COMPUTERIZED TOMOGRAPHY BRAIN SCAN FINDINGS IN SYMPTOMATIC HUMAN IMMUNODEFICIENCY VIRUS INFECTED ADULT PATIENTS AT THE MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA.

BY

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A thesis presented to the School of Medicine in partial fulfillment for the award of the degree of Master of Medicine in Radiology and Imaging

Moi University.

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DECLARATION

Student's Declaration

I declare that this thesis is my original work, written in part fulfillment for the degree of Master of Medicine in Radiology and Imaging. It has not been submitted to any other university or organization. No part of this work may be reproduced without the sole permission of Moi University and, or the investigator.

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This thesis has been submitted for consideration with our approval as supervisors.

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DEDICATION

I would like to dedicate this work to God who has made it possible for me to be who I am today, through the help of my family, friend, and numerous persons, who have in one way or other, helped me realize my true potential.

I am forever grateful.

ABSTRACT

Background: Human Immunodeficiency Virus (HIV)is a major global health issue. HIV is neuro-invasive and neuro-virulent causing Central Nervous System(CNS) complications in 40-70% ofHuman Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) patients. Computerized Tomography (CT) is a non-invasive diagnostic tool use to investigate patients with clinical signs suggestive of central nervous system involvement.

Objective: To describe the Computerized Tomography brain findings of HIV-infected adult patients and relate these findings to Antiretroviral Therapy (ART) use.

Methods: A cross-sectional study conducted between January 2015 and December 2015. Ninety-five HIV-infected adult patients with CNS presentation who underwent a contrast-enhanced brain CT were enrolled. Data was collected using a structured questionnaire. Data on patient demographics, clinical presentation and ART-use were collected at the time of presentation and correlated with brain CT findings. Frequencies were calculated. Odds ratios used to assess associations. A p-values of <0.05 was considered significant.

Results: Ninety-five participants were included in the study. The mean age of participants was 39.8 years. Brain CT scans were abnormal in 65.3%(n=62). Parenchymal pathology was seen in 44.2% (n=42). Most parenchyma lesions are hypodense (n=39), non-enhancing (n=37) and located in the frontoparietal region. Ventricular pathology was seen in 35.8% (n=34). Meningeal pathology was seen in 11.65% (n=11). Encephalitis was the most common finding in 27.4% (n=26). Toxoplasmosis was the only opportunistic infection seen in 2.1% (n=2). Brain pathology was significantly higher in male compared to the female, OR 2.5 (95% CI 1.0-6.0), p=0.046. Prevalence of brain pathology was significantly lower in participants 40 years and below, compared to participants over 40 years, OR 0.3 (95% CI 0.1-0.8), p=0.010. there was no significant association betweenART use and common brain CT findings (p>0.05). Focal and multifocal lesions are significantly higher in patients who were on ARTs (13.5%) while none of their counterparts reported such lesions (p=0.015).

Conclusions: Prevalence of brain pathology was 65.3%. Most lesions were hypodense, non-enhancing and located in the frontoparietal region. The most common finding was Encephalitis. Toxoplasmosis was the only opportunistic infection diagnosed. Antiretroviral therapy use was not a determinant of brain pathology. Focal and multifocal parenchymal lesions were only seen in participants on ARTs.

Recommendation: A large prospective studies should be conducted to further evaluate the relationship, if any, between CT findings and Antiretroviral Therapy use.

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ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatment
ARV	Antiretroviral
CD	Cluster of Differentiation
CDC	Center for diseases control
CM	Cryptococcal meningitis
CT	Computerized Tomography
FND	Focal Neurological Disorder
HAD	Human Immunodeficiency Virus-Associated Dementia
HAND	Human Immunodeficiency Virus-associated neurocognitive dysfunction
HIV	Human Immunodeficiency Virus
IREC	Institutional Research and Ethics Committee
MAC	Mycobacterium Avium Complex
MRI	Magnetic Resonance Imaging
MTRH	Moi Teaching and Referral Hospital
NACC	National AIDS Control Council

NASCOP	National AIDS and STI Control Programme
OI	Opportunistic Infection
PGL	Persistent GeneralizedLymphadenopathy
PLHA	People Living with AIDS
PML	Progressive Multifocal Leukoencephalopathy
SPECT	Single-photon emission Computerized Tomography
STI	Sexually Transmitted Disease
TBM	Tuberculous meningitis
UNAIDS	Joint United Nations Programme on Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome
WHO	World Health Organization

DEFINITION OF TERMS

Focal: well-define lesion localize to a specific area.

Multifocal: focal lesions arising from or occurring in more than one location.

Diffuse: disseminated lesions that appear spread out and not restricted or limited to one location.

Ill-define: lesions lacking a clear boundary or outline with indistinct margins.

CHAPTER ONE: INTRODUCTION

BACKGROUND

HIV/AIDS isa major global public health issue. Ithas claimed more than 34 million lives globally with 1.2 million people dying from Human Immunodeficiency Virus (HIV) related causes in 2014 (WHO, 2015).Sub-Saharan Africa is the most affected with 70% ofnew infection occurring in this region(WHO, 2015). In 2015, 36.7 million people were living with HIV (WHO, 2016a). In Kenya, the 2015 estimated prevalence of HIV infectionin adults 15-49 years was 5.9%, and an estimated 71,000 adults were newly infected with the virus(UNAIDS, 2016).

HIV is a lentivirus which causes latent infection (McGire, 2003). The virustends to cause neurological disease and complications. These complications are caused by the virus, opportunistic infection, Acquired Immune Deficiency Syndrome (AIDS) related tumours, or treatment [Immune Reconstitution Inflammatory Syndrome (IRIS)] (Singer, Valdes-Sueiras, Commins and Levine, 2010).

The virus is neurotrophic, lymphotrophic (Tso, Todd, Groleau and Hooper, 1993) and neurovirulent (Manji and Miller, 2004) with the ability to cross the blood-brain-barrier (Tso et al., 1993) resulting in a plethoric of Central Nervous System (CNS) manifestation. The CNS provides a fertile environment for the virus to grow, replicate, mutate and finally re-infect (Brew et al., 2009).

10-20% of People Living with HIV/AIDS (PLHA) present with neurological manifestations at the time of diagnosis, while 60% of PLHA present with neurological disease in the course of their illness(McGire, 2003).

The commonest neurological complications seen in people living with HIV in Kenya are Cryptococcal meningitis (22%), Encephalitis (18.7%), Cerebral Toxoplasmosis (12.7%), Stroke (12.7%) and Tuberculous Meningitis (10.7%)(Jowi, Mativo and Musoke, 2007).Clinicians should strongly consider the possibility of CNS involvement in HIV/AIDS because PLHA are sometimes unaware of their status and people who have commenced Antiretroviral Therapy (ART) might be exposed to CNS opportunistic infections (Tan et al., 2012). Fortunately, most of these complications are treatable (Manji and Miller, 2004);however, timely diagnosis is critical.

Clinical presentation, Cerebrospinal Fluid (CSF) findings, and radiological features are the fundamental tools used in the diagnosis of HIV/AIDS patients with suspected CNS disease (Tan et al., 2012b). A host of neuroimaging techniques including CT, Magnetic Resonance Imaging (MRI), Thallium Single-Photon Emission Computerized Tomography (SPECT), Positron Emission Tomography (PET) scans (Senocak et al., 2010), assist in the diagnosis of brain lesions in HIV patients.

Countries in sub-Saharan Africahave a lack of sophisticated radiological equipment(AFRO WHO, 2015). The ratio of CT scanner to population is 1 per 64,900 in high-income countries and 1 per 3.5 million people in low-income countries(WHO, 2010b). The lack of radiology equipment limits radiological investigation in a population with high HIV/AIDS prevalence. Contrast-enhanced brain CT is usually the first radiological investigation done in patients with CNS presentation.In Kenya, contrast-enhanced brain CT is the recommended first line radiological tool in HIV/AIDS patients with suspected CNS complications(NACC and NASCOP, 2012).

The complex HIV-nervous system interaction makes neurological manifestations a frequent complication in HIV/AIDS. This study seeks to investigate the different patterns seen on brain CT in adult patients with these complications.

PROBLEM STATEMENT

If not recognized early, CNS involvement in HIV infection is associated with high morbidity and mortality (Offiah and Turnbull, 2006). CNS involvement in HIV is also a major obstacle in the management and eradication of the virus. The CNS is somewhat impermeable to Antiretroviral (ARV), causing reduced levels of ARV in the CNS(Letendre et al., 2008).

In Kenya, 1.6 millionare living with HIV (NACC and NASCOP, 2012), and a fifth of these patients present with neurological complications (Jowi, Mativo and Musoke., 2007).Thesecomplications are seen eitherat the time of diagnosis (McGire, 2003), in all stages of the infection (Manji and Miller, 2004), or during initiation of ART (Tan et al., 2012b).

CT is one of a primary tool in the management of CNS disease in HIV/AIDS (NACC and NASCOP., 2012), however, local data illustrating CT finding among this population is limited.

JUSTIFICATION

Clinical presentation, CSF analysis, and radiology are the primary tool in the management of CNS HIV/AIDS opportunistic infections(Tan et al., 2012b).

Imaging features are characteristic, and this enables detection, diagnosis, and initiation of treatment (Descamps, Hyare, Zerizer, and Jäger, 2008). Imaging should be done for patients with clinical signs suggestive of CNS involvement. Even though these conditions have high mortalities (Thurnher, Thurnher, and Schindler, 1997) theyare treatable (Roullet, 1999).

A hosts of neuroimaging techniques assist in the diagnoses of brain lesions, in this study, CT is the most appropriate tool. It is an imaging tool that is geographically and financially accessible in resource-limited settings (Potchen et al., 2014), and at the study site, it is the most cost effective option compared to MRI.In unstable and agitated patients, CT is a valuable tool in the evaluation of HIV/AIDS patients who present with confusion. It is a known fact that MRI is more sensitive (McGire, 2003) and superior(Ramsey and Geremia, 1988) to CT in detecting neuropathology in HIV/AIDS patients. However, in the early stage of HIV disease MRI and CT may prove nonspecific (Kramer and Sanger, 1990).Contrast-enhanced brain CT also plays a significant role in diagnosis and follow-up of HIV/AIDS patients with CNS disorders (Senocak et al., 2010). The National AIDS and STI Control Programme (NASCOP) of Kenya also recommends CT as the premier imaging modality in PLHA in need of neurological review (NACC and NASCOP, 2012).

There is a paucity of local data on the imaging findings of CNS manifestation in HIV/AIDS infection. The last documented study was in 1999 (Gatune, 1999).

Globally, 36.7 million people are living with the virus;however, only 17 million people are on antiretroviral therapy (WHO, 2016a).

Currently, the WHO recommends a “treat all” policy (WHO, 2016b) with the hope of reducing the risk of HIV/AIDS-related infection; CNS disease included (WHO, 2016c).

This policy change might affect imaging dynamics in this population. In low-income countries, there is a paucity of studies relating ART-use to CT brain findings.

This study seeks to identify the different CT pattern of CNS involvement in HIV/AIDS in the Kenyan population and to relate these findings to ART-use. This informationwillprovide local data for policy makers and contribute to local and international knowledge.

RESEARCH QUESTION

1. What are the imaging findings on CT brain scan of HIV-infected adult patients at Moi Teaching and Referral Hospital?

2. Is there any relationship betweenthe commonimaging findings seen on CT brain scan and Antiretroviral Therapy (ART) use?

RESEARCH OBJECTIVES

1.1.1. Main Objective

To describe the imaging findingson Computerized Tomography (CT) brain scan of HIV-infected adult patients and relate these findings to Antiretroviral Viral Therapy (ART) use.

1.5.2. Specific Objectives

1. To describe the imaging findings on CT brain scans ofHIV-infected adult patients at Moi Teaching and Referral Hospital.

2. To describe the relationship between common imaging findings on CT brain scan ofHIV-infected adult patients and theirAntiretroviral Viral Therapy (ART) use.

CHAPTER TWO: LITERATURE REVIEW

2.1. EPIDEMIOLOGY OF HIV

HIV has claimed more than 34 million lives globally (WHO, 2015). In 2014, 1.2 million people died from HIV-related causes in 2014 (WHO, 2015). Sub-Saharan Africa is the hardest region. Sub-Saharan Africa bear 10% of the world's population and 70% of the global burden of HIV(Morison, 2001). In Kenya, the 2015 estimated prevalence of HIV infection in adults 15-49 years was 5.9%;with 71,000 new infections(UNAIDS, 2016).

2.2. NEUROPATHOGENESIS OF HIV

The virus is neuroinvasive, neurotrophic and neurovirulent(Wiley, Schrier, Nelson, Lampert and Oldstone, 1986). The virus enters the CNS as a passenger and invades the CNS; the "Trojan Horse Mechanism"(Wiley et al., 1986).Infected monocytes will traverse the blood-brain-barrier(Wiley et al., 1986).

CNS cells are prone to infection because these cells have receptor and, or co-receptors for the virus (González-Scarano and Martín-García, 2005). Commonly affected cells are microglia and perivascular macrophages (González-Scarano and Martín-García, 2005), while neurons and the oligodendrocytes are rarely affected (Kaul and Lipton, 2006).There are activation and destruction of astrocytes, loss of neuronal tissue in the basal ganglia, caudate nucleus and the hippocampus (Ghafouri, Amini, Khalili, and Sawaya, 2006).

Other sources of CNS infection include passage of infected $CD4^+$ T cells, the direct entrance of the virus or entrance of virus via transcytosis of brain microvascular endothelial cells (Ghafouri et al., 2006).

During primary infection, there is a sudden increase in viral replication (Patrick, Johnston, and Power, 2002). This results in intense immune response which abates with time, extended subclinical infection, the reappearance of the disease and ultimately death (Patrick et al., 2002).

2.3. CLINICAL PRESENTATION IN NEURO-AIDS

Patients with HIV CNS disease present with a variety of signs and symptoms. Symptoms and signs can be focal and, or non-focal(Byanyima, 2015)(Tso et al., 1993)(Eze and Eze, 2012)(McGire, 2003). Patients may also present with non-specific symptoms of CNS diseases e.g. fever(Byanyima, 2015).

Focal presentations include paresis(McGire, 2003)(Solu, M.D., Dandge, V., Kaira, P., Prajapati, R., Joshi, 2012)(Tso et al., 1993), hemiplegia(Eze and Eze, 2012), facial nerve palsy, and slurred speech (Tso et al., 1993). Focal presentation is seen in PML, CNS Lymphoma and Toxoplasmosis (McGire, 2003), and are predictors for structural lesions (Byanyima, 2015).

The non-focal presentation includes seizures, altered mental status and generalized weakness(Tso et al., 1993). The most common non-focal symptoms are altered consciousness and convulsions (Byanyima, 2015)(Tso et al., 1993)(Solu et al., 2012). Altered level of consciousness is the second commonest predictor of structural lesion seen (Byanyima, 2015) and global cerebral disease can present with altered consciousness (McGire, 2003).

Non-specific symptoms include fever, lethargy, headache and vomiting (Byanyima, 2015)(Tso et al., 1993)(Dhadke, Dhadke, Mahajan, and Korade, 2014).

2.4. COMMON CT BRAIN SCANFINDINGS

Spectra of findings are seen on brain CT scan of HIV/AIDS patients investigated for intracranial diseases. CT scans of HIV/AIDS patients with CNS presentations can be normal or abnormal (Gifford and Hecht, 2001)(Potchen et al., 2014)(Tso et al., 1993).

Single and multiple brain parenchymal lesions have been documented (Byanyima, 2015)(Eze and Eze, 2012). Both are seen in primary CNS lymphoma(PCNSL). Multiple lesions are seen in Toxoplasmosis (Byanyima, 2015).

Multiple lesions can also be seen in up to half of HIV patients with brain lesions on CT (Byanyima, 2015).

Lesions can be located anywhere within the brain. They have been found within the white matter (Potchen et al., 2014), basal ganglia (Byanyima, 2015)(Adeolu et al., 2006), internal capsule, thalamus, cerebral cortex, intraventricular and cerebellum (Adeolu et al., 2006).

Lesions can have variable characteristics. They can be focal (Adeolu et al., 2006)(Byanyima, 2015)(Eze and Eze, 2012), multifocal (Adeolu et al., 2006) and ill-defined(Adeolu et al., 2006). In the majority of HIV-infected patients evaluated for CNS involvement focal lesions are seen on brain CT scans (Byanyima, 2015). Regarding lesion density, the majority of lesionsare hypodense (Byanyima, 2015). Hyperdense lesions are also seen(Adeolu et al., 2006).

After the administration of I.V. contrast lesions can be non-enhancing, enhancing (Potchen et al., 2014), orring-enhancing (Byanyima, 2015)(Eze and Eze, 2012)(Adeolu et al., 2006). Multiple and solitary ring-enhancing lesions have been reported in 11.1% and 2.8% of brain CTs (Eze and Eze, 2012) respectively. Leptomeningeal enhancement hasalso been reported (Potchen et al., 2014).

The mass effect caused by lesions can be variable. Mass effect is seen in multiple ring-enhancing lesions (Eze and Eze, 2012). The mass effect seen in such scenario are caused by perilesional oedema (Eze and Eze, 2012).

Changes in brain volume have been documented. These changes range from normal brain volume to reduction in size (atrophy) or gross swelling due to oedema (Potchen et al., 2014). Relative ventricular size increase can be seen in patients with subcortical atrophy (Potchen et al., 2014).

2.5.CNS MANIFESTATIONS OF HIV/AIDS AND IMAGING PATTERNS

The spectrum of CNS abnormalities in HIV infection can be divided into three major categories(Senocak et al., 2010). A fourth which includes diseases not captured in the first three categories is considered:

HIV-Associated Lesions

HIV Vasculitis

HIV Encephalitis

Opportunistic Infections

Cryptococcosis

Tuberculosis

Toxoplasmosis

Progressive Multifocal Leukoencephalopathy (PML)

Cytomegalovirus (CMV) Infection

Neoplasms

Primary CNS Lymphoma

Others

2.5.1. HIV-Associated Lesions

This category includes CNS disorders that may arise from direct infection by the virus. They include HIV-vasculitis and HIV encephalitis also called AIDS-dementia complex (ADC) or HIV-associated dementia complex(Senocak et al., 2010). They may occur during all stages of the disease, but especially the late stages of infection(Howlett, 2012).

HIV Vasculitis

Presentation in HIV/AIDS-vasculitis includes stenosis and, or aneurysmal dilatation (O'Charoen, Hesselink, and Healy, 2007). Aneurysms mainly affect young black patients (Nair, Abdool-Carrim, Chetty, and Robbs, 1999). Intracerebral bleed (haemorrhage) and infarcts (stroke) may occur due to this process (Shah, Zimmerman, Rorke and Vezina) and patients may also present with subarachnoid haemorrhage(Corr, 2006). CD4 counts are below normal in the majority of these patients (Mulaudzi, 2009).

Stroke has a 1% lifetime prevalence in HIV disease and might occur during asymptomatic stages of the disease when CD4 counts are 200-500cells/cm^3 (Howlett, 2012). In Nigeria infarct-like lesions have been reported in 38.9% of HIV/AIDS patients and intracerebral haemorrhage has been reported in 8.3% (Eze and Eze, 2012). Themajority of stroke in HIV disease are ischaemic, occurring in anterior circulation (Howlett, 2012). In patients with HIV, there are direct and indirect causes of stroke (Corr, 2006).

Direct causes included HIV-associated vasculopathy, while indirect causes include cardioembolism, coagulopathy, meningitis and non-HIV infective vasculitis (Corr, 2006)(Howlett, 2012).Any of these mechanisms may lead to haemorrhagic or ischaemic stroke.

HIV Encephalitis/HIV Encephalopathy

HIV-Encephalitis is also referred to as HIV-1-associated dementia complex, AIDS dementia complex, HIV-associated dementia (HAD), AIDS encephalopathy, and multinucleated giant-cell encephalitis (McGire, 2003). HIV encephalopathy (Di Muzio, B., Ho, 2009) or HIV encephalitis(Smith, Smirniotopoulos, and Rushing, 2008) refers to the imaging patterns seen.

It is a progressive subcortical dementia associated with direct infection of the CNS with HIV(Takeuchi et al., 2005).As the level of immunosuppression increases so does the occurrence of HAD (Howlett, 2012). In Africa, the rate of HAD was shown to decrease significantly after six months of ARV treatment (Howlett, 2012).

CT Imaging Findings

The microscopic nature of the lesions affects the sensitivity of CT and MRI in identifying the early stage of the disease. Brain atrophy is the most common and frequent radiological finding (Senocak et al., 2010).

CT might be unremarkable, however, diffuse symmetric cortical atrophy, out of proportion to patient's age (Smith et al., 2008), and ventricular enlargement is seen on CT.

Increase white matter signal changes are seen in late stages of HIV infection(Singh, N.N.Thomas, F.P., Bollu, 2013). In some cases, foci of demyelination are seen, and these present on CT as low density, non-enhancing areas within the white matter without mass effect (Post et al., 1988). Symmetric abnormal hypodense lesions are also seen in the periventricular regions which do not enhance and do not cause a mass effect (Smith et al., 2008).

2.5.2. Opportunistic Infections

In developing countries, opportunistic infections are the primary cause of neurologic disorders in PLHA (de Almeida et al., 2008)(Bhigjee, Naidoo, Patel, and Govender, 1999)(Fragoso, Mendes, Adamo, Bosco, and Tavares)(Isezuo et al., 2009). Opportunistic infections affecting the CNS are Cryptococcosis, Toxoplasmosis, Tuberculosis, Cytomegalovirus Infection, Syphilis, and Progressive Multifocal Leukoencephalopathy (PML) (Senocak et al., 2010). In Kenya, Cryptococcal meningitis is the commonest neurological complications seen (Jowi, Mativo and Musoke., 2007).

Cryptococcosis

The commonest intracranial fungal infection and the third most frequent infecting pathogen in AIDS are Cryptococcus neoformans (Offiah and Turnbull, 2006). In Africa, Cryptococcus meningitis (CM) is the second commonest form of meningitis after TBM. CM is the leading cause of death in AIDS accounting for up to 25% (Howlett, 2012).

CM and TBM tend to present with similar clinical pictures and can be indistinguishable, but the onset of a headache with fever, nausea and vomiting evolving during the preceding week or two may be highly suggestive of CM (Howlett, 2012).

In up to 75% of cases signs of meningism are typically absent while raised intracranial pressure with papilloedema is a common a presentation in CM, but may occur in both CM and TBM (Howlett, 2012).

CT Imaging Findings

Imaging can be non-specific and variable (Smith et al., 2008)(Thurnher et al., 1997). CT findings may range from being unremarkable to findings suggestive of meningitis, with mild dilatation of the ventricular system. Seldom, nodular meningeal enhancement on contrast-enhanced images is seen (Thurnher et al., 1997).

Dilated Virchow-Robin spaces filled with fungi results in the formation of non-enhancing cystic lesions, which are symmetric and predominantly seen in the basal ganglia and thalamus (Thurnher et al., 1997). On CT scan these lesions appear hypodense (Thurnher et al., 1997). Solid or ring-like contrast-enhancing parenchymal mass is also an imaging feature (Thurnher et al., 1997). Cryptococcoma which is extremely rare can be found preferentially in the ependymal of the choroid plexus (Thurnher et al., 1997). The commonest sites for Cryptococcoma are the basal ganglia, thalamus, and cerebellum (Smith et al., 2008). In appropriate clinical settings these nonspecific findings are suggestive of CNS Cryptococcosis infection (Thurnher et al., 1997).

Tuberculosis (TB)

In Africa disseminated TB occurs in >50% of patients with advanced HIV disease, and TBM has been shown at post mortems to be present in >10% of AIDS patients(Howlett, 2012).

In New Delhi India, more than half of HIV patients (52.9%) with CNS symptoms had TBM(Wadhwa, Kaur, and Bhalla, 2008), while in Kenya tuberculous meningitis occurs in 10.7% of PLHA(Jowi, Mativo and Musoke., 2007).

CT Imaging Findings

CNS TB in AIDS patients presents with similar radiological features as in non-AIDS patients (Thurnher et al., 1997). CT of the brain is usually not very helpful; however basal meningeal enhancement may be seen in TBM. Occasionally patients will have tuberculoma; solitary or multiple with nodular enhancement (Howlett, 2012). Tuberculoma can is seen in the intra- and extra-axial compartment and majority are super-tentorial(Senocak et al., 2010)

Toxoplasmosis

Toxoplasmosis, the most frequent and easily treatable opportunistic infection(Roullet, 1999), causes Toxoplasma encephalitisin 15–50% of HIV-infected patients(Thurnher et al., 1997). Its frequency in Africa varies depending on the local prevalence of toxoplasmosis(Howlett, 2012).In Kenya cerebral toxoplasmosis occurs in 12.7% of PLHA(Jowi, Mativo and Musoke., 2007).

There is a common history of a headache (60%) and fever (40-70%) over preceding days or 1-2 weeks, with a positive Toxoplasma serology (Howlett, 2012). A negative

serology makes the diagnosis unlikely(Howlett, 2012). An established diagnosis of CNS toxoplasmosis must be made in every HIV/AIDS patient presenting with focal neurological signs until proven otherwise(Kurne et al., 2006).

CT Imaging Findings

Classic CT findings of toxoplasmosis abscesses include multiple iso- or hypodense lesions, with ring enhancement or nodular arrangement with peri-focal vasogenic oedema and mass effect (Howlett, 2012). If haemorrhagic the lesions may be hyperdense (Offiah and Turnbull, 2006).

Most frequent sites involved are the corticomedullary junction, basal ganglia, and thalamus(Smith et al., 2008). The brainstem is less commonly affected (Offiah and Turnbull, 2006).

Imaging modalities are very relevant in follow-up. If the lesion size is constant or, increases 10–14 days after the start of treatment brain biopsy is mandated to exclude lymphoma (Thurnher et al., 1997). Distinguishing lymphoma and toxoplasmosis lesions is often challenging; therefore, this might not be possible in certain cases on imaging studies (Senocak et al., 2010).

Progressive Multifocal Leukoencephalopathy (PML)

When a latent virus (John CunninghamVirus), carried by healthy people, is reactivated in advance states of immunosuppression, PML occurs. PML is an opportunistic infection affecting PLHA(Howlett, 2012).

CT Imaging Findings

CT scans lesions are typically multifocal hypodensities which start at the site of highest blood flow; the sub-cortex, and spreading into the deep white matter. It also exhibits accelerated progression in size, which results in the confluence of the lesions(Thurnher et al., 1997).

The presence of contrast enhancement, especially when faint and peripheral, the diagnosis of PML should not be excluded (Roullet, 1999)(Post et al., 1999). A posterior location is an imaging sign favorable to the diagnosis of PML, but it is not pathognomonic of PML(Post et al., 1999).

After the initiation of HAART increased enhancement and mass effect is noted. If seen weeks after therapy, such finding may result from IRIS (Collazos, Mayo, Martínez, and Blanco, 1999)(Thurnher et al., 2001).

Cytomegalovirus (CMV) Infection

Over 90% of adults have antibodies to CMV (Offiah and Turnbull, 2006). During the late stages of HIV infection with CD4 counts <50 cells/cm3, reactivation may occur(Howlett, 2012).Encephalitis is the usual brain involvement seen, with preferential involvement of the periventricular regions and brainstem(Senocak et al., 2010). Other manifestations are ventriculitis, infarcts, and meningitis(Senocak et al., 2010).

CT Imaging Findings

CMV infection of the CNS yield nonspecific radiographic studies and in the majority of cases, CT and MRI reveal no abnormality (Thurnher et al., 1997). In 40% of the cases atrophy and ventricular enlargement are seen (Roullet, 1999).

CT findings include diffuse white matter hypodensities, ependymal enhancement, and focal ring-enhancing or nodular enhancing lesions (Offiah and Turnbull, 2006). The diffuse white matter hypodensities are due to demyelination (Smith et al., 2008).

Since neuroradiology features of CMV infection of the brain are nonspecific diagnosis of CMV infection must be confirmed by identification of typical intranuclear inclusion; owl's eye, on histology (Thurnher et al., 1997).

2.5.3. Neoplasm

Neoplasms related to AIDS, are opportunistic conditions which occur with CD4 counts <200 cells/cm^3(Howlett, 2012). Neurological presentations are dependent on the site, and they include focal neurological deficit, altered level of consciousness or coma(Howlett, 2012).

Lymphoma

As the HIV prevalence increases so does the prevalence of primary CNS lymphoma (PCL) among HIV/AIDS patients (Thurnher et al., 1997).

CT Imaging Findings

Contrary to typical PCL, AIDS-related lymphoma can be cortical, involving gray and white matter. It is associated with leptomeningeal thickening, and may induce vasculitis (Offiah and Turnbull, 2006). PCL affects the basal ganglia, corpus callosum, periventricular white matter, frontal lobes, and thalamus, sometimes restricted to the subependymal regions, or can ultimately involve the intraventricular region (Offiah and Turnbull, 2006)(Thurnher et al., 1997).

On CT appearance may be similar to a Tuberculoma, but they may differ in location and distribution (Howlett, 2012). The primary differential diagnosis is toxoplasmosis (Senocak et al., 2010).

Other Tumours

Case reports have documented the occurrence of high grade meningioma in young patients with HIV(Abbara, M., Tolaymat, A., Battles, O.E., Robinson, 2010)(Khurshid et al., 1999). Meningioma has been reported in the early and advanced stages of HIV/AIDS (Khurshid et al., 1999).

ANTIRETROVIRAL THERAPY USE AND CNS MANIFESTATION OF HIV/AIDS

Over the years, HAART has significantly reduced the incidence of neurological opportunistic infections in high-income countries(Tan et al., 2012b). Currently “treat all” is advocated for (WHO, 2016b). Every HIV infected person is expected to be on ART. The early initiation of ART is expected to reduce the incidence of life-threatening HIV-related infections (WHO, 2016c).

A paradoxical reaction occurs, in which patients who have just started ARTs may experience an up flair of CNS opportunistic infections(Tan et al., 2012b). This phenomenon is known as Immune Reconstitution Inflammatory Syndrome(IRIS).

IRIS occurs because previously unsuspected CNS opportunistic infections may be revealed after treatment initiation(Tan et al., 2012b). IRIS typically develops up to 2 months following HAART initiation(Knipe, H., Stanislavsky, 2011). Imaging patterns vary and may be atypical presenting as prominent, progressive enhancement and mass effect (Smith et al., 2008).

CHAPTER THREE:RESEARCH DESIGN AND METHODOLOGY

3.1.STUDY DESIGN

This was a descriptive cross-sectional study.

3.2.STUDY SITE

The study was conducted at the Radiology and Imaging department of the Moi Teaching and Referral Hospital (MTRH).MTRH isin Eldoret town, which is 350 Kilometers northwest of the Capital Nairobi.MTRH is a tertiary (level 6) health facility, and a teaching hospital making it a conducive centre for this study as it serves as a training center for medical, clinical and nursing officer interns. It is a national referral hospital for the Western part of Kenya and North Rift, with a catchment population approximating 13 million people(Moi Teaching and Referral Hospital, 2013).Departments includingMedicine, Surgery, Pediatrics and Radiology and Imaging among others.

3.3.STUDY POPULATION

The study population includedall referred HIV/AIDS patients 18 years and older who present with CNS signs and symptomsand underwenta brain CT scan at the Radiology Department of the Moi Teaching and Referral Hospital during the study period.

3.4.SAMPLINGTECHNIQUES

3.4.1. Sampling and Recruitment

A census study was done. All patients who met study criteria from January 2015 to December 2015 were included in the study.

All HIV/AIDS patients 18 years and older, referred for a contrast-enhanced CT brain scan and met study criteria were recruited in the study.Consent requested from adult participants with good mental status. For adult participants unfit to give consent, proxy consent was sought from guardians or relatives. The demographic characteristics, clinical history and examination findings of all study participants were entered in the data collection instrument. CT scan images were saved onto a compact disc and subsequently read by myself. Findings verified by three consultant radiologists. Results were entered once a consensus on imaging findings was reached.

3.5. STUDY PROCEDURE

All referred HIV infected patients who met the study criteria, were identified at the CT room of the Radiology and Imaging Department. CT brain scan was done as part of their routine care, as requested by their primary doctor. The MTRH CT brain HIV/AIDS protocol was utilized for all patient.

MTRH CT Brain HIV/AIDS Protocol

- Non-enhanced and enhanced head CT scan done using the PHILIPS MX 4000 Dual Slice CT Scan Machine.
- Request received, and indication for the CT scan confirmed and recorded in the register along with the In-Patient Number.
- Patient informed about the procedure.
- An I.V cannula inserted.
- Patient supine and head secured in position with pads on both sides and strapped in place.

- Patient positioned head first in the gantry and laser light centered at midline, about 2.5 cm from the vertex.
- The following settings used; Kilo-voltage 120Kv, 150Mas, 80 WW and 35 WL.
- The scanogram with necessary collimation was done and the appropriate windows were set i.e. brain window and bone window.
- Non-enhanced brain images were acquired.
- 40 millilitres bolus of contrast media (Ultravist) introduced via the cannula and contrast enhanced images were then acquired.
- All scanning was then done with increments of 5mm from the base of the skull to the vertex.

The images were shown on the computer screen, and any intracranial lesion was visualized. The images were then loaded onto the film format in the computer after which the film was printed, and interpretation was done. A copy of the image was then saved onto a compact disc.

The scans were reported by the principal investigator and findings were verified by two consultant radiologists for internal validity. If any disagreement occurreda third consultant radiologist was consulted and that decision was final.

Parenchymal pathology was assessed based on location, density, enhancement patterns, the presence of perilesional oedema, presence of midline shift and presence of brain herniation. Parenchymal abnormalities, including structural parenchyma changes, were categorised into focal, multifocal, ill-defined and diffuse. Every contrast enhanced CT scan was assessed for the presence of meningeal enhancement.

Objective methods (Cella Media Index, Cortical Sulci Diameter, Bicaudate Indexand Evans Index) were used to assess every participant for brain atrophy. The different subtype of brain atrophy; cortical and sub-cortical brain atrophy were also assessed. The cella media index is the ratio of the biparietal diameter of the skull to the maximum external diameter of the lateral ventricles at the cella media, the widest part of the lateral ventricles in an axial CT scan (Keats and Sistrom, 2001). Evans' Indexis the ratio of maximum width of the frontal horns of the lateral ventricles and the maximal internal diameter of the skull at the same level in an axial CT scan (Ng et al., 2009). Bicaudate index is the ratio of the two lateral ventricles at the level of the head of the caudate nucleus to the distance between outer tables of the skull at the same level (Barr et al., 1979). Cortical atrophy evaluated as cella media index <4.0, Evans index of>0.3 and the presence of enlarged cortical sulci. Subcortical atrophy was assessed using the bicaudate index>0.12.

The ventricles were objectively evaluated for hydrocephalus. Each ventricle diameter was taken. Measurements were not done for study participants with effaced ventricles as this might affect the size.

The Evans ratio was used to evaluate the lateral ventricular size and an Evans index >0.3 with normal sulci was considered as pathological enlargement, while Evans index >0.3 with prominent sulci and, or cortical atrophy, subcortical atrophy, or any other compensatory ventriculomegaly considered "ex-vacuo hydrocephalus."

Finally, the CT-diagnosis was also documented for every study participant.

Data was collected from the medical records and entered in a structured questionnaire. For patients with altered mental states, guardians were interviewed for demographic information (age and gender, address) to authenticate with the medical records and hence ensure accuracy.

Data of Antiretroviral therapy use was collected from study participants. For participants with altered mental state, history of antiretroviral therapy use was collected from care givers and medical files.

All data collected was entered in a questionnaire. Questionnaires were kept in a locked cabinet by the principal investigator during the study period to ensure access to authorized persons only. Data was exported onto a password protected excel worksheet.

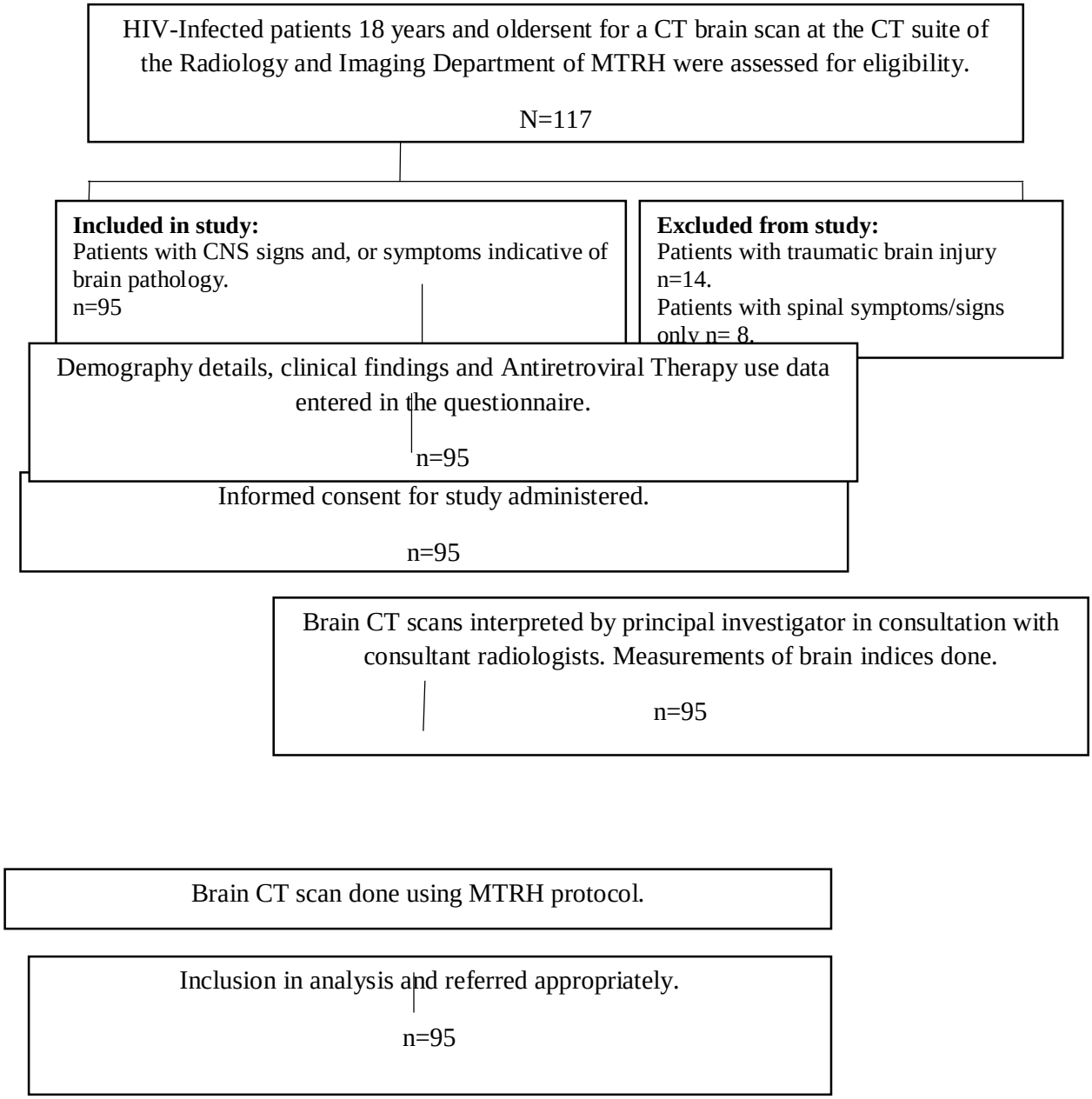


Figure 1: Study Recruitment Schema

3.6. DATA COLLECTION AND MANAGEMENT

3.6.1. Data Collection

Data collection was from January 2015 to December 2015. Questionnaire completed and data transferred to an excel database. Double entry was used to ensure the accuracy of the data. Patients' details were kept confidential. Patients received a copy of their results, and they had the autonomy over who else can view their scan result(s). Serial numbers were used to protect patients' identity. At the end of each day, data collection forms were verified for completeness and coded.

3.6.2. Quality control

All head CT were done at MTRH CT SCAN room, which has internal quality checks. The scans were done either as an emergency or follow-up as per protocol. The scans were read by the registrar (Investigator) doing the study and by two qualified radiologists to correlate the findings. The two radiologists independently viewed the films, and an agreed radiological diagnosis was made. When disagreement occurred, another consultation was done with a third radiologist and a consensus reached.

3.6.3. Data Management and Analysis

Collected data was coded and entered in Microsoft Excel 2013 spreadsheet. Data cleaning was conducted before exporting to SPSS version 21.0 for statistical analysis. The study population was described by summarizing demographic and clinical data into percentages and means or medians for categorical and continuous variables respectively. Patterns of CT scan relating to brain pathology findings were listed and presented as a percentage of all patients. Brain pathology findings were associated with age categories, sex, and Antiretroviral Therapy (ART).

Odds ratios (ORs) were calculated and presented as relative risk (RR) of brain pathology associated with the type of exposure. Statistical tests were interpreted at a p value less or equal to 0.05. Tables and graphs were used to present the study findings.

3.7. ETHICAL CONSIDERATIONS

Authorization to conduct the research was sought from the Institutional Research and Ethics Committee (IREC) and the Director of Moi Teaching and Referral Hospital. Study participants and guardians were informed about the study. They were informed about the study agenda, likely benefits, procedure safety and potential risks. All patients received medical attention as needed, unmindful of their willingness/unwillingness to participate in the study. No incentives or inducements was used to convince patients to partake in the study. Confidentiality was a priority and upheld throughout the study. The data collection forms used neither contain the names of the patients nor their personal identification numbers. During the study period, data collecting material was kept under lock and key.

The findings of the research will be presented to the Hospital's management and the university's Department of Radiology and Imaging for use as necessary. It will also be made available for academic reference at the College of Health Sciences Resource Centre. The results of this research shall be made accessible for publication in a reputable journal of medicine for use by the wider population in the universal advancement of patient management and as a reference for future studies.

3.8. ELIGIBILITY CRITERIA

3.8.1. Inclusion Criteria

All HIV/AIDS patients referred for CT brain scan with CNS signs and, or symptoms.

3.8.2. Exclusion Criteria

HIV/AIDS patients referred for CT brain scan with traumatic brain injury.

HIV/AIDS patients referred for CT brain with signs and, or symptoms suggestive of spinal cord pathology.

CHAPTER FOUR: RESULTS

4.1. INTRODUCTION

The demographics, clinical presentations, Antiretroviral Therapy (ART) use, CT patterns and CT-diagnosis are documented in this chapter.

4.2.DEMOGRAPHIC AND CLINICAL CHARACTERISTICS PARTICIPANTS

The total number of patients assessed for eligibility was 117. Fourteen (14) patients with traumatic brain injury and 8 patients with only spinal cord signs and, or symptoms were excluded from the study. A total of 95 participants were enrolled in the study.

The mean age of study participants was 39.8 years and the standard deviation was 11.6 years). The age range was from 18 years to 68 years. Over half (54.7%) of study participants were 40 years and below. More than a half (55.8%) were females (Table 1). The male to female ratio was 1:1.3.

Almost a third (30.5%) reported focal symptoms with the majority (22.1%) reporting of weakness of one side of the body. Non-focal symptoms were reported by 95.8% of the participants; persistent headache (66.3%) and confusion (54.7%) being the main symptoms reported. Only 57.9% of the patients had focal signs.

Table 1: Demographic and clinical characteristics

Variable	Frequency (%)
Age	
Mean (SD)	39.8 (11.6)
Min-Max	18-68
Category	
<40	52 (54.7)
≥40	43 (45.3)
Gender	
Male	42 (44.2)
Female	53 (55.8)
Focal symptoms	**29 (30.5)**
Weakness of one side of the body	21 (22.1)
Localized seizures	1 (1.1)
Loss of vision	4 (4.2)
Inability to talk	6 (6.3)
Blurred vision	2 (2.1)
Non-focal symptoms	**91 (95.8)**
Generalized seizures	28 (29.5)
Headache	63 (66.3)
Dizziness	17 (17.9)
Memory impairment	6 (6.3)
Confusion	52 (54.7)
Fever	25 (26.3)
Unconscious	18 (18.9)
Focal sign	**55 (57.9)**
Hemiplegia	7 (7.4)
Hemiparesis	12 (12.6)
Coma	2 (2.1)
Bilateral blindness	1 (1.1)
Ataxic gait	1 (1.1)
Non-focal signs	**128 (134) ***
Generalized seizure	16 (16.8)
Memory impairment	2 (2.1)
Confusion	40 (42.1)
Depressed level of consciousness	29 (30.5)
Fever	41 (43.2)

***Participants had multiple non-focal signs.**

4.3. IMAGING FINDINGS SEEN ON CT BRAIN SCAN

Table 2: Brain Abnormalities seen on Computerized Tomography (CT)

Variable	**Frequency (%)**
Presence of Brain pathology (n=95)	
Yes	63 (65.3)
No	33 (34.7)
Meningeal pathology (n=62)	**11 (17.7) ***
Brain parenchyma pathology (n=62)	**42 (67.7) ***
Ventricular pathology (n=62)	**34 (54.8) ***

***Participants had pathologies in multiple locations.**

Detecting any pathology on brain CT was considered as an abnormal scan.

About two-thirds, n=62 (65.3%), of study participants, had brain pathology on CT.

These were further classified based on the anatomical location(s) of the pathology.

Meningeal pathology was found in n=11 (17.7%) of participants with brain scans. N=42 (67.7%) of participants with brain pathology had brain parenchymal pathology and n=34 (54.8%) had ventricular abnormalities.

Table 3: Meningeal Pathology on Computerized Tomography Brain Scans

Variable	Frequency (%)
Meninges pathology (n=62)	11 (17.7)
Meningeal changes (n=11)	
Leptomeningeal enhancement	6 (54.5)
Sub-arachnoid Haemorrhage	1 (9.1)
Subdural Haemorrhage	2 (18.2)
Subdural hygroma	2 (18.2)

Over half, n=6 (54.5%), of participants with meningeal pathology had leptomeningeal enhancement and n=2, (18.2%), of participants had Subdural Haemorrhage. Only one participant had Sub-arachnoid Haemorrhage.

4.3.1. Brain Parenchyma Findings

Table 4: Characteristics of Brain Parenchyma Lesions

CT Pattern		Total	Focal and Multifocal Lesions n (%)	Ill-defined Lesions n (%)	Diffuse Lesions n (%)
Density of lesion	Hypodense lesion	39	5 (12.8)	11 (28.2)	23 (59.0)
	Mixed Isodense and Hyperdense	1	1 (100.0)	-	-
	Hyperdense lesion	2	2 (100.0)	-	-
	Ring-like lesion	1	-	1 (100.0)	-
Enhancement	No enhancement	37	5 (13.5)	10 (27.0)	22 (59.5)
	Mild enhancement	1	-	1 (100.0)	-
	Avid enhancement	1	1 (100.0)	-	
	Ring-enhancement	3	1 (33.3)	1 (33.3)	1 (33.3)
Location of Lesions	Frontal lobe	19	4 (21.1)	3 (15.8)	12 (63.2)
	Parietal lobe	25	1 (4.0)	8 (32.0)	16 (64.0)
	Temporal lobe	3	-		3 (100.0)
	Occipital Lobe	9	-	-	9 (100.0)
	Insular Cortex	1	1 (100.0)	-	-
	Basal Ganglia	8	2 (25.0)	1 (12.5)	5 (62.5)
	Thalamus	1	1 (100.0)	-	-
	Cerebellum	1	1 (100.0)	-	-
Perilesional oedema	Present	5	3 (60.0)	2 (40.0)	-

From Table 4, the majority, n=39, of brain parenchyma lesion were hypodense (88.1%). Most hypodense lesions were diffuse n=23 (59%).

Majority, n=37, of parenchymal lesions did not enhance post-IV contrast. N=22 (59.5%) of non-enhancing lesions were diffuse. Ring enhancement was seen in n=3 participants. Most lesions were in the parietal lobe n=25.

The second common location was the frontal lobe n=19. Few lesions, n=1, were found in the insular cortex, thalamus and cerebellum.

Perilesional oedema was noted in n=5 participants, mostly in participants with focal, multifocal and ill-define lesions.

Midline shift due to mass effect was noted in n=11 (11.6%) of study participants. Midline shift was commonly seen in participants with diffuse lesions. Brain herniation was noted in n= 2 (1%) of participant; both having subfalcine herniation.

Table 5: Prevalence of Brain Atrophy

Variable	Frequency
Brain atrophy (n=84)	
Yes	37 (32.6)
No	47 (49.5)
Type of brain atrophy cortical (n=37)	
Subcortical	31 (83.8)
Both	6 (16.2)

The presence of brain atrophy was assessed in 84 participants. These participants had no significant mass effect or effacement of ventricles. The prevalence of brain atrophy in the study population was 44%. From Table 5, most participants with brain atrophy had subcortical brain atrophy.

Table 6: Brain Atrophy by Age and Sex

	Sub-cortical	Sub-cortical/ cortical	OR (95% CI)	P value	Brain atrophy present	Brain atrophy absent	OR (95% CI)	P value
Age								
≤40	15 (78.9)	4 (21.1)	0.5 (0.1-3.0)	0.660	19 (40.4)	28 (59.6)	0.9 (0.4-2.1)	0.795
>40	16 (88.9)	2 (11.1)	1.0		16 (43.2)	21 (56.8)	1.0	
Gender								
Male	14 (87.5)	2 (12.5)	1.7 (0.3-10.4)	0.680	15 (39.5)	23 (60.5)	0.9 (0.4-2.0)	0.711
Female	17 (81.0)	4 (19.0)	1.0		20 (43.5)	26 (56.5)	1.0	

As shown in Table 6, brain atrophy was not significantly associated with age and gender of participants (p>0.05). N=16 (43.2%) of the participants more than 40 years and n= 19 (40.4%) of participants 40 years and below (p=0.795) had brain atrophy. Similarly, 39.5% of males had brain atrophy compared to 43.5% of the females (p=0.711).

4.3.2. Ventricular Findings

N=12 (12.6%) of participants had effaced ventricles and 23.2% (n=22) has a dilated ventricle (ventriculomegaly).

Ventriculomegaly involving all 4 ventricles was considered as communicating hydrocephalus. Communicating hydrocephalus was the common form of hydrocephalus seen among study participants. Findings are detailed in Table 7.

Table 7: Characteristics of Ventricular Pathology

Variable	Frequency (%)
Effaced ventricles	12 (12.6)
Effaced ventricles location (n=12)	
Lateral ventricle (s)	9 (75.0)
3rd ventricle + lateral ventricles	1 (8.3)
4th ventricle + 3rd + lateral ventricles	2 (16.7)
Dilated ventricles	22 (23.2)
Location of dilated ventricles (n=22)	
Lateral ventricle (s)	8 (36.4)
4th ventricle + 3rd + lateral ventricles	14 (63.6)
Hydrocephalus subtype (n=22)	
Communicating	19 (86.4)
Non-communicating	3 (13.6)

4.3.3. CT-based Diagnosis

As detailed in Table 8, the spectrum of CNS abnormalities was divided into three broad categories, and a fourth category that highlights other conditions.

As shown in Table 8,HIV-associated diseases are the most common pathology. Most participants, 27.4% (n=26), had Encephalitis. Likely complications of vasculitis were infarcts (6.3%), haemorrhagic stroke (2.1%) and 1 patient each with unilateral and bilateral subdural haematoma and subarachnoid haemorrhage.

Toxoplasmosis was the only opportunistic infection diagnosed at 2.1% (n=2). One participant each had a suspected case of CNS Lymphoma and Meningioma. Cerebral abscess was see in 5.3% (n=5) of study participants.

Table 8: Brain CT-Diagnosis of Study Participants

Variable	Frequency (%)
HIV associated diseases	
Encephalitis	26 (27.4)
Complications of Vasculitis	
Ischaemic Stroke	6 (6.3)
Unilateral subdural haematoma	1 (1.1)
Bilateral subdural haematoma	1 (1.1)
Haemorrhagic stroke	2 (2.1)
Sub-arachnoid haemorrhage	1 (1.1)
Opportunity diseases	
Toxoplasmosis	2 (2.1)
Neoplasm	
Suspected lymphoma	1 (1.1)
Others	
Cerebritis	7 (7.4)
Abscess	5 (5.3)
Meningitis	6 (6.3)
Meningioma	1 (1.1)
CSF hygroma	3 (3.2)

4.4.RELATIONSHIP BETWEEN COMMONBRAIN CT FINDINGS AND ANTIRETRIVIRAL THERAPY (ART) USE.

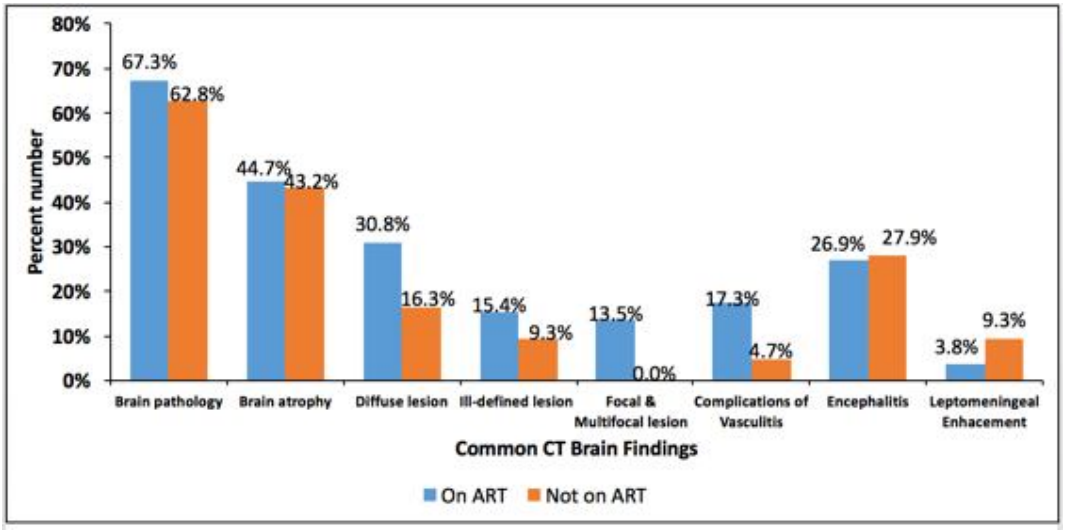
As shown in Table 9, only n=52 (54.7%) of study participants were on ARTs. A handful, n=6 (11.5%) have been on ARTs for 2months or less.

Table 9: Antiretroviral Therapy Use among Participants

Variable	Frequency (%)
ART use	
Yes	52 (54.7)
No	43 (45.3)
Duration of ART use (n=52)	
≤2	6 (11.5)
>2	46 (88.5)
Prophylactic use	
Yes	52 (54.7)
No	43 (45.3)

From Figure 2, brain pathology, brain atrophy, diffuse brain lesions, ill-define lesions and complications of vasculitis was higher in participants on ARTs, compared to participants not on ARTs. Proportion of participants with encephalitis and leptomeningeal enhancement was higher in participants not on ART.

Figure 2: Common Brain CT Findings and ART Use



As shown in Table 10, focal and multifocal lesions were significantly higher in patients who had used ARTs (13.5%) while none of their counterparts reported such lesions ($p=0.015$). Though diffuse and ill-defined lesions (30.8% and 15.4% respectively) were substantially higher in patients using ARTs, the difference was not significant ($p>0.05$). Brain pathology, brain atrophy, and encephalitis were not significantly associated with ART use ($p>0.05$).

Table 10: Relationship between ART Use and Common CT Findings

	ART use		OR (95% CI)	P value
	Yes (%)	No (%)		
Brain pathology				
Yes	35 (67.3)	27 (62.8)	1.2 (0.5-2.9)	0.671
No	17 (32.7)	16 (37.2)	1.0	
Brain atrophy				
Yes	21 (44.7)	16 (43.2)	1.1 (0.4-2.5)	0.895
No	26 (55.3)	21 (56.8)	1.0	
Focal and multifocal lesions				
Yes	7 (13.5)	0	-	0.015
No	45 (86.5)	43 (100.0)		
Ill-defined lesions				
Yes	8 (15.4)	4 (9.3)	1.8 (0.5-6.3)	0.374
No	44 (84.6)	39 (90.7)	1.0	
Diffuse lesions				
Yes	16 (30.8)	7 (16.3)	2.3 (0.8-6.2)	0.101
No	36 (69.2)	36 (83.7)	1.0	
Encephalitis				
Yes	14 (26.9)	12 (27.9)	1.0 (0.4-2.4)	0.915
No	38 (73.1)	31 (72.1)	1.0	
Complications of vasculitis				
Yes	9 (17.3)	2 (4.7)	4.3 (0.9-21.0)	0.104
No	43 (82.7)	41 (95.3)	1.0	
Leptomeningeal enhancement				
Yes	2 (3.8)	4 (9.3)	0.4 (0.1-2.2)	0.405
No	50 (96.2)	39 (90.7)	1.0	

A paradoxical up flair of opportunistic infection is noted up to 2 months after the initiation of ARTs, however, in this study population brain pathology and common CT findings were not significantly associated with the duration of ART use, P>0.05 (Table 11).

Table 11: Relationship between Common CT Findings and Duration of ART use.

	Duration of ART use		OR (95% CI)	P value
	=<2 (%)	>2 (%)		
Brain pathology				
Yes	4 (66.7)	31 (67.4)	1.0 (0.2-5.9)	1.000
No	2 (33.3)	15 (32.6)	1.0	
Brain atrophy				
Yes	3 (50.0)	18 (43.9)	1.3 (0.2-7.1)	1.000
No	3 (50.0)	23 (56.1)	1.0	
Focal and multifocal lesions				
Yes	0	7 (15.2)	-	0.580
No	6 (100.0)	39 (84.8)		
Ill-defined lesions				
Yes	0	8 (17.4)	-	0.573
No	6 (100.0)	38 (82.6)		
Diffuse lesions				
Yes	2 (33.3)	14 (30.4)	1.1 (0.2-7.0)	1.000
No	4 (66.7)	32 (69.6)	1.0	
Encephalitis				
Yes	2 (33.3)	12 (26.1)	1.4 (0.2-8.7)	0.655
No	4 (66.7)	34 (73.9)	1.0	
Complications of vasculitis				
Yes	2 (33.3)	7 (15.2)	2.8 (0.4-18.2)	0.275
No	4 (66.7)	39 (84.8)	1.0	
Leptomeningeal enhancement				
Yes	0	2 (4.3)	1.1 (1.0-1.3)	1.000
No	6 (100.0)	44 (95.7)	1.0	

4.5. DEMOGRAPHY, CLINICAL PRESENTATION ANDCOMMON CT FINDINGS

As shown in Table 12 below, the prevalence of brain pathology was significantly lower (53.8%) in patients aged 40 years and below compared to those who were above 40 years, OR 0.3 (95% CI 0.1-0.8), p=0.010. Similarly, 5.8% of the patients who were 40 years and below had ill-defined lesions compared to 20.9% of those above 40 years [OR 0.2 (95% CI 0.1-0.9), p=0.027]. All the other findings including brain atrophy, focal and multifocal lesions, diffuse lesions and encephalitis were not significantly associated with the age group of the study participants (p>0.05).

Table 12: Common CT Findings by Age Category

Common CT Findings	Age		OR (95% CI)	P value
	≤40 years (%)	>40 years (%)		
Brain pathology				
Yes	28 (53.8)	34 (79.1)	0.3 (0.1-0.8)	0.010
No	24 (46.2)	9 (20.9)	1.0	
Brain atrophy				
Yes	19 (40.4)	18 (48.6)	0.7 (0.3-1.7)	0.451
No	28 (59.6)	19 (51.4)	1.0	
Focal and multifocal lesions				
Yes	4 (7.7)	3 (7.0)	1.1 (0.2-5.3)	1.000
No	48 (92.3)	40 (93.0)	1.0	
Ill-defined lesions				
Yes	3 (5.8)	9 (20.9)	0.2 (0.1-0.9)	0.027
No	49 (94.2)	34 (79.1)	1.0	
Diffuse lesions				
Yes	14 (26.9)	9 (20.9)	1.4 (0.5-3.6)	0.497
No	38 (73.1)	34 (79.1)	1.0	
Encephalitis				
Yes	11 (21.2)	15 (34.9)	0.5 (0.2-1.3)	0.135
No	41 (78.8)	28 (65.1)	1.0	
Complications of vasculitis				
Yes	6 (11.5)	5 (11.6)	1.0 (0.3-3.5)	1.000
No	46 (88.5)	38 (88.4)	1.0	
Leptomeningeal enhancement				
Yes	2 (3.8)	4 (9.3)	0.4 (0.1-2.2)	0.405
No	50 (96.2)	39 (90.7)	1.0	

From Table 13, brain pathology was significantly higher (76.2%) in male patients than females (56.6%), OR 2.5 (95% CI 1.0-6.0), p=0.046. Brain atrophy, the lesions, and encephalitis were not significantly different between males and females (p>0.05).

Table 13: Common CT Findings by Gender

Common CT Findings	Gender		OR (95% CI)	P value
	Male (%)	Female (%)		
Brain pathology				
Yes	32 (76.2)	30 (56.6)	2.5 (1.0-6.0)	0.046
No	10 (23.8)	23 (43.4)	1.0	
Brain atrophy				
Yes	16 (42.1)	21 (45.7)	0.9 (0.4-2.1)	0.744
No	22 (57.9)	25 (54.3)	1.0	
Focal and multifocal lesions				
Yes	4 (9.5)	3 (5.7)	1.8 (0.4-8.3)	0.696
No	38 (90.5)	50 (94.3)	1.0	
Ill-defined lesions				
Yes	4 (9.5)	8 (15.1)	0.6 (0.2-2.1)	0.540
No	38 (90.5)	45 (84.9)	1.0	
Diffuse lesions				
Yes	11 (26.2)	12 (22.6)	1.2 (0.5-3.1)	0.810
No	31 (73.8)	41 (77.4)	1.0	
Encephalitis				
Yes	13 (31.0)	13 (24.5)	1.4 (0.6-3.4)	0.498
No	29 (69.0)	40 (75.5)	1.0	
Complications of vasculitis				
Yes	4 (9.5)	7 (13.2)	0.7 (0.2-2.5)	
No	38 (90.5)	46 (86.8)	0.750	
Leptomeningeal enhancement				
Yes	4 (9.5)	2 (3.8)	2.7 (0.5-15.4)	0.400
No	38 (90.5)	51 (96.2)	1.0	

4.6.SAMPLE IMAGES

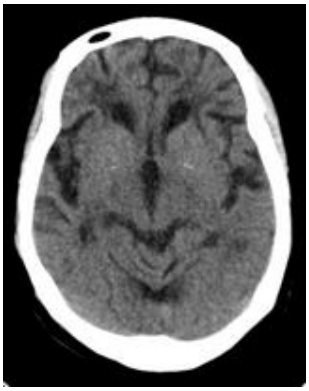


Figure 3: A 23years old male patient with confusion.

An axial brain CT image at the level of the 3rd ventricle illustrates the global, prominent fissures, sulci, and gyri in keeping with cortical brain atrophy. Subtle, bilateral, basal ganglia hyperdensities(calcifications) noted.

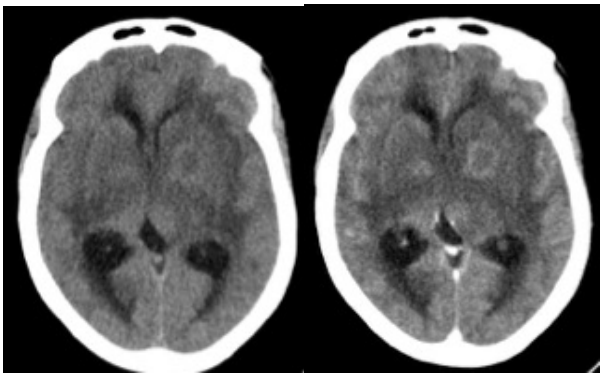


Figure 4: A 52years old patient who presented with hemiplegia.

Pre and post I.V. contrast images of at the level of the basal ganglia. A ring-like lesion is visualized in the left basal ganglia with hypodensities around the basal ganglia, thalami, and peri-ventricular region. Post contrast image depicts a ring-enhancing

lesion in the left basal ganglia with an enhancing focus in the right basal ganglia. A diagnosis of Toxoplasmosis involving the basal ganglia was made.

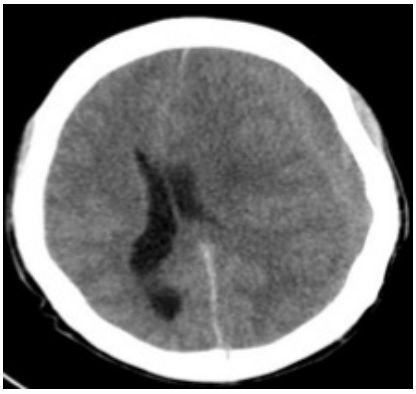


Figure 5: 28 years old male patient. No history of trauma.

Axial brain CT at the level of the atrium of the lateral ventricle illustrating, aleft-sided massive, subacute, subdural haematoma. The lesion is causing the significant mass effect; midline shift to the contralateral side and compression of the ipsilateral lateral ventricle.

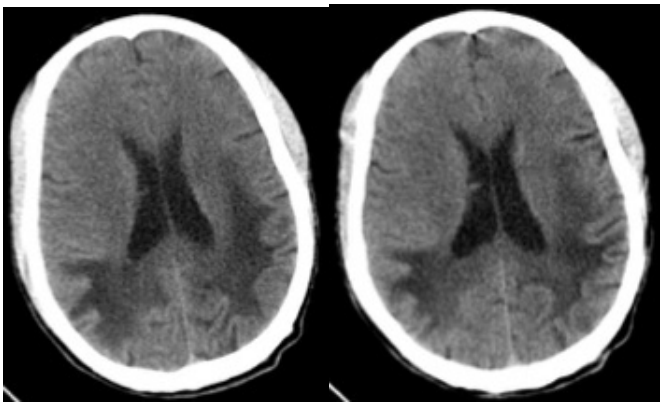


Figure 6: 24 years old patient with history of blindness

Bilateral,symmetrical, non-enhancing, hypodensities noted in both occipital cortices. No significant mass effect noted. A diagnosis of Encephalitis was made involving the occipital region.

CHAPTER FIVE: DISCUSSION

5.1. INTRODUCTION

The purpose of this study was to describe the imaging findings seen on Computerized Tomography (CT) scan of the brain of HIV-infected adult patients with CNS presentation, relating these findings to ART-use.

5.2. DEMOGRAPHIC CHARACTERISTICS

The majority of study participants were females and this was not in keeping with other studies in which male participants either outnumbered (Graham III, Wippold II, Pilgram, Fisher, and Smoker, 2000)(Eze and Eze, 2012)(Hongsakul and Laothamatas, 2008)(Potchen et al., 2014), or equaled female participants (Berhe, Melkamu and Amare, 2012).Of note, in Kenya, the prevalence of HIV infection in females is disproportionately higher compared to males (KAIS 2012), however, the presence ofbrain pathology was significantly higher (76.2%) in malescompared to females (56.6%), OR 2.5 (95% CI 1.0-6.0), p=0.046.

The mean age of study participants was 39.8 years (S.D. 11.6), with a range of 18-68 years. Most participants were less than 40 years old. This age distribution was comparable to other studies in sub-Saharan Africa (Berhe et al., 2012)(Potchen et al., 2014), United States (Graham III et al., 2000) and Asia (Hongsakul and Laothamatas, 2008).

Prevalence of brain pathology was significantly lower (53.8%) in participants 40 years and below compared to participants above 40 years (79.1%), OR 0.3 (95% CI 0.1-0.8), p=0.010. Similarly, ill-defined lesions are more common in participants above 40 years, compared to participants below 40 years [OR 0.2 (95% CI 0.1-0.9), p=0.027]. This

might be because participants over 40 years have a higher incidence of brain pathology due to normal aging process or might have lived longer with the virus.

5.3. IMAGING FINDINGS SEEN ON CT BRAIN SCANS

The prevalence of brain pathology seen on CT in the study population was 65.3%. 34.7% of participants hadunremarkable brain scans. It is not surprising for HIV/AIDS patients with CNS manifestations to have unremarkable brain scans. Reported prevalence of normal brain CT scans ranging from 11% to 98.97%(Gatune, 1999)(Gifford and Hecht, 2001)(Byanyima, 2015)(Tso et al., 1993)(Potchen et al., 2014)(Hongsakul and Laothamatas, 2008).

Most parenchyma pathologies were diffuse, hypodense, non-enhancing and located in the front oparietal region. These findings are due to the high proportion of encephalitic lesions seen in the study population. Similar results were reported in Uganda (Byanyima, 2015).

The parietal lobe was the most frequent site involved, followed by frontal lobe, occipital lobe, and the basal ganglia. These findings are comparable to a study in Nigeria in which the most common site was the front oparietal lobes (Adeolu et al., 2006), however, this was not similar to a Ugandan study in which the basal ganglia was the most common location(Byanyima, 2015). Of note was the different CT diagnosis in both studies. Most participants in this study population had HIV-associated lesions, which favour the cerebral cortex, while most participants in the Ugandan study had opportunistic infections that favour the basal ganglia.

Ring-enhancing lesions were the most common types of enhancement patterns seen. This finding was comparable to findings in a study done in Nigeria(Eze and Eze, 2012), in which multiple ring-enhancing lesions was reported as one of the most common findings (Eze and Eze, 2012). The Ugandan study also reported a high incidence of single and multiple ring-enhancing lesions which are suggestive of opportunistic infection; Toxoplasmosis.

Isolated brain atrophy is a reported finding in HIV-positive patients (Adeolu et al., 2006)(Graham, Wippold, Pilgram, Fisher, and Smoker, 2000)(Potchen et al., 2014)(Tso et al., 1993), however; an objective assessment of brain atrophy among HIV-patients is lacking. A subjective assessment is prone to interobserver (Leonardi et al., 1994) and probably intraobserver variability. Considering the error that might occur in the evaluation of brain atrophy, an objective method of assessment for cortical and subcortical brain atrophy was utilized.

Less than half (44%) of study participants presented with brain atrophy. Similar findings have been reported in developed countries (Graham III et al., 2000)(Tso et al., 1993). A lower prevalence (28%) of brain atrophy was reported in Nairobi (Gatune, 1999). Most participants with brain atrophy had subcortical brain atrophy. Compared to findings among HIV-positive Zambians (Potchen et al., 2014), the proportion of participants with subcortical brain atrophy was high. However, the Zambian study mainly evaluated HIV-positive patients who present with their first seizure and the method used in assessing subcortical brain atrophy was not documented.

Only 17.7% of participants had meningeal enhancement signifying meningitis. This proportion was lower than a Thailand study(Hongsakul and Laothamatas, 2008)in which 32.31% of participants had meningitis. The study site was a regional referral centre; therefore, participants might have been treated before referral. This makes the proportion of participants with detectable meningeal enhancement below the expected.

Lesions that were large enough to cause mass effect can cause effacement of the ventricles. Effacement of ventricles was noted in 12.6% of participants with structural pathology on brain CT. The evaluation of ventriculomegaly on brain CT can be unreliable because of the presence of brain atrophy in this population. In 23.2% of participants, a dilated ventricle was evident. The majority being ex-vacuo dilatation, while pathological dilatation was minimal. Similar findings were noted in Zambia in which 37.21% of participants with imaging abnormalities on CT had enlarged ventricles being associated with subcortical brain atrophy (Potchen et al., 2014). In Nairobi, a low prevalence (4.7%) of hydrocephalus in HIV/AIDS patients was documented.

HIV-associated CNS disease was the most common spectrum of pathology seen. HIV-associated CNS disease results from direct infection by the virus. Most participants had Encephalitis. This was similar to a study in Thailand (Hongsakul and Laothamatas, 2008) which found HIV encephalopathy, also referred to as encephalitis, to be the most common CT diagnosis. Findings are not comparable to a study done in Nairobi in which 9.3% of participants had encephalitis (Gatune, 1999).

Only one (1.1%) diagnosis of suspected CNS Lymphoma was made. This was similar to findings in Thailand, where 1.92% of participants with positive brain CT scan had suspected lymphoma.

Ischemic stroke was commoner compared to hemorrhagic stroke in patients with HIV/AIDS(Howlett, 2012). In the study population, more participants (6.3%) had an ischaemic stroke compared to hemorrhagic stroke (2.1%). A higher proportion (15%) of ischaemic stroke have been documented in HIV/AIDS patients in Nairobi (Gatune, 1999). The percentage of ischaemic stroke was comparable to the Thailand study in which only 5.2% of participants had an ischaemic stroke on CT. It was lower than a study in Nigeria(Eze and Eze, 2012)in which 38.9% of participants had an infarct-like lesion. The study in Nigeria has conducted in a small (n=36) HIV population in which most of the participants were not on ARTs.

In this study, 2.1% of participants had subdural haematoma not related to trauma. Similar findings were reported in another sub-Saharan African country (Adeolu et al., 2006).

Toxoplasmosis was the only opportunistic infection diagnosed in 2.1% of participants. This finding was not comparable to a study done in Uganda (Byanyima, 2015) and Thailand (Hongsakul and Laothamatas, 2008). In Thailand Toxoplasmosis was seen in 21.8% of participants (Hongsakul and Laothamatas, 2008). This study was conducted in a referral hospital. Based on CSF findings, study participants might have been treated prior to referral, or treated prior to imaging.

Cerebral abscess was seen in 5.3% of study participants. The percentage of participants with brain abscess was low compared to a study done in Nairobi (Gatune, 1999) in which 29.9% of study participants had cerebral abscess.

One participant presented with a case of suspected meningioma. Such finding is an uncommon presentation in HIV patients(Abbara, M., Tolaymat, A., Battles, O.E., Robinson, 2010)(Khurshid et al., 1999). Lymphomas are the most common CNS tumors seen in this population. Lesions have been shown to mimic meningioma in HIV patients (Chourmouzi et al., 2012).Therefore, histological diagnosis is crucial.

5.4. RELATIONSHIP BETWEEN COMPUTED TOMOGRAPHY PATTERNS AND USE OF ANTIRETROVIRAL THERAPY

With only 54.7% of study participants on ARTs. HIV-associated diseases were more prevalent in participants not on ARTs. Encephalitis is an HIV-associated disease caused by the direct effect of the virus in the CNS. A higher percentage of Encephalitis was noticed in ART-naive participants. The large proportion of Encephalitis seen among such participants might be caused by the uncontested presence of the virus in the CNS.

In the study population, focal and multifocal lesions were significantly higher in patients on ARTs (13.5%) while none of their counterparts reported such lesions ($p=0.015$). Though diffuse and ill-defined lesions (30.8% and 15.4% respectively) were substantially higher in patients using ARTs, the difference was not significant ($p>0.05$).

Brain pathology, brain atrophy, and encephalitis were not significantly associated with ART use ($p>0.05$).Adherence to ART, which was not assessed in this study, might contribute to our findings.

Even though majority of study participants were on ART for more than 2 months, brain pathology was not significantly associated with the duration of ART use. Toxoplasmosis, an opportunistic infection, was not significantly associated with the duration of ART use.

5.5. STUDY LIMITATIONS

Being a cross-sectional study confounding factors that may cause and, or influence similar disease presentation were not adequately addressed in the study population.

Recall bias. Participants were asked about the duration of Antiretroviral use.

Inability to confirm the diagnosis using histopathology.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1. CONCLUSIONS

Majority of participants' had a detectable pathology on brain CT and the commonest structural abnormality seen was brain atrophy.

The most common CT brain scan diagnosis was Encephalitis, and Toxoplasmosis was the only opportunistic infection diagnosed.

There was no significant association between Antiretroviral Therapy use and common brain CT findings.

6.2. RECOMMENDATIONS

A larger study over a longer duration should be done, to further assess the relationship, if any, between CT findings and Antiretroviral Therapy use.

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APPENDICES

Appendix I: Consent Forms

ENGLISH VERSION

Investigator: My name is Dr. JACKSON-COLE Jennifer. I am a qualified doctor, currently pursuing a Master's degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which will study the Computerized Tomography Brain Scan Findings in Symptomatic Human Immunodeficiency Virus Infected Adult Patients at the Moi Teaching and Referral Hospital, Eldoret, Kenya.

Purpose: This study will seek to describe the Patterns seen on Computerized Tomography scan of the Brain in patients infected with HIV presenting with CNS symptoms, and correlate these findings with demographics and use of Anti-retro viral therapy (ART).

Procedure: All patients infected with HIV who present with CNS signs and symptoms for which consent has been given will be assessed and will undergo brain CT depending on the clinical signs and symptoms. Adult patients will be interviewed for age, area of residence, use of ART. Clinical examination of the patients will be carried out and the type and location of the lesion recorded. Medical records would be accessed to confirm the use of ARTs. Data will be collected on data collection forms. Data collecting material will be kept in a locked cabinet in the office of the principal investigator during the study period.

Benefits: There will be no direct advantages of participating in this study. Study subjects will be given same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants because of this study.

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

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

Sign or make a mark if you agree to take part in the study.

Sign or make a mark if you agree to take part in the study.

Study Participant: …… Investigator: …… Date: …….

Proxy Consent Form

Investigator: My name is Dr. JACKSON-COLE Jennifer. I am a qualified doctor, currently pursuing a Master's degree in Radiology and Imaging at Moi University. I would like to recruit your relative/ward into my research which will study the Computerized Tomography Brain Scan Findings in Symptomatic Human Immunodeficiency Virus Infected Adult Patients at the Moi Teaching and Referral Hospital, Eldoret, Kenya.

Purpose: This study will seek to describe the Patterns seen on Computerized Tomography scan of the Brain in patients infected with HIV presenting with CNS symptoms, and correlate these findings with demographics and use of Anti-retro viral therapy (ART).

Procedure: All patients infected with HIV who present with CNS signs and symptoms for which consent has been given will be assessed and will undergo brain CT depending on the clinical signs and symptoms. Adult patients will be interviewed for age, area of residence, use of ART. Clinical examination of the patients will be carried out and the type and location of the lesion recorded. Medical records would be accessed to confirm the use of ARTs. Data will be collected on data collection forms. Data collecting material will be kept in a locked cabinet in the office of the principal investigator during the study period.

Benefits: There will be no direct advantages of participating in this study. Study subjects will be given same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants as a result of this study.

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

Rights to Refuse: Participation in this study is voluntary. You can refuse to partake or withdraw at any time, on behalf of your relative/ward. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study.

Sign or make a mark if you agree to take part in the study.

Name: ……. Relation to Study Participant: ……

Signature: ……...

Investigator: ……. Date: …….

KISWAHILI VERSION

Mpelelezi: Jina langu ni Dr. JACKSON-COLE Jennifer.Mimi nidaktariniliohitimu na kwa sasa natafutashahada ya uzamili katikaRadiologyna ImagingkatikaChuo Kikuu cha Moi. Ningependakukusajili katikautafiti wanguambao ni wa kupima mfumo mkuu wa neva (CNS) kwa wagonjwa wanaougua Virusi vinavyosababisha Ukimwi (VVU) kutumia CT katika hospitali ya mafundisho na ya rufaa ya moi.

Kusudi: Utafiti huu utaeleza matokea ya CT kwa wagonjwa walio na VVU/ UKIMWI ambao wanamaambukizi kwenye mfumo mkuu wa neva. Matokeo yatakayopatikana yatahusishwa na dalili za mfumo mkuu wa neva, kiasi cha kinga ya mwili matumizi ya madawa ya kurefusha maisha nadalili za mgonjwa.

Utaratibu: Wangonjwa wote ambao wana VVU pamoja na maambukizi kwenye mfumo mkuu wa neva watakao kubali kushiriki, watakaguliwa na kufanyiwa CT ya ubongo. Vigezo kama umri, makazi na matumizi ya madawa ya kurefusha maisha yataangaziwa. Watu wazima watahojiwa na wazazi au walezi watahojiwa kwa niaba ya watoto. Ruhusa itachukuliwa na wagonjwa watakaopeana ridha watapimwa na matokeo ya uchunguzi, aina na eneo ya ugonjwa kuangaziwa. Rekodi za matibabu zitakaguliwa kuthibitisha kiasi cha kinga na utumizi wa dawa ya kurefusha maisha. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa katika nyumba ya mpelelezi mkuu katika kipindi cha utafiti.

Faida: Hakutakuwa na faida yeyote ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa nahaki sawa ya kupatiwa matibabu bora na wale ambao hawatofanyiwa utafiti huo.

Hatari: Utafiti huu haukusudiwi kuwa na hatari yeyote.

Usiri: habari zozote zitakazopatikana katika utafiti huu zitawekwa kwa siri na wala hazitatolewa kwa mtu yeyote asiye husika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni kwa hiari yako, kuna uhuru wa kukubali, kukataa au kutoka kwenye utafiti wakati wowote. Utafiti huu imepitishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha kufundishia Moi na Hospitali ya Rufaa.

Kusaini au kufanya alama kama unakubali kushiriki katika utafiti

Mzazi / Mlezi: ..... Mpelelezi:.....Tarehe: .....

Appendix II: Data Collection Form

1. **INCLUSION/EXCLUSION CRITERIA**

CRITERIA	YES	NO (PLEASE EXCLUDE FROM STUDY)
Patient Tests Positive For HIV		
Over 18 Years Of Age		
Brain CT with I.V contrast done		
Brain associated CNS symptom(s) +/- sign(s)		
Not pregnant		

2. **DEMOGRAPHICS**

Date				
Hospital Medical Record Number				
Ward				
CT number				
Age/Date Of Birth				
Sex	Male			
	Female			
Place of Residence				
	Rural		Urban	

NO: __

3. CLINICAL FINDINGS

a. CLINICAL SYMPTOMS

Clinical symptoms	**Present /Yes**	**Absent /No**
Focal symptoms		
Paralysis of both lower limb		
Weakness of both lower limb		
Weakness of one side of the body		
Localized seizures		
Loss of vision on one eye		
Loss of vision both eyes		
Others please specify		
Non-focal symptoms		
Generalized seizures		
Headache		
Dizziness		
Memory impairment		
Confusion		
Depressed level of consciousness		
Fever		
Others, please specify		

b. CLINICAL SIGNS

Clinical signs	**Present /Yes**	**Absent /No**
Focal neurological sign		
Hemiplegia		
Hemiparesis		
Coma		
Unilateral Blindness		
Bilateral blindness		
Focal seizures		
Others please specify		

6. CT PATTERNS SEEN
Please TICK appropriately

a. Normal or Abnormal scan

	YES	NO
Normal brain scan		
Abnormal brain scan		

b. Location of brain abnormality

i. Anatomical location

	YES	NO
Meninges		
Ventricles		
Brain parenchyma		
Others	Description	

ii. Regional location

	YES	NO
Supratentorial		
Infratemporal		
Both		

c. Meningeal changes

	YES	NO
Leptomeningeal enhancement		
Others		

d. Ventricular changes

i. General ventricular changes

	YES	NO		
Normal				
Effaced				
Dilated			If YES Evans Index (E.I*) Value	
Others				

*E.I: linear ratio of the total width of the frontal horns of the cerebral lateral ventricles to the maximum intracranial diameter.

ii. Dilated Ventricles

	Lateral ventricles	3rd Ventricle	Cerebral aqueduct	4th Ventricle
Location of dilatation				

	YES	NO
Communicating		
Non-communicating		

iii. Effaced Ventricles

	Lateral ventricles		3rd Ventricle	4th Ventricle
	Left	Right		
Location of effacement				

e. Brain parenchyma changes

i. General brain parenchyma changes

		YES	NO		
1	**Brain atrophy, If YES type of brain atrophy**				
a	Cortical brain atrophy (cella media index)			**Cella media index**	
b	Subcortical brain atrophy (Intercaudate distance ratio)			**Intercaudate distance ratio**	
2	**Diffuse lesion, If YES locations**			**Locations**	
3	**Localize lesions**			**Locations**	
4	**Others**	**Description**			

Cortical atrophy: cella media ratio. Ratio of BPD of skull to maximum external diameter of lateral ventricle at cella media (central part of the lateral ventricle) normal >4. Intercaudate distance/inner table width (normal 0.09-0.12).

ii. Diffuse brain parenchyma changes

	Pre-contrast			**Post-contrast**			
	YES	Location(s)	NO	YES	Location	NO	**Measurements (mm)**
Ring-like lesion							
Isodense lesion							
Hypodense lesion							
Hyperdense lesion							
Others							

iii. Description of diffuse brain parenchyma changes

	Description
Ring-like lesion	
Isodense lesion	
Hypodense lesion	
Hyperdense lesion	
Others	

iv. Localize brain parenchyma changes

	Pre-contrast			Post-contrast				Perilesional oedema	
	YES	Location(s)	NO	YES	Location	NO	Measurement (mm)	YES	NO
Ring-like lesion									
Isodense lesion									
Hypodense lesion									
Hyperdense lesion									

Others				

v. Description of localize brain parenchyma changes

	Description
Ring-like lesion	
Isodense lesion	
Hypodense lesion	
Hyperdense lesion	
Others	

f. Other patterns

i. Midline shift

	YES	NO
Midline shift		
Degree of midline shift		
Description		

ii. Brain Herniation

	Present	Absent
Brain herniation		

1. Subtype of brain herniation

		Present	Absent
Subfalcine herniation			
Tonsillar herniation			
Transalar herniation	**Ascending**		
	Descending		
Transtentorial herniation	**Downward uncal herniation**		
	Upward ascending transtentorial herniation		

7. CT-BASED DIAGNOSIS

a. HIV-ASSOCIATED LESIONS

	YES	NO
Encephalitis		
HAD		
Vasculitis		
Others	**TYPE:**	

b. OPPORTUNISTIC INFECTIONS

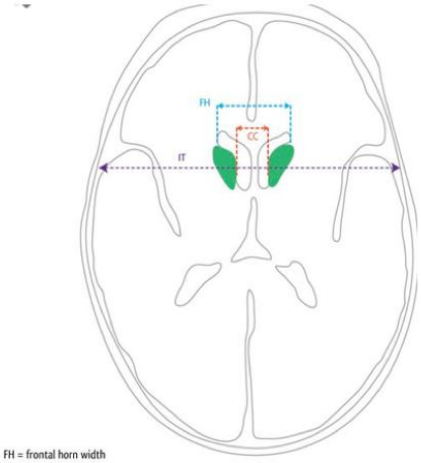
	YES		
Toxoplasmosis		**Site**	
Cryptococcosis		**Site**	
PML			
Cytomegalovirus infection			
Syphilis			
Tuberculous meningitis		**With tuberculoma**	**Site**
		No tuberculoma	
Others			

c. NEOPLASMS

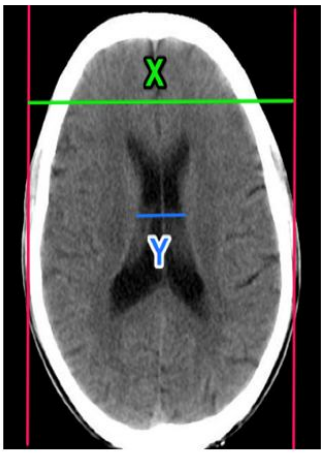
Suspected Lymphoma	YES		SITE
	NO		
Other neoplasms	YES	TYPE	SITE

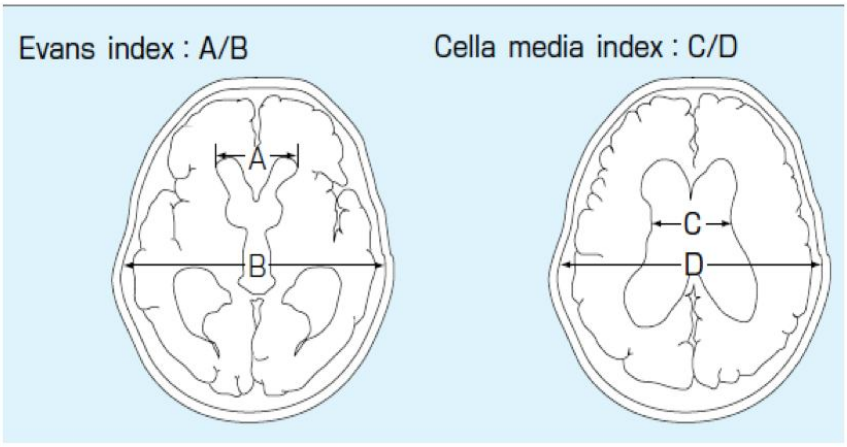
d. OTHERS

Infarcts	YES	Sites	
	NO		
Abscess	YES	SITES	
	NO		
Meningitis	YES		
	NO		
Other lesion	YES Description	Sites	
	NO		



FH = frontal horn width
CC = intercaudate distance
IT = inner table width





KEY

FL; frontal lobe.	PL; parietal lobe.	TL; temporal lobe.	OL; occipital lobe
CBLM; cerebellum.	BG; basal ganglia.	TM; thalamus.	Rt; right, Lt; left

Appendix III: MTRH CT Brain HIV/AIDS Protocol

- Non-enhanced and enhanced head CT scan done using the PHILIPS MX 4000 Dual Slice CT Scan Machine.
- Request received, and indication for the CT scan confirmed and recorded in the register along with the In-Patient Number.
- An I.V cannula inserted.
- Patient supine and head secured in position with pads on both sides and strapped in place.
- Patient positioned head first in the gantry and laser light centered at midline, about 2.5 cm from the vertex.
- The following settings used; Kilo-voltage 120Kv, 150Mas, 80 WW and 35 WL.
- The scanogram with necessary collimation was done and the appropriate windows were set i.e. brain window and bone window.
- Non-enhanced brain images were acquired.
- 40 millilitres bolus of contrast media (Ultravist) introduced via the cannula and contrast enhanced images were then acquired.
- All scanning was then done with increments of 5mm from the base of the skull to the vertex.

Appendix VI: Ethics Committee Approvals

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

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

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2014/132
Approval Number: 0001231

31st July, 2014

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
31 JUL 2014
APPROVED
P.O. Box 4606-30100 ELDORET

Dr. Jennifer Jackson -Cole,
Moi University,
School of Medicine,
P.O.Box 4606-30100
ELDORET-KENYA.

Dear Dr. Cole,

RE: FORMAL APPROVAL

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

"Patterns Seen on Computerized Tomography Scan of the Brain in Patients Infected With HIV at Moi Teaching and Referral Hospital, Eldoret."

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1231*** on 31st July, 2014. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 30th July, 2015. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

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

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
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P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

31st July, 2014

Dr. Jennifer Jackson -Cole,
Moi University,
School of Medicine,
P.O.Box 4606-30100
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

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

***"Patterns* Seen on Computerized Tomography Scan of the Brain in Patients Infected With HIV at Moi Teaching and Referral Hospital, Eldoret."**

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

DR.JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD,HRISM