"ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

BY

REG NO: BS0120009

Dissertation

Submitted to the

KLE Academy of Higher Education and Research, Belagavi, Karnataka

In partial fulfillment

of the requirements for the degree of

M.D.

IN

RADIO-DIAGNOSIS

JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI -590010. KARNATAKA

JUNE/ JULY 2023

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,
BELAGAVI, KARNATAKA

Endorsement by the HOD/Principal/ Head of the Institution

This is to certify that the dissertation entitled **"ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** is a bonafide research work done by **REG NO. BS0120009.**

Dr. PRADEEP H PATIL
M.D. RADIO-DIAGNOSIS
Professor and Head,
Department of Radio Diagnosis,
J. N. Medical College,
Nehru Nagar, Belagavi – 590010
Date: 16/01/2023
Place: Belagavi

Dr. N.S. MAHANTASHETTI
M. D. PEDIATRICS
Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 590010
Date :
Place : Belagavi

ii

UNDERTAKING

I, **Reg No. BS0120009,** hereby declare that the information and the data mentioned in my dissertation entitled " entitled **"ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** belongs to me and is original. I am aware of the definition of plagiarism as detailed below-

- An act or instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized use or imitation.
- The deliberate or reckless representation of another's words, thoughts, or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the dissertation prepared by me is original one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the University.

Date-

Place: Belagavi

Reg No: BS0120009

ETHICAL CLEARANCE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed to be University)
Accredited 'A' Grade by NAAC (2nd Cycle) Ele...ical Category 'A' by MHRD (Govt.)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website http://www.jnmc.edu
E-Mail domc@jnmc.edu
Phone (+91-(0)831 Office 2472550
Principal 2471701
Fax No. +91 (0)831 - 2470759

Ref: MDC/DOME/ 142

Date: 25/01/2021

To

Reg No. BS0120009
PG student in Radio-diagnosis,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

117

ABBREVIATIONS

ADD	-	Acquired demyelinating disorder
CNS	-	Central nervous system
ADEM	-	Acute disseminated encephalomyelitis
NMOSD	-	Neuromyelitis optica spectrum disorder
MS	-	Multiple sclerosis
CIS	-	Clinically isolated syndrome
MOG	-	Myelin oligodendrocyte glycoprotein
MOGAD	-	Myelin oligodendrocyte glycoprotein antibody associated disease
MRI	-	Magnetic resonance imaging
ON	-	Optic neuritis
TM	-	Transverse myelitis
NMO	-	Neuromyelitis optica
NMOSD	-	Neuromyelitis optica spectrum disorder
POMS	-	Pediatric onset multiple sclerosis
DD-NOS	-	Demyelinating disease not otherwise specified
CSF	-	Cerebrospinal fluid
OCBs	-	Oligoclonal bands
IgG	-	Immunoglobulin G index
GM	-	Grey Matter
FLAIR	-	Fluid attenuated inversion recovery
WM	-	White matter
T1W	-	T1-weighted image
T2W	-	T2-weighted image
IV	-	Intra venous
AQP4	-	Aquaporin-4
DWI	-	Diffusion-Weighted Imaging

ABSTRACT

BACKGROUND:

The acquired demyelinating disorder (ADD) is characterized by the destruction or damage of normally myelinated structures of the central nervous system (CNS) which are immunologically mediated. Acquired demyelinating disorders encountered during childhood include acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), Clinically isolated syndrome (CIS) and the more recently discovered anti-myelin oligodendrocyte glycoprotein (anti-MOG)–associated encephalomyelitis.

Radiologists play a major role in the diagnosis and differentiation these diseases. Recent discovery of some key MRI imaging features which can be explained by the pathophysiological basis of these different entities. It helps in identifying magnetic resonance imaging predictors of a particular demyelinating diagnosis in the pediatric population which can have broad implications on treatment of the disease.

The aim of this study is to determine the clinical profile and imaging features of the pediatric acquired demyelinating disorders of the central nervous system.

MATERIALS AND METHODS:

One year hospital based cross sectional study was done in Department of Radio-diagnosis at the KLE'S Dr Prabhakar Kore Hospital & MRC, Belagavi.

30 pediatric patients clinically suspected of having demyelination disease presented to the department of radiodiagnosis were included in the study. The patients were subjected to MRI brain and spine scan.

The study population were analysed based on age, gender, clinical history, abnormalities on MRI brain, optic nerve & spine imaging.

OBSERVATION AND CONCLUSION:

In our study, the majority (43.33%) were aged between 7 to 12 years with mild female predominance. The most common diagnosis was ADEM (53.33%) followed by equal distribution of MOGAD & NMOSD.

ADEM cases showed lesions in bilateral cerebral hemispheres in an asymmetric distribution with predominant supratentorial brain involvement and majority of the cases showed large lesions.

In MOGAD cases, brain parenchyma showed predominantly large lesions in supratentorial distribution. Spinal cord lesion was predominantly LETM with statistically significant involvement of the lumbar spinal cord.

In NMOSD cases, statistically significant association was seen with area postrema syndrome and periaqueductal grey matter & area postrema lesions on MRI brain. Spinal cord lesions in NMOSD was predominantly LETM with involvement of the cervical and thoracic spinal cord involvement.

TABLE OF CONTENTS

SL.NO	CONTENTS	PAGE NO.
1.	INTRODUCTION	1-2
2.	AIM & OBJECTIVES	3
3.	REVIEW OF LITERATURE	4-29
4.	MATERIALS AND METHODS	30-32
5.	RESULTS	33-54
6.	DISCUSSION	55-57
7.	CONCLUSION	58
8.	SUMMARY	59-60
9.	BIBLIOGRAPHY	61-65
10.	ANNEXURES	
	ANNEXURE I – INFORMED CONSENT FORM	66-75
	ANNEXURE II - PROFORMA	76-80
	ANNEXURE-III – IMAGES	81-84
	ANNEXURE IV – MASTER CHART	85-87

LIST OF TABLES

TABLE NO.	DESCRIPTION	PAGE NO.
1.	The 2017 McDonald criteria for diagnosis of multiple sclerosis in patients with an attack at onset	22
2.	Disease-Modifying drugs used in pediatric Multiple Sclerosis	26
3.	Summary of spinal MR imaging features of pediatric demyelinating disorders	26
4.	Descriptive analysis of diagnosis in the population	33
5.	Comparative analysis of diagnosis groups with age	34
6.	Comparison of diagnosis groups with gender	36
7.	Comparison of diagnosis groups with Clinical symptoms	37
8.	Comparison of diagnosis groups with MRI Brain anatomical location	39
9.	Comparison of diagnosis groups with mean number of positive findings in supra tentorial and infra tentorial brain parenchyma	42
10.	Comparison of diagnosis groups with size of lesion	43

11.	comparison of diagnosis group with optic nerve involvement	45
12.	Comparison of diagnosis groups with Optic nerve laterality	46
13.	Comparison of diagnosis groups with Optic nerve segment involved	47
14.	Comparison of diagnosis groups with spinal cord involvement	49
15.	Comparison of diagnosis groups with Type of spinal cord involvement	50
16.	Comparison of diagnosis groups with Spinal cord segment involved	52
17.	Comparison of diagnosis groups with status of Follow up MRI	53

LIST OF FIGURES

TABLE NO.	DESCRIPTION	PAGE NO.
1.	Typical lesions for ADEM	10
2.	MR imaging findings typically seen in anti-MOG associated disease	13
3.	MR imaging findings typically seen in neuromyelitis optica spectrum disorder	18
4.	Typical multiple sclerosis lesions	24
5.	Typical multiple sclerosis lesions in the spine	25
6.	Pie diagram for diagnosis wise distribution	33
7.	bar chart for comparison of diagnosis with age	35
8.	Comparison of diagnosis groups with gender	36
9.	Comparison of diagnosis groups with Clinical symptoms	38
10.	Comparison of diagnosis groups with MRI Brain anatomical location	41
11.	Comparison of diagnosis groups with mean number of positive findings in supra tentorial and infra tentorial brain parenchyma	43

12.	Comparison of diagnosis groups with size of lesion	44
13.	comparison of diagnosis group with optic nerve involvement	45
14.	Comparison of diagnosis groups with Optic nerve laterality	47
15.	Comparison of diagnosis groups with Optic nerve segment involved	48
16.	Comparison of diagnosis groups with spinal cord involvement	49
17.	Comparison of diagnosis groups with Type of spinal cord involvement	51
18.	Comparison of diagnosis groups with Spinal cord segment involved	53
19.	Comparison of diagnosis groups with status of Follow up MRI	54

INTRODUCTION

The acquired demyelinating disorder (ADD) is characterized by the destruction or damage of normally myelinated structures of the central nervous system (CNS) which are immunologically mediated. They are characterized by axonal damage and dysrupture of the myelin sheath which occurs secondary to the neuroinflammatory process.[1]

Acquired demyelinating disorders encountered during childhood include acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), Clinically isolated syndrome (CIS) and the more recently discovered anti-myelin oligodendrocyte glycoprotein (anti-MOG)–associated encephalomyelitis.[2] Demyelinating disorders are challenging to differentiate from each other and they can also mimic anti-MOG encephalitis, because all these disorders can present with nonspecific MRI (magnetic resonance imaging) findings and with overlapping clinical symptoms. Detailed clinical history and clinical examination helps in improved diagnostic accuracy. The discovery of antibody-based biomarkers have led to changes in defining criteria of these disorders[2].

Radiologists play a major role in the diagnosis and differentiation these diseases. There was recent discovery of some key MRI imaging features which can be explained by the pathophysiological basis of these different entities. It helps in identifying magnetic resonance imaging predictors of a particular demyelinating diagnosis in the paediatric population which can have broad implications on treatment of the disease. Radiologists can also use history and biomarkers to improve the interpretation of the MRI imaging. This composite approach improved the understanding, diagnosis, prognosis and treatment of these disease entities.[2]

The widespread access to MRI, along with refinement of neuroimaging techniques and advanced knowledge of the spectrum of these diseases lead to an increase in the number of diagnosed and reported cases of ADD. Even then, the ADD still represents a group of rare diseases of the childhood [(1)].

AIMS & OBJECTIVES

- To determine the clinical profile and imaging features of the pediatric acquired demyelinating disorders of the central nervous system

- To differentiate the imaging features of different subtypes of acute demyelinating disorders

REVIEW OF LITERATURE

Acquired demyelinating disorders (ADD) can be defined as disorders caused by inflammatory demyelination of the central nervous system (CNS) resulting in single (mono-focal) or multiple (poly-focal) lesions. [3]

Monophasic ADD:

- Clinically isolated syndrome (CIS): mono-focal or poly-focal deficits without encephalopathy, which includes;
  - Optic neuritis (ON)
  - Transverse myelitis (TM)
  - Other clinically mono-focal or poly-focal ADD
- Acute disseminated encephalomyelitis (ADEM): polyfocal deficits with encephalopathy

Recurrent ADD:

- Neuromyelitis optica (NMO)
- Myelin oligodendrocyte glycoprotein (MOG) antibody associated disease
- Pediatric onset multiple sclerosis (POMS)
- Recurrent demyelinating disease not otherwise specified (DD-NOS) [3]

Pediatric patient presenting with new onset subacute focal neurologic deficits occurring after a known infection, and in the absence of trauma, metabolic derangements, or known underlying structural abnormalities, should be suspected of having acquired CNS demyelination. Suggested workup for these children includes

detailed history and physical examination, the cerebrospinal fluid (CSF) analysis, serum antibody analysis and neuroimaging.[3]

Clinical features[4]

Usually the presentation will be subacute, with symptoms appearing over 24 to 48 hours. Common symptoms of acute demyelination in children include:

- Fever
- Seizure
- Encephalopathy which is indicated by behavioral change (confusion or excessive irritability) or alteration in consciousness (lethargy or coma)
- Visual disturbance like blurred vision or loss of vision
- Limb weakness like paraparesis, hemiparesis, quadriparesis or weakness of bilateral upper limbs
- Cranial nerve involvement
- Extrapyramidal signs like akathisia, dystonia or dyskinesia
- Cerebellar symptoms like ataxia, uncoordinated movements, imbalance, speech problems(dysarthria), visual problems (nystagmus) and vertigo
- Sensory disturbances
- Signs and symptoms of meningism like sudden high fever, stiff neck, severe headache, nausea or vomiting or confusion
- Bowel and bladder disturbances

Laboratory findings[3]

Laboratory features, suggestive of acquired demyelination, include:

- Mild to moderate CSF pleocytosis
- Elevated CSF protein
- Presence of oligoclonal bands (OCBs)
- Increased immunoglobulin G index (IgG)
- Presence of antibody-based biomarkers like anti-MOG antibody or anti-AQP4 antibody

Neuroimaging features[4]

Magnetic resonance imaging (MRI) of the brain, orbits and spinal cord may show:

- Multifocal white and grey matter abnormalities of the supra tentorial and infratentorial brain parenchyma
- Spinal cord lesions
- Optic nerve thickening or hyperintensity on T2-weighted imaging
- Post contrast enhancement of lesions after the administration of gadolinium

Management

Management of acute demyelinating symptom can be done with symptomatic treatment and in the cases of chronic or polyphasic disease, disease-modifying treatment can be started. The management team should include a pediatric neurologist, nurse, counsellor and a neuropsychologist to provide both medical and supportive services.[5]

Multiple sclerosis (MS), acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), and the more recently identified anti-myelin oligodendrocyte glycoprotein (anti-MOG)-associated encephalomyelitis are among the demyelinating illnesses that can affect children. Both in terms of clinical presentation and imaging, pediatric demyelinating diseases can manifest in startling ways. Positive CSF values may not be a good predictor of a demyelinating condition as that of a positive MR imaging result. Despite the fact that many of the radiologic characteristics of these diseases are similar, certain new developments may enable radiologists to distinguish between various disease processes. The criteria for various conditions have changed as a result of advancements, such as the identification of antibody-based biomarkers. As a result, many disorders now have better knowledge, diagnosis, prognosis, and therapy.(2)

ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)

ADEM represents a monophasic acute inflammatory and demyelinating event of brain parenchyma and spinal cord with encephalopathy which will usually follow a recent vaccination or viral infection.[6]

Pathogenesis

Like MS, the exact etiology of the ADEM is uncertain. It causes immune-mediated CNS demyelination and is linked to an antigenic challenge in certain febrile illnesses or postvaccination. According to the current theory, myelin components react with antigens of viral origin and, as a result trigger a secondary immune-mediated reaction that, in turn causes demyelination in a perivenular distribution.[7]

Clinical Features

ADEM is usually a monophasic event which can happen at any age group. But the incidence is more common in pediatric population especially children younger than 10 years old. Slight male predominance is also noted (1.3:1). [8]

In ADEM the symptoms are usually generalized than focal neurological deficits which includes:

- Fever
- Headache
- Reduced level of consciousness which ranges from lethargy to coma
- Seizure
- Multifocal neurologic symptoms such as cranial nerve involvement, hemiparesis, paraparesis or quadriparesis and other movement disorders
- Behavioral changes [9]

Classification

International Pediatric MS Study Group A proposed a classification system for defining monophasic ADEM, recurrent ADEM and multiphasic ADEM.[8]

- Monophasic ADEM: No evidence of development of new lesions or demyelinating event.
- Recurrent ADEM: New demyelinating event developing more than 3 months after the initial event and more than 4 weeks after steroid treatment completion which will shows demyelination in the same areas on MR imaging.

- Multiphasic ADEM: New demyelinating event developing more than 3 months after the initial event and more than 4 weeks after steroid treatment completion. The new lesions involves newer areas of the CNS on neurologic examination and MR imaging.

Diagnosis

Laboratory Diagnosis

Cerebrospinal Fluid analysis: may show pleocytosis and an increase in myelin basic protein.

Neuroimaging

BRAIN

- Bilateral WM involvement in an asymmetric distribution (Fig 1A).
- Multiple oval shaped lesions with indistinct margins and which are usually >2 cm.
- Lesions are distributed along central white matter, juxtacortical white matter (Fig 1B), brain stem, periventricular and cerebellar regions.
- Symmetrical involvement of the GM like basal ganglia and thalami (Fig 1C) can be seen.
- Active lesions may show ring, punctate or arc like (open ring sign) enhancement.[10-11]

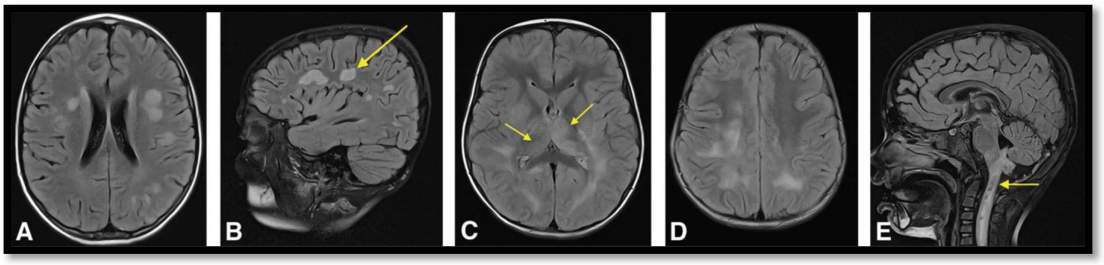


Figure 1: Typical lesions for ADEM.[2]

Figure 1 A, Axial FLAIR image showing moderate size oval hyperintense lesion in bilateral (left> right) cerebral hemispheric WM. B, Sagittal FLAIR image showing multiple areas of FLAIR hyperintensity in the cerebral hemispheric WM (arrow). C, Axial FLAIR image showing near-symmetric FLAIR hyperintensity in the bilateral thalami (arrow) and posterior periventricular WM. D, Axial FLAIR image showing hyperintensity in the posterior subcortical and deep WM of the cerebral hemispheres. E, Sagittal FLAIR image showing confluent FLAIR hyperintensity in the lower brain stem extending into the upper cervical spine (arrow).

SPINAL CORD

Variable involvement of the spinal cord can be seen. Spinal cord can be involved in 10%–30% of cases. Longitudinally extensive transverse myelitis, predominantly affecting the thoracic spinal cord with involvement of grey or white matter was commonly observed.[2]

Management

A 5-day course of intravenous steroids can be given in acute presentation and plasma exchange or IV immunoglobulin (IVIg) is considered in case of refractory disease.[12]

ANTI-MYELIN OLIGODENDROCYTE (MOG)–ASSOCIATED DISEASE (MOGAD)

MOGAD is a distinct clinical entity which represents a group of acquired demyelinating disorders by the presence of IgG antibodies to the myelin oligodendrocyte glycoprotein (MOG). Clinical and neuroimaging features of MOGAD overlaps with acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorders (NMOSD) and the multiple sclerosis (MS). [13]

Pathology

Myelin oligodendrocyte glycoprotein (MOG) is a protein situated on the outermost surface of myelin sheaths and oligodendrocyte membranes. MOG antibody is thought to have a role in cell adhesions and it can be a cellular receptor. Some studies have suggested that, MOG can be a marker of myelin maturation.[2]

Clinical features

It can follow a monophasic or relapsing course of demyelinating event, with absence of typical criteria for multiple sclerosis or any other known demyelinating disorder and it occurs with the presence of serum MOG antibodies. The most common presenting complaints are: [14]

- Optic neuritis (ON)
- Transverse myelitis
- Acute disseminated encephalomyelitis
- ADEM-like presentation

DIAGNOSIS

LABORATORY DIAGNOSIS

- Serum- MOG antibody immunoglobulin G (IgG) is tested in serum using indirect fluorescence test or fluorescence-activated cell sorting
- Cerebrospinal fluid-CSF pleocytosis[14]

NEUROMINAGING

Certain imaging features are now being increasingly recognized as typical of MOGAD spectrum.

BRAIN

Parenchymal lesions tend to be less in number but larger in size compared to NMOSD. Lesions typically involves supratentorial WM and more commonly involves nearby grey matter (GM) and shows ill-defined borders relative to the NMOSD. Compared with NMOSD cases, MOGAD cases shows thalamic and pontine lesions more commonly with bilateral thalamic lesions (Fig.2A) being frequent [15]

OPTIC NERVES

Involvement of the optic nerves can be seen in majority of the MOGAD patients, usually at the time of its presentation. Typically, bilateral optic nerve involvement is seen with a predilection to the anterior segment (Fig.2C). Optic nerves can be thickened and edematous. Periorbital enhancement or involvement of the posterior parts of optic nerve or optic chiasma is uncommon.[16]

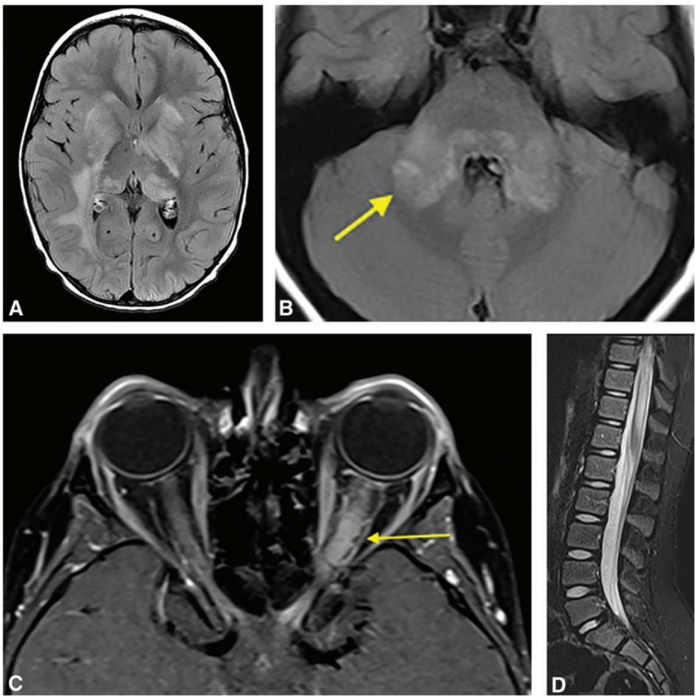


Figure 2: MR imaging findings typically seen in anti-MOG associated disease

Figure 2 A, Axial FLAIR image showing bilateral thalamic signal abnormality. B, Axial FLAIR image of the posterior fossa showing symmetric expansion and confluent FLAIR hyperintense lesions involving the bilateral brachium pontis/middle cerebellar peduncle (arrow) and the dorsal pons. C, Contrast-enhanced axial T1-weighted image with fat saturation showing enhancement and enlargement of the intraorbital segment of the left optic nerve (arrow). D, Sagittal T2-weighted image showing abnormal T2 hyperintensity and expansion of the distal cord and conus.

SPINAL CORD

Spinal cord involvement is usually central affecting central grey matter and also white matter. Based on length of the spinal cord involved, it can be longitudinally extensive spinal cord lesions, if the lesion involves more than 3 vertebral body height or focal spinal cord lesions, if short segment is only involved.

Both these patterns can be seen simultaneously. The involvement of central grey matter results in the appearance of "H" sign on axial images and linear thin T2 hyperintense signals are seen on sagittal view.[16] The distribution of cord lesions is more likely to be seen in the lower cord or conus as compared to the cervicothoracic spinal cord (Fig.2D).

Management

The management of MOGAD is divided into the treatment of acute attacks & treatment for attack prevention.

Acute Attacks: Acute attacks will respond to methylprednisolone or other high-dose IV steroids, usually 3- to 7-day course is recommended.

Preventive therapy: In case of relapsing diseases of MOGAD immunomodulatory drugs are given. The most commonly used drugs are rituximab and mycophenolate mofetil.[12]

NEUROMYELITIS OPTICA SPECTRUM DISORDERS (NMOSD):

It is an immune-mediated demyelinating CNS condition, formerly known as Devic's disease. The blood biomarker for the immunoglobulin G (IgG) autoantibody, which distinguishes NMO from MS, was found in 2004. Following the demonstration that this marker attaches to the aquaporin-4 (AQP4) water channel in a specific manner, this demyelinating condition began to be called as AQP4 antibody associated demyelination.[17]

Pathogenesis

AQP4-seropositive patients will demonstrate pathologic features which are distinct from that of MS. The immune related destruction is more focused on the astrocytes, along with secondary damages to the axons and myelin. Various immune mediated cells, including T cells, B cells, neutrophils and plasma cells can be found in NMOSD patients. Complement and antibody deposition is also found in lesions. [18–19]

Clinical Features

The most common presenting features include:

- Optic neuritis -unilateral or bilateral
- Transverse myelitis
- Brainstem/cerebellar syndromes
- Area postrema syndrome- nausea, vomiting and intractable hiccups
- AQP4-IgG–positive patients can have coexisting autoimmune disorders such as systemic lupus erythematosus or Sjogren syndrome[20]

Diagnosis

In 2015, new diagnostic criteria was created using nomenclature that defines the term NMOSD and stratifies patients by serologic testing in NMOSD with and without AQP4-IgG.

According to these criteria, six core clinical characteristics for diagnosis of NMOSD were identified, including ON, TM, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical

syndrome, and symptomatic cerebral syndrome. For diagnosis in AQP4-IgG positive NMOSD patients, only one core criterion is enough. For seronegative NMOSD patients, two core criteria are necessary for diagnosis occur as a consequence of one or more clinical events, and at least one of these two core criteria should be ON, TM with longitudinally extensive transverse myelitis (LETM), or area postrema syndrome.[21]

Laboratory Diagnosis

About 65% of pediatric NMOSD patients will show AQP4 antibody seropositivity; however AQP4 antibody may not be tested positive at the time of the first demyelinating event but it can become positive up to 4 years later.

CSF analysis typically shows pleocytosis with predominance of lymphocytes. Positive oligoclonal band testing and elevated IgG index can also be the associated features. [20]

Neuroimaging

MRI is the diagnostic modality of choice for the suspected cases of NMOSD and the orbits, brain and spinal cord imaging should be done.

BRAIN

Brain lesions usually mirror the distribution of aquaporin 4 water channels, which involves the periependymal regions abutting the ventricles:[21]

- Periventricular white matter (Fig. 3Gb)
- Periaqueductal grey matter

- Diencephalic lesions (Fig. 3Ga) surrounding the third ventricles and cerebral aqueduct and extend to involve the thalami, hypothalamus, and anterior border of the midbrain
- Dorsal pons (area postrema) (Fig. 3E&F), dorsal medulla and the solitary nucleus

Corpus callosum, deep white matter lesions (similar to that of MS) and corticospinal tract involvement can also be seen.

OPTIC NERVE

Targeted MRI imaging of the orbits, including T2 weighted sequences and fat-saturated T1 contrast sequence will demonstrate:

- T2 hyperintense and edematous optic nerves with or without contrast enhancement.
- Optic nerve is usually involved bilaterally with predilection to posterior optic nerve, which might extend into the chiasma. [22]

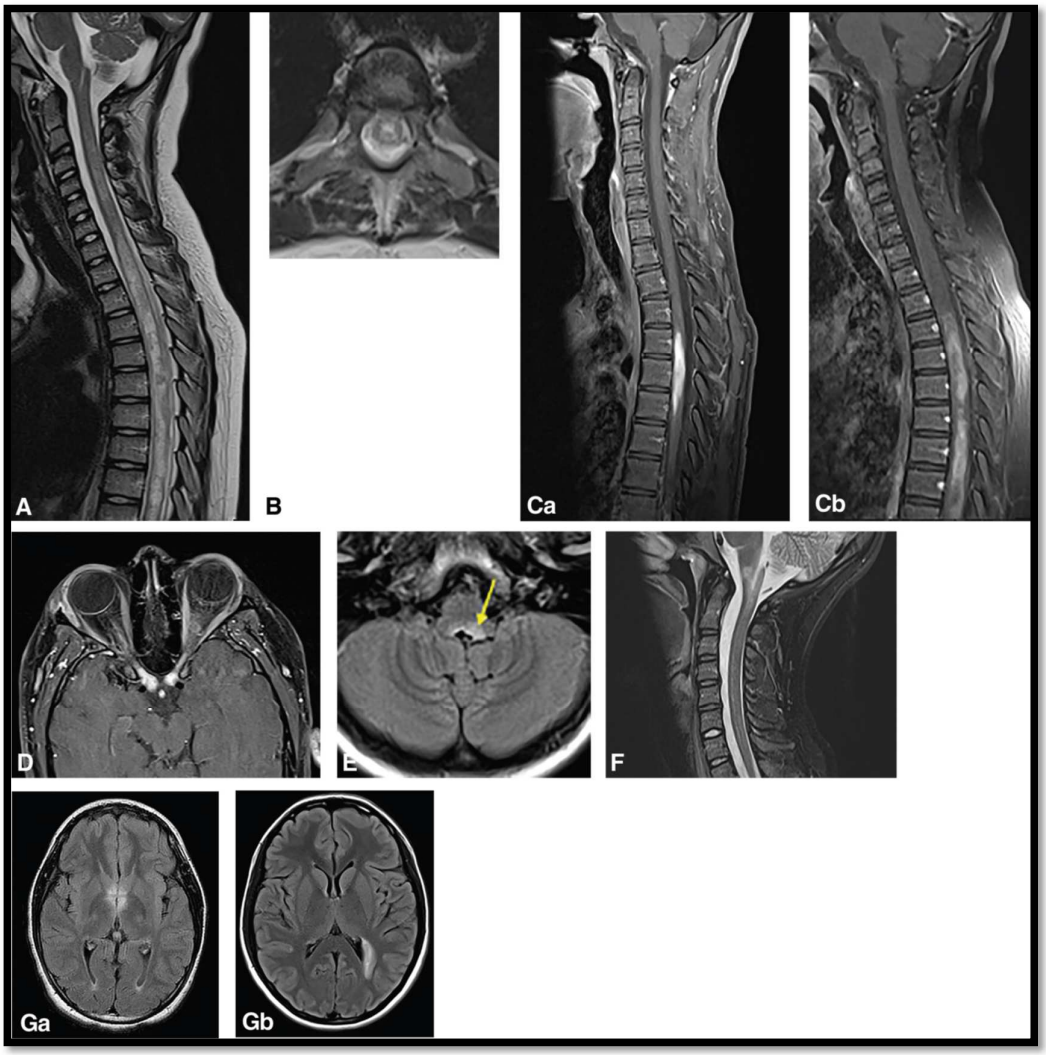


Figure 3: MR imaging findings typically seen in neuromyelitis optica spectrum disorder.[2]

Figure 3 A, Sagittal T2-weighted image of the spine showing expansion and abnormal T2 hyperintensity in the cervicothoracic cord. B, Axial T2-weighted image showing T2 hyperintensity involving the central gray matter with some cord expansion. C, Two contrast-enhanced sagittal T1-weighted images showing varying degree of enhancement in the cord. D, Axial postcontrast T1-weighted image showing enhancement of the bilateral pre-chiasmatic segments of the optic nerves. E, Axial FLAIR image showing focal enlargement and FLAIR hyperintensity in the dorsal left

lower brain stem (arrow) in area postrema. F, Sagittal T2- weighted image showing abnormal signal in the cervicomedullary region. Ga, Axial FLAIR images showing near-symmetric FLAIR hyperintensity in the diencephalon. Gb, Axial FLAIR showing confluent abnormal FLAIR increase signal along the periependymal regions surrounding the lateral ventricles.

SPINAL CORD

NMOSD can involve long segments of the spinal cord, which can be seen as T2 & FLAIR hyperintense signal involving more than three vertebral body heights (LETM lesions) (Fig. 3A).

Lesions usually involve more than 50% of the cross-sectional area of spinal cord with a central grey matter predominance. This reflects the localization of AQP4 protein channels along the ependymal lining in the central canal (Fig 3B).

There can be associated cord edema and varying patterns of enhancement on postcontrast study (Fig 3C). An upper cervical spinal cord lesion can also be seen to extend into the brain stem (Fig 3F).[22]

Management

Management of NMOSD consists of treatment of acute attacks and preventive treatment.

Acute attacks: IV methylprednisolone at 20 mg/kg to 30 mg/kg for 5 days. If the symptoms worsen or there is no evidence of any improvement, then immediately plasma exchange is started.

Preventive therapy: It reduces the risk of relapse of the disease and also associated disability. Disease-modifying drugs consists of mycophenolate mofetil, azathioprine and rituximab. [23-24]

MULTIPLE SCLEROSIS

MS is still not fully understood, despite decades of study and recent improvements in therapy. The most common way to define it as a CNS demyelinating illness with an immune-mediated origin.

Although the MS often appear in early adulthood, frequently between the ages of 20 and 40, around 5% of people have symptoms as children. MS that manifests before the age of 16 is known as paediatric MS, also known as pediatric onset MS (POMS), early-onset MS, or juvenile MS. There are distinct distinctions between POMS and adult-onset MS despite their similarities.[25]

Associations

The development of the illness is influenced by environmental variables as well as hereditary predisposition. Human leukocyte antigen (HLA) genes have been proven to enhance the likelihood of developing MS; HLA-DR15 in particular has the best correlation with early-onset MS.[25]

Pathology

The most prevalent pathologic pattern has been identified as perivenous lesions attenuated with T cells, myelin-laden macrophages, and complement activation. This appearance resembles lesions seen in anti-MOG sensitised

experimental animal models and is suggestive of an antibody-mediated mechanism.[26] However, the exact underlying immune-pathologic process remains unclear.

Clinical features[27]

Clinical presentation is highly variable depending upon varying plaque location, as well as over time. Examples of common clinical features include

- Brainstem and cranial nerve involvement: Optic Neuritis, Diplopia or Vertigo
- Cerebellum involvement: Ataxia and gait disturbance
- Cerebrum and spinal cord involvement:
    - Upper motor neuron signs
    - Limb sensory loss or paresthesias
    - Urinary incontinence
- Others: Fatigue, Depression or Cognitive decline

Diagnosis

The diagnosis of multiple sclerosis is made by a combination of clinical features and various other investigations. The McDonald diagnostic criteria comprises of clinical, laboratory and radiographic criteria for multiple sclerosis diagnosis. It was introduced in the year 2001 and then revised multiple times, most recently in the year 2017.[28]

Laboratory diagnosis

- Oligoclonal bands in CSF
- Immunoglobulin G in serum

Neuroimaging:

Multiple sclerosis can be diagnosed if any one of these five criteria is fulfilled.[28]

	Number of lesions with objective clinical evidence	Additional data needed for a diagnosis of multiple sclerosis
≥2 clinical attacks	≥2	None*
≥2 clinical attacks	1 (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location†)	None*
≥2 clinical attacks	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI‡
1 clinical attack	≥2	Dissemination in time demonstrated by an additional clinical attack or by MRI§ OR demonstration of CSF-specific oligoclonal bands¶
1 clinical attack	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI‡ AND Dissemination in time demonstrated by an additional clinical attack or by MRI§ OR demonstration of CSF-specific oligoclonal bands¶

Table 1 The 2017 McDonald criteria for diagnosis of multiple sclerosis in patients with an attack at onset[28]

- Dissemination in space

Dissemination in space requires more than one T2-hyperintense lesions (≥3 mm in long axis), that are specific of multiple sclerosis present in 2 or more of the 4 following locations:

1. Periventricular
2. Cortical or juxtacortical
3. Infratentorial
4. Spinal cord

- Dissemination in time

Dissemination in time is established in one of the 2 ways:

1. New appearance of a T2-hyperintense or enhancing lesion as compared to the previous MRI scan.
2. Presence of an enhancing lesion and a non-enhancing T2-hyperintense lesion simultaneously in any MRI scan.

BRAIN

MS lesions can be found anywhere in the brain parenchyma, but characteristic lesions of MS make the diagnosis more likely. Cortical grey matter, juxtacortical white matter and the periventricular white matter (Fig. 1A), are characteristic locations of MS. Juxtacortical lesions (Fig 1B) are at the interface of cortical grey matter (GM) and subcortical white matter (WM). This is a significant finding since it is one of the McDonald 2017 MRI criteria for dissemination in space. Other specific lesions that are seen in MS as areas of T2 & FLAIR hyperintensity are Dawson's fingers and corpus callosum lesions. Dawson's fingers are ovoid or elliptical lesions arranged like pointing fingers away from the walls of the lateral ventricle (Fig.1C). On T1-weighted sequences, the lesions of MS will have the typical "black hole" (Fig.1E) appearance.[29]

OPTIC NERVES

Optic neuritis (ON) in MS patients are typically short segment lesions predominantly involving unilateral optic nerve (Fig.1G).

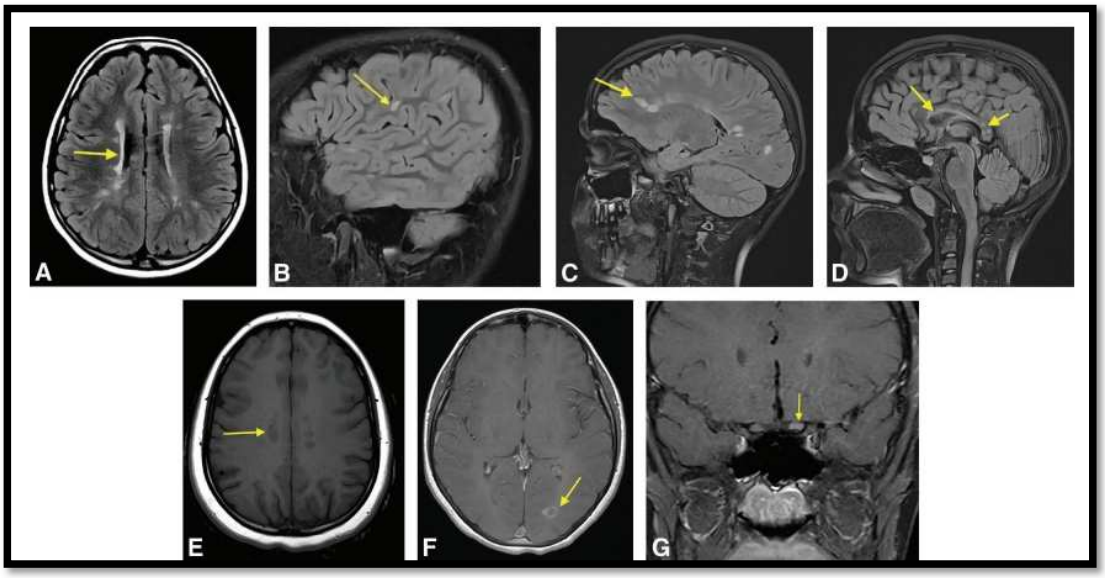


Figure 4: Typical multiple sclerosis lesions.[2]

Figure 4 A, Axial FLAIR sequences shows abnormal FLAIR signal along the right periventricular WM (arrow) with additional multifocal foci of abnormal FLAIR in the bilateral periventricular WM. B, Sagittal FLAIR image shows a hyperintense lesion most likely in the subcortical WM (arrow). C, Sagittal FLAIR image shows oval FLAIR hyperintense lesion orientated in a radial fashion (arrow) from the ventricular margin (Dawson's finger lesion). D, Sagittal FLAIR image in the midline showing abnormal signal (arrows) involving the corpus callosum. E, Arrow indicates a low-attenuating lesion on axial T1-weighted sequence, indicating a "black hole" lesion. F, Axial T1-weighted image with contrast shows a ring-enhancing lesion in the left occipital lobe (arrow). G, Coronal T1-weighted image with fat saturation shows abnormal enlargement and enhancement of the left prechiasmatic optic nerve (arrow).

SPINAL CORD

MR imaging of the spinal cord is valuable because asymptomatic spinal lesions can be seen in MS. Cervical to cervicothoracic cord is preferentially involved

in MS but it can also manifest as several focal lesions in case of diffuse spinal cord involvement. Typically MS lesions are located peripherally involving less than half of the cross-sectional area of the spinal cord[30] (Figure 5).

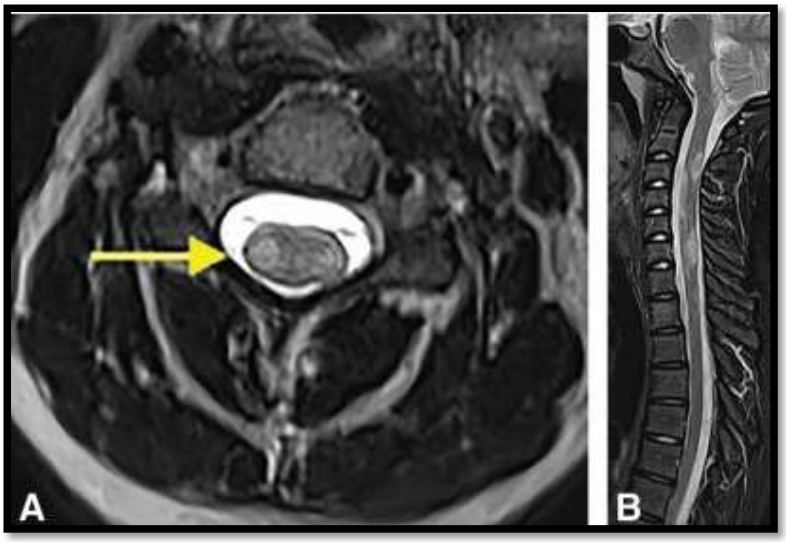


Figure 5: Typical multiple sclerosis lesions in the spine[2]

Management

Immunotherapy is generally used for acute attacks to mitigate attack severity and duration. Disease-modifying therapies are strongly recommended once a diagnosis of pediatric MS has been established.

Disease-Modifying Treatment	Level of Evidence	Potential Side Effects
Fingolimod (oral)	US Food and Drug Administration (FDA) approved for pediatric multiple sclerosis (2018) based on phase 2 randomized controlled trial[40]	Bradycardia, macular edema, lymphopenia, infections, seizures (rare)
Interferon beta-1a and interferon beta-1b (IM or subcutaneous injections)	European Medicines Agency approval for children >12 years of age; prospective and retrospective observational studies[44,45]	Injection site reactions, flulike symptoms, depression
Glatiramer acetate (subcutaneous injections)	Retrospective observational studies[8]	Injection site reactions, postinjection tachycardia
Natalizumab (IV infusion)	Prospective observational studies[9,10]	Progressive multifocal leukoencephalopathy, infusion reactions
Rituximab (IV infusion)	Retrospective observational studies[46–48]	Infusion reactions, infections, hypogammaglobulinemia

Table 2: Disease-Modifying drugs used in pediatric Multiple Sclerosis. [31]

MR Imaging Spine Findings	POMS	ADEM	NMOSD	Anti-MOG
Spine region (CTL)	C	T	CT can extend into lower brain stem	TL conus
Extent in vertebral segments	<2	>3	>3	>3
Cord location (GM or WM)	Lateral WM <50% of cross-sectional area. Peripheral predominance	Swollen GM or WM	Central GM >50% of cross-sectional area; central predominance	Central GM >50% of cross-sectional area; central predominance
Enhancement	Active plaques can enhance	Variable	Variable	Variable
DWI restriction	Active plaques can restrict	Variable	Not typical	Not typical
Other features	Relapsing remitting	Monophasic Prodromal illness Encephalopathy Often positive brain MR imaging findings Variable involvement of the spinal cord Follow up should show overwhelming resolution of lesions	Multiphasic Bulbar or visual symptoms	Multiphasic Often visual symptoms

Table 3: Summary of spinal MR imaging features of pediatric demyelinating disorders[2].

MRI IMAGING – DEMYELINATION PROTOCOLS

Demyelination protocols include the group of MRI sequences which have been used together to get the optimum imaging of the white matter disorders. These disorders can be of different etiology like infective, inflammatory, toxic or ischemic in origin.

For the diagnosis and follow-up of MS, the same protocol was used.

Consortium of Multiple Sclerosis Centers is the distinguished resource for MRI protocol recommendations used now which was updated in 2018. [32]

4 different protocols were recommend depending on the clinical presentation:

- Clinically Isolated Syndrome or new diagnosis
- Routine follow up
- Progressive Multifocal Leukoencephalopathy (PML) surveillance
- Imaging of the spinal cord

Protocols

T1 sequence

Preferable 3D isotropic acquisition of ≤1.0 mm.

Purpose: for proper imaging the anatomy and assessing the volume loss. This is preferable in cases of MS as disease severity and disability can be correlated with loss of brain volume. [33,34]

T2 sequence

Preferable 3D isotropic acquisition of ≤1.0 mm.

Purpose: for evaluation of the signal abnormality involving the white matter. For imaging of the infratentorial lesions, T2 sequence is more sensitive than that of FLAIR. <3 mm slice thickness without any skip if only 2D is available.[32,35]

FLAIR sequence

Preferable 3D isotropic acquisition of ≤1.0 mm.

Purpose: for evaluation of the signal abnormality involving the white matter. For the detection of periventricular and juxtacortical plaques, FLAIR is more sensitive than that of T2 sequence. <3 mm slice thickness without any skip if only 2D is available.[32,35]

DWI/ADC sequence:

Routine 2D DWI (diffusion-weighted imaging)

Purpose: Restricted diffusion may be demonstrated in active demyelinating MS plaques.

T1 C+ (Gd) sequence

Contrast is required for clinically isolated syndrome or new diagnosis,

Preferable 3D isotropic acquisition of ≤1.0 mm or 2D sequence.

Purpose: Enhancement can be seen in active demyelinating lesions, peripherally it is usually incomplete (open ring sign). Dissemination in time can be established based on the enhancement. [32,35]

Spinal cord imaging

Imaging of the entire spinal cord will take additional time, so usually a second appointment is given in many patients. If the patient is clinically stable, imaging of the cervical spinal cord till the level of T4 vertebra can be done. but if there are symptoms related to the involvement of the thoracic spinal cord, or any alternative diagnosis is considered then entire spinal cord should be imaged.

Any two among the following sagittal sequences are recommended as per CMSC:

- T2
- Proton Density
- STIR
- T1-PSIR

It should be <3 mm slice thickness without any skip.

If any lesion is seen on sagittal axial T2 images should be done at that level.

These should be <5 mm slice thickness without any skip. [32]

MATERIAL & METHOD

Source of data: Patients clinically suspected of having pediatric demyelinating disorder presenting to the Department of Radio-Diagnosis at the KLE's Dr. Prabhakar Kore Hospital & MRC, Belagavi.

Method of collection of data:

Study design: Hospital based Cross sectional study.

Sample size: On an average around 30 cases undergo MRI for the detection of pediatric demyelinating disorders per year at KLES Dr Prabhakar Kore Hospital& MRC, Belagavi.

So the present study included all patients clinically suspected of having pediatric demyelinating disorder presenting to the Department of Radio-Diagnosis **from 1st January 2021 to 31st December 2021.**

Sampling method: Universal sampling.

Study duration: 1stJanuary 2021- 31stDecember 2021.

Inclusion criteria:

A. Age below 18 years.
B. Inflammatory demyelinating event of the central nervous system in the period from 1st January 2021 to 31st December 2021.

Exclusion criteria

A. Patients with alternative diagnosis such as
    1. Infectious diseases
    2. Metabolic diseases
B. Pre existing malignancy, psychiatric disorders, or human immunodeficiency virus infection.

Methodology

Written informed consent was obtained from all the study participants. Data was collected in patients with clinical suspicion of acquired demyelinating disorders from the pediatric neurology department at KLE's Dr.Prabhakar Kore Hospital & MRC, Belagavi and referred for magnetic resonance imaging (MRI) study to the Department of Radio-Diagnosis at the KLE's Dr. Prabhakar Kore Hospital & MRC, Belagavi. Patients who underwent brain, orbit and spinal cord 3T magnetic resonance imaging scan including T1 & T2 weighted imaging and FLAIR sequence. The lesions were observed in regards to their size, location, longitudinal extension and involvement of optic nerves. Differentiating imaging features of the subtypes of pediatric demyelinating disorders like anti MOG (Myelin Oligodendrocyte Glycoprotein) associated encephalomyelitis, ADEM (Acute Disseminated Encephalomyelitis) and NMOSD (Neuromyelitis Optica Spectrum Disorder) were noted. All the data collected will be entered in a pre-designed and pretested questionnaire. The questionnaire consists of socio-demographic data, clinical history, physical examination and MRI findings. All the data collected were entered into MS Excel sheet, and master chart will be prepared. Tables, graphs and charts were

prepared. All diagnosed cases of pediatric demyelinating disorders were referred to pediatric neurology for further management.

Does the study require any investigations or interventions to be conducted on patients or other humans or animals? If so, please describe briefly:

Yes, magnetic resonance imaging of paediatric patients with acquired demyelinating disorders was done. Healthy humans or animals are not involved in this study.

STATISTICAL ANALYSIS

Since the study is of observational study the plan of analysis was as follows.

The categorical data were expressed in terms of rates, ratios and percentages. The association between the MRI features, clinical and demographic characteristics were tested using Chi-square test or Fisher's exact test.

Discrete variables were represented by median.

Nonparametric tests was used for comparing discrete variables.

Suitable diagrams was used to depict the comparison.

For all the tests the value of p less than 5% (0.05) was considered significant.

RESULTS

The final analysis included a total of 30 participants.

Table 4 : Descriptive analysis of diagnosis in the population(N=30)

Diagnosis	Number	percentage
ADEM	16	53.33%
MOGAD	7	23.33%
NMOSD	7	23.33%
Total	30	100.00%

Among the study population, the most common diagnosis was ADEM in 53.33% (16) participants followed by equal number of MOGAD and NMOSD cases, accounting for 23.33% (7) participants each (Table 4 & Figure 6).

Figure 6: Pie diagram for diagnosis wise distribution

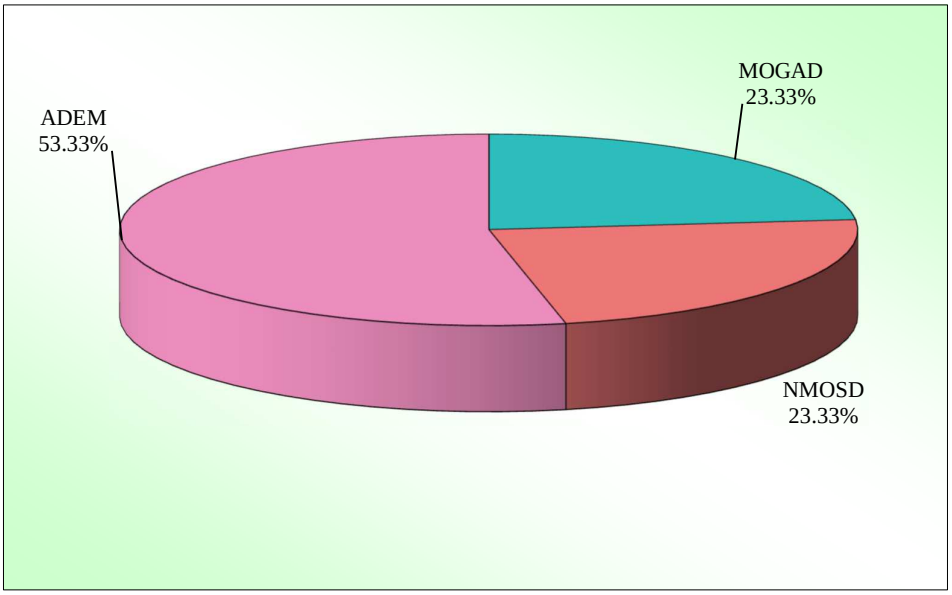


Table 5: Comparative analysis of diagnosis groups with age

Age groups	ADEM	%	MOGAD	%	NMOSD	%	Total	%
1-6yrs	7	43.75	1	14.29	2	28.57	10	33.33
7-12yrs	8	50.00	4	57.14	1	14.29	13	43.33
13-18yrs	1	6.25	2	28.57	4	57.14	7	23.33
Total	16	100.00	7	100.00	7	100.00	30	100.00
Mean age	6.88		10.00		11.57		8.70	
SD age	4.05		4.00		6.63		5.01	
Chi-square=8.6780, p=0.0700								

Among the study population, most of the participants (43.33%) was included in the age group of 7-12 years, followed by 1-6 years (33.33%) and 13-18 years (23.3%).

Among ADEM majority of the participants belonged to the age group of 7-12 years (50.00 %) and 1-6 years (43.75 %). Among MOGAD majority of the participants belonged to the age group of 7-12 years (57.14 %) whereas in NMOSD, most of the participants were aged 13-18 years (57.14 %) (Table 5 & Figure 7).

Figure7 : bar chart for comparison of diagnosis with age

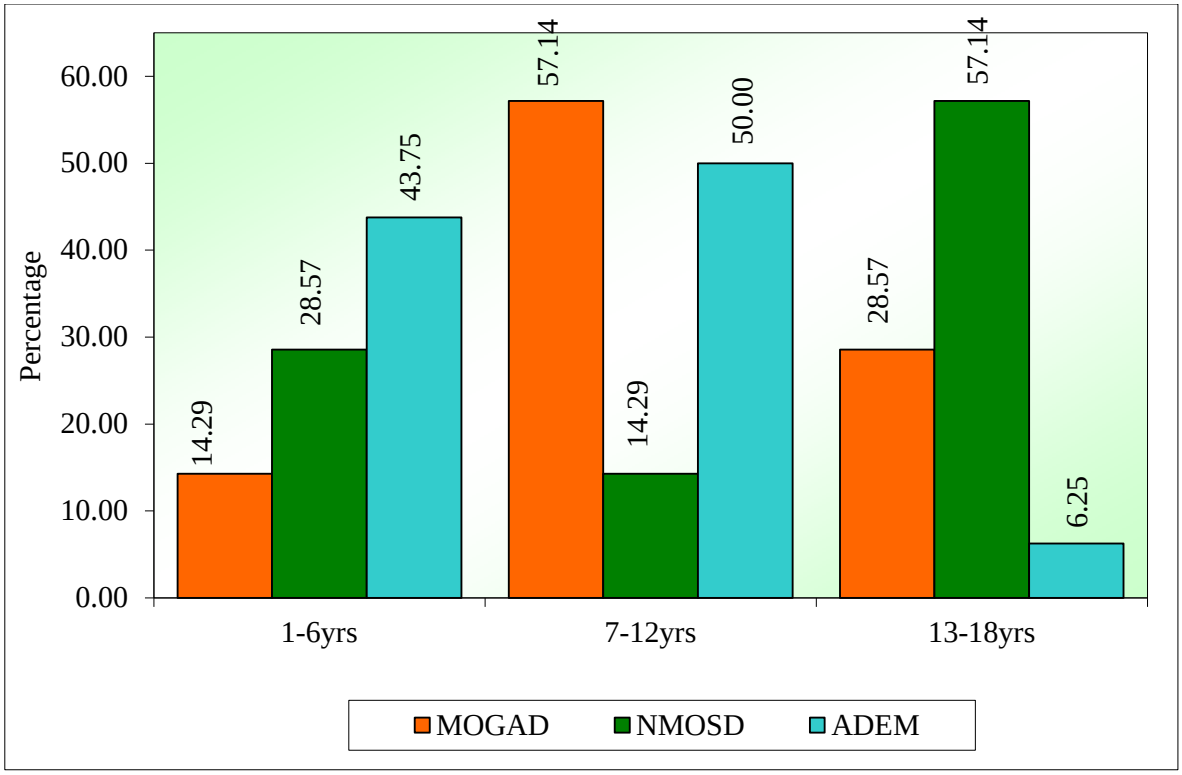


Table 6: Comparison of diagnosis groups with gender

Gender	ADEM	%	MOGAD	%	NMOSD	%	Total	%
Male	8	50.00	3	42.86	2	28.57	13	43.33
Female	8	50.00	4	57.14	5	71.43	17	56.67
Total	16	100.00	7	100.00	7	100.00	30	100.00
Chi-square=0.9110, p=0.6340								

Among the study population, there was a slight female predominance with a female: male ratio of 1.3: 1. ADEM group showed equal number of male and female participants whereas MOGAD and NMOSD showed female predominance with a female: male ratio of 1.33: 1 and 2.5: 1 respectively (Table 6 & Figure 8).

Figure 8: Comparison of diagnosis groups with gender

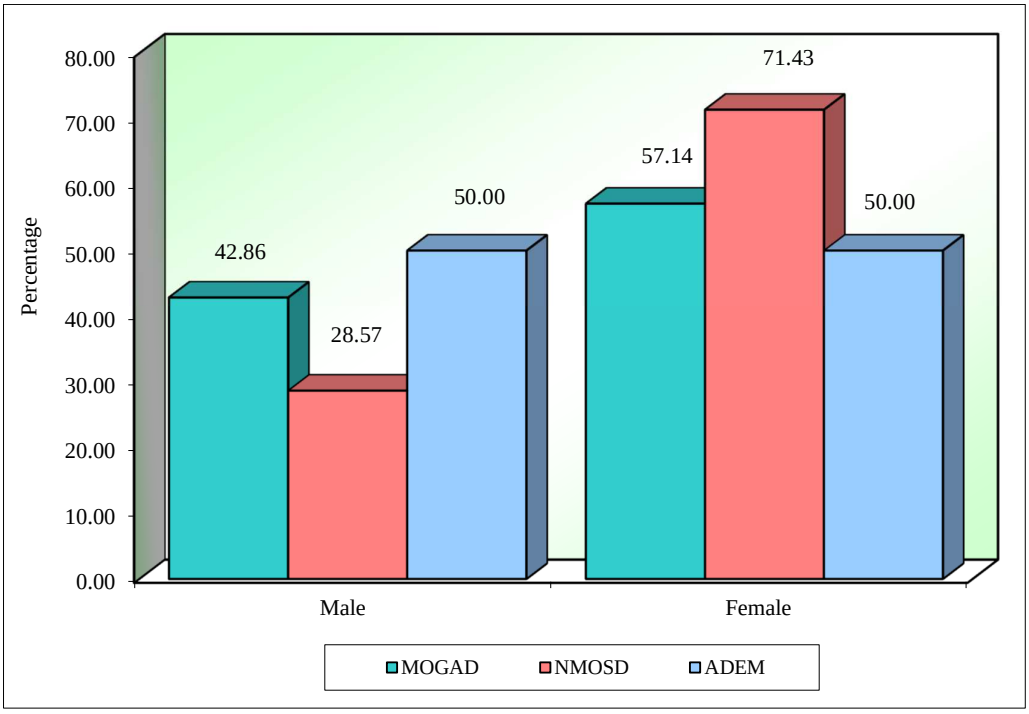


Table 7: Comparison of diagnosis groups with Clinical symptoms

Clinical symptoms	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Fever	12	75.00	3	42.86	3	42.86	18	60.00	3.2140	0.2000
Seizure	6	37.50	3	42.86	2	28.57	11	36.67	0.3180	0.8530
Encephalopathy	9	56.25	2	28.57	2	28.57	13	43.33	2.3300	0.3120
Visual disturbance	2	12.50	3	42.86	3	42.86	8	26.67	3.5190	0.1720
Limb weakness	3	18.75	4	57.14	3	42.86	10	33.33	3.6030	0.1650
Area postrema syndrome	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Cerebellar Symptoms	4	25.00	3	42.86	2	28.57	9	30.00	0.7480	0.6880
Head ache	7	43.75	3	42.86	3	42.86	13	43.33	0.0020	0.9990

*p<0.05 indicates significant association

Among the study population, the major symptoms were fever for 18 (60.00%) participants followed by encephalopathy and head ache for 13 (43.33 %) participants each.

In ADEM group the most common symptom was fever for 12 (75.00%) participants, followed by encephalopathy for 9 (56.25 %) and headache for 7 (43.75 %) participants however none of the ADEM cases had area postrema syndrome.

Among MOGAD group the major symptom was limb weakness for 4 (57.14 %) participants and fever, seizure, visual disturbances, cerebellar symptoms & headache for 3 (42.86 %) participants each.

Among NMOSD group the major symptoms were fever, visual disturbances, limb weakness, area postrema syndrome and headache for 3 (42.86 %) participants each. Area postrema syndrome showed statistically significant (p value = 0.0210) association with NMOSD cases as compared to ADEM & MOGAD cases (Table 7 & Figure 9).

Figure 9: Comparison of diagnosis groups with Clinical symptoms

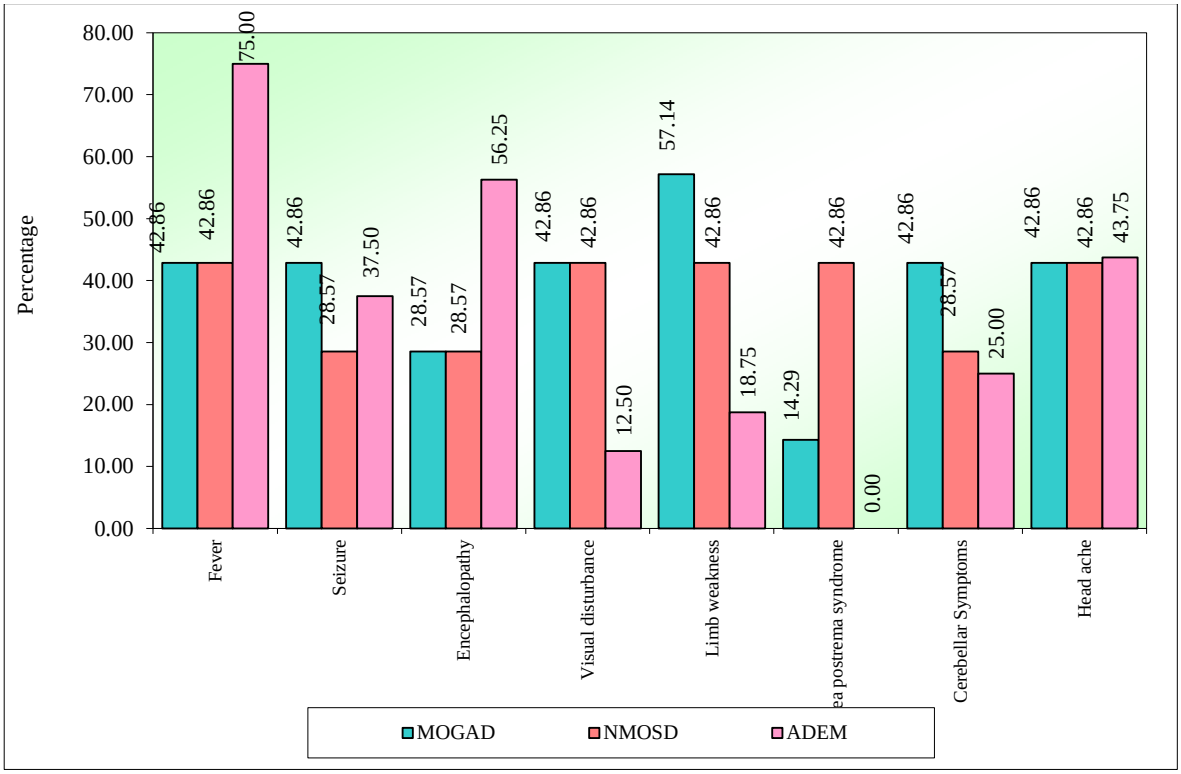


Table 8: Comparison of diagnosis groups with MRI Brain anatomical location (T2 and FLAIR hyperintensity)

MRI Brain	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Cortical grey matter	5	31.25	2	28.57	0	0.00	7	23.33	2.7980	0.2470
Juxta cortical white matter	8	50.00	3	42.86	0	0.00	11	36.67	5.3930	0.0670
Deep white matter	11	68.75	4	57.14	4	57.14	19	63.33	0.4330	0.8050
Periventricular white matter	6	37.50	2	28.57	4	57.14	12	40.00	1.2800	0.5270
Periaqueductal grey matter	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Corpus callosum	3	18.75	3	42.86	2	28.57	8	26.67	1.4640	0.4810
Thalamus	8	50.00	4	57.14	3	42.86	15	50.00	0.2860	0.8670
Basal ganglia	8	50.00	3	42.86	3	42.86	14	46.67	0.1530	0.9260
Brain stem	7	43.75	4	57.14	4	57.14	15	50.00	0.5360	0.7650
Area postrema	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Cerebellum	6	37.50	3	42.86	3	42.86	12	40.00	0.0890	0.9560

*$p<0.05$ indicates significant association

Among the study population the most common anatomical location of the lesion on MRI Brain was deep white matter in 19 (63.33 %) participants followed by thalamus and brain stem in 15 (50.00 %) participants each.

ADEM cases showed deep white matter lesions in 11 (68.75 %) cases followed by juxta cortical white matter, basal ganglia and thalamus in 8 (50.00 %) cases each, however none of the patients showed periaqueductal grey matter and area postrema involvement.

MOGAD group showed equal distribution of deep white matter, thalamus and brain stem lesions accounting for 57.14 % (4) participants each.

Among NMOSD the common anatomical locations of the brain lesions were deep white matter, periventricular white matter and brain stem lesions in 4 (57.13 %) participants followed by periaqueductal grey matter, area postrema, thalamus, basal ganglia and cerebellum in 3 (42.86 %) participants each. None of the patients showed cortical grey matter and juxta cortical white matter involvement. Involvement of area postrema and periaqueductal grey matter showed statistically significant (p value = 0.0210) association with NMOSD cases as compared to ADEM & MOGAD cases (Table 8 & Figure 10).

Figure 10: Comparison of diagnosis groups with MRI Brain anatomical location (T2 and FLAIR hyperintensity)

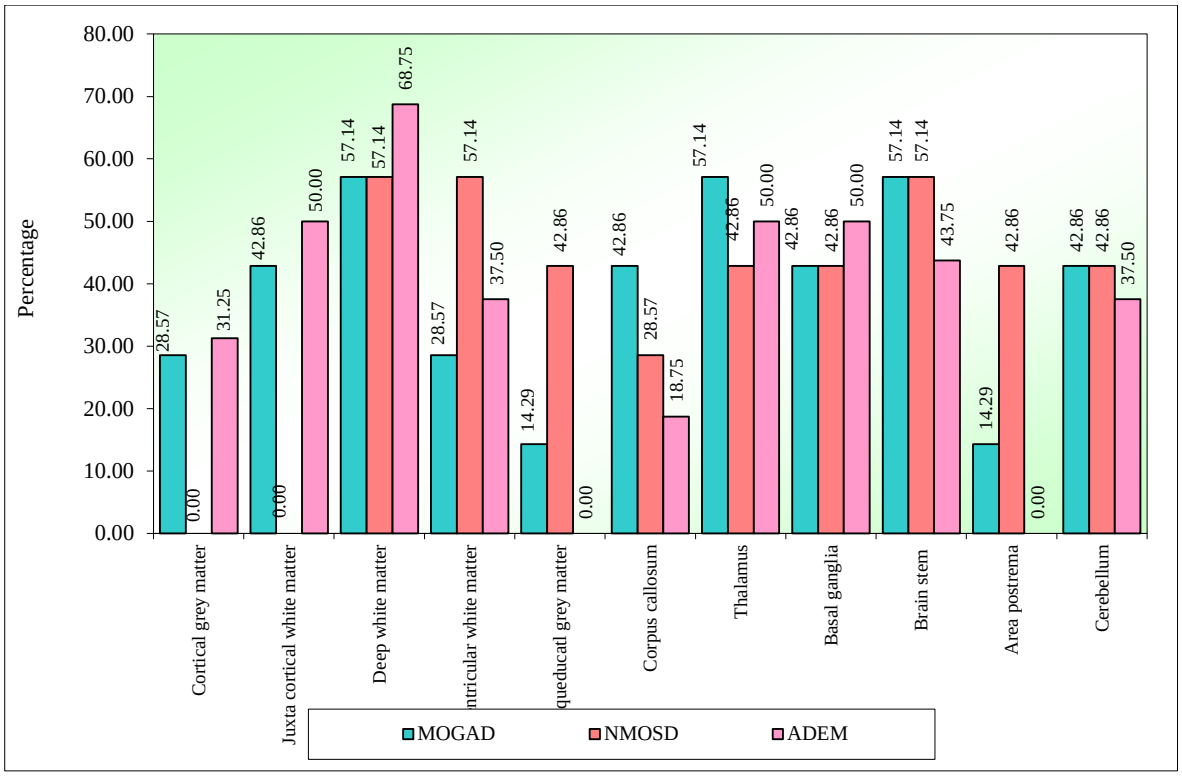


Table 9: Comparison of diagnosis groups with mean number of positive findings in supra tentorial and infra tentorial brain parenchyma by one way ANOVA

Diagnosis	Supra tentorial			Infra tentorial		
	Mean	SD	Median	Mean	SD	Median
ADEM	3.19	1.05	3.00	0.81	0.98	0.00
MOGAD	3.17	2.14	3.00	1.67	1.51	1.00
NMOSD	1.88	1.64	1.50	1.75	1.91	1.00
Total	2.83	1.53	3.00	1.23	1.41	1.00
F-value	2.3266			1.6051		
P-value	0.1169			0.2195		

Among the study population, the positive findings were more common in supratentorial brain parenchyma with a mean value of 2.83 as compared to the infratentorial findings with mean value of 1.23.

In ADEM and MOGAD the findings were more common in supratentorial brain parenchyma with a mean value of 3.19 and 3.17 respectively, whereas NMOSD showed relatively equal number of positive of findings involving both the supratentorial & infratentorial brain parenchyma.

However the supratentorial and infratentorial involvement was not statistically significant with any of the diagnosis groups (Table 9 & Figure 11).

Figure11: Comparison of diagnosis groups with mean number of positive findings in supra tentorial and infra tentorial brain parenchyma

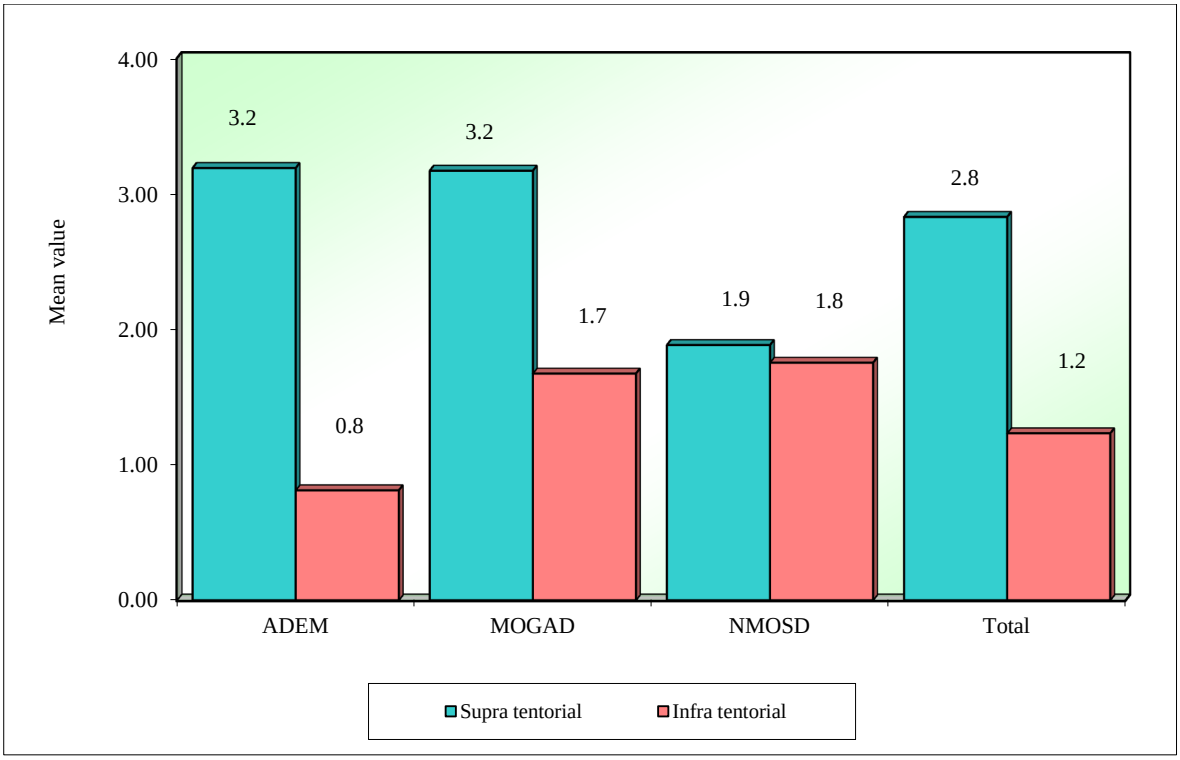


Table 10: Comparison of diagnosis groups with size of lesion

Size of lesion	ADEM	%	MOGAD	%	NMOSD	%
Large lesion	11	68.75	3	57.14	2	28.57
Small lesion	5	31.25	4	42.86	5	71.43
Total	16	100.00	7	100.00	7	100.00

Large lesions are de-myelinating lesion with a diameter greater than 2 cm in the transversal plane and small lesions are those with a diameter 0.3–2 cm in the transversal plane.

Majority of the ADEM and MOGAD cases showed large lesions in about 68.75 % and 57.14% participants each. But most of the NMOSD cases showed small lesions (71.43%). (Table 10 & Figure 12).

Figure 12: Comparison of diagnosis groups with size of lesion

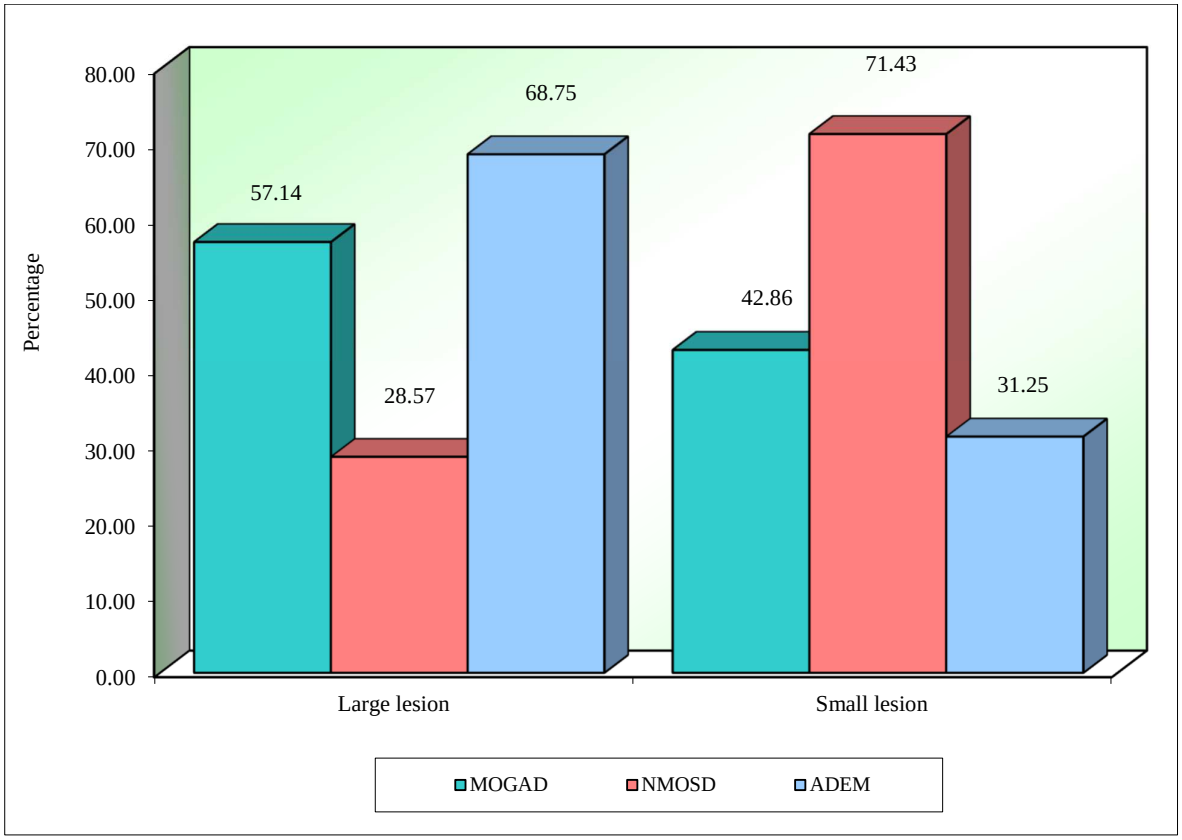


Table 11: comparison of diagnosis group with optic nerve involvement

Optic nerve	ADEM	%	MOGAD	%	NMOSD	%	Total	%
Not involved	14	87.50	5	71.43	4	57.14	23	76.67
Involved	2	12.5	2	28.57	3	42.86	7	23.33
Total	16	100.0	7	100.00	7	100.00	30	100.00

Among the study population, optic nerve involvement was seen in 23.33% of the participants. In NMOSD 42.86% participants showed optic nerve involvement where as MOGAD and ADEM showed optic nerve involvement in 28.57% and 12.5% cases respectively. (Table 11 & Figure 13).

Figure 13: comparison of diagnosis group with optic nerve involvement

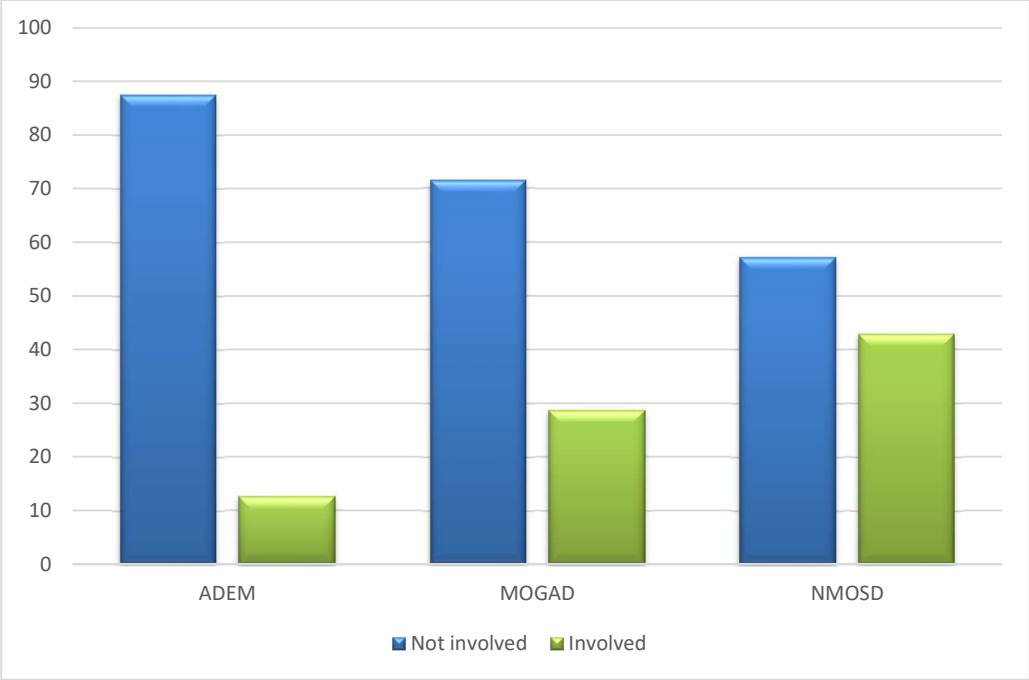


Table12: Comparison of diagnosis groups with Optic nerve laterality

Optic nerve	ADEM	%	MOGAD	%	NMOSD	%	Total	%
None	14	87.50	5	71.43	4	57.14	23	76.67
Unilateral	1	6.25	1	14.29	0	0.00	2	6.67
Bilateral	1	6.25	1	14.29	3	42.86	5	16.67
Total	16	100.00	7	100.00	7	100.00	30	100.00
Chi-square=5.6450, p=0.2290								

Among the study population bilateral optic nerve involvement (16.67%) was more common than unilateral optic nerve involvement (6.67 %).

Among ADEM & MOGAD cases, there was equal distribution of unilateral & bilateral optic nerve involvement in 6.25 % & 14.29% cases respectively. Among NMOSD, 42.86 % cases showed optic nerve involvement and all the cases showed bilateral involvement. However, the diagnosis groups do not show any statistical significance with the optic nerve laterality. (Table 12 & Figure 14).

Figure 14: Comparison of diagnosis groups with Optic nerve laterality

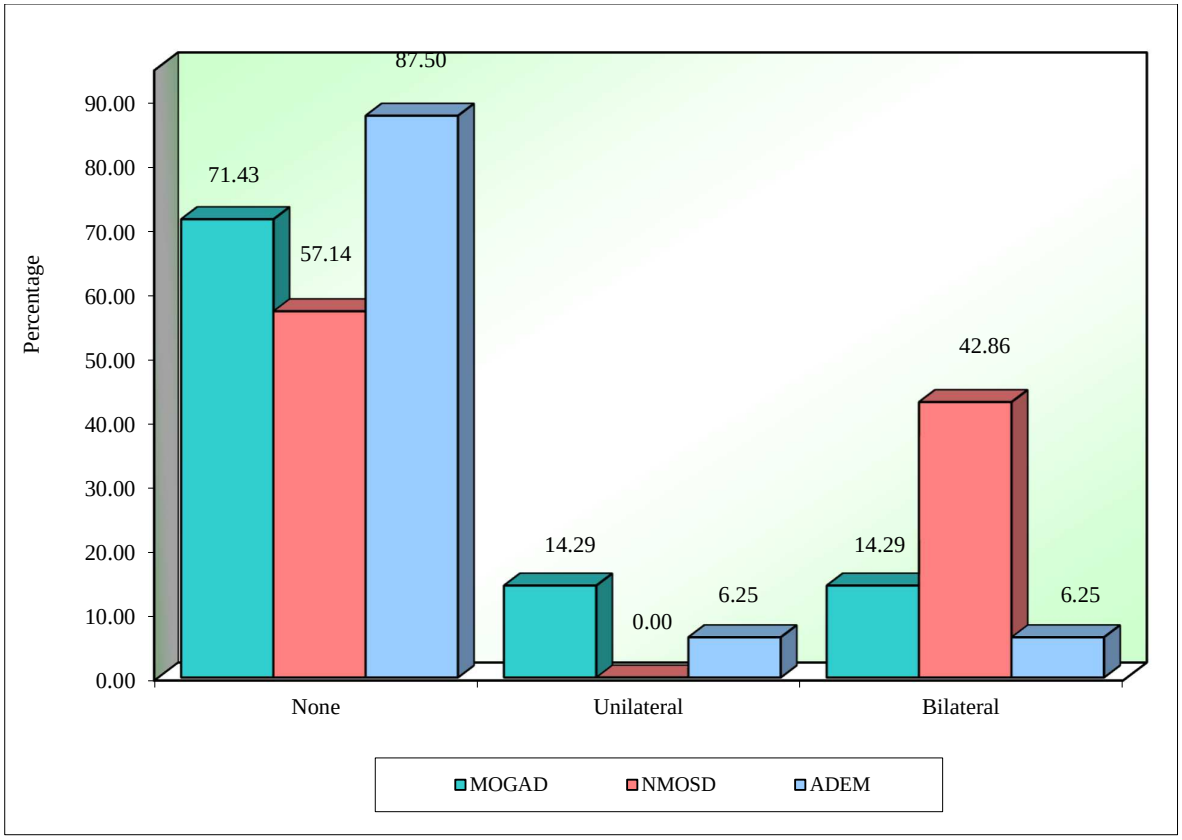


Table 13: Comparison of diagnosis groups with Optic nerve segment involved

Optic nerve	ADEM	%	MOGAD	%	NMOSD	%	Total	%
None	14	87.50	5	71.43	4	57.14	23	76.67
Anterior	2	12.50	2	28.57	1	14.29	5	16.67
Posterior	0	0.00	0	0.00	2	28.57	2	6.67
Total	16	100.00	7	100.00	7	100.00	30	100.00
Chi-square= 7.9750, p=0.0920								

Among the study population, majority of the optic nerve involvement was along the posterior segment, accounting for 28.57% of participants, however 16.67 % showed anterior optic nerve involvement.

ADEM & MOGAD cases showed only anterior optic nerve involvement in 12.5% & 28.57 % cases respectively and none of them showed posterior involvement. Among NMOSD cases posterior optic nerve involvement was more common (28.57 %) than anterior involvement (14.29 %). However, the diagnosis groups do not show any statistical significance with the optic nerve segment involved. (Table 13 & Figure 15).

Figure 15: Comparison of diagnosis groups with Optic nerve segment involved

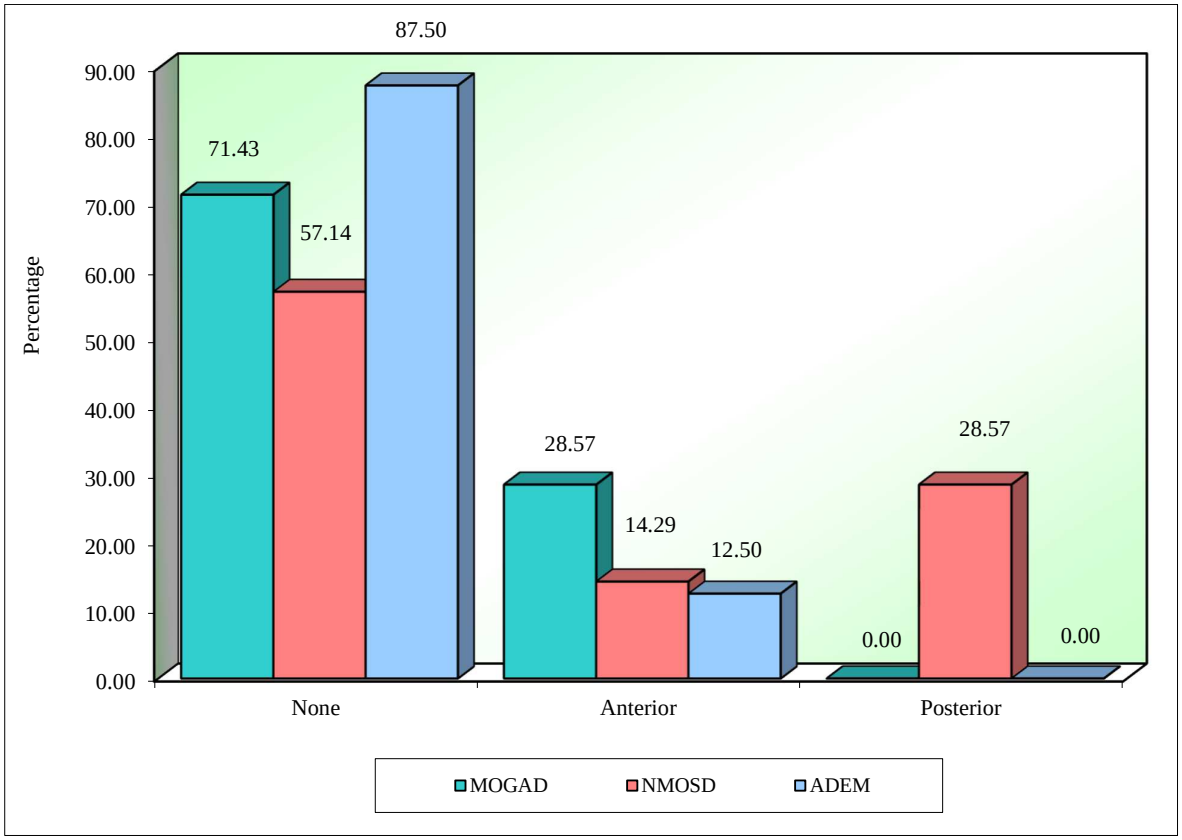


Table 14: Comparison of diagnosis groups with spinal cord involvement

Spinal cord	ADEM	%	MOGAD	%	NMOSD	%	Total	%
Not involved	13	81.25	3	42.86	3	42.86	19	76.67
Involved	3	18.75	4	57.14	4	57.14	11	23.33
Total	16	100.0	7	100.00	7	100.00	30	100.00

Among the study population, spinal cord involvement was seen in 23.33% cases and spinal cord was not involved in 76.67 % cases.

In ADEM group, most of the cases didn't show spinal cord involvement (76.67%) and spinal cord was involved only in 18.75 % cases where as spinal cord involvement was seen in 57.14% cases of MOGAD & NMOSD (Table 14 & Figure 16).

Figure 16: Comparison of diagnosis groups with spinal cord involvement

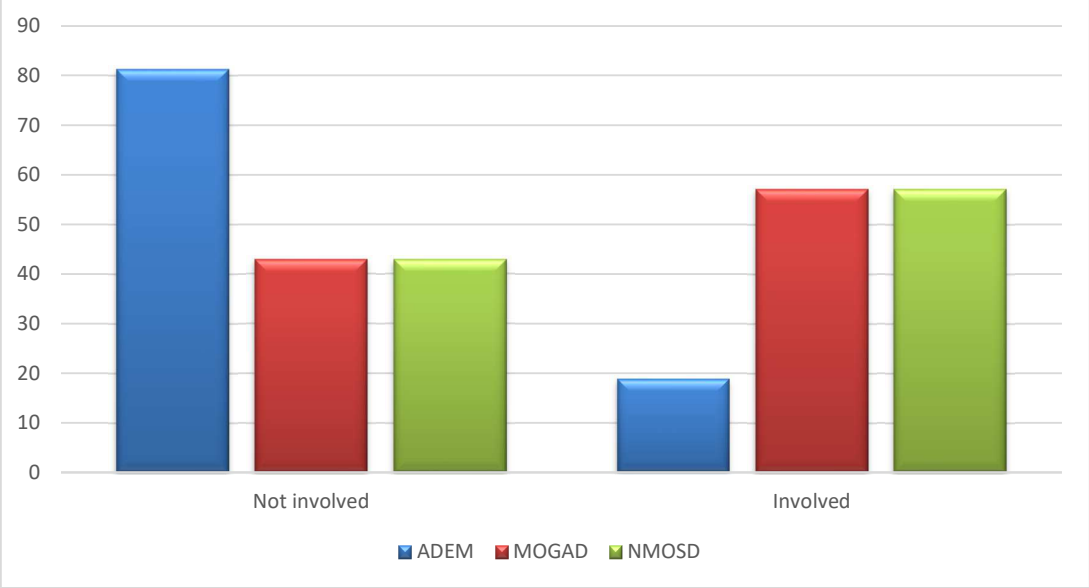


Table 15: Comparison of diagnosis groups with Type of spinal cord involvement

Spinal cord involvement	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
LETM	2	12.5	3	42.86	3	42.86	8	26.67	3.519	0.172
Focal spinal cord lesion	1	6.25	1	14.29	1	14.29	3	10.00	0.536	0.765

Longitudinally extensive transverse myelitis (LETM) is defined as a T2 hyperintense spinal cord lesion extending for three or more vertebral levels and focal spinal cord lesions will extend for less than three vertebral levels.

Among the study population, LETM (26.67 %) was more common than focal spinal cord lesions (10.00 %).

In ADEM group, LETM was seen in 12.50 % (2) participants and foal spinal cord lesions in 6.25 % (1) cases. Among MOGAD & NMOSD, the most common type of spinal cord involvement was LETM in 3 (42.86 %) participants and foal spinal cord lesions in 1(14.29 %) participant each. (Table 15 & Figure 17).

Figure 17: Comparison of diagnosis groups with Type of spinal cord involvement

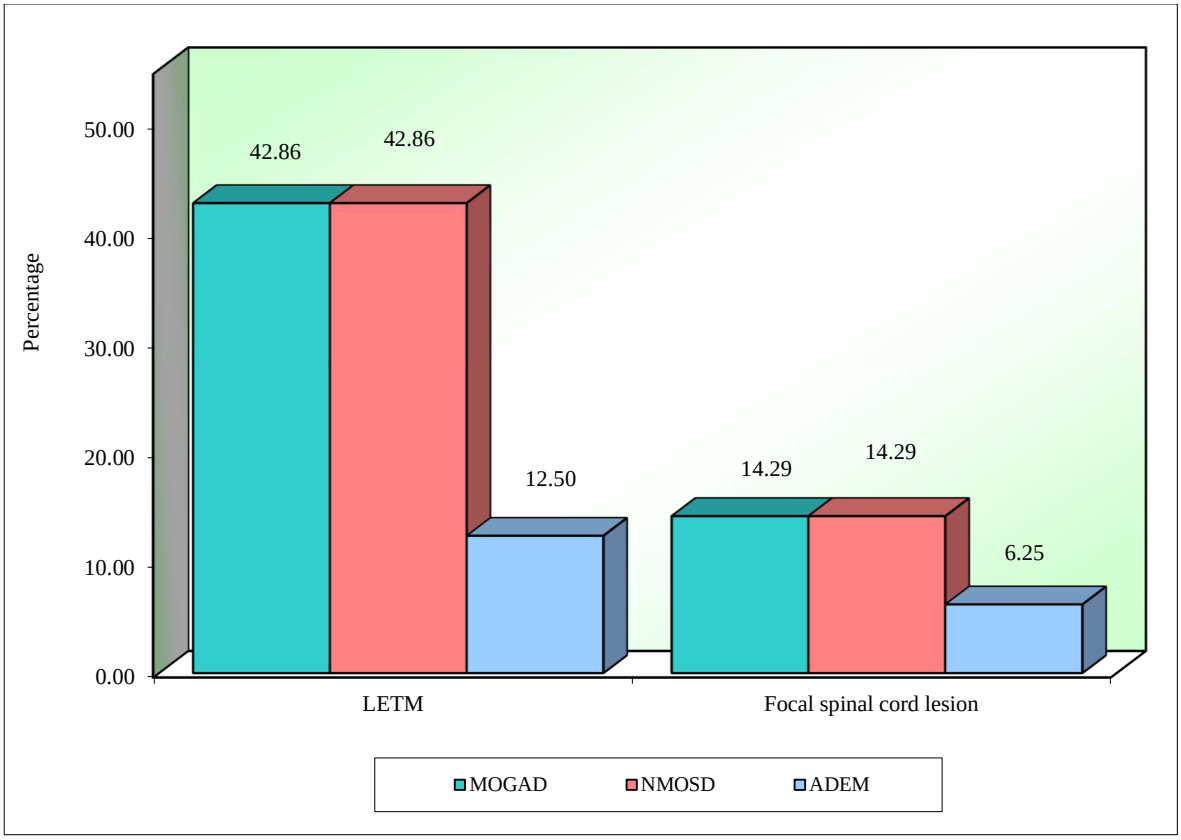


Table 16: Comparison of diagnosis groups with Spinal cord segment involved

Spinal cord segment involved	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Cervical	3	18.75	2	28.57	4	57.14	9	30.00	3.4270	0.1800
Thoracic	2	12.50	3	42.86	3	42.86	8	26.67	3.5190	0.1720
Lumbar	1	6.25	4	57.14	1	14.29	6	20.00	8.0690	0.0180*
Conus medullaris	1	6.25	2	28.57	1	14.29	4	13.33	2.1070	0.3490

*p<0.05

Among the study population, cervical (30.00 %) spinal cord involvement was more common followed by thoracic (26.67%) & lumbar (20.00%) spinal cord and least involved was conus medullaris (13.33%).

Cervical (18.75 %) spinal cord involvement was more common in ADEM than thoracic (12.50%), lumbar (6.25 %) and conus medullaris (6.25 %) involvement. Among MOGAD cases, majority showed lumbar spinal cord involvement (57.14%) which showed statistical significance (p value= 0.0180). MOGAD also showed thoracic (42.86%), conus medullaris (28.57 %) & cervical (28.57 %) spinal cord involvement. Majority of the NMOSD showed involvement of cervical spinal cord (57.14 %) followed by thoracic (42.86%), lumbar (14.29%) and conus medullaris in (14.29%) involvement. (Table 16 & Figure 18).

Figure 18: Comparison of diagnosis groups with Spinal cord segment involved

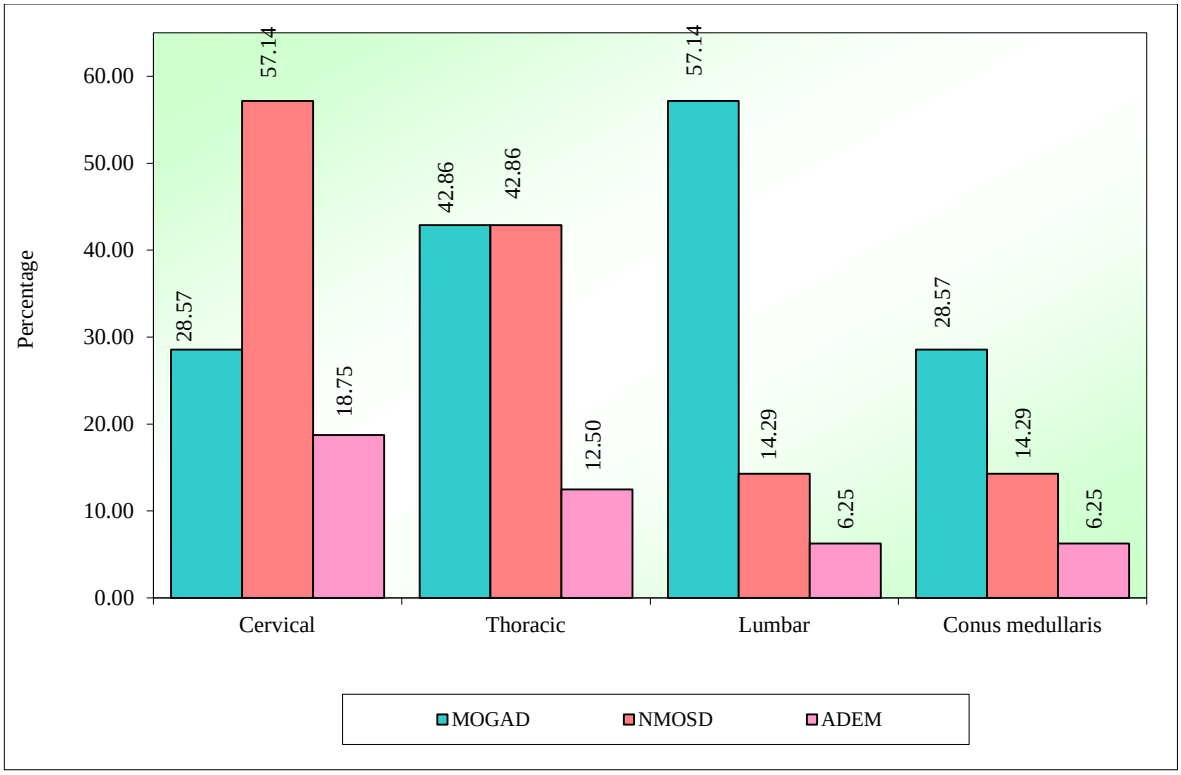


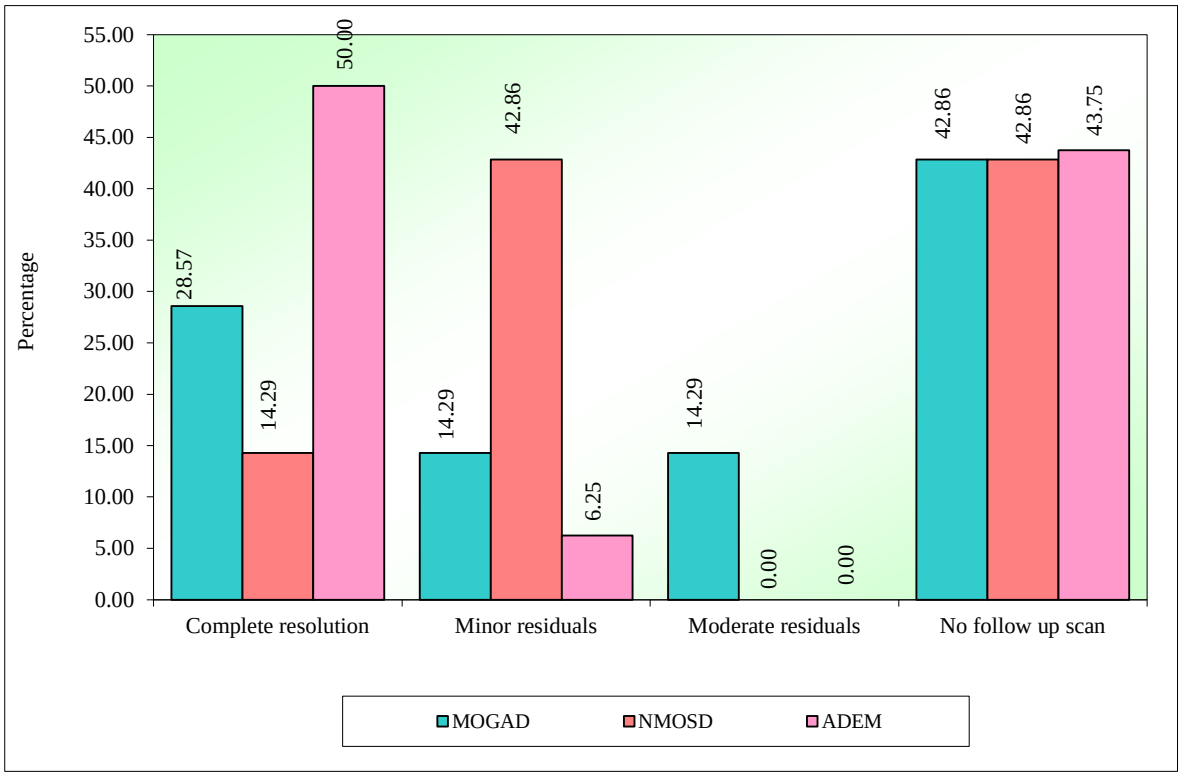
Table 17: Comparison of diagnosis groups with status of Follow up MRI

Follow up MRI	ADEM	%	NMOSD	%	MOGAD	%	Total	%
Complete resolution	8	50.00	1	14.29	2	28.57	11	36.67
Minor residuals	1	6.25	3	42.86	1	14.29	5	16.67
Moderate residuals	0	0.00	0	0.00	1	14.29	1	3.33
No follow up scan	7	43.75	3	42.86	3	42.86	13	43.33
Total	16	100.00	7	100.00	7	100.00	30	100.00
Chi-square=9.0910, p=0.1690								

Among the study population on follow up scan, majority had complete resolution (36.67%) and minor residuals were seen in 16.67% and moderate residuals in 3.33% of cases. No follow up scan was done for 13 (43.33%) participants.

Among ADEM on follow up scan complete resolution was seen in 50.00 % cases with minor residuals in 6.25% and no follow up scan was done for 43.75% participants. Among MOGAD on follow up scan, complete resolution was seen in 28.57 % cases but minor & moderate residuals were seen in 14.29% cases each (1) and no follow up scan was done for 3 (42.86 %) participants. Among NMOSD on follow up scan 42.86 % (3) cases showed minor residuals and14.29% (1) showed complete resolution. No follow up scan was done for in 3 (42.86 %) participants. (Table 17 & Figure 19).

Figure 19: Comparison of diagnosis groups with status of Follow up MRI



DISCUSSION

The present hospital based cross sectional study was done on 30 subjects aged between 1 and 18 years with clinical features suggestive of acute demyelinating disorder, attending the radiodiagnosis department in a tertiary care institute. MRI of the brain, optic nerves and spinal cord were done with 3.0 tesla MRI scanner.

The present study is one of the pioneer studies in India, focussing on the paediatric age group, comparing the clinical and imaging features of different acquired demyelinating disorders encountered in childhood.

Classification of acquired demyelinating disorders

The acquired demyelinating disorders encountered during childhood include acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), clinically isolated syndrome (CIS) and the more recently discovered anti-myelin oligodendrocyte glycoprotein (anti-MOG)–associated encephalomyelitis.[2]

In this study all pediatric patients with clinical features suggestive of acute demyelinating disorder who underwent MRI brain and spine imaging were included. All MOG antibody positive cases were considered as MOGAD. All NMO antibody positive cases and other cases fulfilling the new diagnostic criteria of NMOSD (2015)[21] was considered as NMOSD. All demyelinating cases seronegative for NMO or MOG antibodies and presenting with polyfocal deficits in the presence of encephalopathy and was considered as ADEM.

In this study of 30 cases of paediatric acquired demyelinating disorders, the most common diagnosis was ADEM in 16 (53.33%) cases followed by MOGAD & NMOSD, which accounted for 7 (23.33%) cases each.

Similarly in a study by Salma Zouari mallouli[36] showed that the most common acquired demyelinating disorder in the paediatric age group was ADEM (36%), followed by CIS (24%), MS (19%), NMOSD (7%) and MOGAD (2%).

Age distribution

In the present study, children between 1 to 18 years were included. The peak incidence of the paediatric acquired demyelinating disorders was seen between 7-12 years (43.33%) and the mean age was 8.7 ± 5.01years.

Similarly in a study by Vykuntaraju K [4], the mean age of ADD presentation was 7.8 years (ranges from 9 months–17 years).

Gender distribution

In this study mild female predominance was noted with a female: male ratio of 1.3: 1. Among 30 cases, 17 (56.67%) patients were females and 13 (43.33%) patients were males.

Similarly in a study by Santa Ignêz L[1], mild female predominance was noted as 12 (55%) out of 22 ADD cases were females.

Clinical features

The most common clinical presentation in the present study was fever in 18 (60%) patients, followed by encephalopathy and head ache in 13 (43.33%) patients each. Other common symptoms were seizure in 11 (36.67%), limb weakness in 10 (33.33%), cerebellar symptoms in 9 (30.00%) patients.

Similarly in a study by Vykuntaraju K [4], the most common presenting features of acute demyelinating disorders was fever (53.12%) followed by limb weakness & bowel and bladder complaints (43.75%), encephalopathy (37.50 %), seizure (28.12%) and visual disturbances (21.87 %).

ADEM

In this study of 30 cases of paediatric acquired demyelinating disorders, majority of the cases (53.33%) were ADEM. The mean age of presentation in the ADEM group was 6.88 ± 4.05 years, ranges from 1 year to 13 years. Similar age distribution was noted in a previous study by Vykuntaraju K [4] where the mean age of presentation was 5.5 years (ranges from 9 months–15 years). The study showed equal distribution of males and females, with a male: female ratio of 1:1.

In ADEM group the most common clinical presentation was fever (75.00%) followed by encephalopathy (56.25%) and head ache (43.75%). Similarly in a study by Vykuntaraju K [4] the commonest symptom was fever (80%), encephalopathy (53.3%) and seizure (40%). Encephalopathy which is one of the important criteria for the diagnoses ADEM, was found in 56.25 % patients in this study. This is similar to study conducted by Vykuntaraju K [4] where 53 % patients had encephalopathy. None of the ADEM cases had area postrema syndrome.

MRI brain showed demyelination in the form of T2 & FLAIR hyperintensities in the supratentorial and infratentorial brain parenchyma. ADEM showed lesions in bilateral cerebral hemispheres in an asymmetric distribution. Supratentorial brain involvement was 4 times as compared to infratentorial brain involvement. Majority of the cases showed large lesions (68.75%) with size >2 cm. The most common location involved was deep white matter (68.75%) followed by juxta cortical white matter (50%), thalamus (50%), basal ganglia (50%), brain stem (43.75%), cerebellum (37.5%), periventricular white matter (37.5%) and cortical grey matter (31.25%) cases. None of the ADEM cases showed peri aqueductal grey matter or area postrema involvement. This was similar to the observations in a study by Alpert et.al[38] in 2009 where most common site of brain lesions were deep white matter (68%), cerebellum (50%), basal ganglia (43%), brain stem (41%), juxta cortical white matter (21%) and periventricular white matter (18%).

Only 2 (12.5%) cases of the ADEM group showed optic nerve involvement which was anterior in both cases, however one patient showed unilateral involvement while the other one showed bilateral involvement. 3 ADEM cases showed spinal cord involvement which was LETM in 2 (12.5%) patients and focal lesion was seen in one patient. All the 3 (18.7%) cases showed cervical spinal cord involvement, whereas thoracic involvement was seen in 2 (12.5%) cases and lumbar and conus medullaris involvement was seen in 1 (6.2%) case each. Similarly in a study by Matthias Baumann et-al[37], the most common site spinal cord involvement was in the cervical (73%) region, followed by thoracic (54%), lumbar (35%) and conus medullaris (27%).

On follow up MRI, majority of the ADEM cases showed complete resolution (50%) and in 1 case, minor residuals were seen, however follow up MRI was not done in 43.3 % of the cases.

MOGAD

In our study of 30 cases of paediatric demyelinating disorders, 7 (23.33%) cases had the diagnosis of MOGAD. The mean age of presentation in the MOGAD group was 10 ± 4.0 years, ranging from 3 years to 15 years and showed female predominance with a female: male ratio of 1.33: 1.

In MOGAD the most common presenting feature was limb weakness (57.14%) followed by fever, seizure, visual disturbance, cerebellar symptoms, headache. Area postrema syndrome was seen in 1 (14.29%) case. In a study by M Baumann et-al[39] the most common clinical presentation among MOG antibody positive MOGAD was altered consciousness (89.5%) followed by limb weakness (52.6%), cerebellar (52.6%) signs and optic neuritis (15.8%), however in our study, altered sensorium was seen in only 2 (28.57%) cases.

On MRI Brain study, MOGAD group showed equal distribution of deep white matter, thalamus and brain stem lesions in 57.14 % (4) participants each, followed by basal ganglia, cerebellar and corpus callosal lesions. Cortical grey matter and juxta cortical white matter lesions were seen in 28.5% and 48.2% cases respectively. Although periaqueductal grey matter and area postrema lesions are specific for NMOSD cases, in our study one MOGAD case (14.29%) showed these lesions. Similarly in a study by Sara Salama et al[40], 7% of the MOG antibody disease showed area postrema involvement and 57% cases showed cortical/juxta cortical involvement.

In our study MOGAD cases showed supratentorial distribution of the lesions more than infratentorial lesions in the ratio of 1.9: 1. MOGAD cases showed more number of large lesions (57.14%) as compared to small lesions (42.8%). Optic nerve involvement was seen in 2 (28.5%) cases of MOGAD which showed involvement of the anterior segment in both cases, however one had unilateral involvement while the other showed bilateral involvement. 4 (57.15%) cases of MOGAD showed spinal cord involvement, among which 3 cases had LETM and 1 case showed focal spinal cord lesion. All of them showed involvement of the lumbar spinal cord with a statistically significant p value (0.0180), thoracic involvement was seen in 3 (42.8%) cases and conus medullaris and cervical spinal cord involvement was seen in 2 (28.5%) cases each.

4 (57.15 %) out of the 7 MOGAD cases had follow up MRI, which showed minor residuals in 3 cases (42.8%) and complete resolution in 1 case (14.29%).

NMOSD

In our study of 30 cases of paediatric demyelinating disorders, 7 (23.33%) cases had the diagnosis of NMOSD. The mean age of presentation in the NMOSD group was 11.57 ± 6.63 years, ranging from 1 year to 18 years and showed female predominance with a female: male ratio of 2.5: 1. Similarly in a study by E. Bulut [41] the mean age of presentation in the NMOSD group was 10.3 ± 5.6 years and showed female predominance with a female: male ratio of 2.3: 1.

In NMOSD cases, the commonest presenting complaint was fever, visual disturbance, limb weakness, area postrema syndrome and head ache for 3 (42.86%)

cases each followed by seizure, encephalopathy and cerebellar symptoms in 2 (28.57%) cases each. For area postrema syndrome p value was statistically significant with NMOSD as compared to ADEM & MOGAD cases.

On MRI Brain NMOSD group showed equal distribution of deep white matter, brain stem and periventricular white matter lesions in 57.14 % (4) participants each, followed by periaqueductal grey matter, area postrema, thalamus, basal ganglia and cerebellar lesions. Periaqueductal grey matter and area postrema lesions which are specific for NMOSD cases was seen in 42.8% cases in our study. Cortical grey matter and juxta cortical white matter lesions were not seen in NMOSD cases. Similarly in a study by Sara Salama et al[40], 50% of the NMOSD cases showed area postrema involvement and none of the cases showed cortical/juxta cortical involvement.

In our study NMOSD cases showed equal distribution of lesions in the supratentorial and infratentorial brain parenchyma in the ratio of 1.07: 1 cases respectively. NMOSD cases showed more number of small lesions (71.43 %) as compared to small lesions (28.57 %). Optic nerve involvement was seen in 3 (42.8 %) cases of NMOSD which showed bilateral involvement in all the 3 cases. Posterior segment involvement was more common as it was seen in 2 (28.57%) cases as compared to anterior involvement in 1 case (14.29%). 4 (57.15%) cases of NMOSD showed spinal cord involvement, among which 3 cases had LETM and 1 case showed focal spinal cord lesion. Most of the cases showed cervical and thoracic involvement, 57.15 % and 42.8% cases respectively. Lumbar and conus medullaris involvement was seen only in 1 (14.29%) case each. Similarly in a study by M. Baumaann[37], the most common site of involvement was cervical spinal cord followed by thoracic, lumbar and conus medullaris.

4 (57.15 %) out of the 7 cases of NMOSD had follow up MRI which showed, which showed complete resolution in 2 cases (28.57%), minor residuals and moderate residuals in 1 (14.28%) case each.

CONCLUSION

The present hospital based cross sectional study was conducted in the department of radiodiagnosis, KLES Dr. Prabhakar Kore Hospital Belagavi, aimed to study the role of MRI in pediatric demyelinating disorders.

Magnetic resonance imaging scan of brain and spinal cord was performed in 30 patients with suspected pediatric acquired demyelinating disorders.

- The majority (43.33%) were aged between 7 to 12 years.
- Mild female predominance was noted with a female: male ratio of 1.3: 1.
- The most common diagnosis was ADEM in16 (53.33%) cases followed by equal distribution of MOGAD & NMOSD.
- ADEM cases showed lesions in bilateral cerebral hemispheres with predominant supratentorial brain involvement and majority of the cases had large lesions.
- In MOGAD cases, brain parenchyma showed predominantly large lesions in supratentorial distribution. Spinal cord lesion was predominantly LETM with statistically significant involvement of the lumbar spinal cord.
- In NMOSD cases, statistically significant association was seen with area postrema syndrome and periaqueductal grey matter & area postrema lesions on MRI brain. Spinal cord lesions in NMOSD were predominantly LETM with involvement of the cervical and thoracic spinal cord.

SUMMARY

The acquired demyelinating disorder (ADD) is characterized by the destruction or damage of normally myelinated structures of the central nervous system (CNS) which are immunologically mediated. Acquired demyelinating disorders encountered during childhood include acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), Clinically isolated syndrome (CIS) and the more recently discovered anti-myelin oligodendrocyte glycoprotein (anti-MOG)–associated encephalomyelitis. The recent discovery of some key MRI imaging features which can be explained by the pathophysiological basis of these different entities helps in identifying magnetic resonance imaging predictors of a particular demyelinating diagnosis. Hence the present study is to asses the role of MRI in pediatric demyelinating disorders.

The present hospital based cross sectional study was conducted on 30 subjects aged between 1 to 18 years suspected of acute demyelinating disorder, presented to the department of radiodiagnosis, KLES Dr. Prabhakar Kore Hospital Belagavi. MRI Brain and spinal cord was done.

The majority were aged between 7 to 12 years and majority were females with a female: male ratio of 1.3: 1. Among 30 cases, the most common diagnosis was ADEM (53.33%) followed by equal distribution of MOGAD & NMOSD.

ADEM cases showed equal distribution among males and females. Most common clinical presentation was fever & encephalopathy. MRI Brain showed lesions in bilateral cerebral hemispheres in an asymmetric distribution with predominant supratentorial brain involvement and majority showed large lesions.

None of the ADEM cases showed peri aqueductal grey matter or area postrema involvement. Spinal cord involvement in ADEM was predominantly LETM with majority showing cervical spinal cord involvement. On follow up MRI, majority of the cases showed complete resolution.

23.33% cases had the diagnosis of MOGAD which showed a slight female predominance with a male: female ratio of 1.33: 1. The most common presenting feature was limb weakness, fever and seizures. On MRI Brain MOGAD cases showed predominant supratentorial distribution of lesions with majority of large lesions as compared to small lesions. MOGAD group showed majority of deep white matter, thalamus and brain stem lesions. Optic nerve involvement was seen in the anterior segment and spinal cord lesions was predominantly LETM with majority of cases showing involvement of the lumbar spinal cord. On follow up MRI majority showed minor residuals.

NMOSD cases accounted 23.33% of the subjects and showed female predominance with a female: male ratio of 2.3: 1. The commonest presenting complaint was fever, visual disturbance, area postrema syndrome and limb weakness. MRI brain showed predominantly small lesions in NMOSD with majority of deep white matter, brain stem, periventricular white matter, periaqueductal grey matter and area postrema lesions. Cortical grey matter and juxta cortical white matter involvement were not seen in NMOSD cases. Optic nerve involvement was more common in the posterior segment and spinal cord lesions were predominantly LETM with involvement of the cervical and thoracic spinal cord.

BIBLIOGRAPHY

1. Santa Ignêz L. J., Silveira de Souza A., Amâncio A. P. R. L., Almeida J.V., Gamarano G. M. F., Costa A. A. B. P, et al. Magnetic Resonance Imaging in the Acquired Demyelinating Disorders: A Pediatric Cohort Study. J Pharm Pharmacol. 2018;6(1).
2. Aw-Zoretic J, Harrell A, Rubin JP, Palasis S. Pediatric Demyelinating Disease: Emerging Patterns from Multiple Sclerosis to Anti-Myelin Oligodendrocyte Glycoprotein-Associated Encephalomyelitis. Neurographics. 2020;10(3):139–51.
3. Maryam Nabavi Nouri & E. Ann Yeh, et al. Neuroinflammatory and Demyelinating Disorders of Childhood. Clinical Child Neurology June 2020 pp 651–677.
4. Vykuntaraju K. Gowda1 , Deepthi Shetty et al. Clinical and Radiological Profiles, Treatment, and Outcome of Pediatric Acquired Demyelinating Disorders of Central Nervous System. J Pediatr Neurosci 2019;14:76-81.
5. Dekate PS. Acquired demyelinating disorders of central nervous system. Indian J Child Health. 2014;1(3):128–135.
6. Hynson JL, Kornberg AJ, Coleman LT et-al. Clinical and neuroradiologic features of acute disseminated encephalomyelitis in children. Neurology. 2001;56 (10): 1308-12.
7. Wender M. Acute disseminated encephalomyelitis (ADEM). J Neuroimmunol. 2011;231(1–2):92–9.
8. Anilkumar AC, Foris LA, Tadi P. Acute Disseminated Encephalomyelitis (ADEM). StatPearls ublishing; 2019. Available from: https://www.ncbi.nlm.nih.gov/books/ NBK430934

9. Inglese M, Salvi F, Iannucci G et-al. Magnetization transfer and diffusion tensor MR imaging of acute disseminated encephalomyelitis. AJNR Am J Neuroradiol. 2002;23 (2): 267-72.
10. Weng WC, Peng SS, Lee WT, et al. Acute disseminated encephalomyelitis in children: one medical center experience. Acta Paediatr Taiwan 2006;47:67–71.
11. Baum PA, Barkovich AJ, Koch TK, et al. Deep gray matter involvement in children with acute disseminated en-cephalomyelitis. AJNR Am J Neuroradiol 1994;15:1275–83.
12. Korporal M, Haas J, Balint B, et al. Interferon beta-induced restoration of regulatory T-cell function in multiple sclerosis is prompted by an increase in newly generated naive regulatory T cells. Arch Neurol 2008;65(11):1434–1439.
13. Hart BA, van Kooyk Y, Geurts JJ, et al. The primate autoimmune encephalomyelitis model; a bridge between mouse and man. Ann Clin Transl Neurol 2015;2:581–93. 10.1002/acn3.194
14. Ray Wynford-Thomas,1,2 Anu Jacob,3 and Valentina Tomassini et al. Neurological update: MOG antibody disease. J Neurol. 2019; 266(5): 1280–1286.
15. Kitley J, Waters P, Woodhall M, et al. Neuromyelitis optica spectrum disorders with aquaporin-4 and myelinoligodendrocyte glycoprotein antibodies: a comparative study. JAMA Neurol 2014;71:276–83. 10.1001/ jamaneurol.2013.5857
16. Mona Shahriari, Elias S. Sotirchos, Scott D. Newsome, David M. Yousem. MOGAD: How It Differs From and Resembles Other Neuroinflammatory Disorders. (2021) American Journal of Roentgenology.

17. Roemer SF, Parisi JE, Lennon VA, et al. Pattern-specific loss of aquaporin-4 immunoreactivity distinguishes neuromyelitis optica from multiple sclerosis. Brain 2007; 130(pt 5):1194–1205. doi:10.1093/brain/awl371. 75
18. Misu T, Höftberger R, Fujihara K, et al. Presence of six different lesion types suggests diverse mechanisms of tissue injury in neuromyelitis optica. Acta Neuropathol 2013;125(6):815–827. doi:10.1007/s00401-013-1116-7
19. Papadopoulos MC, Verkman AS. Aquaporin water channels in the nervous system. Nat Rev Neurosci. 2013;14(4):265–77.
20. Michela Ada Noris Ferilli, Roberto Paparella, Ilaria Morandini et-al. Pediatric Neuromyelitis Optica Spectrum Disorder: Case Series and Literature Review. Research Updates in Pediatric Neuroscience. Life 12, no. 1: 19.
21. Dutra BG, Jose´ da Rocha A, Nunes RH, et al. Neuromyelitis optica spectrum disorders: spectrum of MR imaging findings and their differential diagnosis. RadioGraphics 2018;38:169– 93. 10.1148/rg.2018170141
22. Chitnis T, Ness J, Krupp L, et al. Clinical features of neuromyelitis optica in children: US Network of Pediatric MS Centers report. Neurology 2016;86(3): 245–252. doi:10.1212/WNL.0000000000002283
23. Barnett Y, Sutton IJ, Ghadiri M et-al. Conventional and Advanced Imaging in Neuromyelitis Optica. AJNR Am J Neuroradiol. 2013
24. Prat A, Antel J. Pathogenesis of multiple sclerosis. Curr Opin Neurol. 2005;18(3):225–30.
25. Popescu BFG, Lucchinetti CF. Pathology of Demyelinating Diseases. Annu Rev Pathol Mech Dis. 2012;7(1):185–217.
26. Weinshenker B, Bass B, Rice G et al. The Natural History of Multiple Sclerosis: A Geographically Based Study. I. Clinical Course and Disability. Brain.

1989;112 (Pt 1)(1):133-46.

27. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162–73.
28. Lycklama G, Thompson A, Filippi M, Miller D, Polman C, Fazekas F, et al. Spinal-cord MRI in multiple sclerosis. Lancet Neurol. 2003 Sep;2(9):555–62.
29. Tartaglino LM, Friedman DP, Flanders AE, Lublin FD, Knobler RL, Liem M. Multiple sclerosis in the spinal cord: MR appearance and correlation with clinical parameters. Radiology. 1995;195(3):725–32.
30. Tanuja Chitnis et al. Pediatric Central Nervous System Demyelinating Diseases. continuum (minneap minn) 2019;25(3, multiple sclerosis and other cns inflammatory diseases):793–814 .
31. Consortium of MS Centers (CMSC) MRI protocol for the diagnosis and follow-up of MS (Proposed 2017 guidelines).
32. Radue EW, Barkhof F, Kappos L et-al. Correlation between brain volume loss and clinical and MRI outcomes in multiple sclerosis. Neurology. 2015;84 (8): 784-93.
33. De Stefano N, Airas L, Grigoriadis N et-al. Clinical relevance of brain volume measures in multiple sclerosis. CNS Drugs. 2014;28 (2): 147-56.
34. A. Traboulsee, J.H. Simon, L. Stone, E. Fisher, D.E. Jones, A. Malhotra, S.D. Newsome, J. Oh, D.S. Reich, N. Richert, K. Rammohan, O. Khan, E.-W. Radue, C. Ford, J. Halper, D. Li. Revised Recommendations of the Consortium of MS Centers Task Force for a Standardized MRI Protocol and Clinical Guidelines for the Diagnosis and Follow-Up of Multiple Sclerosis. (2016) American Journal of Neuroradiology. 37 (3): 394.

35. Michael Absoud, Ming J Lim, Wui K Chong et-al. Paediatric acquired demyelinating syndromes: incidence, clinical and magnetic resonance imaging features. Multiple Sclerosis Journal 19(1) 76–86.
36. Salma Zouari mallouli et-al. Acute Demyelinating Syndromes: A report of child neurology department of Sfax University Hospital. Multiple sclerosis and related disorders. Volume 56, November 2021, 103291.
37. Matthias Baumann, Astrid Grams, Tanja Djurdjevic et-al. MRI of the first event in pediatric acquired demyelinating syndromes with antibodies to myelin oligodendrocyte glycoprotein. Journal of Neurology.08 february 2018. s00415-018-8781-3.
38. Alpert G., Heyman R., Wang L. Multiple sclerosis and acute disseminated encephalomyelitis diagnosed in children after long-term follow-up: comparison of presenting features. Dev Med Child Neurol. 2009;51:480–486.
39. M Baumann, K Sahin, C Lechner, E M Hennes et-al. Clinical and neuroradiological differences of paediatric acute disseminating encephalomyelitis with and without antibodies to the myelin oligodendrocyte glycoprotein. J Neurol Neurosurg Psychiatry. 2014-308346.
40. Sara Salama, Majid Khan, Amirali Shanechi et-al. MRI differences between MOG antibody disease and AQP4 NMOSD. Mult Scler. 2020 Dec; 26(14): 1854-1865.
41. E. Bulut, X J. Karakaya, X S. Salama, X M. Levy et-al. Brain MRI Findings in Pediatric-Onset Neuromyelitis Optica Spectrum Disorder: Challenges in Differentiation from Acute Disseminated Encephalomyelitis. AJNR Am J Neuroradiol. February 2, 2019.

ANNEXURE-I-INFORMED CONSENT

WRITTEN INFORMED CONSENT

TITLE OF THE STUDY: "ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

INVESTIGATOR: REG NO: BS0120009

GUIDE: DR. _____

CO-GUIDE: DR. _____

INTRODUCTION AND PURPOSE: The purpose of this study is to determine the clinical profile and imaging features of the pediatric acquired demyelinating disorders of the CNS and to differentiate the imaging features of different subtypes of acute demyelinating disorders. Magnetic resonance imaging provides some key imaging features of pediatric demyelinating disorders.

Demyelinating diseases are challenging to differentiate from each other, especially because the various disorders can present with nonspecific radiologic findings and overlapping CNS features. Identifying magnetic resonance imaging predictors of a particular demyelinating diagnosis in the pediatric population can have broad implications on treatment.

PROCEDURE: I request you to kindly allow your child to participate in the study titled **"ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** at Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, being

conducted by **REG NO: BS0120009,** Post graduate in Radio diagnosis at J.N. Medical College, Belagavi, Karnataka, under the guidance of **Dr._____**, Dept. of Radio-diagnosis, J. N. Medical College, Belagavi and co-guidance of **Dr._____**, Dept. of Pediatrics, J. N. Medical College, Belagavi.

We request your child to participate in this study as you are eligible to be included. The purpose of the study will be explained and written informed consent will be obtained from you prior to participation. During the study, you will be asked questions regarding your child's present and past medical history and you will be required to answer to the best of your knowledge. Your child will also be clinically examined as per the protocol drawn. As part of the study your child will be subjected to MRI scan of the brain and spinal cord. Remove any metal objects including jewellery and eye glasses prior to the scan. The technologist will explain the steps involved in the scan in detail. Your child will then be asked to lie flat on your back on the MRI table. The technologist will convey further instructions in your desired language over the intercom. Your child will be asked to lie very still till the scan is over.

If you agree to participate in the study, please furnish the details pertaining to the study.

BENEFITS:

- No use of surgical equipment /risk associated with it.

COMPLICATIONS:

- No risk to the patient has been documented from MRI imaging of brain and spinal cord conducted earlier.

ALTERNATIVES: If you are not willing to take part in the study, your treatment or any other further investigations the patient wants to undergo, in future, in KLE hospital will not be affected by your decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL: Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part, you can later change my mind and withdraw from the study. Your decision will not change the present or future health care or other services that your child receive. The study doctor or the sponsor may stop your child's participation in this study. You will tell if any important new findings that may change my willingness to continue to take part. If you choose not to take part in the study, you will receive the standard treatment for patients with your child's condition.

COSTS: NIL (The study is to be conducted on the participants who are advised MAGNETIC RESONANCE IMAGING as an investigation by the referring consultant and the participants will bear the charges for it.)

Payment for Participation: No incentive will be paid to you for participating in this study.

COMPENSATION: In the event that you become injured as a result of taking part in this study, treatment whatever available at KLE charitable hospital,

Belagavi, will be offered to you. No reimbursement, compensation or free medical care is given.

CONFIDENTIALITY: All information collected about you during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be kept confidential in any publication/ presentation.

QUESTION: If you have any enquiries in the future or in case of research related injury illness, you may contact following persons:

REG NO: BS0120009	**Dr. _____**	**Dr. HARSHA HEGDE**
Post-Graduate, Department of Radio-Diagnosis, J.N. Medical College,Belagavi.	Guide, Professor,Department of Radio-Diagnosis, J.N. Medical College, Belagavi.	Chairperson JNMC, IEC & Scientist D ICMR National Institute Of Traditional Medicine, Belagavi

PARENTAL CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. "I understand that my child is participating in the study, which includes MRI BRAIN AND SPINAL CORD".

2. I confirm that I have read and understood the information in the patient information sheet. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent my child's participation in the trial outlined above.

3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.

4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my child's body, for medical, scientific or educational purposes provided my child's identity is not revealed in the pictures or by the descriptive texts accompanying them.

5. I understand that there is no significant risk involved in the test that would be done in this study.

6. No guarantee or assurance has given by anyone as to the results that may be obtained.

7. My signature on this form signifies that I have willingly decided to participate my child after understanding the above information".

Participant's Name _____

Parent's Name _____

Signature _____

Name and signature of witness _____

Name and signature of interviewer _____

Date: _____

Place_____

VERBAL ASSENT FROM MINOR (7-12 years)

1. "I understand that I am participating in the study, which includes MRI BRAIN AND SPINAL CORD".

2. I confirm that the information in the patient information sheet has been read to me in the language known to me. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.

3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.

4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.

5. I understand that there is no significant risk involved in the test that would be done in this study.

6. No guarantee or assurance has given by anyone as to the results that may be obtained.

7. My signature on this form signifies that I have willingly decided to participate after understanding the above information".

Participant's Name _____

Signature/ left hand thumb impression_____

Name and signature of witness _____

Name and signature of interviewer _____

Date: _____

Place_____

WRITTEN ASSENT FROM MINOR (13-18 years)

1. "I understand that I am participating in the study, which includes MRI BRAIN AND SPINAL CORD".

2. I confirm that the information in the patient information sheet has been read to me in the language known to me. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.

3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.

4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.

5. I understand that there is no significant risk involved in the test that would be done in this study.

6. No guarantee or assurance has given by anyone as to the results that may be obtained.

7. My signature on this form signifies that I have willingly decided to participate after understanding the above information".

Participant's Name _____

Signature/ left hand thumb impression _____

Name and signature of witness _____

Name and signature of interviewer _____

Date: _____

Place_____

ANNEXURE-II-PROFORMA

KAHER

J. N. MEDICAL COLLEGE, BELAGAVI.

DEPARTMENT OF RADIODIAGNOSIS

TITLE: "ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS-ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

INVESTIGATOR: REG NO: BS0120009

GUIDE: DR. _____

CO-GUIDE: DR._____

PROFORMA FOR DATA COLLECTION

Date of interview : _____

Name : _____

Age : _____ Sex: M/F

OP/IP No _____

Mobile Number: _____

MRI Number: _____

Compalints :

1.Fever –

- Duration :

2. Seizures :

- Generalized –
- Focal –
- Generalized -

3. Altered sensorium –

4. Abnormal behavior :

- Irritability –
- Crying –
- Hallucinations –
- Others –

5. Speech abnormalities –

6. Vision:

- Loss of vision
- Blurred vision
- Eye pain on movement
- Loss of color vision

7. Others :

- Hemiparesis –
- Ataxia –
- Autonomic dysfunction –
- Vertigo
- Headache
- Sensory disturbances
- Bowel and /or bladder dysfunction

8.Recurrent history-

Examination :

1. 1.GCS / MMSE –
2. 2.Speech –
3. 3.Cranial nerves :
4. 4.Motor

system examination:

Tone	Right	Left
Upper limb		
Lower limb		

Power	Right	Left
Upper limb		
Lower limb		

Deep tendon Reflexes	Right	Left
Biceps		
Triceps		
Supinator		
Knee		
Ankle		

6.Coordination –

7.Signs of meningeal irritation –

Investigations

Serum MOG antibody

Serum NMO antibody

MRI findings :

1.Brain

Distribution	T1	T2	FLAIR
Cortical grey matter			
Juxtacortical white matter			
Deep white matter			
Periventricular white matter			
Callosal			
Deep grey matter			
Thalamus			
Basal ganglia			
Brain stem			
Cerebellar			

- Quality of lesion
  - Large (>2 cm)
  - Small(0.3-2cm)
  - Extensive confluent

2.Orbits

Optic nerve	**T1**	**T2**	**FLAIR**
Right			
Left			

- ON sheath thickening
- Edematous ON
- Posterior segment
- Anterior segment

3.Spinal cord

	T1	**T2**	**FLAIR**
Cervical involvement			
Thoracic involvement			
Lumbar involvement			
Conus involvement			

- LETM
- Focal spinal lesion

DIAGNOSIS:

ANNEXURE - III - MRI IMAGES

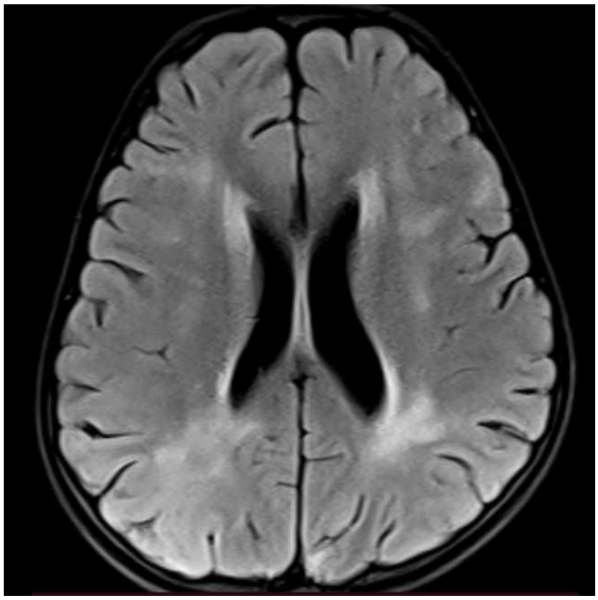


IMAGE 1: ADEM 10 year old male patient- Axial FLAIR weighted brain image showing hyperintensities along the periventricular, deep white matter, cortical and juxta cortical white matter

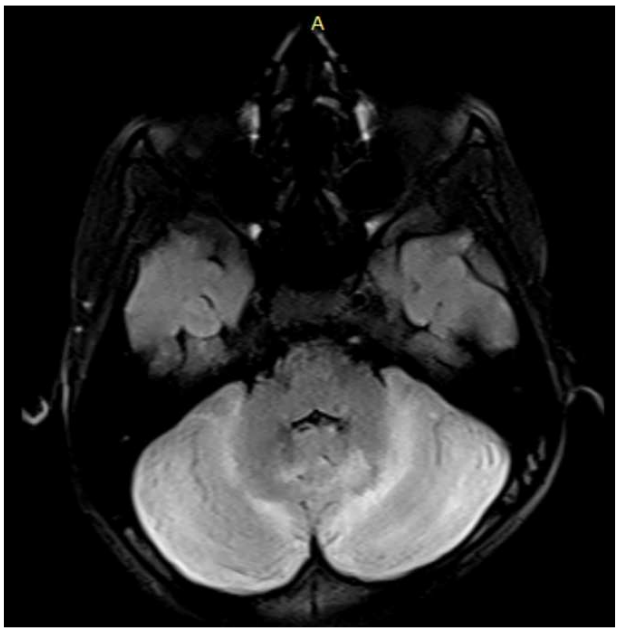


IMAGE 1: ADEM 6 year old female patient- Axial FLAIR weighted brain image showing hyperintensities along the bilateral cerebellar hemisphere and vermis

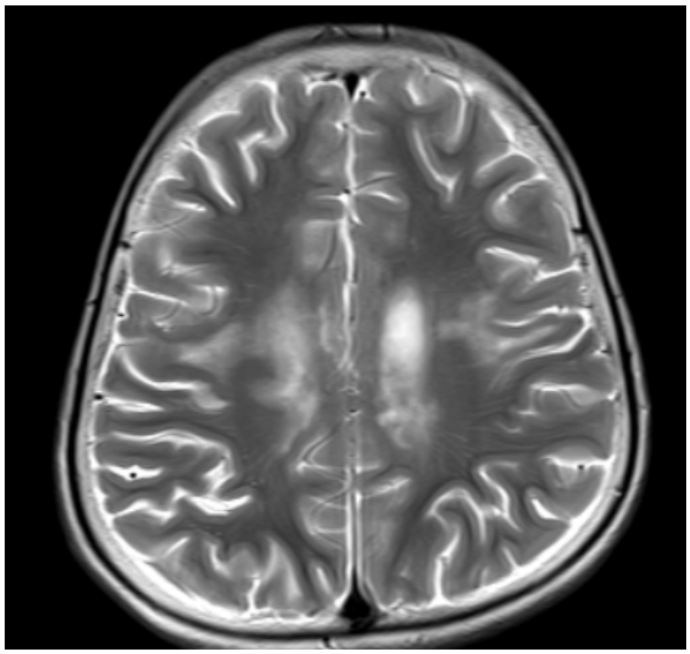


IMAGE 3: MOGAD 12 year old male patient -Axial T2 weighted image showing T2 hyperintensities noted involving the bilateral centrum semiovale and subcortical white matter

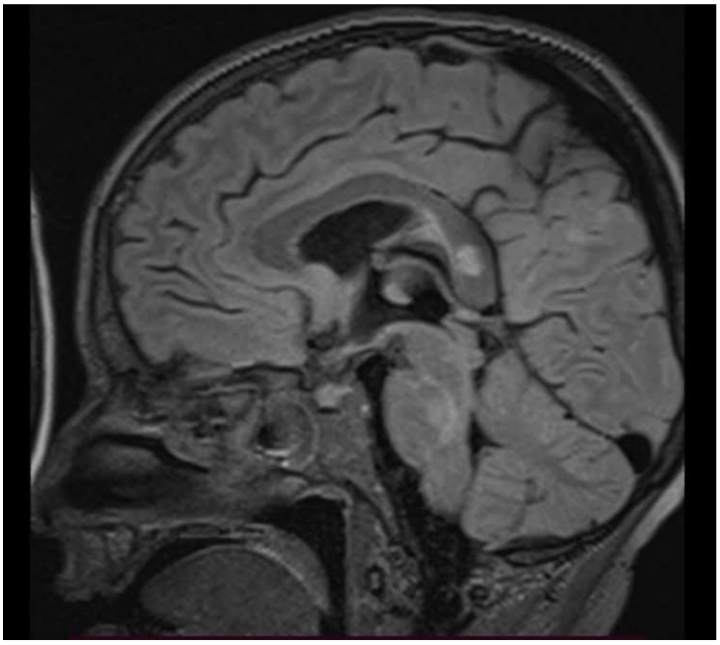


IMAGE 4: MOGAD 7 year old male patient -Sagittal FLAIR weighted brain image showing Hyperintensities along the corpus callosum, pons and juxtacortical white matter

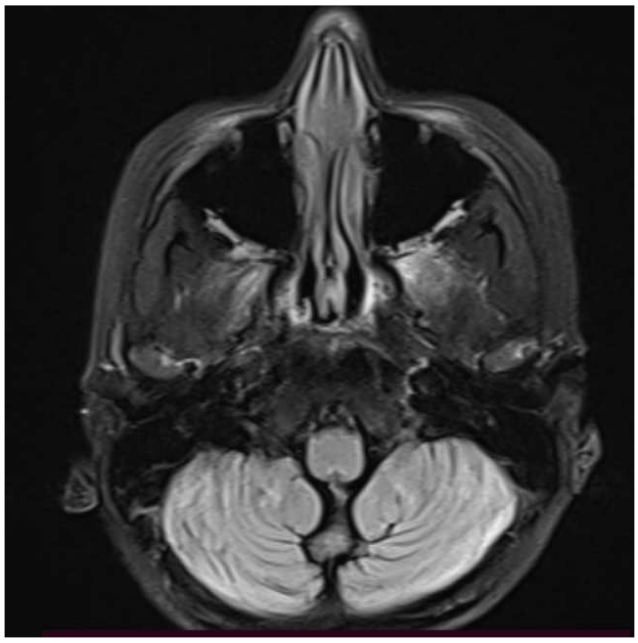


IMAGE 5: NMOSD 17 year old male patient -Axial FLAIR weighted brain image showing hyperintensities along the area postrema

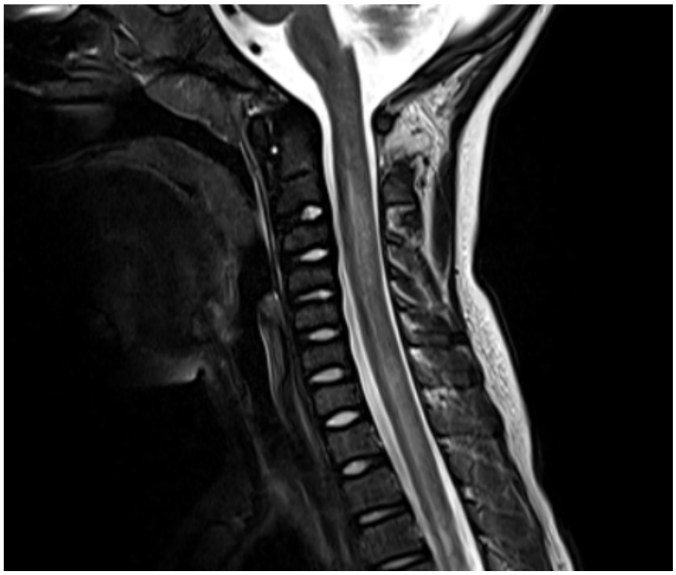


IMAGE 6: NMOSD 13 year old male patient -Sagittal FLAIR weighted spine image showing hyperintensities along the cervical spinal cord

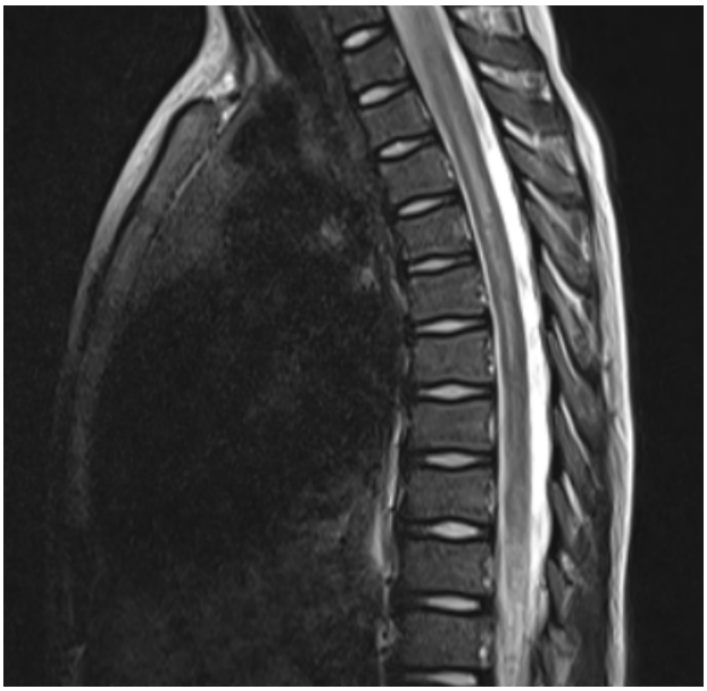


IMAGE 7: NMOSD 10 year old male patient showing Sagittal FLAIR weighted spine image showing hyperintensities along the thoracic spinal cord

			Clinical symptoms										Physical examination		
SL.NO	Age (Years)	Gender	Fever	Seizure	Altered sensorium	Visual disturbance	Limb weakness	Area postrema syndrome	Cerebellar Symptoms	Head ache	Birth history	Immunization history	GCS	Tone	Power
1	15	M	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	NORMAL	Up to age	15	HYPERTONIA	NORMAL
2	13	M	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
3	8	M	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
4	12	F	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	14	HYPERTONIA	REDUCED
5	8	F	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Up to age	15	NORMAL	NORMAL
6	11	F	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	HYPOTONIA	REDUCED
7	3	F	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	NORMAL	Not up to age	15	NORMAL	NORMAL
8	14	F	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
9	18	F	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	NORMAL	Up to age	13	NORMAL	NORMAL
10	1	F	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
11	18	F	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
12	8	M	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	HYPOTONIA	REDUCED
13	16	F	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	NORMAL	Up to age	15	NORMAL	NORMAL
14	6	M	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	PRESENT	NORMAL	Not up to age	15	NORMAL	NORMAL
15	3	M	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	13	NORMAL	NORMAL
16	8	F	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Up to age	15	NORMAL	NORMAL
17	11	M	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	NORMAL	Up to age	13	NORMAL	NORMAL
18	1	M	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NICU admission	Up to age	15	NORMAL	NORMAL
19	13	F	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Up to age	12	NORMAL	NORMAL
20	3	M	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	HYPERTONIA	REDUCED
21	12	F	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
22	8	M	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Not up to age	15	NORMAL	NORMAL
23	9	F	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Up to age	15	NORMAL	NORMAL
24	6	M	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	NORMAL	Not up to age	15	HYPERTONIA	REDUCED
25	11	M	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
26	10	F	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	NICU admission	Up to age	13	HYPERTONIA	REDUCED
27	1	F	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	NORMAL	Up to age	14	NORMAL	NORMAL
28	3	M	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	NORMAL	Up to age	13	NORMAL	NORMAL
29	8	F	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	NORMAL	Up to age	15	NORMAL	NORMAL
30	3	F	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	NORMAL	Not up to age	15	NORMAL	NORMAL

Antibody		MRI Brain findings (T2 and FLAIR hyperintensity)												
MOG antibody	NMO antibody	Cortical grey matter	Juxta cortical white matter	Deep white matter	Periventricular white matter	Periaqueducatl grey matter	Corpus callosum	Thalamus	Basal ganglia	Brain stem	Area postrema	Cerebellum	Large lesion (> 2 cm)	Small lesion(0.3–2 cm)
POSITIVE	NEGATIVE	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT
POSITIVE	NEGATIVE	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
POSITIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT
POSITIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT
POSITIVE	NEGATIVE	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT
POSITIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT
POSITIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT
NEGATIVE	POSITIVE	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT
NEGATIVE	POSITIVE	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT
NEGATIVE	NEGATIVE	PRESENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT
NEGATIVE	NEGATIVE	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT

Orbit				e of spinal cord involver		Spinal cord segment involved					
Unilateral optic nerve	Bilateral optic nerve	Anterior optic nerve	Posterior optic nerve	LETM	Focal spinal cord lesion	Cervical	Thoracic	Lumbar	Conus medullaris	DIAGNOSIS	Follow up MRI
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	MOGAD	MINOR RESIDUALS
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	MOGAD	MODERATE RESIDUALS
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	ABSENT	MOGAD	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	MOGAD	NO FOLLOW UP SCAN
PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	MOGAD	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	MOGAD	NO FOLLOW UP SCAN
ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	MOGAD	COMPLETE RESOLUTION
ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	NMOSD	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	NMOSD	MINOR RESIDUALS
ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NMOSD	COMPLETE RESOLUTION
ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NMOSD	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	NMOSD	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	NMOSD	MINOR RESIDUALS
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	NMOSD	MINOR RESIDUALS
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	PRESENT	PRESENT	ADEM	NO FOLLOW UP SCAN
ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	PRESENT	ABSENT	PRESENT	PRESENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	MINOR RESIDUALS
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	NO FOLLOW UP SCAN
PRESENT	ABSENT	PRESENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ABSENT	ADEM	COMPLETE RESOLUTION