BRAIN MAGNETIC RESONANCE IMAGING FINDINGS IN WHITEMATTER DISEASES.

A DISSERTATION SUBMITTED IN PART FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN DIAGNOSTIC IMAGING AND RADIATION MEDICINE, UNIVERSITY OF NAIROBI.

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DECLARATION

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This dissertation is my original work and has not been presented for a degree in any other university.

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DEDICATION

With love and gratitude to my family.

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ABSTRACT

BACKGROUND

Background:-The white matter of the brain is located in the central and subcortical regions of the cerebral and cerebellar hemispheres and accounts for about 60 % of the total brain volume. The white matter includes the major commissural tracts, the cortical association fibers, and all the cortical afferent and efferent fibers. The white matter contains nerve fibers, supporting cells, interstitial space, and vascular structures.

Magnetic resonance imaging (MRI) is a non-invasive method of mapping the internal structure of the body which completely avoids the use of ionizing radiation. It employs radiofrequency (RF) radiation in the presence of carefully controlled magnetic fields in order to produce high quality cross-sectional images of the body in any plane. Several MRI sequences are deployed to further characterise lesions.

Objective:-The objective of the study is to determine MRI findings in white matter diseases.

Study Design:-A prospective cross sectional study was carried out at the Kenyatta National Hospital and plaza imaging solutions.

Method: - A total of 136 patients with white matter lesions were enrolled in the study from September 2008 to April 2009.Data were filled into questionnaires, which were later transferred into a data mastersheet.Data analysis was done using a statistical software (SPSS version 17.0).A p-value of less than 0.05 was considered statistically significant.

Results

99.2% and 99.3% of the studied patients had high signal intensities with T2WI and FLAIR sequences respectively in the white matter of the brain. The commonest clinical presentations were limb weakness and seizures 53 and 23 patients respectively. The periventricular location was the commonest site for the lesion (66%) of the all studied locations in the brain.

Conclusion

MRI of the brain especially with T2WI and FLAIR sequences plays a critical role towards the diagnosis of white matter disease and hence contributing to the total patient management.

ABBREVIATIONS

CT	Computed Tomography
CNR	Contrast to Noise Ratio
CSF	Cerebral Spinal Fluid
CECT	Contrast Enhanced Computed tomography
DTPA	Diethylene Triamine Penta-acetic Acid
DWI	Diffusion Weighted Imaging
GE	Gradient Echo
FSE	Fast Spin Echo
FLAIR	Fluid Attenuated Inversion Recovery
MITC	Medical Imaging and Therapeutic Centre
MRI	Magnetic Resonance Imaging
NECT	Non Enhanced Computed Tomography
NEX	Number of Excitations
KNH	Kenyatta National Hospital
MRS	Magnetic Resonance Spectroscopy
PD	Proton Density
STIR	Short Tau Inversion Recovery
T	Tesla
TE	Echo Time
TR	Repetition Time
T1W	T1 Weighted images
T2W	T2 Weighted images
TTP	Time To Peak
SE	Spin Echo
SNR	Signal to Noise Ratio

INTRODUCTION

Earlier on before 1946 Einstein and Isidor Isaac Rabi had studied magnetic properties and internal structures of molecules and atoms .later on,Bloch and Purcell studied MR phenomenon in 1946 and for their discovery they were jointly awarded the Nobel Prize for Physics in 1952. [1,2].

Soon after its discovery, MR-spectroscopy has been employed as a laboratory tool for studying the properties of matter at the molecular level [3]. Its use for medical imaging required a method for spatial localization which was discovered in 1973 by Lauterbur [4].The first human images were produced in 1977 by Mansfield, Maudsley, Damadian et al and Hinshaw et al[5,6,7].

Magnetic resonance imaging (MRI) is a noninvasive method of mapping the internal structure of the body which completely avoids the use of ionizing radiation and today appears to be without hazard[1]

It employs radiofrequency (RF) radiation in the presence of carefully controlled magnetic fields in order to produce high quality cross-sectional images of the body in any plane. It portrays the distribution of hydrogen nuclei and parameters relating to their motion in water and lipids.

MRI has now rapidly progressed from being a technique with great potential to one which has become the primary, and often the only, diagnostic method required for many clinical problems.

Its application, which began in the central nervous system, has now extended into all regions of the body. An increased knowledge base has provided a better understanding of how it can best be used, either alone or in conjunction with other techniques to reduce diagnostic uncertainty.

New applications and clinical roles for MRI have emerged in the last few years including evaluation of white matter diseases.

Technical advances have included improvements in spatial resolution, contrast and in particular, speed of imaging compared to the past.

An advance in MRI sequences is providing fascinating insights into cerebral pathology [8].Sequence manipulation can enable one to narrow down the differential diagnosis.

In 1974, differences in the relaxation times of gray and white matter were first described [9].

Studies done about four years later using a highly T1-dependent inversion recovery sequence produced images with high level of contrast between gray and white matter[10].
This stimulated a considerable interest in the ability of MRI to detect changes in white matter diseases [11].

Early in 1980's the use of spin echo sequence produced images with lower contrast between gray and white matter but with high sensitivity of detecting a wide varieties of pathological change.
In addition to that, partial volume artifacts were minimized resulting in making diagnosis less ambiguous [11].

Furthermore,TR and TE could be selected to provide a higher T2-dependent contrast while concurrently reducing the CSF signal in comparison to that of adjacent brain. Partial volume effects were thus easily differentiated from MS lesions which produced higher signal than brain [11].
More recently since 2005,FLAIR and DWI sequences have been employed to yield a high contrast resolution images in white matter diseases [12].

Mechanism for changes in demyelinating disease seen on MRI
Different authors agree that, demyelinating disorders reduce myelin content. This results in increased water content of white matter, because myelin (rich in solids) is lost, leaving behind more hydrated material. In other words white matter becomes less hydrophobic and takes on more water. Less myelin and more water protons prolong the relaxation times of both T1 and T2, resulting in higher signal on T2-weighted and a lower signal on T1-weighted images [11,13,14].

Why MRI
Several study groups indicate that MR imaging is exquisitely sensitive for detecting brain abnormalities, particularly in the evaluation of white matter diseases, MR far outperforms ultrasound and CT.
Ultrasound is not useful as it is impossible for ultrasound waves to interrogate the calvarium.CT has poor soft tissue characterization compared to MRI. Lesions that may be quite subtle or even invisible on CT are often clearly seen on the MR scan [3,11,14.15].

LITERATURE REVIEW

Demyelination (myelinoclysis) implies destruction of myelin after it has formed normally.On the other hand, dysmyelination refers to defective formation of myelin resulting from dysfunction of the oligodendrocytes. Most of the dysmyelinating disorders are caused by metabolic defects that present in infancy [13].Most of these defects are due to enzyme deficiency [11].These two entities are the major groups of diseases affecting white matter, collectively termed white matter disease [15].

NORMAL WHITE MATTER

The white matter of the brain is located in the central and subcortical regions of the cerebral and cerebellar hemispheres and accounts for about 60 % of the total brain volume. The white matter includes the major commissural tracts, the cortical association fibers, and all the cortical afferent and efferent fibers [13].

Histologically, white matter contains nerve fibers, supporting cells, interstitial space, and vascular structures. It consists mostly of axons with their envelope of myelin, along with two types of neuroglia, oligodendrocytes and astrocytes. Axons are extensions of neurons that reside within the gray matter of the brain, spinal cord, and ganglia. Myelin is produced and maintained by oligodendrocytes and myelin functions as an insulator of the axons. Its structure facilitates rapid transmission of impulses [13].

Nerve conduction in myelinated axons is of saltatory manner, whereby the nerve impulse jumps from one node of ranvier to the next without depolarization of the axonal membrane underlying the myelin sheath between the nodes. This produces faster conduction velocities (~70m/s) compared to slow velocities (~1m/s) produced in unmyelinated nerves [13]

It has been documented that, an infant's white matter differs significantly from that of an adult. There is progressive myelination soon after birth which is extensive and relatively slower myelination throughout childhood and adolescence. Immature myelin has a much greater water content compared to the adult form which has a predictable effect, seen on MRI images [14].

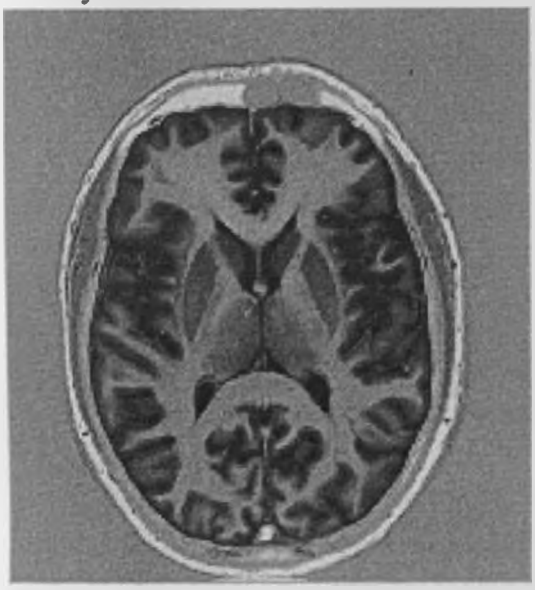
MRI APPEARANCE OF NORMAL WHITE MATTER

T1 and T2 relaxation values in normal white matter are shorter than in gray matter. Thus on T1W images white matter is relatively brighter in signal intensity while on T2W images white matter is less intense or darker.

The white matter is affected by many disease processes.The primary demyelinating disease is multiple sclerosis, but many other metabolic and inflammatory disorders result in deficient or abnormal myelination.

Several study groups indicate that the MR signal characteristics of white matter lesions are primarily periventricular and subcortical hyperintensities. These can be specific or relatively non-specific as ones due to age.Other distinguishing features are often present to assist in diagnosis such as, the pattern of the abnormality, location, imaging protocol used and enhancement features [16,17,18].

Therefore despite some similar imaging appearances of white matter lesions, the above features together with adequate clinical history are of importance towards making a diagnosis. DWI further characterizes brain tissue especially white matter.This is a valuable technique in the identification of myelination disorders. DWI is very sensitive to hypoxic ischaemic injury. It is very sensitive in the direction of axons in white matter [23,24,25].



A normal MRI appearance of white matter with inversion recovery sequence.

DEMYELINATING DISEASES

Demyelinating diseases are characterized by inflammation and selective destruction of CNS myelin. The peripheral nervous system is spared. Most patients have no evidence of associated systemic illnesses [13].

White matter diseases in older children and adults are generally demyelinating or a combination of the two processes i.e. demyelinating and dysmyelinating [13].

The demyelinating diseases can be sub classified into primary (of unknown etiology e.g. MS) or secondary when associated with variety of infections, toxic, anoxic-ischemic or other factors [11].

These diseases include:

- Multiple sclerosis (primary demyelinating disease)
- Infectious and inflammatory disorders (ADEM, PML and HIV encephalitis)
- Deep white matter ischaemia
- Acquired toxic metabolic disorders
- Posterior Reversible Encephalopathy Syndrome(PRESS)
- Central and extra pontine Myelinolysis
- Radiation injuries

MULTIPLE SCLEROSIS

Epidemiology

Literature shows that, MS is approximately twice as common in women as in men. However, studies carried out in India indicate a male preponderance [19].

The age of onset is typically between the second and fourth decades. The highest known prevalence is 250 per 100000 in Scotland. The disease most often occurs in temperate zones. There is a noted general increase in prevalence with increasing distance from the equator. It is seen predominantly in Caucasians though common to all races. Low prevalence rates have been documented in studies done in Japan(2 per 100000),but researchers from western and middle eastern countries suggest an increase in prevalence of MS [12.20].

Aetiology

The precise cause of the disease is unknown [11,21] .However some authors have attributed it to autoimmune mechanisms as the probable cause of demyelination in genetically susceptible individuals [15, 16].

Clinical presentation

(1)Weakness of the limbs

This may manifest as loss of strength or dexterity, fatigue or disturbance of gait. Exercise induced weakness is characteristic symptom of MS.

(2)Sensory symptoms

These include both paresthesias (e.g. tingling, prickling sensations, formications, pins and needle or painful burning) and hypesthesia (e.g. reduced sensation, numbness or a dead feeling). Others include, unpleasant sensation (e.g. feeling that body parts are swollen, wet, raw or tightly wrapped).

(3)Visual disturbances

Impaired or double vision of acute optic neuritis and blindness [14,20].

(4)Bladder and bowel dysfunction

Symptoms of bladder dysfunction are present in up to 90% of MS patients [20]

(5)Spasticity

More than 30% of MS patients have moderate to severe spasticity, especially in the lower limbs [20]. Other presentation includes constipation, cognitive dysfunction, depression, fatigue, sexual dysfunction, facial weakness and vertigo.

Four clinical types of MS have been described

1. Relapsing/remitting.
2. Secondary progressive.
3. Primary progressive.
4. Progressive/relapsing.

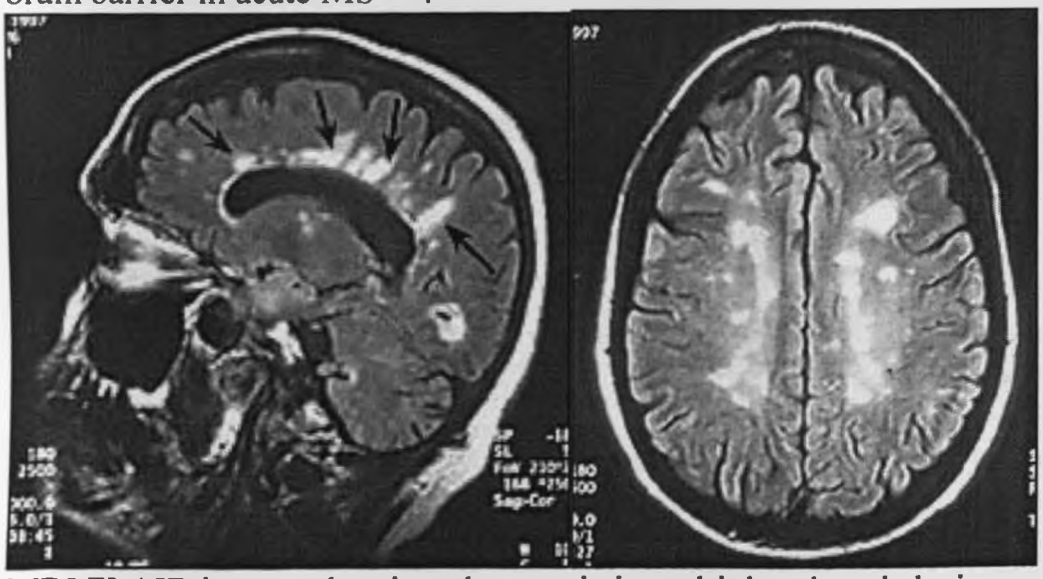
MRI FINDINGS

Typical MS lesions are hypointense on T1 weighted images. These also are called black holes [12] In chronic cases, the lesions have a hypointense centre with hyperintense rim. It has been documented that standardT1 weighted images have low sensitivity in detecting MS lesions with a noted exception for chronic plaques [14].This is ameliorated by employing the T1 inversion recovery study which accentuates grey white matter contrast.

With standard T2 weighted sequences MS plaques appear as hyperintense lesions [11, 12, 14, 15]
Some authors have reported hypointense lesions in the basal ganglia in (10-20%) of cases of chronic MS [12].

FLAIR sequence shows bilateral, asymmetric linear or ovoid hyperintensities and perivenular extensions. With severity of the disease the hyperintensities may become confluent [12] .Dawson finger along the path of medullary veins has been cited as being specific for MS. A horseshoe pattern of contrast uptake is specific for tumefactive multiple sclerosis [19] FLAIR and proton density sequences are diagnostically important. High signal of CSF on T2 is suppressed (low CSF signal), leaving high signal plaques standing out adjacent to ependymal surfaces[11.22].Typical lesions are seen at the callososeptal interphase hence the importance of FLAIR sagittal view.
Typically with DWI, MS lesions appear hyper intense. Acute lesion appears as concentric ring with hyperintense rim. Subacute or chronic lesions, shows an increase in ADC values with moderate decrease in anisotropy compared with white matter [16] .T1W +contrast shows transient enhancement during active demyelination which disappears within 6 months in up to 90%.[12]

Some authors indicates that intravenous Gadolinium is used to study activity of MS lesions.[14]
Gadolinium enhancement is explained by transient breakdown of the blood brain barrier in acute MS [26].



MRI FLAIR images showing characteristic multiple sclerosis lesions

ADEM (ACUTE DEMYELINATING ENCEPHALOMYELITIS)

This is an autoimmune mediated white matter demyelination of the brain and or spinal cord, usually with remyelination [12].

ADEM usually has a monophasic course and is frequently associated with antecedent immunization (postvaccinal encephalomyelitis) or infection (post infectious encephalitis).
The hallmark of ADEM is the presence of widely scattered small foci of perivenular inflammation and demyelination.

Postvaccinal encephalitis may follow the administration of smallpox and certain rabies vaccine.
Post infectious encephalomyelitis is mostly associated with viral exanthems of childhood.
Age
A long term follow up study reveal that the mean age at onset of ADEM is 5.3+-3.9 years.
Sex
Similar study indicated slight male preponderance [27], however a study done by Khosoroshahi revealed no sexual preponderance [28].Another study done in London between 1985-1999, revealed that no patient presented with ADEM before 3 years of age [29].

Clinical presentation

The patient may present with fever, headache, menigismus, seizure, lethargy and coma [20]. Prof.Lakhar working in India found that the common clinical presentation included, altered consciousness(50%),motor symptoms(23.3%) and urinary retention(23.3%).All patients in the study had fever prior to onset of clinical symptoms[19].

MRI FINDINGS

T2-weighted images are the most sensitive in demonstrating asymmetrical white matter foci of hyperintensities.on FLAIR sequences the lesion stand out.
T1 with intravenous gadolinium shows prominent enhancement which may be a punctate foci or less commonly,ring like [14].

Location

May involve both brain and spinal cord. The distribution is predominantly white matter but also gray matter can be involved [12,14].

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

PML is a rare subacute demyelinating disease caused by replication of polyoma virus (JC virus) in the brain of an individual with immunosuppression [14,30].

Clinical presentation

Clinical presentation is related to the location and size of the lesion. Symptoms may include, lack of coordination of an arm or leg, partial hemiparalysis, partial loss of vision, impairment of thought and speech pattern, memory problems and dementia.

MRI-findings

The white matter lesions of PML are patchy and round or oval at first, but then become confluent and large. The process is often distinctly asymmetric and initially involves the peripheral white matter, following the contours of the gray-white matter interface to give outer scalloped margins. Lesions tend to be homogeneous with well-defined margins. The prolonged T_1 and T_2 relaxation times reflect the loss of myelin and increased water. Mass effect and contrast enhancement are rarely seen.

Location

It is not primarily a periventricular process, but as the disease progresses, the deeper white matter is also affected. Any white matter structures can be involved, but lesions of the corpus callosum are much less common than in multiple sclerosis. Brain stem and cerebellar lesions are found in about one-third of patients. Occasionally, they can be the sole presenting lesion. Basal ganglia and thalamic sites generally represent extension from lesions in the internal capsule or damage to white matter fibers coursing through the gray matter structures [30].

HIV-ENCEPHALITIS

This is a subacute encephalitis involving the white matter seen in up to 30% of patients with AIDS.A neurotropic retrovirus, human immunodeficiency virus type 1 (HIV),directly invades the neurons.

Clinical presentation

Patients present with headache, memory loss, language difficulty, movement

disorders, and various sensory deficits. More advanced disease is signaled by behavioral disorders, loss of bowel and bladder control, and the AIDS dementia complex. HIV and cytomegalovirus often coexist in brain specimens taken from patients with AIDS. However, HIV seems to be the predominant etiology for the microglial nodules and multinucleate giant cells, the pathologic hallmarks of the white matter encephalitis [31,32].

MRI-findings
There is bilateral diffuse and patchy to confluent areas of increased signal intensity on T_2-weighted images with poorly defined margins. HIV encephalitis does not enhance with gadolinium.

The MR appearance is distinct from that of PML, and the clinical setting readily separates it from other white matter abnormalities. As with PML, the white matter abnormality on MRI often improves or remains stable after therapy with protease inhibitors, correlating with clinical improvement [33].

Location
The white matter of the cerebrum, cerebellum and brain stem.

DEEP WHITE MATTER ISCHAEMIA
The deep white matter of the cerebral hemispheres receives its blood supply from long, small-caliber arteries and arterioles that penetrate the cerebral cortex and traverse the superficial white matter fiber tracts.

The white matter does not have as generous blood supplies as the gray matter and is more susceptible to ischemia. As the nutrient arteries become narrowed by arteriosclerosis and lipohyaline deposits within the vessel walls, the white matter becomes ischemic on a chronic basis [34]
Therefore, leukoencephalopathy can be the result of longstanding hypertension or a single/prolonged episode of hypotension e.g. global hypo perfusion syndrome [14].

Pathologically, one of the first changes in the aging brain is an increase in the perivascular interstitial fluid, predominantly at the arteriolar level of the vascular tree. With continued progressive ischemia of the white matter, additional histologic changes are observed, including atrophy of axons and myelin and tortuous, sclerotic, and thickened vessels. Vasculitis and lacunar infarct ensues.

Maintenance of myelin becomes deficient, resulting in "myelin pallor" on microscopic sections. Mild gliosis and increased interstitial fluid accompany the changes in the myelin. Necrosis is not seen until severe ischemia leads to frank infarction of brain tissue [34].

MRI FINDINGS

Hyperintense on T2 and FLAIR, mild hypointense on T1.No enhancement with contrast [35].

Location

The most common locations for the hyperintensities are the subcortical and periventricular white matter, optic radiations, basal ganglia and brain stem, in decreasing order of frequency [36].

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

The posterior reversible encephalopathy syndrome (PRES) describes the combination of posterior cerebral involvement and brain dysfunction that occurs with this entity.

Clinical presentation

Patients present with headache, confusion, visual disturbance, and seizures. Several diseases and clinical conditions are associated with PRES, but the root cause seems to be acute or subacutely elevated blood pressure. Hypertension can occur with drug ingestion, chronic renal disease, autoimmune nephritis (systemic lupus erythematosus), Wegener's granulomatosis, acute renovascular hypertension, pheochromocytoma, preeclampsia and eclampsia, and immunosuppressant therapy [36].

MRI-findings

MRI reveals lesions with high signal intensity on FLAIR and T2 weighted nonenhanced images. There is a predilection for the posterior cerebral white matter, and in severe cases the adjacent gray matter can be involved. Extension into the frontal lobes is not uncommon, but isolated anterior white matter involvement is unusual.

Contrast enhancement is patchy if at all present. The white matter lesions of PRES do not exhibit restricted diffusion.The white matter injury is largely reversible. At least, with correction of the hypertension, the MRI findings resolve within a few weeks and follow clinical recovery [37].

ACQUIRED TOXIC METABOLIC DISORDERS

The BBB is said to limit entry of substances into the brain, however this barrier can be broken down by disease process or chemotherapeutic agents. Therapeutic agents may be instituted deliberately to open the BBB,so that the agents have access to the disease process e.g. Tumour mass. Similarly, intrathecal administration and lipid solubility increase delivery to the brain. The commonly documented agent associated with leukoencephalopathy are-

a)Antineoplasmagents,methotrexate,carmustine,cisplatin,cytarabine,fluorouracil,levamisole,fludarubine,thiotepa,interleukin-2,interferon-alpha

b) Immunosuppressive drugs (cyclosporine, tacrolimus)

c) Antimicrobial agents (amphotericineB, hexachlorophen)

d) Drugs of abuse (toluene, ethanol, cocaine, 3,4-methylenedioxymethamphetamine, intravenous heroin, inhaled "heroin" pyrolysate, psilocybin),

e) Environmental toxins (carbon monoxide, arsenic carbon tetrachloride)[38].

Clinical presentation

Different study groups agree that, leukotoxic agents tend to disrupt or abolish neural transmission in neurobehaviour pathway, resulting in changes in mental status, which is the classic presentation. Patient may present with chronic confusion states with inattention, memory loss, emotional dysfunction, dementia, abulia, stupor and coma.Language is usually spared [38,39,40,41]

MRI FINDINGS

MR imaging initially reveals patchy involvement of the periventricular white matter and centrum semiovale, which over time evolves to a confluent pattern. Enhancement is seen in severe cases. Cerebral calcification has been documented [42].

Location

Most lesions are seen in periventricular white matter and centrum semiovale. Deep white matter tracts, brainstem and cerebellum tend to be spared [42].

CENTRAL AND EXTRAPONTINE MYELINOLYSIS

Central pontine myelinolysis, also called osmotic demyelination syndrome, is a disorder characterized pathologically by dissolution of the myelin

sheaths of fibers within the central aspect of the basis pontis [43]. In extreme cases, there may be extension to the pontine tegmentum, midbrain, thalamus, internal capsule, and cerebral cortex, where it is termed as extrapontine myelinosis. The nerve cells and axon cylinders are spared.

It is aid to be associated with excessive alcohol consumption, hyponatremia, especially rapidly corrected hyponatremia and exacerbated by over hydration and administration of diuretic medications[11.14].Other aetiologic factors reported are, systemic hypotension, cerebral oedema, drug induced inappropriate ADH secretion[11,14,43].

Clinical-presentation
Typically the patient present with a rapidly progressive pontine neurologic deficit, spastic quadriparesis, pseudobulbar palsy, change in mental state. Bulbar symptoms often progress to a "locked in" syndrome [14,43].

MRI-findings
The lesions are seen as areas of hypointensity on inversion recovery sequences and hyperintensity on T_2-weighted images in the central pons with sparing of the pontine tegmentum and ventrolateral pons. Lesions have an oval shape on sagittal images, a bat-wing configuration on coronal images and various shapes on the axial images [44].

Location
Characteristic lesions are seen in pons and brainstem. In extreme cases, thalamus, internal capsule and cerebral cortex are involved [11,43].

RADIATION INJURY

Radiation injury to the brain may cause radiation necrosis or diffuse leukoencephalopathy (most common).These two entities differ in their clinical course, pathology and radiographic appearance. In our case we are going to discuss mainly diffuse radiation induced leukoencephalopathy [14].

Clinical-presentation
Has a progressive and insidious course. The effects on the brain can be focal or diffuse, depending on whether whole brain or more focused radiation was given.

The clinical picture is variable. Many patients are entirely asymptomatic. As a rule, severe imaging abnormalities are required for symptomatic patients.

Impairment of mental function is the most common problem, and may include personality change, memory deficiencies, confusion, learning difficulties, and in severe cases, dementia [45].

The pathologic changes of radiation necrosis continue to evolve for a number of years after the initial radiation. The location and amount of brain injury are related to the radiation dose, fractionation methods, and the portals used.

MRI-findings

The characteristic pattern of diffuse radiation injury is asymmetric, high-signal foci on T_2-weighted images in the periventricular white matter. There is initial sparing of the corpus callosum and the subcortical arcuate fibers. The changes parallel those seen in ischemia, but the lesions are more prevalent and a confluent pattern usually develops. As the process extends outward to involve the peripheral arcuate fibers of the white matter, the margins become scalloped, a helpful feature in the differential diagnosis [46].

Location

Diffuse leukoencephalopathy may involve all visible cerebral white matter (when the whole brain has been radiated) or only irradiated parts of the brain.

DYSMYELINATING DISORDERS

This is a spectrum of disorders where there is abnormal formation or maintenance of myelin or myelin is not formed or at best if formed is not maintained.

It includes the following major groups:

- Metachromatic leukodystrophy.
- Globoid leukodystrophy(Krabbe's disease).
- Spongiform degeneration (Canavan's disease).
- Adrenoleukodystrophy.
- Fibrinoid leukodystrophy (Alexander's disease).
- Others (Gangliosidoses,mitochondrial cytopathies,aminoacidopathies,Wilson disease, mucopolysaccharidoses).

The term leukodystrophy is commonly used to refer to Dysmyelination disorders.

METACHROMATIC LEUKODYSTROPHY

Most common of all the familial leukodystrophies.

Aetiology

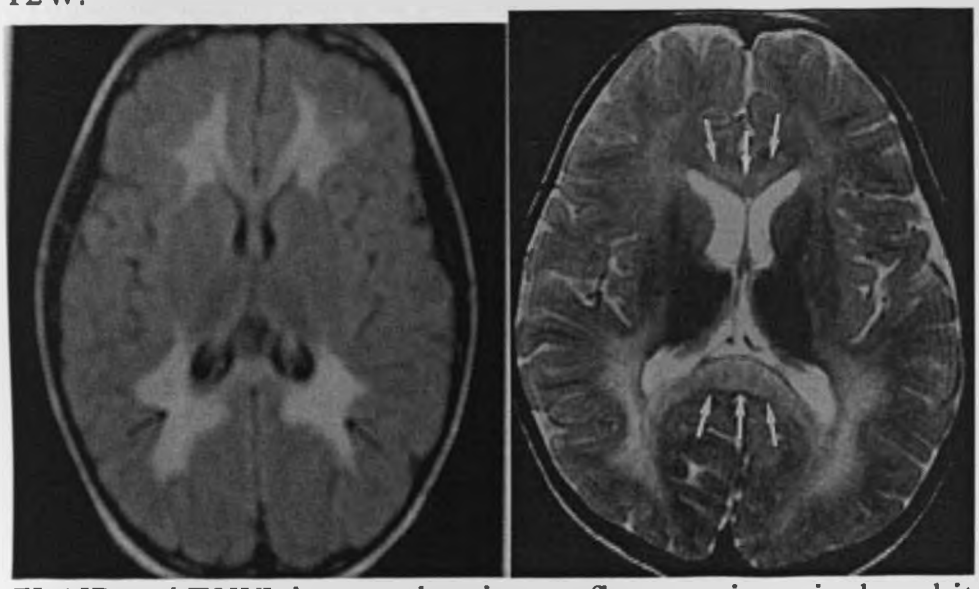
Caused by deficiency of the enzyme arlysulfatase.Diagnosis is confirmed by demonstration of absent or low levels of sulfatase in urine,leukocytes or cultured fibroblast.

Clinical presentation

Symptoms begin in the second or third year of life.They include irritability,frequent crying,anorexia,hypotonicity/hypertonicity, lack of truncal control,extensor postural abnormalities,intellectual decline and blindness.

MRI Findings

Shows symmetrical areas of hypointensity on T1W and hyperintensity on T2W.



FLAIR and T2WI images showing confluent periventricular white matter hyperintensity from MLD in a ''butterfly pattern.the corpus callosum is also involved see arrows in T2WI.

GLOBOID LEUKODYSTROPHY (KRABBE'S DISEASE)

This is a rare autosomal recessive disorder caused by deficiency of the enzyme Beta galactocerebrosidase.This deficiency results in excessive accumulation of galactocerobrosides in myelin,found in the so called globoid cells that are characteristic of the disease.

Clinical presentation

The clinical course mimic that of metachromatic leukodystrophy.

MRI findings

MRI shows white matter hyperintensity.

Location

The deep white matter and thalamic and cerebral cortex

SPONGIFORM DEGENERATION (CANAVAN'S DISEASE)

This is Familial spongy degeneration of CNS affecting infants of Ashkenazi jewish extraction. It is transmitted as an autosomal recessive trait and is caused by deficiency of the enzyme N-aspartoacylase.

Clinical presentation

Symptoms usually begin at 1-3months of age and the patient usually dies by the age of 4. The infants have motor and mental retardation, hypotonia,decorticate posturing,blindness and progressive megalencephally.

MRI findings

Symmetrical low intensity on T1W and high signal on T2W images.

Location

The outer zone of white matter, subcortical U shaped fibers and deep cortical layers. Canavan disease shows some of the most extensive white matter abnormalities. In a child with progressive megalencephaly, this can be almost pathognomonic of the disease.

ADRENOLEUKODYSTROPHY.

This is a hereditary Dysmyelination disease associated with adrenocortical insufficiency and melanoderma. The disease is caused by deficiency of the enzyme acyl-coaenzyme A synthetase, transmitted as an X-linked recessive

gene.Therefore is almost exclusively confined to males,although a few sporadic cases of females do occur.

Clinical presentation.

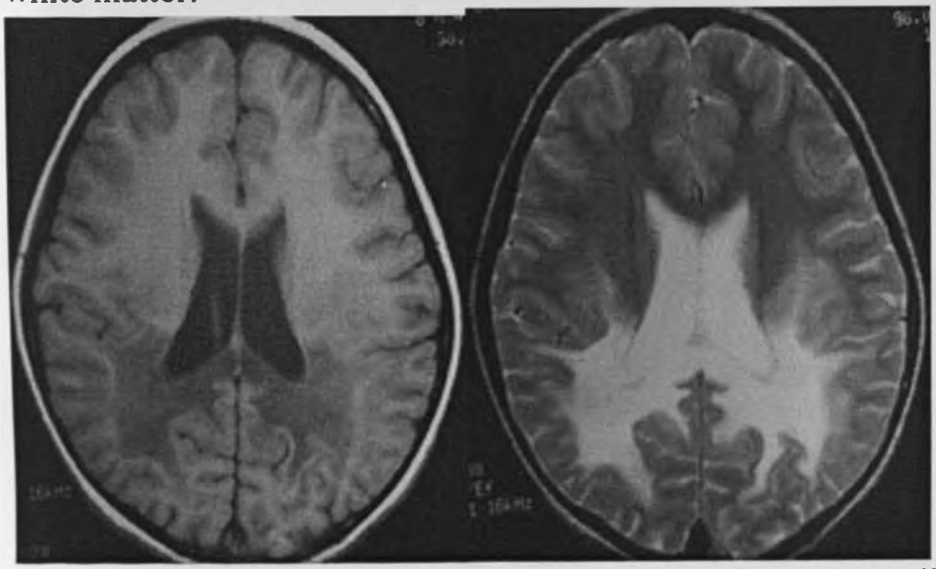
The onset usually in childhood. Progressive behavioral aberrations, visual loss and ataxia are characteristic for the disease. Patients can survive for several years but vegetative state leading to death is almost inevitable. Rare cases of remission, long-term survival and response to steroid medications have been reported.

MRI findings

Symmetrical white matter hyperintensities are seen on T2W images in parietal-occipital regions adjacent to the atria of the lateral ventricles and splenium. These are hypointense on T1W images. The overlying gray matter is entirely spared.

Location.

Parietal,occipital,posterior temporal white matter,corpus callosum,fornix,hippocampal commissure, posterior cingulum and cerebellar white matter.



T1WI and T2WI images showing symmetric confluent demyelination in the peritrigonal white matter and the corpus callosum in 5 year old boy with ALD.

FIBRINOID LEUKODYSTROPHY (ALEXANDER'S DISEASE)

This is a form of spongy sclerosis, a very rare sporadic dysmyelinating disease. It is similar to spongiform degeneration (Canavan's disease) in that,there is megalencephaly.Sometimes they are collectively termed as megalencephalic leukodystrophies.

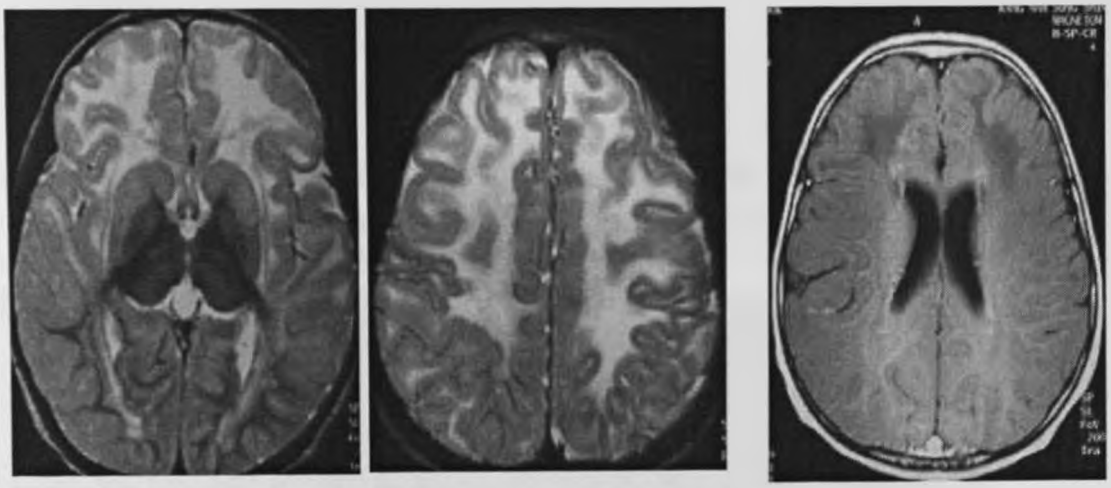
The distinguishing feature of Alexander's disease is histologic feature of fibrinoid astroglial changes, the so called Rosenthal fibers.

MRI findings

White matter hyperintensity on T2W images.

Location

Wide spread but have predilection for frontal lobes.



Bilateral frontal whitematter hyperintensity in a case of Alexander`s disease.

GANGLIOSIDOSES

Tay - Sachs disease (GM2gangliosidosis) is associated with a form of Dysmyelination.

MRI findings

Deep white matter may be prominent.Thalami may show changes consistent with calcification.

MITOCHONDRIAL CYTOPATHIES

Leigh's disease (sub acute necrotizing encephalomyelopathy) is a rare inherited disorder characterized with symmetrical vacuolation of the basal ganglia, the brain stem, cortex and to a lesser degree the white matter.

Location
Most characteristic demyelination is found in the lentiform nuclei, the cerebral peduncles, the periaqueductal gray matter, the pons and medulla.

MRI findings
T2W hyper intensities

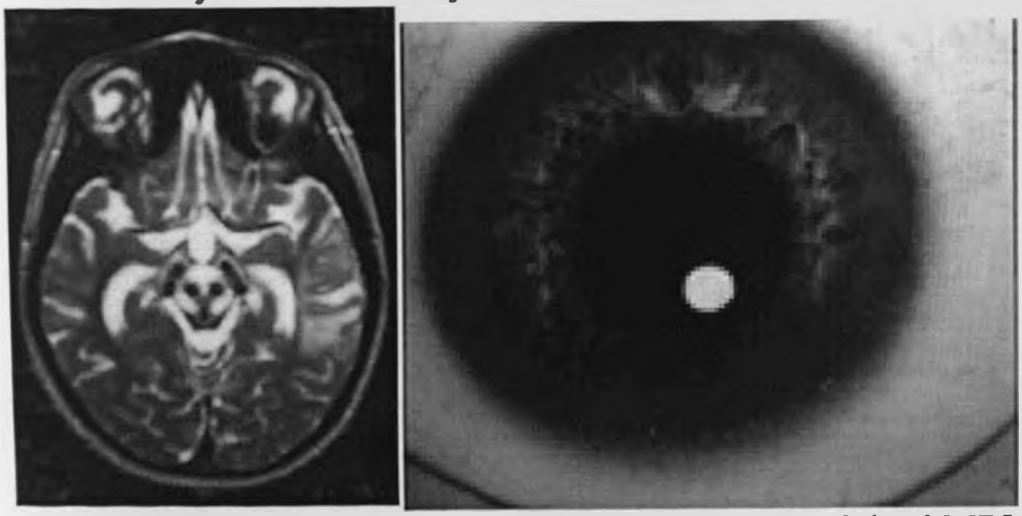
AMINOACIDOPATHIES

These are hereditary disorders of amino acid metabolism accompanied by neurologic dysfunction. They include marple syrup urine disease, phenylaketonuria, ketotic hyperglycinemias, urea cycle enzyme errors and nonketotic hyperglycinemias.

MRI findings
White matter oedema

WILSON`S DISEASE

This is a rare autosomal recessive disorder of copper metabolism. The basal ganglia are predominantly affected. White matter tract abnormalities have been routinely characterized by MRI.



The typical 'face of the giant in the midbrain on T2-weighted MRI of brain with a Kaiser-Fleischer rings of the eyes in a case of Wilson disease.

MUCOPOLYSACCHARIDOSES

The disorder caused by enzyme defects resulting in accumulation of glycosaminoglycans in many organs. There are six well recognized syndromes but Hurler's syndrome is a prototype.

Demyelination is not a prominent neuropathic feature but white matter changes simulating demyelination have been reported.

STUDY RATIONALE AND JUSTIFICATION

Recently there have been a notably increasing number of white matter lesions. Multiple sclerosis is being diagnosed more frequently compared to the previous experiences, especially in our set up, as it was known to be a disease of the Jews [3.19.48].

MRI plays an important role towards early diagnosis and management of white matter disease. In multiple sclerosis alone, MRI characteristic abnormalities are found in more than 95% of the patients [19.20] .Therefore, studying MRI findings of these lesions will provide the primary physician with an effective imaging modality towards diagnosis of white matter diseases.

To the best of my knowledge, so far I have not encountered a local publication of similar study. A search done at the University of Nairobi College of health science website on past research revealed no similar study for the available listed research topics for the last 27years.Results from this study will serve as a local database and will add value to the diagnosis of disease.

OBJECTIVES

BROAD OBJECTIVE

To study brain-MRI findings in white matter diseases.

SPECIFIC OBJECTIVES

1. To determine the socio-demographic pattern of the study population by age and sex.
2. To determine the clinical presentations of the study population.
3. To determine the MRI findings of the study population.
4. To determine the location/distribution of the white matter disease within the brain.

METHODOLOGY

Study area

The study was carried out at Kenyatta National Hospital's imaging department and plaza imaging centre in Nairobi, Kenya. Both centers have the same MRI machines (Phillips).

Study Population

Patients referred for MRI-brain with suspected or known white matter disease.

Inclusion criteria

Patients with MRI-brain with either 3 or more lesions(both focal and diffuse) in the white matter region.The lesions were picked by using standard T2W and FLAIR sequences.Because of variability of brain mri protocols not all patient underwent DWI.

Exclusion criteria

Patients with CNS tumours were excluded by clinical history and suggestive radiological findings.

Standardization of results

A 1.5T MRI Phillips machine with standardized sequences was used to generate images.

All imaging results were discussed with consultant radiologist.

Study design

This was a prospective descriptive cross-sectional study

SAMPLING TECHNIQUE

A simple Random sampling was used.Patients with MRI scans for the brain with findings in the white matter in KNH and PIS were included in the study from September 2008 to april 2009.

SAMPLE SIZE

The sample size was determined by the using the following formulae
$n = Z^2 crit * p (1 - P) / D^2$

Where
n = required sample size
p = Prevalence of white matter disease-based on a study done by Lakhkar B.N et al [19]
D = Precision of the study set at 0.10 (10%).
Zcrit. is the cut off points along the X – axis of the normal probability distribution that represents probability matching the 95% confidence interval

Substituting the above formulae
We get

n = 80.23

Therefore the minimum sample size is 80 patients however, 136 patients were obtained to increase the power of the study.

DATA ANALYSIS

The data were collected using a structured questionnaire. The filled questionnaire will be kept in a safe place ready for the data entry and for confidentiality of the patient details.

After cross checking the questionnaire for any missing entries a data base was designed in the M S which allowed the researcher to set controls and validation of the variables.
On completion of the data entry exercise the data were exported in a statistical package (SPSS – Version 17.0) for analysis.

The analyzed results are presented in tables and figures.
P value of less than 5 % was considered statistically significant.

ETHICAL CONSIDERATIONS

- Patient's identity was not registered during the study to maintain confidentiality. For reference purposes only the patient's identification number was used.

- No information or examination results were obtained without prior patient consent or institution permission.

- Before commencement of the study a request was submitted together with the proposal copy to the ethical and research committee KNH for approval. An approval was granted on 22nd September 2008.

STUDY LIMITATIONS

1. Inadequately or incompletely filled clinical information.
2. This study relied on strong clinical suspicion of white matter disease coupled with radiological diagnosis.

The study dwelled into the findings of the whole spectrum of white matter disease, therefore leading to poverty of information with regard to specific disease-entity

RESULTS

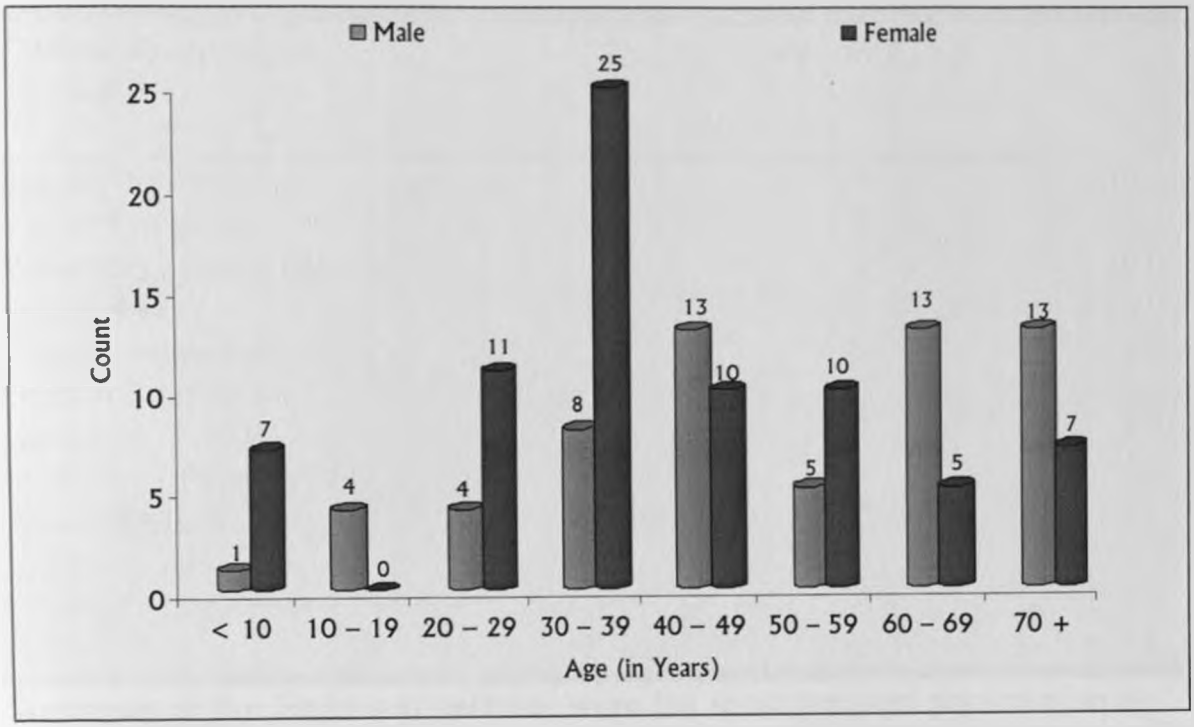
A total of 136 patients were recruited during the study period and the results are presented below.

Table 1: Age by Sex distribution among Study Participants (n = 136)

Age (in Years)	*Sex*		*Total*
	Male, n (%)	*Female, n (%)*	
< 10	1 (1.6)	7 (9.3)	8 (5.9)
10 – 19	4 (6.6)	0	4 (2.9)
20 – 29	4 (6.6)	11 (14.7)	15 (11.0)
30 – 39	8 (13.1)	25 (33.3)	33 (24.3)
40 – 49	13 (21.3)	10 (13.3)	23 (16.9)
50 – 59	5 (8.2)	10 (13.3)	15 (11.0)
60 – 69	13 (21.3)	5 (6.7)	18 (32.1)
70 +	13 (21.3)	7 (9.3)	20 (14.7)
Total	61 (100.0)	75 (100.0)	136 (100.0)

Most patients were aged between 30 and 39 years.

Figure 1: Age by Sex Distribution



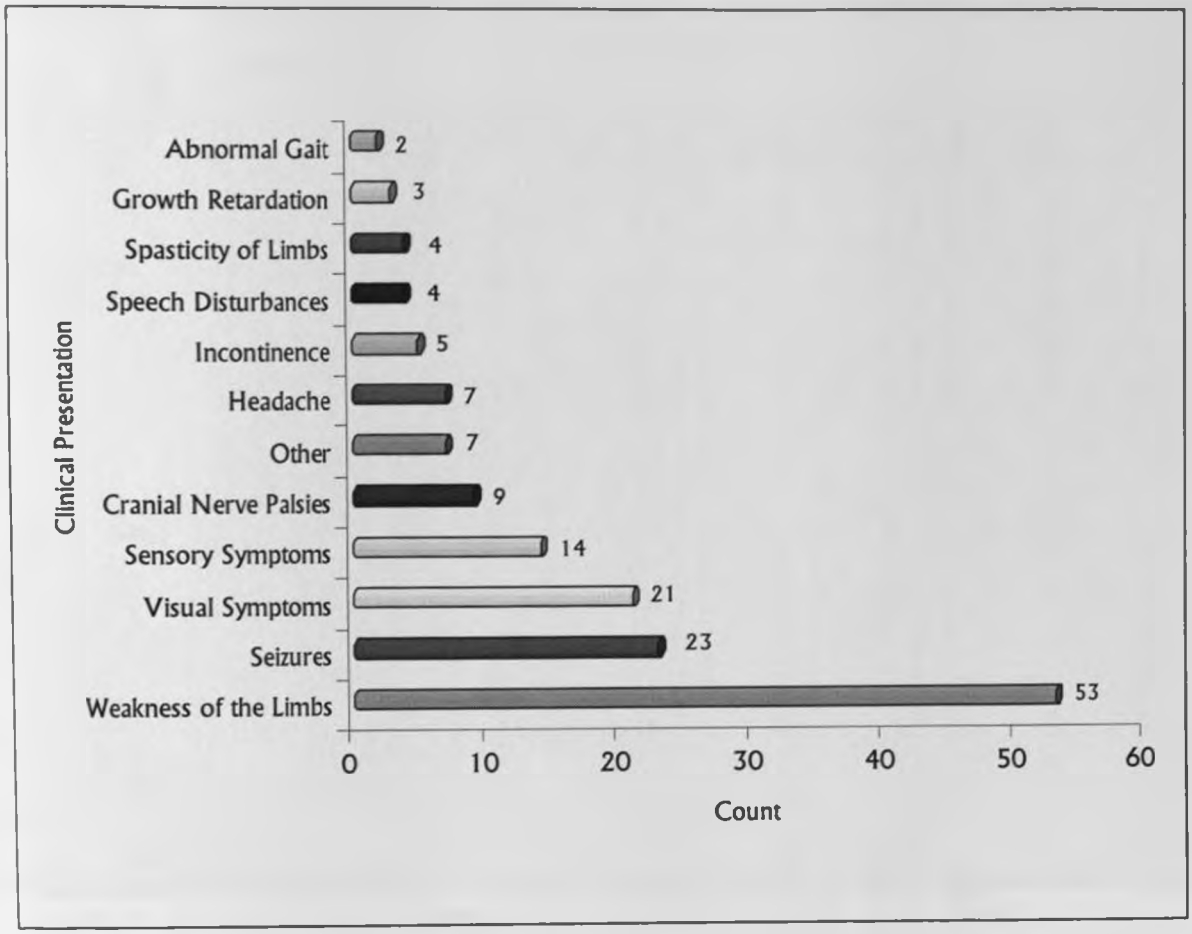
Most of the female participants were aged between 30and 39years of age, while male majority were aged between 60and 69

Table 2: Frequency Distribution of Clinical Presentation (n = 136)

Clinical Presentation	*Frequency*	*Percent*
Sensory Symptoms	14	10.3
Visual Symptoms	21	15.4
Weakness of the Limbs	53	39.0
Seizures	23	16.9
Cranial Nerve Palsies	9	6.6
Growth Retardation	3	2.2
Headache	7	5.1
Spasticity of Limbs	4	2.9
Abnormal Gait	2	1.5
Incontinence	5	3.7
Speech Disturbances	4	2.9
Other	7	5.1

Weakness of the limbs and seizures were the most reported presentation at 39% and 16.9% respectively.

Figure 2: Frequency Distribution of Clinical Presentation (n = 136)



53(39%) patients of the total clinical presentations of the participants had weaknesses of the limbs.

Table 3: Clinical Presentation vs Age (in years)

Clinical Presentation	*Age (in Years)*								*Total*
	< 10	10 - 19	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 +	
Sensory Symptoms	1	0	0	3	2	5	0	3	14
Visual Symptoms	1	2	7	2	5	0	3	1	21
Weakness of the Limbs	1	0	5	24	9	1	5	8	53
Seizures	4	2	0	4	5	2	4	2	23
Cranial Nerve Palsies	0	0	2	0	1	2	4	0	9
Growth Retardation	3	0	0	0	0	0	0	0	3
Headache	0	0	2	0	2	2	0	1	7
Spacicity	2	0	0	0	0	0	0	2	4
Abd. Gait	0	0	0	0	2	0	0	0	2
Incontinence	0	0	0	0	0	2	0	3	5
Speech Disturbances	0	0	0	4	0	0	0	0	4
Other	1	0	0	4	0	0	2	0	7

The mean age for those patients who had limb weakness was 44yrs compared to those who didn't have was 45.5yrs p-value =0.684 which was not statistically significant.

Table 4: Clinical Presentation vs. Sex

Clinical Presentation	Sex		Total
	Male	Female	
Sensory Symptoms	1	13	14
Visual Symptoms	15	6	21
Weakness of the Limbs	19	34	53
Seizures	15	8	23
Cranial Nerve Palsies	6	3	9
Growth Retardation	0	3	3
Headache	4	3	7
Spacicity Dist.	2	2	4
Abd. Gait	2	0	2
Incontinence	3	2	5
Speech Disturbances	0	4	4
Other	3	4	7

Females had more clinical symptoms compared to males.

Table 5: Signal intensity

MRI SEQUENCES	SIGNAL INTENSITY	
	Hyper	Hypo
T1W1	2 (1.5)	134 (98.5)
T1W1 + C	13 (9.6)	123 (90.4)
T2W2	126 (92.6)	10 (7.4)
FLAIR	135 (99.3)	1 (0.7)

FLAIR hyperintensities were seen in 99.3% of the study population.

Table 6a: Association between Signal Intensity vs. Clinical Presentation

Clinical Presentation	Signal Intensity T1W1	
	Hyper	Hypo
Sensory Symptoms	0	14
Visual Symptoms	0	21
Weakness of the Limbs	2	51
Seizures	0	23
Cranial Nerve Palsies	0	9
Growth Retardation	0	3
Headache	0	7
Spasticity of Limbs	0	4
Abnormal Gait	0	2
Incontinence	0	5
Speech Disturbances	0	4
Other	0	7

Table 6b

Clinical Presentation	Signal Intensity T1W1 + C	
	Hypo	Hyper
Sensory Symptoms	12	2
Visual Symptoms	19	2
Weakness of the Limbs	46	7
Seizures	23	0
Cranial Nerve Palsies	9	0
Growth Retardation	3	0
Headache	7	0
Spasticity of Limbs	4	0
Abnormal Gait	2	0
Incontinence	3	2
Speech Disturbances	4	0
Other	7	0

Table 6c

Clinical Presentation	Signal Intensity T2W2	
	Hypo	Hyper
Sensory Symptoms	0	14
Visual Symptoms	1	20
Weakness of the Limbs	6	47
Seizures	2	21
Cranial Nerve Palsies	0	9
Growth Retardation	0	3
Headache	0	7
Spasticity of Limbs	2	2
Abnormal Gait	2	0
Incontinence	5	0
Speech Disturbances	4	0
Other	7	0

Table 6d

Clinical Presentation	Signal Intensity FLAIR	
	Hypo	Hyper
Sensory Symptoms	0	14
Visual Symptoms	1	20
Weakness of the Limbs	1	52
Seizures	0	23
Cranial Nerve Palsies	0	9
Growth Retardation	0	3
Headache	0	7
Spasticity of Limbs	0	4
Abnormal Gait	0	2
Incontinence	0	5
Speech Disturbances	0	4
Other	0	7

Table 6a-d above shows that fewer cases had post contrast enhancement.

Table 7: Frequency distribution of Location

Location	Frequency	Percent
Periventricular	90	66.2
Calloso-septal	8	5.9
Corpus Callosum	10	7.4
Centrum Semiovale	60	44.1
Subcortical region	27	19.9
Basal Ganglia	17	12.5
Frontal Lobe	8	5.9
Parietal	7	5.1
Temporal	2	1.5
Pons	4	2.9
Mid-Brain	4	2.9
Infratentorial	21	15.4
Other	4	2.9

Periventricular site was the commonest location for white matter disease.

Table 8: Location by Sex

	Sex	
Location	Male	Female
Periventricular	45	45
Calloso-septal	2	6
Corpus Callosum	5	5
Centrum Semiovale	26	34
Subcortical region	12	15
Basal Ganglia	4	13
Frontal Lobe	5	3
Parietal	4	3
Temporal	0	2
Pons	0	4
Mid-Brain	4	0
Infratentorial	8	13
Other	2	2

There is no significance association sex predilection for the site of the lesion.

Table 9: Location v/s Signal Intensity.

Location	Signal Intensity T1W1	
	Hyper	Hypo
Periventricular	2	88
Calloseptal	0	8
Corpus Callosum	0	10
Centrum Semiovale	0	60
Subcortical u fiber	0	27
Basal Ganglia	2	15
Frontal Lobe	0	8
Pariental	0	7
Temporal	0	2
Pons	0	4
Mid-Brain	0	4
Infratentorial	0	21
Other	0	4

Table 9b: Location v/s Signal Intensity.

Location	Signal Intensity T1W1 + C	
	Hypo	Hyper
Periventricular	82	8
Calloseptal	4	4
Corpus Callosum	8	2
Centrum Semiovale	55	5
Subcortical u fiber	26	1
Basal Ganglia	13	4
Frontal Lobe	6	2
Pariental	6	1
Temporal	2	0
Pons	2	2
Mid-Brain	0	4
Infratentorial	16	5
Other	0	4

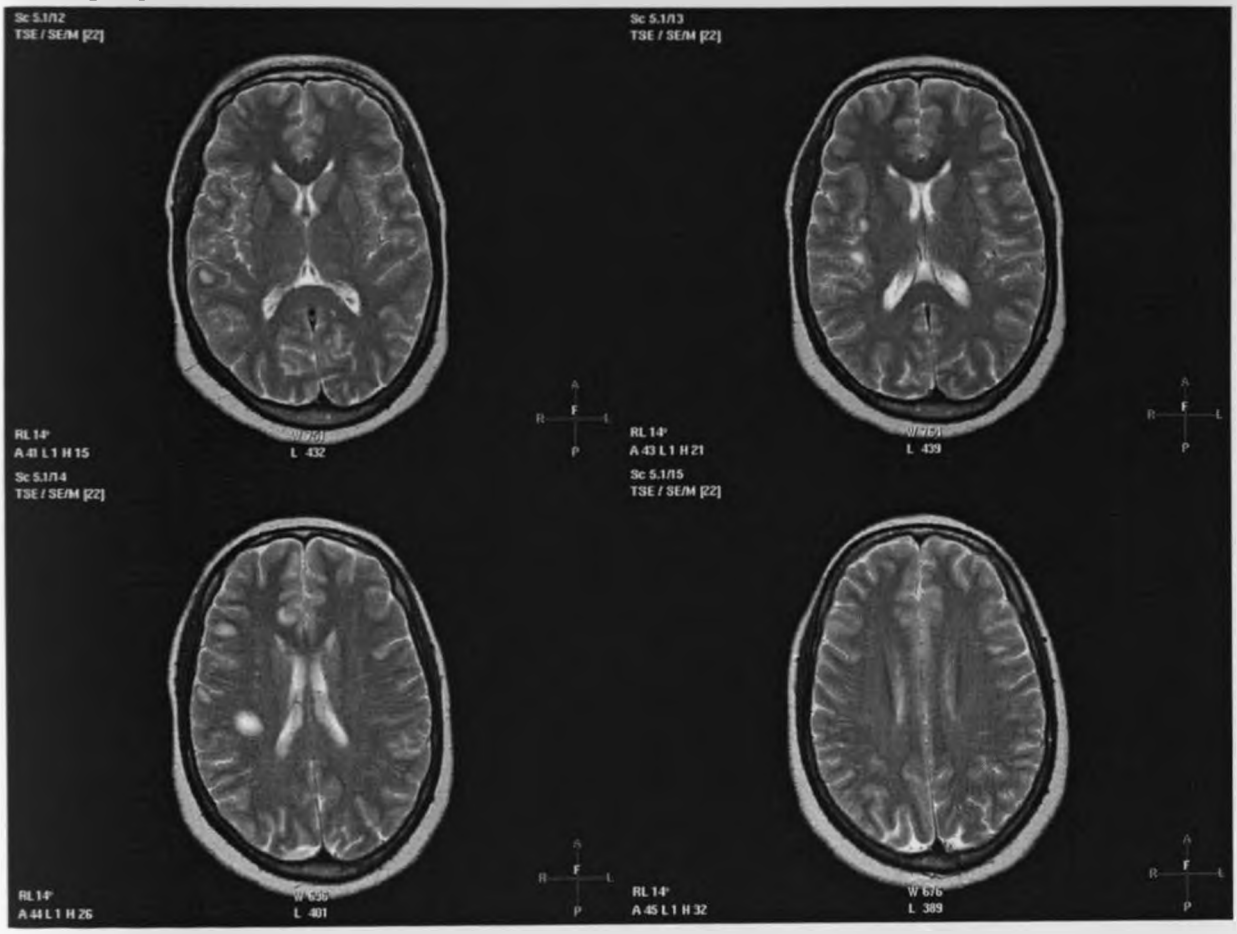
Table 9c: Location v/s Signal Intensity.

Location	Signal Intensity T2W2	
	Hypo	Hyper
Periventricular	7	83
Calloseptal	0	8
Corpus Callosum	2	8
Centrum Semiovale	5	55
Subcortical u fiber	7	20
Basal Ganglia	0	17
Frontal Lobe	1	7
Pariental	0	7
Temporal	2	0
Pons	2	2
Mid-Brain	0	4
Infratentorial	0	21
Other	0	4

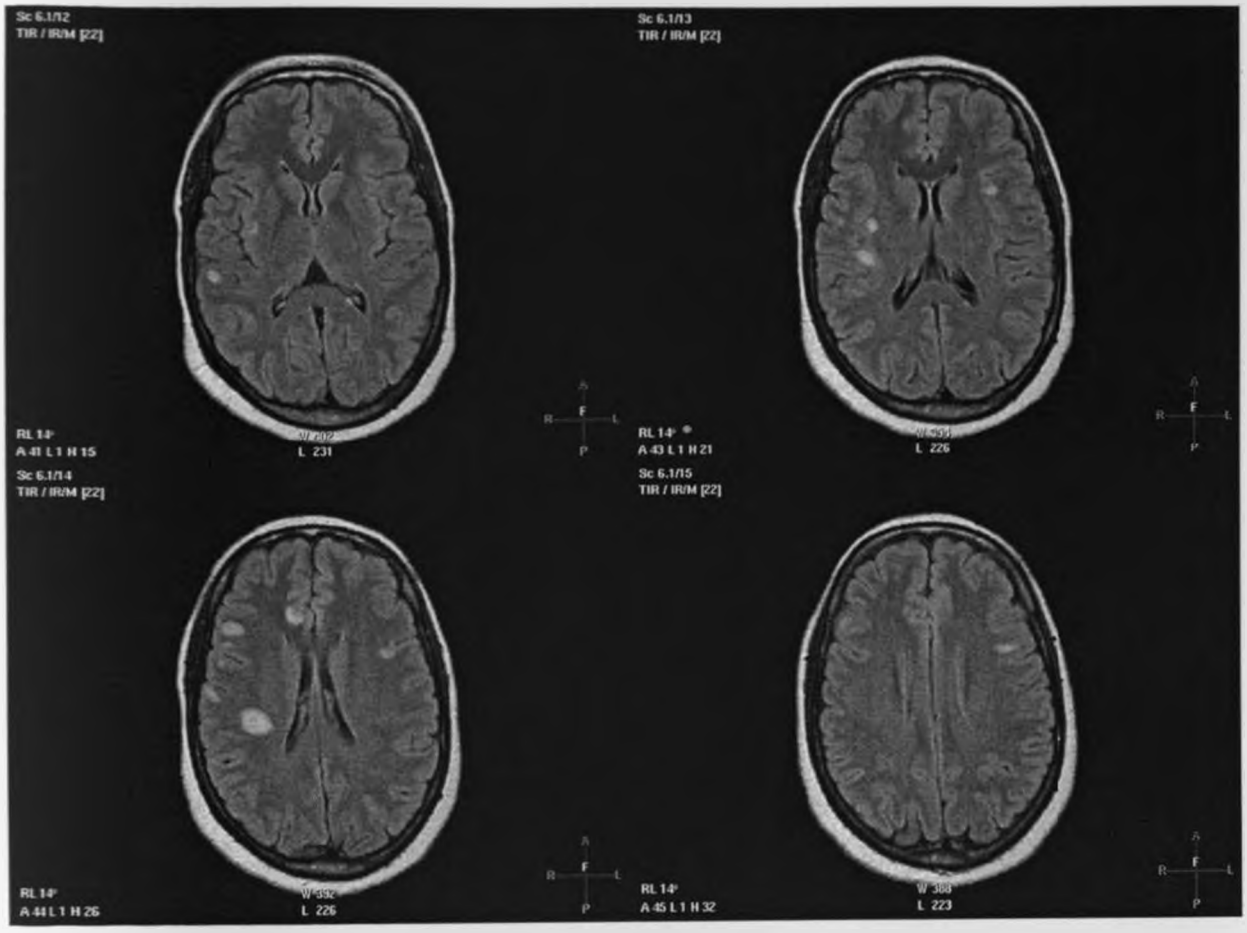
Table 9d: Location v/s Signal Intensity.

Location	Signal Intensity FLAIR	
	Hypo	Hyper
Periventricular	0	90
Calloseptal	0	8
Corpus Callosum	0	10
Centrum Semiovale	0	60
Subcortical u fiber	0	27
Basal Ganglia	0	17
Frontal Lobe	1	7
Pariental	0	7
Temporal	0	2
Pons	0	4
Mid-Brain	0	4
Infratentorial	0	21
Other	0	4

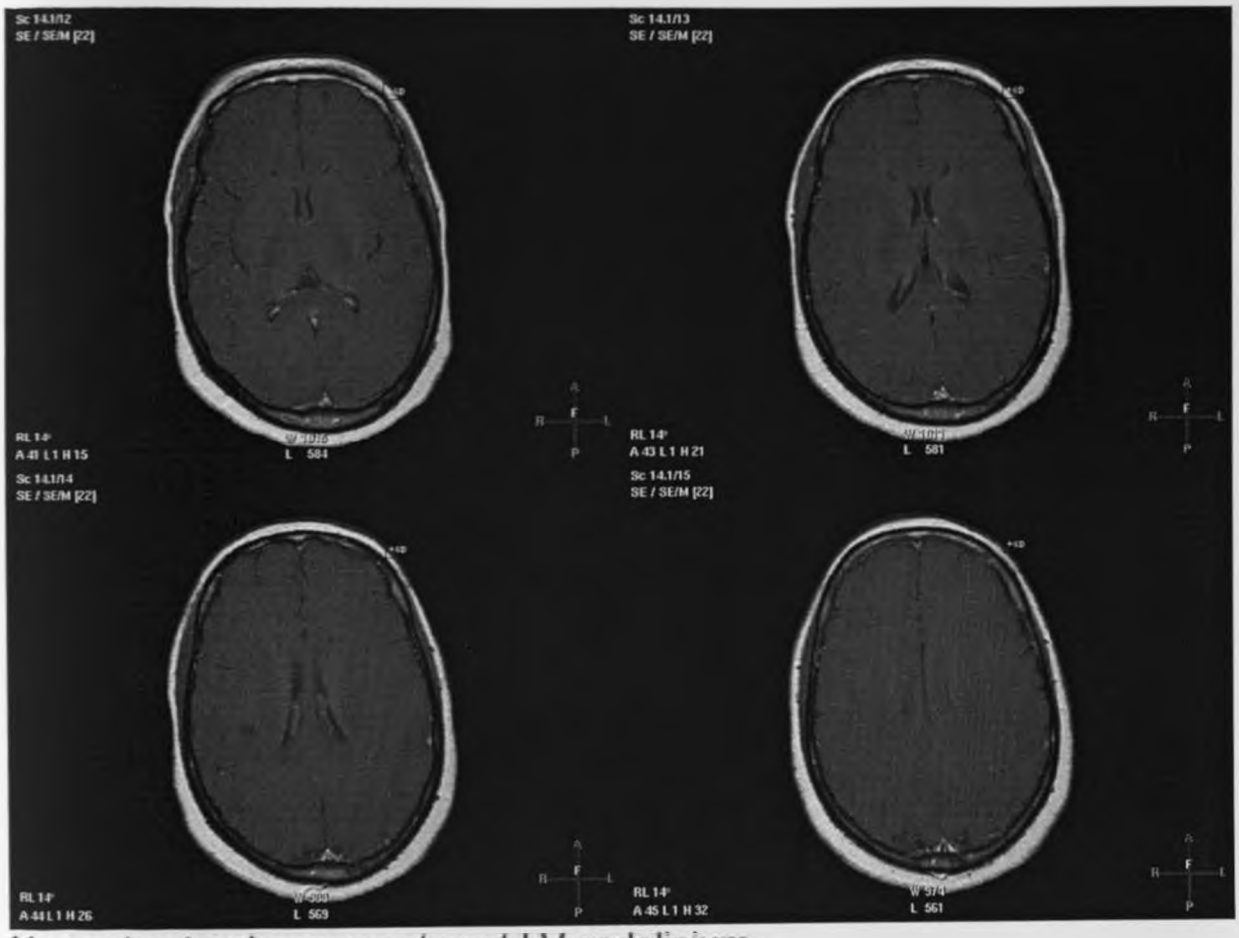
SELECTED SAMPLE IMAGES



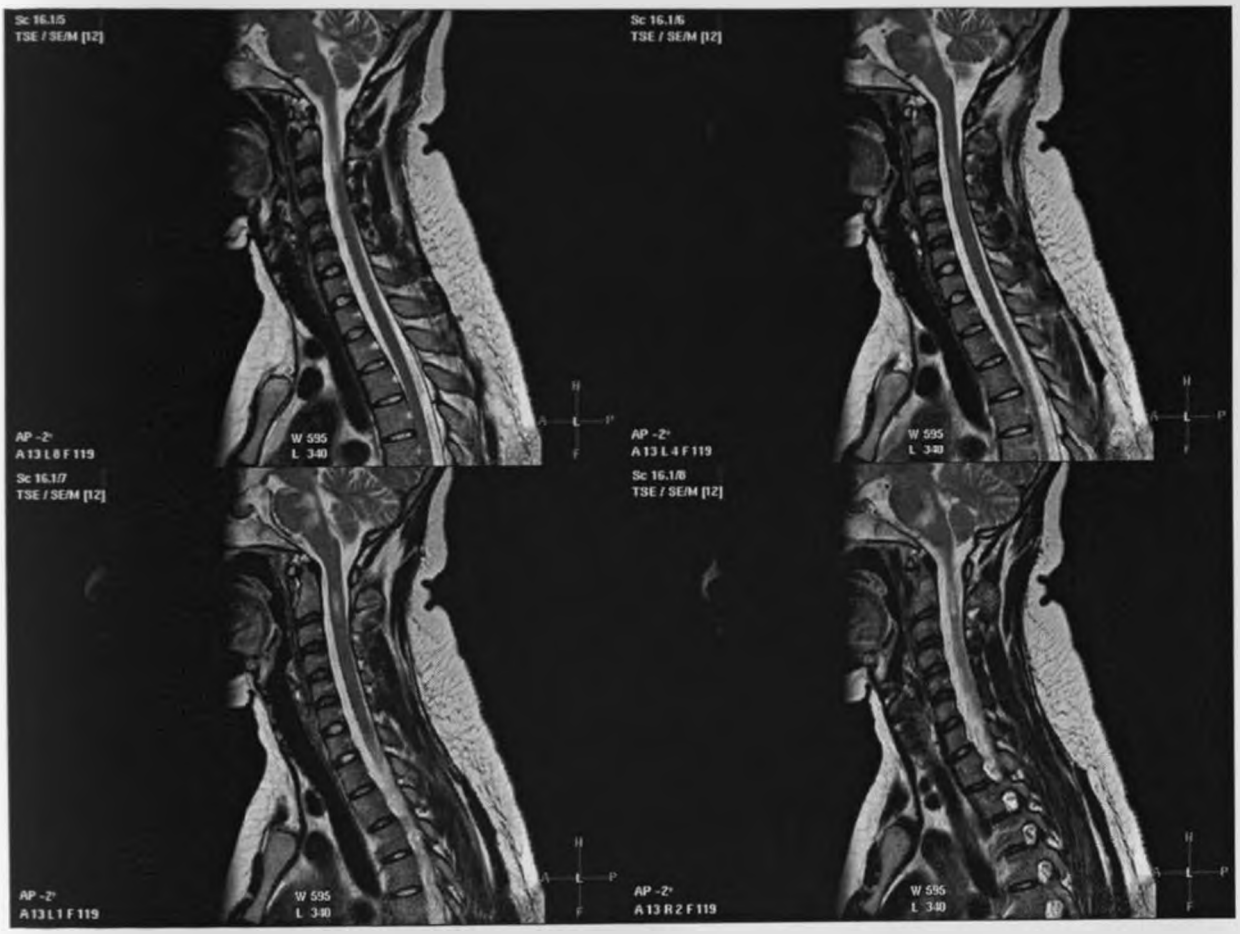
Axial T2WI shows periventricular white matter hyperintensities.



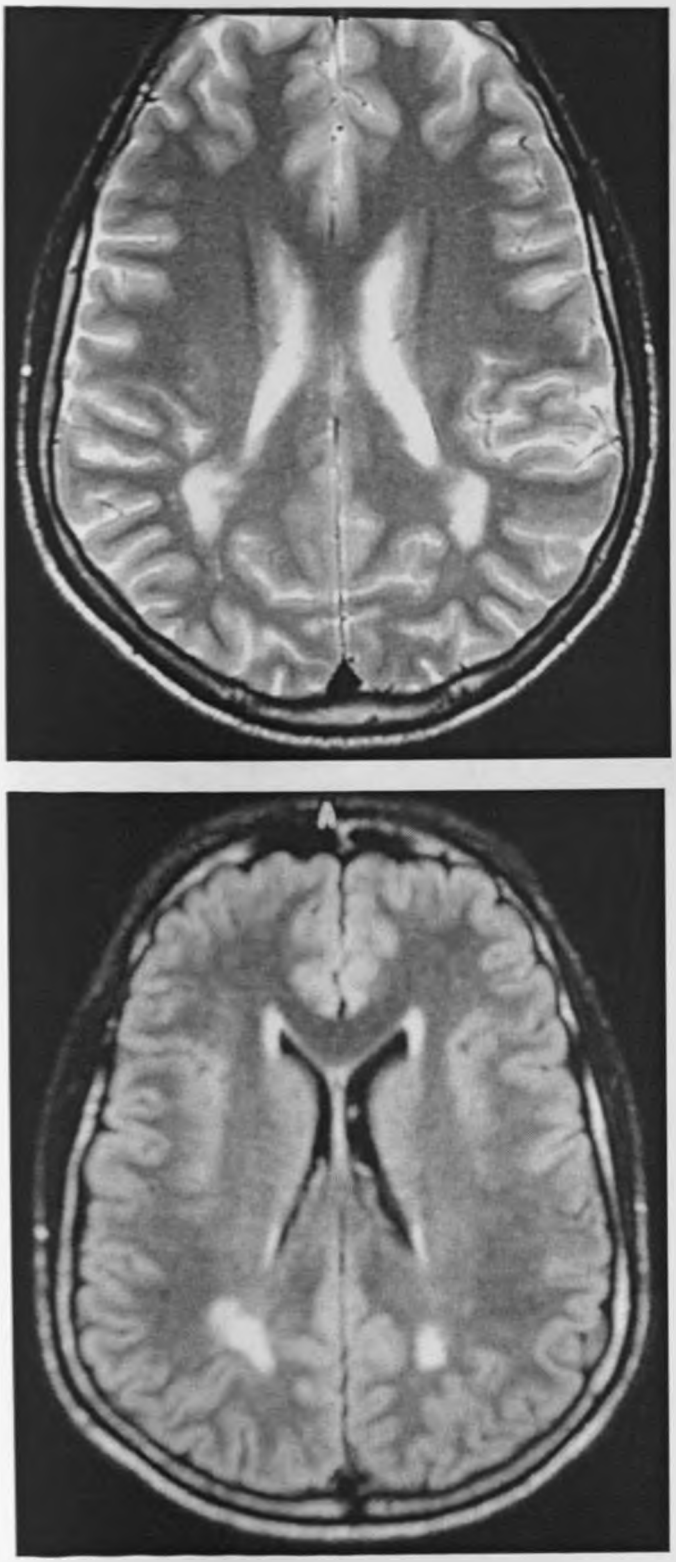
Axial FLAIR images of the same patient showing white matter hyperintensities.



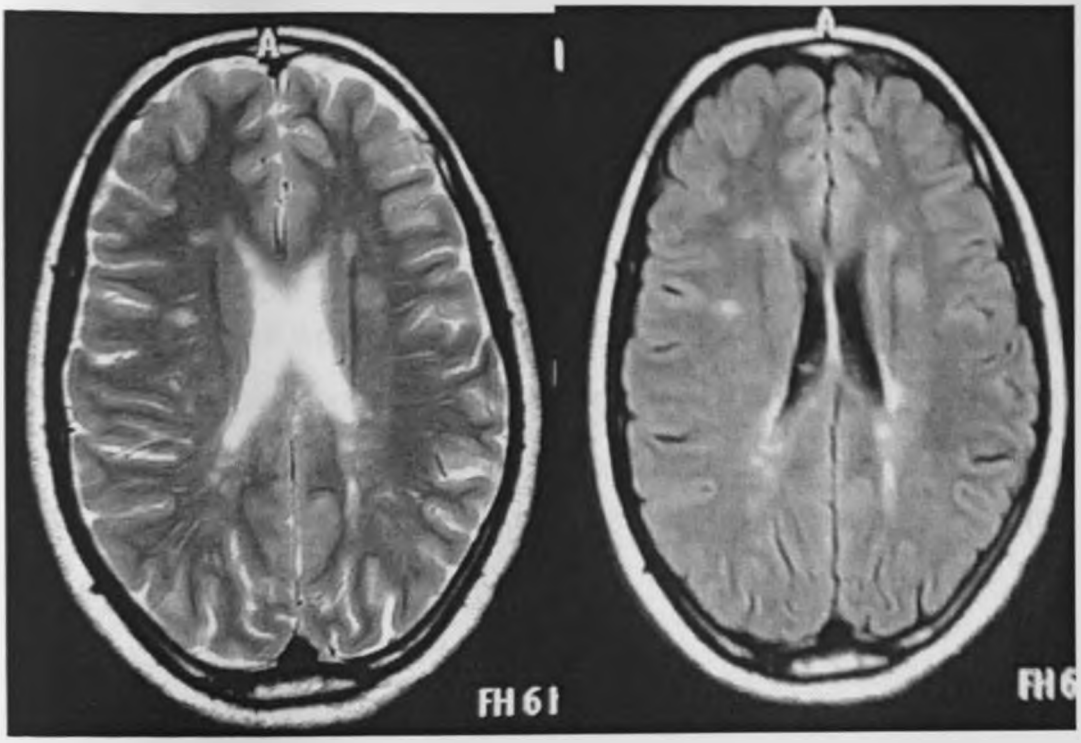
No contrast enhancement post I.V gadolinium.

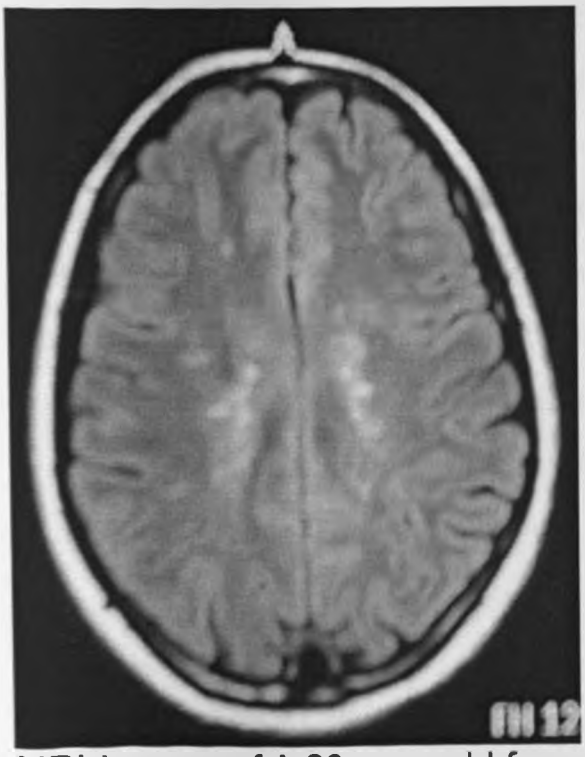


The same patient saggital T2WI showing hyperintensities extending to involve the spinal cord.



Axial T2WI and FLAIR images of 5year old boy,shows a peritrigonal whitematter hyperintensities.





MRI Images of A 28years old female who presented with lower limb weakness,white matter hyperintensities are suggestive of multiple sclerosis.

RESULTS

Age and Sex

The mean age of the patients was 44.9 (SD1.4) years with the minimum age being 0.25 years while the oldest patient was 76 years.

The main age of male patients was 50.7years while that of female was at 40.2 years. There was a significant difference in the mean age between male and female patients with the women being older than male (P-value=0.002), showing that females were significantly younger than males.

Most patients were female at 75(55.01%) while males were at 61(44.9%). The sex ratio being female: male 1.2:1

Clinical presentation of the study population

Weakness of the limbs was the outstanding clinical presentation at 53(39.0) among the study population. This was followed by a seizure which was seen in 23(16.9%).

The speech disturbance contributed only 2.9%.

Growth retardation was exclusively found in those below 10 years contributing 2.2% of the clinical presentation.

There was a significant association between sensory symptoms, visual symptoms and seizures with the sex of the study participants with p-values of 0.003,0.008 and 0.003 respectively.

MRI Findings:

Cross tabulation of signal intensities were reviewed, 126 (92.6%) and 135 (99.3%) of the study participants exhibited high signal intensities for both T2 W2 and FLAIR sequences respectively.

Of those with high signal intensity on T2W2 71(56.3%) were females and 55(43.7%) were males. On FLAIR sequences high signal was found in 74(56.5%) in females and 61(45.2%) males.Extreme age groups i.e. <10years and above 70 years demonstrated fewer cases of high signal intensity on T2W2 and FLAIR sequences.

There were 9 cases of patients in the age group (20-31) who showed contrast enhancement.

The mean age for the patients who sowed contrast enhancement was 45.9 the p-value was 0.063 which was not significant.

Location/distribution of white matter disease.

90 patients were found to have lesions in the periventricular white matter region, which constituted 66% of the study sample.

The second commonest location in this study was the region of the centrum semiovale. 60 patients (44.1%) were found to have a lesion at this site.

This study also, found that 15.4% of the study participants had a lesion in the infratentorial region. Only 2 patients (1.5%) had lesions in the temporal lobes.

There was no sex predilection for the commonest site. The study found 1:1sex presentation.

DISCUSSION

The objectives of this study were to determine the social demographic characteristics, clinical presentations, MRI findings and distribution of white matter diseases of the study population.

Age and sex

Previous studies suggest that age of onset for demyelinating disease is between 2nd and 4th decades, while that for dysmyelinating disease present early in childhood[12,20].

This study found that, the commonest age group is 30 – 39 years.

8 patients less than 10 years of age were found to have white matter lesions. Similar results were found by Valk-J-et al[49].

The study also, revealed that, there is slight female preponderance among the study population with sex ratio of M: F=1: 1.2.Some specific studies suggest definate female preponderance is seen in multiple sclerosis.

Two patients among the study units, who had undergone monoclonal antibody test (a specific test for multiple sclerosis) and found positive were both females.

Clinical presentation

The study established that, commonest clinical presentation in white matter diseases is weakness of the limbs (39%) followed by seizures(16.9%) visual symptoms and urinary incontinence were found in 21(15.4%) and 5(3.7%) respectively.

However, Prof. Lakhar working in India found that common clinical presentation was motor symptoms (23-31%) and urinary retention (23.3%).

These differences can be attributed by the large sample size recruited by Prof. Lakhar [19]

Other literatures suggest more than 30% of the patients with white matter diseases have weakness of the lower limbs while bladder dysfunction may be found in 90% of the patients[19].

MRI findings

The literature document that white matter lesions are of high signal intensity on proton density, T2WI and FLAIR sequences [11, 12, 14, 22, 35]

Similar results were obtained in this study whereby 126(92.6%) and 135(99.3%) of the cases had hyperintense signal on T2W1 and FLAIR sequences.

13 patients showed enhancement post intravenous gadolinium. Some authors propose that; enhancement typically reflects active disease in multiple sclerosis. [14]

Specific disease for example ADEM, PRESS Encephalitis, may also show enhancement. [37].While disease entities such as deep white matter ischaemia and HIV encephalitis does not show contrast enhancement [33, 35]

Location/distribution

Different authors indicate that the common sites for white matter lesions are in the periventricular and centrum semi ovale [11, 22, 36, 42]

These correlate with findings in this study as 90 patients (66.2%) and 60 patients (44.1%) had white matter lesions in the periventricular and centrum semiovale sites, respectively.

Specific disease entities have been reported to have a predilection for certain particular location. For example, Adrenoleukodystrophy has predilection to

peritrigonal white matter (area adjacent to atrial of lateral ventricle and splenium) [12].

In our study one patient who was a 3 years old male had hyperintense lesions in the peritrigonal region on both T2W2 and FLAIR, was diagnosed to have adrenoleukodystrophy, this was later confirmed by a senior neuroradiologist.

CONCLUSIONS

1. White matter lesions are common in our local set-up.
2. Lower limb weakness and seizures are the commonest clinical manifestation of white matter diseases.
3. MRI of the brain especially with T2W2 and FLAIR sequences plays a pivotal role toward diagnosis of white matter lesions.
4. Periventricular and centrum semiovale are the important sites to look for white matter disease.

RECOMMENDATIONS

1. Studies to examine MRI characteristics for specific disease entities e.g. multiple sclerosis are recommended.
2. The same study with Radiological-histopathology correlation should be done to increase the validity of the results obtained.

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A: QUESTIONNAIRE (DATA COLLECTION FORM)

entification number …….. MRI Number……..
……..

……male ☐ female ☐

:ase of White matter disease

☐ b) NO ☐

presentation
/ symptoms ☐ b) Visual symptoms ☐

ess of limbs ☐ d) seizures ☐

nerve palsy ☐ f) growth retardation ☐

; ☐

esults
ı) T1WI with an abnormal increased intensity ☐

ɒ) T1WI with an abnormal decreased intensity ☐

c) T1WI+C-with contrast enhancement ☐

d) T1WI+C with no contrast enhancement ☐

e) T2WI with an abnormal increased intensit ☐

f) T2WI with an abnormal decreased intensit ☐

g) FLAIR with an abnormal increased intens ☐

h) FLAIR with an abnormal decreased intens ☐

e) above is YES, location of T2 hyper intensity

a) Periventricular ☐ b) Calloseptal ☐

c) Corpus callosum ☐ d) centrum semiovale ☐

e)subcortical u fiber ☐ f)basal ganglia ☐

g) Infratentorial ☐ h) Others… ☐

APPENDIX B: PATIENT CONSENT FORM

I am Dr.Mechris Mango. A postgraduate student at the department of Diagnostic imaging and radiation medicine University of Nairobi. As part of my postgraduate studies, am required to do a research project.

My project is based on the MRI findings in white matter diseases. With your permission, I would like to use the results of the procedure done on you and relevant clinical details for my study.

Your rights will be respected and confidentiality maintained at all times.
No names will be mentioned in the study report except the serial numbers.

Participation in this study is purely voluntary and you can withdraw from the study at any point in time if you wish so, without jeopardizing your right to medical care.
You are free to ask any question pertaining to this study.

Thanks for your cooperation.

I..... have been adequately explained about the study and I voluntarily consent to participate in the study.

Signature.....

Date.....

Serial number.....

APPENDIX C: PATIENT CONSENT FORM-SWAHILI VERSION

KIBALI CHA KUSHIRIKI KATIKA UTAFITI.

Jina langu ni Daktari Mechris Mango, ni mwanafunzi katika chuo cha udaktari, Chuo Kikuu cha Nairobi. Ninafanya utafiti kuhusu matokeo ya kipimo cha MRI ya kichwa katika magonjwa ya maada nyeupe ya ubongo na ningependa kukuchagua kama mshiriki wa utafiti huu.

Haki zako zitalindwa,habari utakayotoa au ile itakayopatikana kukuhusu, itakuwa siri wakati wote na itatumika katika utafiti huu tu.

Jina lako halitatumika, bali ile nambari ya matibabu tu,ndiyo itakayotumika.

Ni muhimu kuelewa ya kwamba ushiriki ni wakujitolea,sio lazima kushiriki katika huu utafiti, na pia waweza kubadili nia yako wakati wowote kuhusu kuendelea kushiriki,bila ya kuathiri huduma zako za kiafya.

Asante sana kwa ushirikiano wako.

Mimi .....nimeelezewa kikamilifu kuhusu utafiti huu na nakubali kushiriki.

Sahihi.....

Tarehe.....

Nambari.....