ii. To describe the MRI brain imaging findings in relation to ARV status in HIV/AIDS patients presenting with clinical neurological complaints at MNH from September 2017 to March 2018 and to;
iii. To describe the MRI brain imaging findings in relation to the level of CD4 in HIV/AIDS patients presenting with clinical neurological complaints at MNH from September 2017 to March 2018.

CHAPTER TWO

2.0 METHODS

2.1 Study design

This was a hospital based cross-sectional study.

2.2 Study setting

The study was conducted at MNH, Radiology and Internal medicine departments in Dar es Salaam, Tanzania. Muhimbili National Hospital is a major tertiary hospital with at least 1400 beds. It has all major medical specialties. The Radiology and Imaging department has most of the imaging modalities. There are about 8 MNH staff radiologists and 8 radiologists based at MUHAS/MAMC.

The study was conducted at the MNH MRI unit which has a Philips Achieva 1.5 Tesla MRI machine (Philips Endiehoven, Best The Netherlands). It has a mini PACS system (Siemens Frankfut, German) and well-established image management system. Images are offered recorded on CDs and DVDs, with hard copies printed on laser films , available on request.

2.3 Study population

The study population involved confirmed HIV positive patients who presented with neurological symptoms attending MNH outpatient clinics, wards and MRI unit from September 2017 to March 2018 and their MRI findings and reports as well as most recent records of CD4 counts, viral load, CSF findings and ARV status details were collected and reviewed.

2.4 Inclusion Criteria

The inclusion criteria included all adult patients (aged 18 years and above) confirmed to be HIV positive with primary clinical neurological complains. In this study, four clinical criteria suggested by Rothman et al to warrant immediate neuro-imaging, namely new onset seizures, depressed or altered orientation (or confusion), a headache that had changed in quality or one that was prolonged (>3 days) or a focal neurological deficit, were used as the main neurological symptoms (48).

2.5 Exclusion Criteria

Non-consenting adult HIV/AIDS patients were not involved in this study. No individuals with prior history of mental illness and other pre-existing neurological diseases were enrolled.

2.6 Sampling method

Convenient sampling method was used in this study where all participants who sought for MRI scans at our department and fulfilled inclusion criteria were enrolled into the study.

2.7 Sample size

The sample size included all HIV/AIDS patients with neurological complaints undergoing MRI brain imaging who fulfilled the inclusion criteria within the study duration.

2.8 Data collection

All HIV patient who underwent MRI scan of the brain for the specified reasons and who fulfilled the inclusion criteria were identified at the MRI unit of the MNH Radiology department. Their hospital case notes were then traced and information retrieved. The following data was collected: MRI reported findings, CD4 levels, viral load, ARV status and CSF results if available.

2.9 Imaging and Evaluation

Patients enrolled in the study underwent magnetic resonance imaging of the brain using Philips Achieva 1.5 Tesla MRI machine and a standardized MRI brain protocol for was used. The protocol included the following MRI sequences: T1 and T2 weighted, fluid-attenuated inversion recovery (FLAIR) imaging, diffusion weighted (DWI), apparent coefficient (ADC) and T1 weighted gadolinium contrasted sequences.

Table 1:MRI Brain Protocol

Sequence	Imaging plane
T1W	SAGITTAL+AXIAL
T1W with gadolinium contrast	AXIAL
T2W	AXIAL+CORONAL
FLAIR	AXIAL+ CORONAL
ADC	AXIAL
DWI	AXIAL

Despite overlapping of the neuroimaging findings, positive imaging characteristics were broadly classified into four groups: focal lesions with mass effect and enhancement; focal lesions without significant mass effect or enhancement; diffuse global CNS (cerebral atrophy with or without symmetrical white matter hyper-intensities) abnormalities; and ventriculitis, meningitis, and infarcts. A table(shown in appendix IV) which summarizes the various detailed MRI imaging findings(patterns) of CNS lesions was used to guide in establishing the differential diagnosis of brain diseases in HIV/AIDS patients enrolled in the study presenting with neurological manifestations(10).

For the purpose of this study extra cranial findings such as sinusitis were not included as abnormal MRI finding. The MRI brain images were reported by Principal Investigator and Radiologists, and the final diagnosis was a consensus of both.

2.10 Data Analysis

Descriptive analyses were performed to summarize the data collected, presented as measures of central tendency, proportions, and figures. To assess different associations, *t*-test or Wilcoxon test was used for continuous variables as appropriate while for categorical variables, a Chi-square test or Fisher exact test was used accordingly. For the purpose of this study, during multivariate lo-

gistic regression, we categorized viral load into ≤50 copies/mL and >50 copies/mL, CD4 cell count into ≤200 cells/μL and >200 cells/μL. We considered findings to be significant at an alpha level of 0.05. Variables were included in the multivariate model if thought to be clinically or socially relevant or had a p value of <0.20 following univariate analysis. Results for multivariate model are presented as adjusted odds ratios and plotted in a coefficient plot. All analyses were performed in Stata software version 13.1 (Stata Corporation, College Station, Texas, USA).

2.11 Ethical considerations

The researcher sought informed consent from the research participants and ensured that the patients' information and image findings were kept confidential. Anonymity was ensured by coding instead of using patients' names and registration numbers. All data was then stored in a secured place. Refusal to participate into the study did not affect patient care.

2.12 Ethical clearance

Ethical clearance was sought from the Research and Publication Committee of the Muhimbili University of Health and Allied Sciences as well as the Muhimbili National Hospital.

2.13 Study Challenges

Recurrent breakdown of the laboratory machines and inconsistent supply of the necessary reagents for laboratory tests, posed a hindrance in the acquisition of recent CD4 counts and viral load results that could have aided a more comprehensive analysis. Moreover, during the study duration, the recurrent malfunction of the MRI machine and considerable time taken to fix it limited the number of patients that could have been enrolled in the study. MRI imaging in itself is an expensive investigation hence limiting the number of patients who could afford to pay for it and hence be enrolled in study.

Acquiring the relevant medical information required for this study from outpatients referred from other hospitals outside Muhimbili was also a challenge. Poor record keeping and missing data were also a hindrance in acquiring the relevant information that was necessary for this research and possibly for future researches.

Generalization of the results to the public are limited due to the study being a hospital based cross-sectional study. Furthermore, there was a lack of confirmatory laboratory tests to confirm the MRI brain diagnosis.

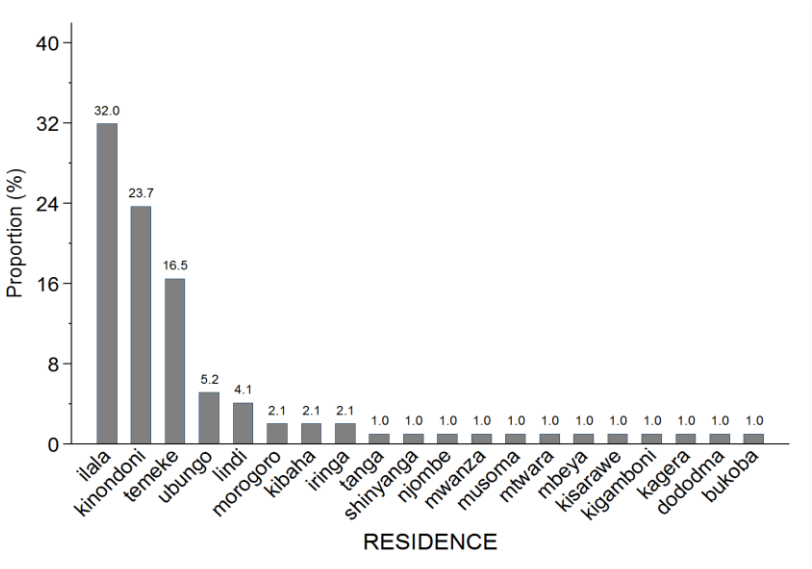
CHAPTER THREE

3.0 RESULTS

3.1 Participants 'baseline characteristics

A total of 101 study participants were recruited (between September 2017 until March 2018), of which females were predominant 75 (74.26%). Dar es Salaam had majority of patients sampled 70 (75.2%), compared with participants coming from other regions of Tanzania as shown by figure 1. Participants' age ranged from 18-66 years and a mean age of 44.4 years ± 10.8 years standard deviation (figure 2) with male participants being significantly older than female participants (mean age 50 years, [95% CI 45.4-54.5 years] vs., 42.5 years, [95% CI 40.2-40.7 years], *P* = 0.002) shown in figure 3.

Figure 1: Distribution of participants' residence.



Over representation of participants from Dar es Salaam is seen in the bar graph above. This is because the study site is located within Dar es Salaam.

Figure 2: Histogram showing the frequency distribution of participants' age

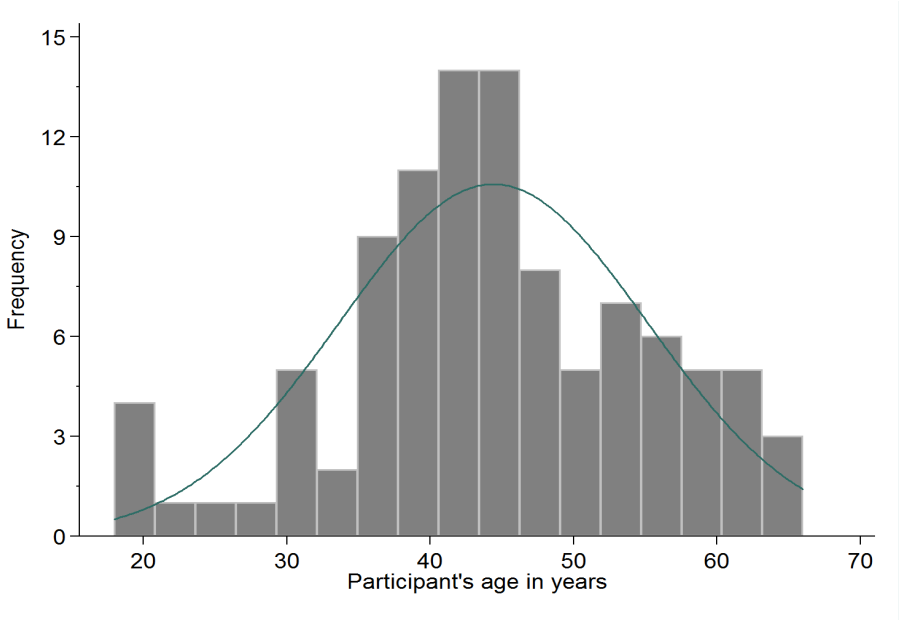
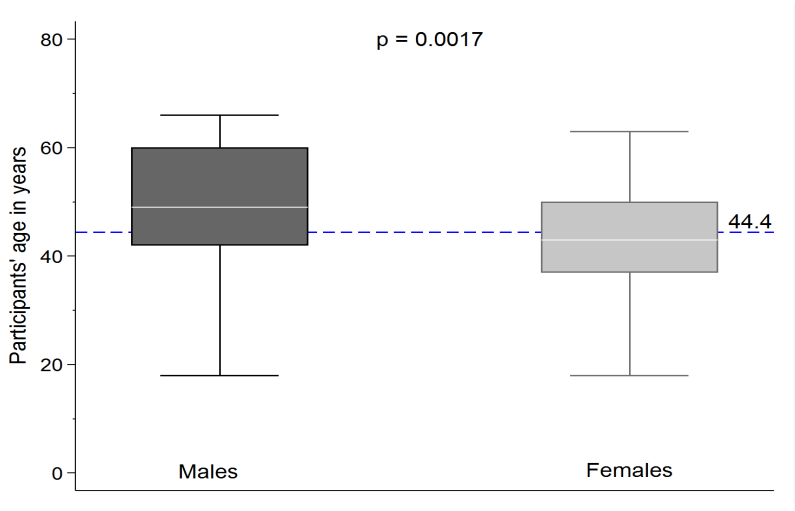


Figure 3: Box plots showing age distribution of study participants stratified by sex.



Briefly, the box plots above show the median and interquartile ranges, with the whiskers showing the minimum and maximum ages. The blue dotted line shows the mean age of study participants which was 44.4 years.

Table 2: Patient Characteristics

Characteristic, n (%)	Male, 26 (25.7)	Female, 75 (74.3)	Total, 101 (100)
Age group, n (%)			
<35 years	1 (3.85)	13 (17.33)	14 (13.86)
35-50 years	13 (50.0)	47 (62.67)	60 (59.41)
>50 years	12 (46.15)	15 (20.0)	27 (26.73)
Marital Status, n (%)			
Single	4(15.38)	23(33.33)	27 (28.42)
Married	19(73.08)	30(43.48)	49(51.58)
Separated	2(7.69)	7(10.14)	9 (9.47)
Widowed	1 (3.85)	9(13.04)	10(10.53)
Education level, n (%)			
Primary level	12(46.15)	29(43.28)	41(44.09)
Secondary level	7(26.92)	26(28.81)	33(35.48)
College level	3(11.54)	7(10.45)	10(10.75)
University level	4(15.38)	5(7.46)	9(9.68)
WHO clinical stage, n (%)			
Stage III		1(1.33)	1(0.99)
Stage IV	26(10)	74(98.67)	100(99.01)
CD4+counts, n (%)			
<200 cells/µL	9(34.62)	28(37.33)	37(36.63)
201-499 cells/µL	5(19.23)	17(22.67)	22(21.78)
>500 cells/µL	2(7.69)	6(8.0)	8(7.92)
Not done	10(38.46)	24(32.0)	34(33.66)

Most participants had primary (44.1%) or secondary education (35.5%), with the remaining lesser proportion (20.5%) occupied by either those who attained college or university level education. About a half of study participants were married (51.6%) while approximately a quarter of study participants (i.e., 28.4%) were single. Almost all participants 100 (99.01%) were classified as stage 4 in WHO clinical staging of HIV/AIDS illness of whom 68 (67.33%) were already on ARV as shown in table 2 (50).

3.2 Neurological symptoms

Table 3: Neurological manifestations among participants

Neurological symptoms, n	Males	Females	Total
Altered mental status	13(50.0%)	31(41.33%)	44(43.56%)
Headache	5(19.23%)	37(49.33%)	42(41.58%)
Neurological deficit	9(34.62%)	24(32.0%)	33(32.67%)
Seizures	7(26.92%)	14(18.67%)	21(20.76%)

All participants exhibited at least one neurological symptom defined as presence of headache, altered mental status, neurological deficit or presence of a seizure disorder. Altered mental status was the predominant symptom among those who sought care, followed by headache (i.e., 43.56% and 41.58% respectively) as shown in table 3 above.

3.3 Abnormal MRI findings

Table 4: Proportion of MRI findings among 101 study participants.

MRI Findings	Male	Female	Total
Normal	7(26.92%)	27(36%)	34(33.66%)
Abnormal	19(73.08%)	48(64%)	67(66.34%)
Total	26(100%)	75(100%)	101(100%)

A total of 101 MRI brain scans were done among HIV/AIDS patients presenting with neurological complaints, of which 67 (66.34%) had abnormal findings. This proportion ranges from 56.4% up to 74.9% in the general population (i.e., 95% confidence interval ranged from 57.4% to 75.9%).

Table 5: MRI Diagnosis of CNS lesions in HIV/AIDS Patients

MRI Diagnosis	Number of patients, n
Meningitis	8
Tuberculoma	3
Toxoplasmosis	6
Brain Abscess	3
Cryptococcosis	6
PML	5
CVA	16
HIVE	14
PCNSL	1
Subdural empyema	1
CMV	1
Hydrocephalus	2
UWMH	12

CMV-Cytomegalovirus, CVA-Cerebrovascular accident, HIVE- HIV encephalopathy, PML-Persistent multifocal leukoencephalopathy, PCNSL-Primary central nervous system lymphoma, UWMH- Unexplained white matter hyper-intensities

The table above depict the number of different diagnosis of CNS lesions in HIV/AIDS patients with neurological complaints, based on the MRI various imaging patterns and characteristics. Cerebrovascular accident (CVA) was the most common (n=16) diagnosis followed by HIV encephalopathy (HIVE) (n=14). Meningitis (n=8), toxoplasmosis and cryptococcosis (n=6 each) were the most common opportunistic infections. Some patients had more than one diagnosis.

Table 6: Relationship between CD4 levels and MRI findings (P=0.27)

CD4	Normal MRI	Abnormal MRI	Total
<200 cells/µL	9(45%)	28(59.57%)	37(55.22%)
≥ 200 cells/ µL	11(55%)	19(40.43%)	30(44.78%)
Total	20(100%)	47(100%)	67(100%)

Abnormal MRI findings differed across two CD4 groups i.e., ≤200 cells/µL and >200 cells/µLout of 67 study participants who had CD4 cell counts. Patients who had CD4 cell counts above 200 cells/µL had lower proportion of abnormal MRI findings (40.4%, 95% CI 27.1%-55.3%) than patients with CD4 cell counts below 200 cells/µL (59.6%, 95% CI 44.7%-72.9%) as shown in table 6 above. The difference was however, not statistically significant (P value 0.27).

Table 7: Relationship between CD4 levels and MRI Diagnosis

Diagnosis	CD4 ≤200 cells/µL n=37	CD4 >200 cells/µL n=30	P Value
Meningitis	7(18.92%)	-	0.01
Tuberculoma	2(5.41%)	1(3.33%)	1.00
Toxoplasmosis	3(8.11%)	1(3.33%)	0.62
Brain Abscess	-	1(3.33%)	0.45
Cryptococcosis	3(8.11%)	1(3.33%)	0.62
PML	2(5.41%)	1(3.33%)	1.00
CVA	8(21.62%)	3(10.00%)	0.32
HIVE	2(5.41%)	5(16.67%)	0.23
PCNSL	1(2.70%)	-	1.00
Subdural empyema	-	1(3.33%)	0.45
CMV	-	1(3.33%)	0.45
Hydrocephalus	1(2.70%)	1(3.33%)	1.0
UWMH	4(10.81%)	6(20.00%)	0.32

CMV-Cytomegalovirus, CVA-Cerebrovascular accident, HIVE- HIV encephalopathy, PML-Persistent multifocal leukoencephalopathy, PCNSL-Primary central nervous system lymphoma, UWMH- Unexplained white matter hyper-intensities

The table 7 above show the MRI diagnosis between the two CD4 count groups, with majority of the opportunistic infections and non-infectious diseases occurring in patients who had CD4 levels lower than 200 cells/µL. There was a significant association between meningitis and CD4 levels lower than 200 cells/µL (P=0.01). Despite no statistical significance, tuberculoma (3 /4) and cryptococcosis (3/4) were more prevalent in patients with CD4≤200 cells/µL. For more detail of table 7 above see appendix V.

Table 8: Relationship between ARV status and MRI findings (P=0.08)

ARV Status	Normal MRI	Abnormal MRI	Total
<6months	1(2.94%)	11(16.42%)	12(11.88%)
>6months	18(52.94%)	38(56.72%)	56(55.45%)
No	13(38.24%)	18(25.37%)	30(29.70%)
Not documented	2(5.88%)	1(1.49%)	3(2.97%)
Total	**33(100%)**	**68(100%)**	**101(100%)**

Only 68, out of 101 HIV/AIDS patients recruited in the study were on ARV therapy. The proportion of abnormal brain findings among people on ARV was higher than those who were not on ARV i.e., 72.1% (95% CI 60-81.6%) vs., 57.6% (95% CI 40%-73.4%). 11 out 12 patients who were on ARV for less than 6months has abnormal MRI. They accounted for 16% out of the 72% of the abnormal MRI in patients on ARV. This difference was however, not statistically significant. (P=0.08)

Table 9: Relationship between Viral Load and MRI findings (P-value 0.62)

Plasma Viral Load	Normal MRI	Abnormal MRI	Total
≤50 copies/mL	6 (33.33%)	8(26.67%)	14(29.17%)
>50 copies/mL	12(66.67%)	22(73.33%)	34(70.83%)
Total	18(100%)	30(100%)	48(100%)

Abnormal MRI findings differed slightly among patients with plasma viral suppression (defined as viral load ≤50 copies/mL) as compared to those without plasma viral suppression among 48 participants who had viral load results. Patients with plasma viral suppression had lower proportion (57%, 95% CI 30.2-80.5%) of abnormal MRI findings than patients without plasma viral suppression (64.7%, 95% CI 46.8-79.2%), however this difference was not statistically different.

Table 10: Relationship between Viral load and MRI diagnosis

Diagnosis	VL ≤50 copies/mL n=14	VL >50 copies/mL n=34	P Value
Meningitis	1(7.14%)	5(14.71%)	0.66
Tuberculoma	-	2(5.88%)	1.00
Toxoplasmosis	-	3(8.82%)	0.54
Cryptococcosis	-	2(5.88%)	1.00
Brain Abscess	-	2(5.88%)	1.00
PML	-	1(2.94%)	1.00
CVA	1(7.14%)	5(14.71%)	0.66
HIVE	2(14.29%)	4(11.76%)	1.00
PCNSL	1(7.14%)	-	0.29
UWMH	3(21.43%)	4(11.76%)	0.40

CMV-Cytomegalovirus, CVA-Cerebrovascular accident, HIVE- HIV encephalopathy, PML-Persistent multifocal leukoencephalopathy, PCNSL-Primary central nervous system lymphoma, UWMH- Unexplained white matter hyper-intensities

Table 10 above depicts the relationship between MRI radiological diagnosis and viral load. Most of the opportunistic infections and non-infectious diseases were seen in patients without viral load suppression, (VL>50 copies/mL). Tuberculoma, toxoplasmosis, cryptococcosis, brain abscess and persistent multifocal leukoencephalopathy (PML) were found only in patients with viral load above 50 copies/mL. These findings were, however not statistically significant. For more detail of table 10 above see appendix V.

Table 11: MRI Imaging Patterns in HIV patients with Neurological Manifestation

MRI Pattern	Male	Female	Total
Abnormal MRI, n (%)	19(73.08)	48(64)	67(6.34)
FML with mass effect/ enhancement, n (%)	3(15.79)	11(22.92)	14(20.9)
FML without mass effect /enhancement, n (%)	3(15.79)	6(12.5)	9(13.43)
Diffuse global abnormality n (%)	6(31.58)	9(18.75)	15(22.39)
Hydrocephalus, n (%)	-	2(4.17)	2(2.99)
Ventriculitis, n (%)	1(5.26)	2(4.17)	3(4.48)
Leptomeningeal enhancement, n (%)	3(15.76)	6(13.43)	9(13.43)
Infarcts, n (%)	5(26.32)	11(22.92)	16(23.88)
Non-specific WMH, n (%)	3(15.76)	9(18.75)	12(17.91)

FML-Focal mass lesion, WMH-White matter hyperintensities

Among the 67 abnormal MRI brain findings, infarct was the most prevalent pattern with a proportion of 23%. This was followed by diffuse global abnormalities (defined as cerebral atrophy with/without symmetrical white matter hyper-intensities) and focal mass lesions with mass effect which had a proportion of 22% and 20% respectively (Table 11).

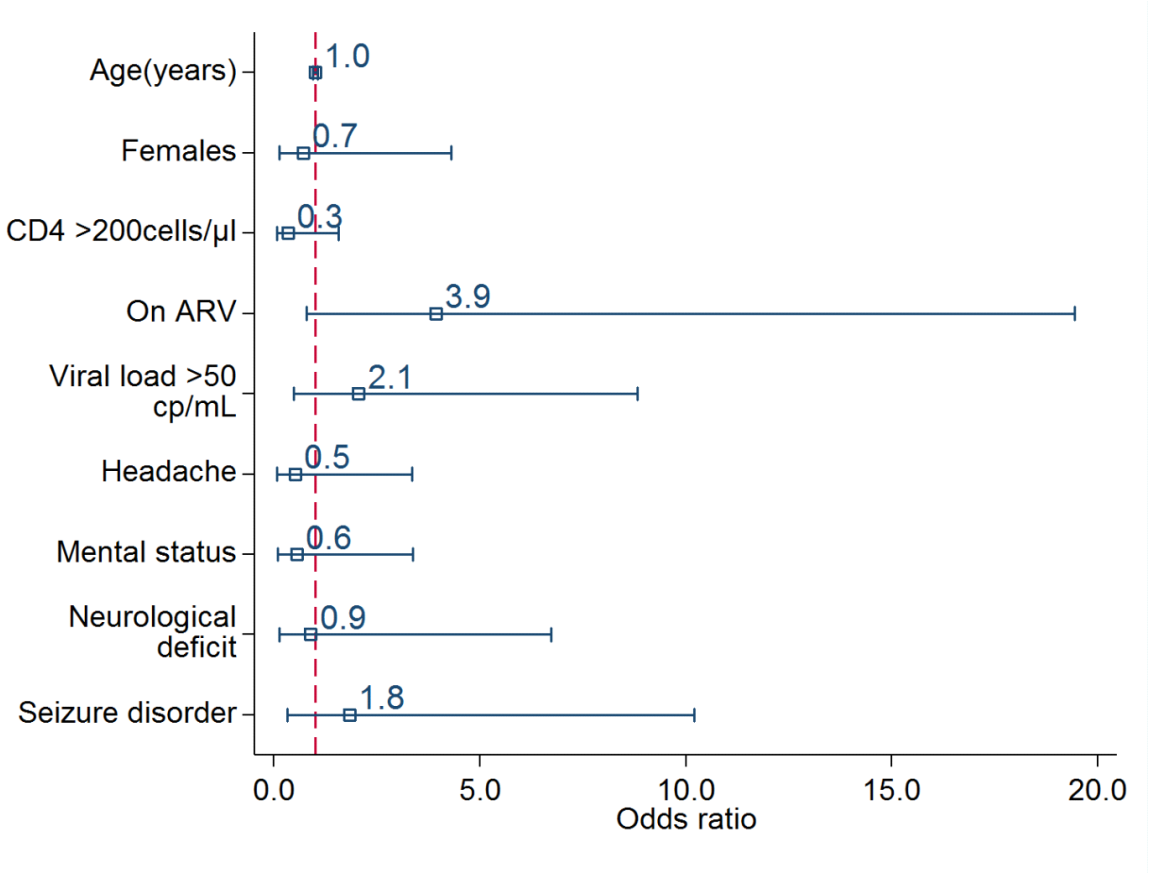
Out of the 14 focal mass lesions with mass effect and enhancement pattern, toxoplasmosis accounted for the majority 6(42.86%) of the MRI diagnosis. Others diagnoses included tuberculoma (n=3), brain abscess (n=3) and cryptococcoma (n=2). (P=0.01)

On the other end, PML was the most prevalent MRI diagnosis, 5(55.56%), among mass lesions without enhancement or mass effect. Presence of seizures showed borderline significant association with leptomeningeal enhancement 4 (44.44%) vs. 9 (15.52%), *P*=0.059.

3.4 Associations of abnormal MRI findings

Figure 4: Coefficient plot showing odds ratio of predictors of abnormal MRI findings

Odds ratio from a multivariate logistic regression model adjusted for age, sex, CD4 status, viral load, ARV status, and neurological symptoms. Red dashed line indicates an Odds ratio of 1.



In a multivariate logistic regression model adjusted for age, sex, CD4 counts, viral load, ARV status, and neurological symptoms (i.e., headache, altered mental status, neurologic deficit and seizure disorder), for every one-year increase in age, the odds of a participant having abnormal MRI finding decreases by 2% (adjusted OR [aOR] 0.98, 95% CI 0.94-1.03). Also, females had approximately a 29% decrease in the odds of having abnormal MRI findings as compared to male participants (aOR 0.71, 95% CI 0.12-4.3) as shown in figure 4.

Patients with viral loads above 50 copies/mL had twice the odds of abnormal MRI as compared to those with less than 50 copies/mL of viral load (i.e., aOR 2.06, 95% CI 0.48-8.82) while those whose CD4 cell counts were above 200 cells/μL had 67% decrease in the odds of having abnormal MRI findings (aOR 0.33, 95% CI 0.07-1.5). Participants with seizure disorder had a 83% increase in the odds of having abnormal MRI finding (see Figure 4) as compared to patients without seizure disorders (aOR 1.83, 95% CI 0.33-10.4), however all these observations were not statistically significant as the study was not powered to assess these associations.

CHAPTER FOUR

4.0 DISCUSSION

In this hospital based cross-sectional study, the mean age of the participants was 44 years with females accounting for a greater proportion of the total study population. This is similar, to the 2011-12 National HIV/AIDS and Malaria Indicator Survey, which showed that HIV prevalence was higher among women (6.2%) than men (3.8%) (4). About a half of the participants were married, contrary to the 2011-12 National HIV/AIDS and Malaria Indicator Survey, where prevalence of HIV was higher among the widowed and separated/divorced (4). In this study Ilala district had the most number of HIV positive participants, followed by Kinondoni and Temeke , contrary to UNAIDS report of Tanzania subnational estimates of HIV prevalence of 2014 which showed the HIV prevalence per district to be highest in Temeke (8.9%) followed by Ilala (7.6%) and lastly Kinondoni (6.8%) (51). These differences could be due to nature of this study being cross-sectional and hospital based focussing only HIV/AIDS patients with neurological complaints hence unable to reflect the burden and distribution of the disease in the population. Altered mental status followed by headaches was the most frequent neurological complaints in this study.

About sixty seven percent (67%) of the HIV patients, who had neurological complaints, had abnormal brain MRI imaging findings. This is contrary to a study by study by Ajith et al, who had a higher proportion (85%) of abnormal MRI brain scans among HIV/AIDS patients with neurological symptoms (52).

Participants on HAART were found to have a higher proportion of the abnormal MRI findings. We would expect to find people on ARV to have less abnormal MRI brain findings due to improved immune status. Out 12 patients who were on ARV for less than 6months, 11 had abnormal MRI. This counterintuitive finding may be due to immune reconstitution inflammatory response to HAART or poor adherence. Furthermore, late initiation of HAART when the immune system is significantly compromised resulting in poor and delayed restoration of the immune defense systems hence increasing the risk of morbidity may also attribute to this finding (53-55).

The nature of the study being cross sectional in design with no longitudinal follow up could also be an alternative explanation to this unexpected observation found in this study.

Participants who had CD4 counts less than 200cell/μL had a higher proportion of abnormal MRI findings. CVA, HIVE and opportunistic infections such as meningitis, tuberculoma, and toxoplasmosis were higher among patients with CD4 counts ≤200 cells/μL as shown in table 7. Similar findings were seen in a study done by Graham et al, where he found, out of the 76(37.3%) positive brain scans, all 18(23.7%) scans which showed mass lesions or white matter lesions in HIV patients with headaches had a CD4 cell count of less than 200 cells/μL (P = .04) (41). Studies done in India by Camera et al and Jency et al, also found CNS manifestations to be more common in patients, who were having low (200μL) CD4 count. (P value – 0.0026) (56, 57). This could be attributed to the more weakened immune system that is more vulnerable to opportunistic infections(39).

Patients with plasma viral suppression (viral load of ≤50 copies/mL) had less abnormal MRI findings than those without viral suppression (viral load >50copies/mL). In addition, based on the multivariate logistic regression model, participants with plasma viral loads of above 50 copies/mL had twice the odds of having abnormal MRI. This could be attributed to increased vulnerability to direct effects of the HIV virus itself as well as to the opportunistic infections and tumors that may result in neurological diseases. A study by Kaplan et al, report increasing viral load as an independent risk factor for opportunistic infections (58).

Infarcts, diffuse global abnormality (cerebral atrophy with or without symmetrical white matter hyperintensities) and focal mass lesions with mass effect accounted for more than half (62%) of the abnormal brain MRI imaging patterns. In this study, the most common MRI diagnosis was CVA followed by HIVE. Meningitis, toxoplasmosis and cryptococcosis were the most common opportunistic infections. A study done by Ajith et al, reported cerebral atrophy and infarct as the most common CT abnormalities while the common abnormalities identified by MRI scan were HIVE (16.67%), toxoplasmosis (12.50%), and infarcts (10.42%) (52). Primary HIV vasculopathy and opportunistic infection associated vasculitis; vasospasm plus thrombosis are possible patho-

logical processes that could attribute to the high proportion of infarcts in this study (59). Based on a study done by Laura et al, the rates of stroke in HIV individuals is increased compared to non-HIV patients, particularly in females (60).

Furthemore, the risk of cerebrovascular events is reported to increase when associated with low CD4 count before ART, and abacavir (61). Confounding variables such as hypertension and diabetes could also have influenced this finding; however, we did not have such valuable information in order to adjust for such predictors in the model.

Diffuse global abnormality and focal mass lesions with mass effect which accounted for about 40% of the abnormal MRI brain findings, could be attributed to the fact that, direct involvement of the CNS by the virus itself as being the most common cause of neurological disease in AIDS while toxoplasmosis as being the most frequent opportunistic CNS infection in the AIDS population (59).

Non-specific white matter hyper-intensities which accounted for 16% of the abnormal MRI findings in this study are documented as incidental finding with no difference in incidence between seropositive and seronegative individuals. These are small (sub 5mm) areas of increased signal on T2 and FLAIR. They are thought to represent focal areas of mild gliosis, increased perivascular fluid and pathological partial demyelination possibly due to arteriosclerosis as seen in elderly patients, prior inflammation/vasculitis, and drug abuse (59).

CHAPTER FIVE

5.1 CONCLUSION

Neuro-imaging is an essential component in the management of HIV/AIDS patients who present with clinical neurological manifestations. The excellent soft tissue resolution of MRI and availability of multiple sequences in MRI simplifies the identification and characterizations intracranial lesions. Out of 101 participants in this study, 67% had abnormal MRI findings, with infarcts, diffuse global abnormality and focal mass lesions accounting for about two thirds of the abnormal brain MRI patterns. Patients with CD4≤200cells/μL and viral load >50copies/mL had higher proportion of abnormal MRI findings than their counterparts. Neuro-imaging hence forth, not only aids in the diagnosis of the disease culprit but also in assessing treatment response especially in patients with low CD4 count and no viral suppression.

Only one out of 101 clients enrolled in the study had a follow up MRI which showed considerable improvement in the lesions after treatment initiation.

5.2 RECOMMENDATIONS

This study sets the groundwork for future studies which can assess specifically on individual associations of the MRI brain findings in HIV patients with neurological manifestations. With the counterintuitive finding of higher proportion of abnormal MRI in patients on HAART, further analysis on the relationship between the MRI findings and ARV status of the HIV patient with consideration of the time since ARV initiation and adherence is recommended.

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7.0 APPENDICES

Appendix 1: Questionnaire

A: Demographics

1	Patient initials/ID	
2	Sex	
3	Age	
4	Residence	
5	Level of education	
6	Occupation	
7	Marital status	single married separated widowed

B: HIV Disease history

8	WHO HIV stage	
11	CD 4 count (within 6mo)	
12	Viral load	
13	ARV status	On treatment:
		Not on treatment
14	Duration on ARV	6months > 6months

C: Presenting Neurological Complaint

	Neurological Complaint	yes	no
15	Headache: prolonged > 3dys increasing severity		
16	altered /depressed mental status		
17	focal neurological deficit		
18	new onset seizures		

D: CSF Analysis

19	Done	Yes	No
20	Biochemistry	Glucose Protein	
21	Cytology	Lymphocytes Neutrophils Abnormal cells	
22	Antigen test	Toxoplasmosis Cryptococcal	
23	Microbiology	Gram stain ZN stain Indian ink Culture/sensitivity	

D: Neuro-Imaging (MRI) findings

24	Normal		
25	Focal lesions with significant mass effect /enhancement		
26	Focal lesions without significant mass effect/enhancement		
27	Diffuse globular disease	Cerebral atrophy	White matter lesions
28	Ventriculitis		
29	Meningitis		
30	Infarcts		
31	Other findings		
32	Conclusion		

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. Haika Maro; I am conducting a study on MRI brain findings in HIV/AIDS patients with neurological findings among HIV/AIDS adult patients at Radiology department at MNH.

Study Purpose

The study is conducted as partial fulfillment of the requirements of Mimed Radiology at MUHAS. The study is also conducted to establish the imaging findings of HIV/AIDS patients with CNS symptoms that can serve as a foundation of future studies as well as aid in patient management

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 evaluate the MRI radiographic findings among HIV/AIDS adult patients with CNS manifestations, thus the study outcomes will help to 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.Haika Maro,

Muhimbili University of Health and Allied Sciences,

P. O. Box 65001, Dar es Salaam

Tel: 0624 717 629**.**

In case you have questions about your rights of participation in this study you may contact:

Dr Joyce Masalu, Chairperson of the Senate Research and Publications Committee,

P. O. Box 65001 DSM.

Telephone**:** +255 022 2152489

Dr. Ramadhani Kazema who is the supervisor of this study

Tel. +255 754 288 644

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

Jina langu ni Dr. Haika Maro nafanya utafiti wenye lengo la kuangalia madiliko katika ubungo wa wagonjwa wa maambukizi ya VVU wanaofanyiwa MRI ya kichwa kwenye idara ya vipimo vya mionzi katika Hospitali 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 Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili. Hali kadhalika kupata vipimo ambavyo vinaweza kutumika kwenye matibabu ya wagonjwa hao.

Jinsi ya kushiriki

Ukikubali kushiriki katika utafiti huu, utasailiwa halafu utatakiwa kujibu maswali kutoka kwenye dodoso lililoandaliwa halafu mgongwa ataendelea 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.Haika Maro,
Chuo Kikuu cha Afya na Sayansi ya Tiba Muhimbili,
S. L. P. 65001, Dar es Salaam.
Simu: 0624 717 629.

Dr Joyce Masalu,

Mwenyekiti wa kamati ya Utafiti na Uchapishaji,
S.L.P 65001,
Dar es Salaam.
Simu+255 022 2152489

Msimamizi wa utafiti huu Dr. Ramadhani Kazema
Simu +255 754 288 644

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…….

Appendix IV: Table and images MRI patterns of CNS manifestations

MRI Imaging Characteristic of CNS lesions in patients with AIDS

Diagnosis	Nonenhanced CT scans	Nonenhanced MR images	Enhancement pattern	Surrounding edema	Location of lesion	No. of lesions
Toxoplasmosis	Low attenuation; occasional hemorrhagic lesions	Low signal intensity on T_1W image; high signal intensity on T_2W image; occasional hemorrhagic lesion	Nodular (small); ring (small to large)	++	Basal ganglia; grey-white junction	Single to many
Primary CNS lymphoma	Varies, but high attenuation is characteristic	Low to isointense signal on T_1W image; low to isointense to decreased signal on T_2W image	Uniform to ring (necrotic)	++	Periventricular white matter; basal ganglia; subependymal spread characteristic	One to a few
Cryptococcosis (pseudocyst)	Low attentuation	Low signal intensity on T_1W image; high signal intensity on T_2W image	None	None	Perivascular spaces (particularly basal ganglia)	One to many
Tuberculosis (granuloma)	Low attenuation	Low signal intensity on T_1W image; high signal intensity on T_2W image	Ring or nodular	None	Variable	One to many
Syphilis (gumma)	Low attenuation	Low signal intensity on T_1W image; high signal intensity on T_2W image	Uniform	++	Cortex or dura	One to a few
Abscess (cryptococcal, tuberculous, or bacterial)	Low attenuation	Low signal intensity on T_1W image; high signal intensity on T_2W image	Thin ring	+++	Varies	One to a few

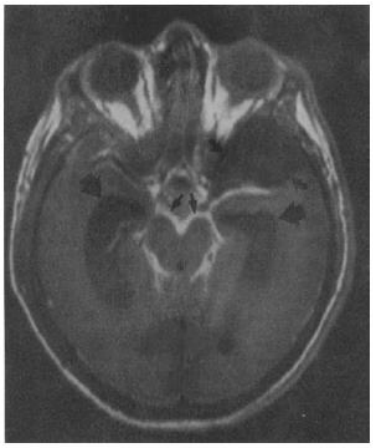
NOTE. MR = magnetic resonance; T_1W = T_1 weighted; T_2W = T_2 weighted; ++ = mild to moderate surrounding edema; +++ = large amount of surrounding edema.

Imaging Characteristic of CNS lesions in patients with AIDS

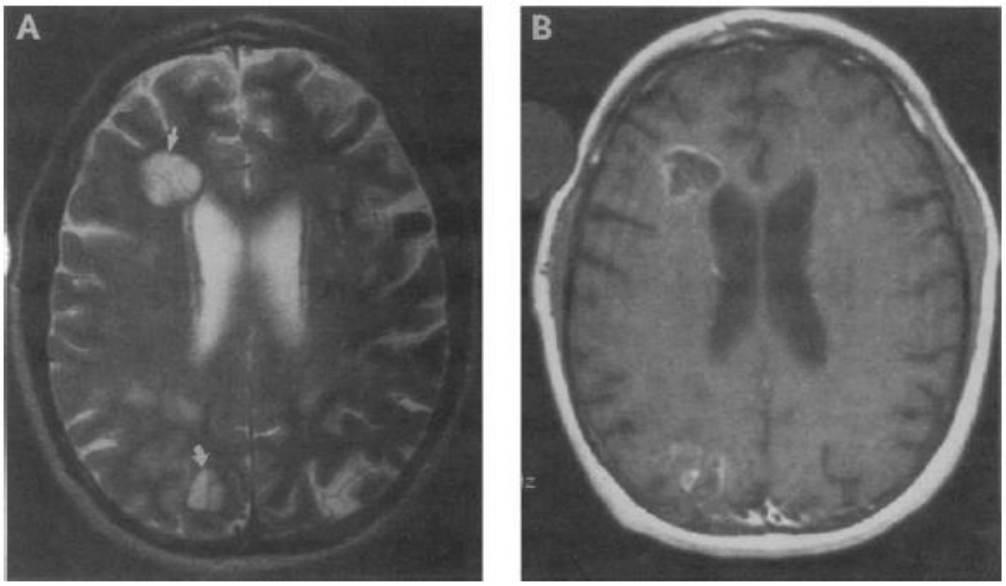
Pattern	Diagnosis	Nonenhanced CT scans	Nonenhanced MR images	Enhancement pattern	Surrounding edema	Location	No. of lesions
Focal lesion without mass effect	Progressive multifocal leukoencephalopathy	Low attenuation	Low signal intensity on T_1W image, high signal intensity on T_2W image	Rare rim enhancement	None	White matter	Single to a few
Diffuse abnormality	Infection with HIV and CMV	Low attenuation, atrophy	Low signal intensity on T_1W image, high signal intensity on T_2W image; atrophy	None	None	Deep white matter	Diffuse, ill defined
Ventriculitis, meningitis, and infarcts	Infection with CMV	Low attenuation	Low signal intensity on T_1W image, high signal intensity on T_2W image	Linear ependymal enhancement and ill-defined periventricular enhancement	+++	Ependyma, periventricular spaces	Confluent
	Tuberculosis	Thickened meninges, infarcts, hydrocephalus	Thickened meninges; infarcts; hydrocephalus	Uniform	++	Meninges (particularly basilar meninges)	Confluent
	Neurosyphilis	Infarcts	Infarcts	Variable	Variable	Variable	Variable

NOTE. CMV = cytomegalovirus; MR = magnetic resonance; T_1W = T_1 weighted; T_2W = T_2 weighted; ++ = mild to moderate surrounding edema; +++ = large amount of surrounding edema.

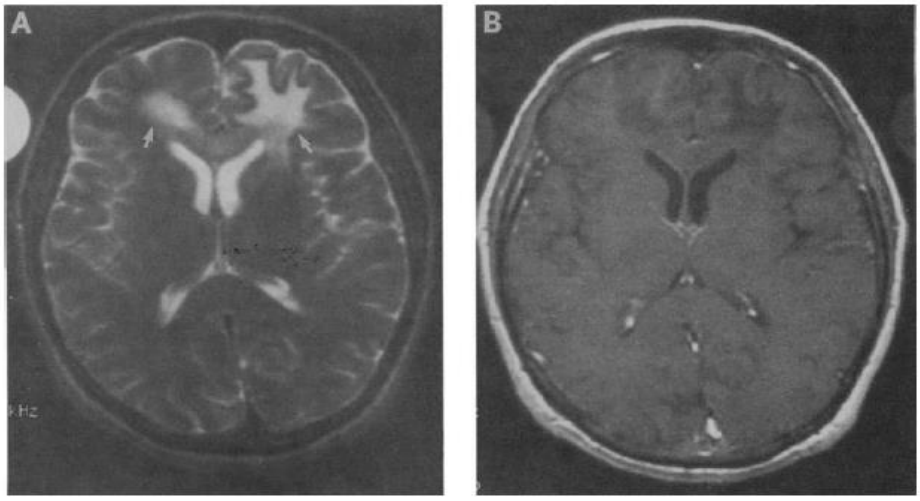
MR image of a patient with tuberculous meningitis and hydrocephalus. T,W contrast-enhanced axial MR *(600/2012)* image reveals thickened enhancing meninges surrounding the brainstem *(arrows)* and dilated temporal horns of the lateral ventricles *(large arrows).* An arachnoid cyst in the left middle fossa *(curved arrows)* is an incidental finding. T,W = TI weighted; numbers in parentheses are repetition time/echo time/excitations



MR image of a patient with a cryptococcal brain abscess. *A,* T2W fast spin echo axial MR (3000/10212) image at the level of the top of the lateral ventricles shows two well-defined lesions of high signal intensity (one in the right frontal lobe adjacent to the right lateral ventricle *[an-ow]* and another small lesion in the right occipital lobe *[curved an-ow]). B,* contrast-enhanced TjW MR (600/10/2) image at the same level shows both lesions to be oflow signal intensity with thin rim enhancement. T2W = T2 weighted; T.W = T) weighted; numbers in parentheses are repetition time/ echo time/excitations.



MR image of a patient with progressive multifocal lleukoencephalopathy.*A,* T2Wfast spin echo axial MR *(4000/10211)* image shows iIIdefined white matter lesions in both frontal lobes *(arrows);* no mass effect is seen. *B,* contrast-enhanced T,W axial MR (66/10/1) image at the same level shows the lesion to be of low signal intensity with minimal, if any, contrast enhancement



Appendix V: Tables of MRI Diagnosis with Viral load and CD4 countsTable

Diagnosis	CD4 ≤200 cells/µL n=37	CD4 >200 cells/µL n=30	P Value
Meningitis			
yes	7(18.92%)	0	0.01
no	30(81.08%)	30(100%)	
Tuberculoma			
yes	2(5.41%)	1(3.33%)	1.00
no	35(94.59%)	29(96.67%)	
Toxoplasmosis			
yes	3(8.11%)	1(3.33%)	0.62
no	34(91.89%)	29(96.67%)	
Brain Abscess			
yes	0	1(3.33%)	0.45
no	37(100%	29(96.67%)	
Cryptococcosis			
yes	3(8.11%)	1(3.33%)	0.62

no	34(91.89%)	29(96.67%)	
PML			
yes	2(5.41%)	1(3.33%)	1.00
no	35(94.59%)	29(96.67%)	
CVA			
yes	8(21.62%)	3(10.00%)	0.32
no	29(78.38%)	27(90.00%)	

7A: Relationship between CD4 levels and MRI Diagnosis
Table 7B: Relationship between CD4 levels and MRI Diagnosis

Diagnosis	CD4 ≤200 cells/µL n=37	CD4 >200 cells/µL n=30	P Value
HIVE			
yes	2(5.41%)	5(16.67%)	0.23
no	35(94.59%)	25(83.33%)	
PCNSL			
yes	1(2.70%)	0	
no	36(97.30%)	30(100%)	1.00
Subdural Empyema			
yes	0	1(3.33%)	0.45
no	37(100%)	29(96.67%)	
CMV			
yes	0	1(3.33%)	0.45
no	37(100%)	29(96.67%)	
Hydrocephalus			
yes	1(2.70%)	1(3.33%)	1.00
no	36(97.30%)	29(96.67%)	
UWMH			
yes	4(10.81%)	6(20.00%)	0.32
no	33(89.19%)	24(80.00%)	

Table 10 A: Relationship between Viral load and MRI diagnosis in HIV patients

Diagnosis	VL ≤50 copies/µL n=14	VL >50 copies/µL n=34	P Value
Meningitis			
yes	1(7.14%)	5(14.71%)	
no	13(92.86%)	29(85.29%)	0.66
Tuberculoma			
yes	0	2(5.88%)	
no	14(100%)	32(94.12%)	1.00
Toxoplasmosis			
yes	0	3(8.82%)	
no	14(100%)	31(91.18%)	0.54
Cryptococcosis			
yes	0	2(5.88%)	
no	14(100%)	32(94.12%)	1.00
Brain Abscess			
yes	0	1(2.94%)	
no	14(100%)	33(97.06%)	1.00
PML			
yes	0	1(2.94%)	
no	14(100%)	33(97.06%)	1.00

Table 10 B: Relationship between Viral load and MRI diagnosis in HIV patient

Diagnosis	VL ≤50 copies/µL n=14	VL >50 copies/µL n=34	P Value
CVA			
yes	1(7.14%)	5(14.71%)	
no	13(92.13%)	29(85.29%)	0.66
HIVE			
yes	2(14.29)	4(11.76)	1.00
no	12(85.71)	30(88.24)	
PCNSL			
yes	1(7.14%)	0	
no	13(92.86%)	34(100%)	0.29
UWMH			
yes	3(21.43%)	4(11.76%)	
no	11(78.11%)	30(88.24%)	0.40