"ROLE OF MAGNETIC RESONANCE IMAGING CLASSIFICATION SYSTEM (MRICS) IN EVALUATION OF CEREBRAL PALSY IN CHILDREN UNDER FIVE YEARS OF AGE: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

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Dr. SANTOSH D. PATIL
M.D.(Radio-Diagnosis)
Professor & HOD
Dept. of Radio-diagnasis
J.N. Medical College, BELAGAVI-10.
KMC Reg No: 58499

Dr. Santosh D Patil M.D. RADIO-DIAGNOSIS

Professor and Head,

Department of Radio Diagnosis,

J. N. Medical College,

Nehru Nagar, Belagavi – 590010

Date: 24.03.25

Place: Belagavi

Dr. N.S. Mahantashetti M. D. PEDIATRICS

Principal,

J. N. Medical College,

Nehru Nagar, Belagavi 590010

PRINCIPAL
Jawaharlal Nehru Medical College
BELAGAVI

Date:

Place: Belagavi

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Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu incipal@jnmc.edu

Ref No: MDC/PG/ Date: 17-03-2025

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Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BS0122014
Postgraduate Student,
2022-23 Batch,
Department of Radio-Diagnosis
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
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Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 300 **Date: 21/07/2023**

To.
BS0122014
PG Student in Radio-Diagnosis
J. N. Medical College,
BELAGAVI.

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

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

ABSTRACT

Background: Cerebral Palsy (CP) is a neurodevelopmental disorder that affects movement, posture, and muscle coordination due to early brain injury or malformation. Magnetic Resonance Imaging (MRI) plays a crucial role in diagnosing and classifying CP, aiding in understanding the underlying pathology and guiding clinical management.

Objective: This study aims to evaluate the role of the MRI Classification System (MRICS) in the assessment of cerebral palsy in children under five years of age.

Methods: A hospital-based, cross-sectional study was conducted over one year at Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 51 children under five years with suspected or diagnosed CP underwent MRI brain imaging. Clinical parameters such as muscle tone, seizures, and developmental delay were recorded. MRI findings were categorized based on MRICS into five classifications: maldevelopments, predominant white matter injury, predominant gray matter injury, miscellaneous lesions, and normal MRI. Data analysis was performed using statistical software R version 4.2.2.

Results: The study showed a male predominance (64.7%) among CP cases. Positive MRI findings were observed in 84.6% of cases, with the most common classification being miscellaneous lesions (25.5%), followed by maldevelopments (21.6%) and predominant gray matter injury (21.6%). Predominant white matter injury and normal MRI findings each accounted for 15.7% of cases. Poor muscle tone was the most frequently observed clinical feature, followed by developmental delay and seizures. The findings of this study highlight differences in MRI classifications compared to previous research, where white matter injury was more commonly reported.

Conclusion: MRICS serves as a valuable tool in the assessment of CP by identifying distinct brain abnormalities and their correlation with clinical presentations. The predominance of miscellaneous lesions in this study suggests that CP pathology varies among populations. MRI-based classification can enhance diagnostic accuracy, aid in prognosis, and inform treatment strategies for children with CP.

[Keywords: Cerebral Palsy, MRI Classification System (MRICS), Brain Imaging, Pediatric Neurology, Neurodevelopmental Disorders, Magnetic Resonance Imaging (MRI).]

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ABBREVIATION	MEANING
CP	Cerebral palsy
MR	Magnetic resonance
MRI	Magnetic Resonance Imaging
CT	Commuted tomography
MRICS	MRI classification system
PVL	Peri-ventricular Leukomalacia
MCA	Middle Cerebral Artery
IUGR	Intra Uterine Growth Restriction
IL-6	Interleukin 6
TNF- α	Tumor necrosis factor- α
HIE	Hypoxic-Ischemic Encephalopathy
IVH	Intraventricular Hemorrhage
CHD	Congenital heart disease
CVI	Cortical visual impairment
SNHL	Sensory-neural hearing loss
GMFCS	Gross Motor Function Classification System
DTI	Diffuse Tensor Imaging
fMRI	functional Magnetic Resonance Imaging
DWI	Diffusion-weighted imaging
NINDS	National Institute of Neurological Disorders and Stroke
NICHD	National Institute of Child Health and Human Development
DNA	Deoxyribonucleic acid
CIT	Constraint-Induced Therapy
Botox	Botulinum toxin
OPD	Outpatient department

Min	Minimum
Max	Maximum
SD	Standard Deviation
PVHI	Periventricular Hemorrhagic Infarction

INTRODUCTION

Cerebral palsy (CP) is neurological disorder which impacts muscle movement, coordination, and posture. Etiology is by damage to the developing brain parenchyma before, during, or shortly after birth [(1)].

The severity of CP usually varies significantly among individuals, with some experiencing mild motor impairments while others facing severe disabilities affecting mobility and daily life activities [(2)]. Although CP, in itself, is a lifelong condition; early intervention, physical therapy, and assistive technologies can enhance function and overall quality of life [(3)].

CP results from disturbances in brain development or injury occurring at an early stage. Several prenatal factors, like maternal related infections (e.g., rubella or cytomegalovirus), genetic influences and oxygen deprivation, contribute to its onset [(4)]. Additionally, complications during birth—including premature delivery, low birth weight, and birth asphyxia—can increase the risk [(5)].

In some cases, postnatal factors such as severe infections (e.g., meningitis), untreated jaundice, or traumatic brain injuries may lead to CP [(6)].

Types

CP is classified on the basis of movement disorders, which include:

1. **Spastic type:** Most prevalent type, usually affects ~70-80% of individuals with CP. It is marked by muscle stiffness, which can be unilateral side of body (hemiplegia), bilateral legs (diplegia), or all four limbs (quadriplegia) [7].

2. **Dyskinetic (Athetoid) type:** Characterized by involuntary movements, often making voluntary actions difficult. It may also impact facial muscles, affecting speech and expressions [8].

3. **Ataxic type:** Primarily affects coordination and balance, which leads to unsteady movements and difficulties executing fine motor skills (like writing or buttoning clothing) [9].

4. **Mixed type:** Some individuals exhibit symptoms of more than one type, leading to a combination of motor impairments [7].

MRI Classification System

Magnetic Resonance Imaging (MRI) is an essential tool in identification of the brain abnormalities associated with cerebral palsy.

MRI findings are categorized into **five** primary patterns [10]:

1. White Matter Injury (Peri-ventricular Leukomalacia - PVL): Most commonly observed abnormality, particularly in preterm infants. It results from reduced oxygen supply to the peri-ventricular white matter, which plays key role in motor control [11].

2. Gray Matter Injury: Damage to deeper brain structures like basal ganglia or thalamus, typically due to birth asphyxia. It is more commonly seen in full-term infants [12].

3. Cortical Malformations: These structural abnormalities, including conditions like lissencephaly and polymicrogyria, arise from disruptions in fetal brain development [13].

4. Miscellaneous Lesions: This category includes brain injuries caused by strokes, congenital infections, or other conditions that do not fit into the primary classifications [14].

5. Normal MRI Findings: In some cases, children diagnosed with CP may exhibit no apparent abnormalities on MRI scans, indicating **potential** genetic or metabolic factors as underlying causes [15].

Aim & Objective of the study

To assess the role of MRI classification system (MRICS) in evaluation of cerebral palsy in children under five years of age.

REVIEW OF LITERATURE

Cerebral Palsy

Cerebral Palsy (CP) is a group of neurological disorders that primarily impact the movement, muscular tone, and body posture. It results from damage to the brain occurring before/ during/ shortly after birth [16].

While CP predominantly affects muscle control, the severity of its effects varies significantly among individuals, ranging from mild motor impairments to profound disabilities that can influence mobility, speech, and cognitive function [17].

Understanding the patterns of brain abnormalities associated with CP is essential, as these patterns are linked to different stages of brain parenchymal development.

Human brain undergoes intricate both structural & functional changes during both intrauterine and postnatal development.

The specific type of abnormality or lesion depends on the timing of the insult. CP pathology is largely determined by the period during which harmful events interfere with or damage the developing brain.

Magnetic Resonance Imaging (MRI) is a valuable tool for visualization of these abnormalities and further assisting in diagnosis [18].

During 1st & 2nd trimesters of pregnancy, cortical neurogenesis occurs, involving processes like gain, relocation and organization of neuronal precursor cells. Any disruptions in these processes can lead to structural abnormalities few of them like classic lissencephaly, pachygyria, or polymicrogyria.

If the motor cortex is affected, CP may develop. Few malformations are associated with genetic factors, particularly when symmetrically distributed [13].

In 3rd trimester, once foundational architecture of brain has largely been formed, growth and differentiation processes dominate, continuing into the postnatal period.

Events such as axon and synapse formation, dendritic branching, and myelination play crucial roles in brain maturation. Disruptions at this stage often lead to **clastic** lesions, with key contributing factors including inflammation, excessive cytokine production, oxidative stress, and an overabundance of glutamate (which triggers excitotoxic damage).

These mechanisms, often initiated by hypoxic-ischemic or infectious conditions, may interact and exacerbate neurological injury [19].

A primary site of injury in CP is the cortical white matter, particularly in cases of periventricular leukomalacia (PVL) or complications of intraventricular hemorrhage. This form of brain injury, referred to as **"encephalopathy of prematurity"** is also associated with neuronal and axonal damage, affecting regions such as the thalamus, basal ganglia, cortex, brainstem, and cerebellum.

However, the most commonly observed pathology linked to CP is white matter injury [11].

In late 3rd trimester, lesions affecting the cortical gray matter, basal ganglia, and thalamus are common causes of CP.

MCA infarcts, particularly in full-term infants, are frequently associated with unilateral spastic CP. Preterm infants may also experience infarcts, primarily affecting the lenticulostriate arteries [20,21].

The pathological patterns associated with CP can be broadly categorized as maldevelopments, predominant white matter injury, and predominant gray matter injury.

These classifications correspond to distinct time periods of brain development, providing insight into the underlying mechanisms of CP and aiding in prompt early diagnosis and intermediation [22].

Causes of Cerebral Palsy

Causes of CP are multifaceted, involving pre-, perinatal and postnatal factors that contribute to abnormal brain development or injury. Identifying these causes is essential for early diagnosis, prevention, and effective management strategies.

1. **Prenatal** Causes (70-80% of CP Cases)

Prenatal factors represent the predominant cause of CP, occurring due to genetic, infectious, inflammatory, or vascular disruptions that affect fetal brain development [16].

- **Genetic and Developmental Disorders**: Genetic mutations and chromosomal abnormalities can disrupt neuronal migration, leading to brain malformations such as lissencephaly or polymicrogyria, which are linked to CP [23]. Advances in genetic testing have helped identify monogenic mutations associated with CP [24].
- **Intrauterine Infections**: Maternal infections, including cytomegalovirus, rubella, toxoplasmosis, herpes simplex, and Zika virus, can trigger neuroinflammation and fetal brain damage, contributing to CP [25].
- **Placental Insufficiency and Hypoxia**: Conditions like preeclampsia, intra-uterine growth restriction (IUGR), and placental abruption may result in chronic hypoxia, leading to periventricular leukomalacia (PVL), a significant cause of CP in preterm infants [26].

- **Maternal Inflammation and Autoimmune Conditions**: Exposure to inflammatory cytokines like IL-6 and TNF- α during pregnancy has been linked to fetal brain injury and an increased risk of CP [27].
- **Toxins & Drug Exposure:** Alcohol, tobacco, and illicit drug in pregnant state can impair fetal brain development. Fetal alcoh3ol syndrome is known to have been associated with a higher incidence of CP [28].

2. **Perinatal** Causes (10-20% of CP Cases)

Perinatal factors involve complications occurring around birth that may result in hypoxic-ischemic injuries, stroke, or infections affecting the developing brain.33

- **Post-natal Asphyxia & Hypoxic-Ischemic Encephalopathy (HIE):** Post-natal asphyxia, where oxygen deprivation occurs during labor, is a major contributor to CP in term infants. Severe HIE is particularly associated with spastic quadriplegia and dyskinetic CP [29].
- **Prematurity and Low Birth Weight:** Preterm birth (<32 weeks) significantly increases CP risk due to immature brain vasculature, making the brain susceptible to PVL and intraventricular hemorrhage (IVH) [30]. Nearly half of preterm infants diagnosed with PVL develop CP [31].

- **Neonatal Stroke:** Perinatal arterial ischemic stroke, often involving the middle cerebral artery, can lead to hemiplegic CP. Risk factors are thrombophilia, CHD and maternal infections [32].
- **Perinatal Infections and Sepsis**: Conditions such as chorioamnionitis, neonatal meningitis, and sepsis can trigger neuroinflammation and white matter injury, contributing to CP [33].

3. **Postnatal** Causes (10% of CP Cases)

Brain injuries occurring postnatally but within first few years of life can also result in CP. Many of these cases are preventable with appropriate healthcare interventions.

- **TBI:** Severe head trauma from accidents, falls, or non-accidental injuries (e.g., shaken baby syndrome) can lead to motor impairments resembling CP [34].
- **Neonatal Infections (Meningitis and Encephalitis):** Bacterial and viral infections such as meningitis, encephalitis, or herpes simplex virus can cause inflammation and brain damage, increasing the likelihood of CP [35].
- **Severe Jaundice (Kernicterus):** Untreated hyperbilirubinemia in newborns can lead to bilirubin toxicity in the basal ganglia, resulting in athetoid or dyskinetic CP [36].

- **Hypoxic Events (Near-Drowning, Cardiac Arrest, Respiratory Failure):** Postnatal hypoxia due to near-drowning, suffocation, or cardiac arrest can lead to brain damage and subsequent CP [37].

Symptoms of Cerebral Palsy

The severity of CP symptoms varies based on the location and extent of brain damage. Some individuals exhibit mild motor difficulties, whereas others experience significant impairments in mobility, speech, and cognition. Symptoms typically manifest in infancy or early childhood and remain stable over time, though associated complications may change.

1. **Motor Impairments:** Motor dysfunctions are a defining feature of CP, affecting muscle tone, reflexes, and voluntary movements.
    - **Abnormal Muscle Tone**: CP is characterized by either excessive (hypertonia) or diminished (hypotonia) muscle tone. Hypertonia results in stiff and rigid muscles, while hypotonia causes muscle weakness and floppiness. Some individuals may experience fluctuating muscle tone [38].
    - **Spasticity and Rigidity**: Spastic CP, the most prevalent form, leads to increased muscle stiffness and exaggerated reflexes (hyperreflexia), which hinder voluntary movements [39].

- **Involuntary Movements**: Dyskinetic CP is associated with uncontrolled twisting, writhing, or jerking movements, particularly in the limbs and facial muscles [40].
- **Coordination and Balance Difficulties**: Ataxic CP disrupts balance and coordination, making fine motor tasks, such as writing or fastening buttons, challenging [4].
- **Delayed Motor Milestones**: Children with CP often experience delays in rolling over, sitting, crawling, or walking. Some may require mobility aids such as walkers or wheelchairs [41].

2. **Postural and Gait Abnormalities**: Many individuals with CP exhibit difficulties in posture and walking patterns.
   - **Scissoring Gait**: Leg crossing at the knees due to increased muscle tone in the thighs, which impairs walking.
   - **Toe-Walking**: Persistent walking on the toes, often resulting from tight calf muscles.
   - **Asymmetrical Movements**: Uneven limb use, such as dragging one leg or favouring one hand when reaching for objects.

3. **Speech and Communication Difficulties:** Speech and language challenges often arise due to muscle impairments affecting the mouth and vocal cords.

   - **Dysarthria**: Weak or uncoordinated oral muscles lead to slurred or slow speech [42].
   - **Aphasia**: Impaired language comprehension or production, commonly associated with brain damage in language-processing areas.
   - **Drooling and Swallowing Difficulties (Dysphagia)**: Poor muscle control in the mouth and throat can lead to excessive drooling and swallowing difficulties, increasing the risk of aspiration pneumonia [43].

4. **Cognitive and Intellectual Impairments**: While not all children with CP have cognitive deficits, approximately 50% may experience intellectual disabilities, with severity dependent on brain injury extent [44].

   - **Learning Difficulties**: Issues with memory, attention, and problem-solving.
   - **Intellectual Disability**: Ranges from mild to severe, affecting independence and daily functioning.

5. **Seizures and Epilepsy:** Epilepsy affects about 30-50% of individuals with CP, particularly those with extensive brain abnormalities [45]. Seizures may be focal, generalized, or absence seizures and often require long-term management with medication.

6. **Sensory Impairments**: Many individuals with CP experience sensory challenges related to vision, hearing, and touch perception.

   - **Visual Impairments**: Conditions such as strabismus (crossed eyes), cortical visual impairment (CVI), or optic nerve damage can result in partial or complete vision loss [46].
   - **Decreased Hearing**: Some paediatric population with CP develop SNHL due to brainstem damage or congenital infections [15].
   - **Tactile Sensory Deficits**: Difficulties in processing touch, pain, or temperature, impacting movement and spatial awareness.

7. **Pain and Musculoskeletal Complications:**

   - **Chronic Pain**: Muscle stiffness, contractures, and joint deformities may cause persistent pain, particularly in adulthood [47].
   - **Hip Displacement and Scoliosis**: Spasticity can lead to hip misalignment (hip dysplasia) or spinal curvature abnormalities (scoliosis), requiring orthopaedic management [48].

- **Contractures and Joint Deformities:** Tight muscles can progressively lead to joint deformities, restricting movement and posture.

8. **Growth and Nutritional Challenges:**

- **Failure to Thrive:** Feeding and swallowing difficulties can result in inadequate weight gain and malnutrition. Some children may require feeding tube support [49].
- **Short Stature:** Growth delays may arise from poor nutrition or hormonal imbalances.

Early Signs

Early indicators of CP often manifest as developmental delays, where infants take longer than usual to achieve motor milestones like rolling over, sitting, crawling, or walking.

Some children may exhibit hypotonia (low muscle tone), making them appear overly relaxed or floppy, whereas others may have hypertonia (high muscle tone), causing stiffness or rigidity in their movements.

Additionally, children with CP may show abnormal posture or demonstrate one-sided preference when reaching, crawling, or moving.

Signs in less than 6 Months of Age

- Head lag when lifted while lying on back
- Unusually body stiffness or, conversely, overly limp.
- Legs stiffness and cross (scissoring motion) when picked up

Signs from 6-10 Months of Age

- Inability to roll over in either direction
- Difficulty bringing hands together or towards the mouth
- Favorism of one hand while keeping the other clenched in a fist

Signs After 10 Months of Age

- Crawling appears asymmetrical, with the baby using one side more dominantly while dragging the opposite side.
- The child is unable to stand while holding onto support.

Early recognition of these signs is essential for prompt intervention, which may include physical therapy, developmental monitoring, and medical support to optimize later years of life and improve motor & sensory function.

Diagnosis and Radiological Findings

Diagnosis of CP is primarily diagnosed through clinico-neural evaluation of motor impairments and developmental history. Neural structures imaging plays crucial role in confirming the findings & diagnosis and identifying potential causes. The diagnostic process involves:

- **Clinical Assessment:** Evaluation of motor function, muscle tone, reflexes, and developmental progress. GMFCS is commonly used to determine motor severity [53].

- **Neuroimaging:** MRI is recommended in all suspected CP cases to identify underlying brain abnormalities [10].

- **Genetic and Metabolic Testing:** If imaging findings are atypical or no clear brain injury is detected, genetic and metabolic tests may be conducted to exclude other neurological disorders [54].

Radiological imaging, particularly MRI, is integral to diagnosing and classifying CP. It assists in identifying patterns of brain injury, predicting prognosis, and differentiating CP from other neurological conditions. Early imaging and intervention can significantly improve outcomes for affected children.

MRI is usually chosen in evaluation of brain pathology, while CT and cranium USG serve as complementary tools in specific cases.

1. **MRI**- Considered gold standard because of the ability to provide detailed visualization of brain internal structures, detect white & gray matter injuries and identify congenital anomalies [16].

   Common findings in individuals with CP include:

   - Periventricular Leukomalacia (PVL): Frequently observed in preterm infants, this condition involves white matter injury near the ventricles, which is associated with motor and cognitive impairments [11].
   - Cortical and Deep Gray Matter Damage: Injuries affecting basal ganglia & thalamus are often linked to hypoxic-ischemic events in full-term and can contribute to spastic or dystonic CP [50].
   - Brain Malformations: Developmental anomalies such as lissencephaly, polymicrogyria, or schizencephaly may result from genetic factors or prenatal disruptions [13].
   - MCA Infarcts: Commonly observed in population with unilateral spastic CP which are usually caused by perinatal stroke [14].

2. **CT**- Serves as an alternative imaging tool, particularly in cases where MRI is unavailable. They are valuable for detecting calcifications indicative of intrauterine infections, such as congenital cytomegalovirus (CMV) or toxoplasmosis [51].

   However, CT lacks the sensitivity of MRI in identifying white matter damage.

3. **Cranial Ultrasound**- Widely used in preterm infants for monitoring brain development and detecting early indicators of PVL, intraventricular hemorrhage (IVH), and hydrocephalus [52]. While it provides a convenient bedside assessment, its resolution is lower compared to MRI.

Types

CP is classified on the basis of movement disorders and muscle tone abnormalities.

Four main types are spastic, dyskinetic, ataxic, and mixed. Each type has distinct clinical features and MRI findings that assist in diagnosis and severity assessment.

1. **Spastic type:**

   - Spastic CP is the most common type, affecting approximately 70-80% of individuals with CP [39].
   - It is characterized by muscle stiffness (spasticity), exaggerated reflexes, and difficulty with voluntary movements.
   - Depending on the limbs affected, it can be further classified into:
     - Spastic Hemiplegia (one side affected)
     - Spastic Diplegia (both legs affected but more than arms)
     - Spastic Quadriplegia (all four limbs affected, severity is usually highest)

MRI Findings:

- PVL: White matter insult in peri-trigonal regions, commonly seen in pre-terms [55].
- Cortical and Subcortical Atrophy: Thinning of the cerebral cortex, impacting motor function [16].
- Enlarged Ventricles: Resulting from loss of surrounding brain tissue [50].

2. **Dyskinetic type:**

   - Characterized by involuntary, uncontrolled movements that worsen with voluntary actions.
   - Caused by damage to the basal ganglia
   - 2 major subtypes:
     - Dystonic type: Sustained muscle contractions leading to posture abnormality.
     - Choreoathetoid type: Rapid, jerky (chorea) or slow, writhing (athetosis) movements, often affecting the face, arms, and trunk.

MRI Findings:

- Basal Ganglia Lesions: Damage involving putamen & globus pallidus, commonly due to hypoxic-ischemic injury at birth [15].
- Thalamic Damage: Disruption in sensory-motor integration, affecting movement control [56].
- Cerebellar Atrophy (in some cases): Leading to additional motor dysfunction [4].

3. **Ataxic type:**

- Least common type, affecting 5-10% of total cases (44).
- Marked by poor coordination, balance difficulties, and tremors.
- Children with ataxic type struggle with precise movements, such as writing or buttoning clothes.
- Walking is often unsteady (wide-based gait), and speech may be slow or slurred (dysarthria).

MRI Findings:

- Cerebellar Hypoplasia or Atrophy: Underdevelopment or degeneration of the cerebellum, responsible for balance and coordination [57].
- Brainstem Abnormalities: Affecting posture and fine motor control [58].
- Delayed Myelination in the cerebellum, impacting nerve signal transmission [59].

4. **Mixed type:**

   - When features of two or more types of CP are present, it is classified as mixed CP.
   - The most common combination is spastic-dyskinetic type, where both stiffness (spasticity) and involuntary movements (dyskinesia) coexist.
   - Symptoms vary widely depending on the areas affected.

MRI Findings:

- Multiple Brain Abnormalities: Damage to both white and gray matter, showing features suggesting PVL, basal ganglia injury, and cerebellar atrophy [10].
- Diffuse Cortical and Subcortical Damage: Leading to a combination of motor and coordination difficulties [60].
- Ventriculomegaly (enlarged ventricles): Seen in some cases, indicating brain volume loss [61].

MRI plays a crucial role in classifying CP types and understanding underlying brain abnormalities. Common linking patterns in different types:

- Spastic type- PVL and cortical atrophy
- Dyskinetic type- Basal ganglia damage
- Ataxic type- Cerebellar atrophy
- Mixed type- Widespread brain injury

MRI findings not only confirm the diagnosis but also aid in prognosis and treatment planning.

MRI Classification System for Cerebral Palsy

MRI is a crucial diagnostic modality for CP, providing valuable insights into brain abnormalities, determining the timing of injury, and guiding treatment approaches. Research indicates that over 80-90% of individuals with CP exhibit abnormal MRI findings, reinforcing its role in confirming clinical diagnoses [(10)].

The MRI classification system (MRICS) categorizes brain abnormalities into five primary patterns, which help in understanding CP's underlying pathology and predicting outcomes [(62)].

1. **White Matter Injury** (Peri-ventricular Leukomalacia - PVL): PVL is the most frequent MRI abnormality in preterm infants with CP. It is characterized by damage to the periventricular white matter due to ischemic events or infections, commonly leading to spastic diplegia or quadriplegia [11].

   Advanced techniques such as diffusion tensor imaging (DTI) have upgraded the capacity to evaluate white matter integrity in such cases [63].

2. **Gray Matter Injury**: Frequently found in term infants with CP, this pattern results from hypoxic-ischemic encephalopathy (HIE) and is marked by damage to deeper gray matter structures like basal ganglia and thalamus.

   Such injuries are strongly associated with dyskinetic CP, where involuntary movements significantly impact motor function [12].

3. **Malformations of Cortical Development**: These structural anomalies arise from disruptions during early brain formation and include conditions such as lissencephaly, polymicrogyria, and schizencephaly.

   These malformations are linked to severe motor and cognitive impairments in individuals with CP [13].

4. **Miscellaneous Lesions**: MRI can also detect other contributors to CP, including congenital strokes, infections (e.g., congenital cytomegalovirus), or metabolic disorders. For instance, perinatal strokes can lead to hemiplegic CP [64].

5. **Normal MRI Findings**: Despite advanced imaging techniques, 10-20% of CP cases present with normal MRI scans. These cases suggest the possibility of genetic, metabolic, or neurochemical factors as underlying causes [15].

   Increasingly, genetic testing and advanced metabolic screenings are used alongside MRI to determine the etiology in these patients [65].

MRI-based classification plays a crucial role in understanding its etiology thus subsequently shaping treatment strategies. Specific injury patterns correlate with different levels of motor impairment, aiding in prognosis [61].

Emerging advancements including functional MRI (fMRI) and diffusion-weighted imaging (DWI) are enhancing the assessment of subtle brain abnormalities and connectivity issues, offering deeper insights into CP's pathophysiology [66].

These evolving imaging technologies hold promise for early diagnosis and targeted therapeutic interventions, potentially improving long-term outcomes in such patients [67].

Therapeutic options and Management

While CP is incurable, various methods help reduce symptoms and improve functionality [68-74]:

1. **Physical Therapy**
   Enhances mobility, strength, and balance through stretching and muscle training

2. **Occupational Therapy**
   Focusing on improving daily skills like dressing, feeding, and writing.

3. **Verbal communication and Language Therapy**
   Helping individuals with speech difficulties & impairments, and swallowing issues.

4. **Medications**

   - **Muscle Relaxants:** Baclofen and botulinum toxin (Botox) help reduce spasticity.
   - **Anticonvulsants:** Used to manage seizures in individuals with epilepsy.
   - **Pain Relievers:** Help alleviate discomfort caused by muscle stiffness.

5. **Assistive Devices**

   Wheelchairs, braces, and communication devices enhance independence.

6. **Surgical Interventions**

   - **Orthopedic Surgery:** Corrects bone deformities and muscle contractures.
   - **Selective Dorsal Rhizotomy (SDR):** Reduces spasticity by cutting selective nerve fibres.

7. **Alternative Therapies**

   - **Aquatic Therapy:** Improves muscle strength and coordination in a low-impact environment.
   - **Hippotherapy:** Uses horseback riding to enhance balance and muscle control.
   - **Stem Cell Therapy:** A potential future treatment currently under research.

Future Directions and Research

Ongoing research is focused on improving the diagnosis and treatment of CP through various approaches:

- **Neuroplasticity-Based Interventions:** Studies have been investigating the neuronal ability to reorganize itself and enhance motor function through rehabilitation.
- **Genetic and Molecular Studies:** Researchers are exploring genetic mutations that may contribute to CP, potentially leading to targeted therapies.
- **Advanced Robotics and AI-Assisted Therapy:** Innovations in robotics and artificial intelligence are aiding in personalized rehabilitation programs.
- **Regenerative Medicine:** Stem cell therapy and neurotrophic factors are being explored for potential neuro-regeneration.

Latest Updates on Cerebral Palsy Research

The NINDS and the Eunice Kennedy Shriver NICHD are leading research efforts into cerebral palsy (CP). Their work has provided insights into risk factors, improved treatment options, and advanced diagnostic methods [75,76].

Genetic Research

Emerging research indicates that genetic mutations have shown to play a role in CP by affecting neural development. Scientists are analyzing DNA from individuals with CP and their families to establish links between specific genes and the condition.

Identifying these genetic factors could enhance early diagnosis and lead to targeted therapies [24].

Brain Damage Mechanisms and Neurochemical Research

Studies show that bleeding in the brain, epileptic seizures, and circulatory issues can trigger an excessive release of neurochemicals, such as glutamate, which, in high concentrations, can damage neurons.

Understanding these mechanisms may help develop drugs to mitigate neurotoxic effects [29].

Periventricular White Matter Damage

Damage to periventricular white matter, a leading cause of CP, is under investigation. Researchers funded by NINDS are exploring how inflammation contributes to white matter injury.

Additionally, a new mouse model and cell-based therapies are being developed to study perinatal white matter damage [77].

Stem Cell Therapy

Stem cell research offers a promising avenue for brain repair in CP patients. Clinical trials are evaluating the safety and effectiveness of umbilical cord blood stem cell infusions in children with CP.

While the results are still pending, this therapy holds potential for neural regeneration [38].

Neuroimaging and Biomarkers

Advanced neuroimaging techniques and blood biomarkers are being used to predict CP in preterm infants.

Wireless imaging systems are being tested to monitor brain activity in children with CP, potentially enabling earlier diagnosis and personalized treatment plans [78].

Systemic Hypothermia

Therapeutic hypothermia has been found to reduce the impact of hypoxic-ischemic encephalopathy (HIE).

Research continues to refine cooling treatments to improve survival rates and neurodevelopmental outcomes in newborns with HIE [79].

Rehabilitation and Therapy Advances

Several rehabilitative techniques are being evaluated to improve motor function in patients with CP:

- **Constraint-Induced Therapy (CIT)** – A method where the stronger limb is restricted, forcing the weaker limb to perform exercises.

  A clinical study funded by NICHD is comparing different durations of CIT to establish best practices [80].

- **Functional Electrical Stimulation (FES)** –Use of low-level electrical currents to stimulate muscles, which may improve strength and mobility.

  Researchers are studying its application in stationary cycling and robotic-assisted gait therapy [81].

- **Botulinum Toxin (Botox) Therapy** – Botox is widely used to reduce muscle stiffness in CP. However, recent studies indicate that it may contribute to bone degradation.

  A NICHD clinical trial is assessing whether combining Botox with low-intensity vibration therapy can preserve bone density in children with CP [82].

Ongoing research continues to enhance our understanding of CP, improve early detection, and expand treatment options.

The findings from these studies will shape future therapeutic interventions, offering a better quality of life for individuals with CP.

MATERIALS AND METHODS

Source of Data:

Children under 5 years of age with clinical suspicion and diagnosis of Cerebral Palsy coming to the Paediatric OPD and are advised and referred for MR brain imaging to Department of Radio-diagnosis in Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.

Study Design:

Cross sectional study

Study Period:

A one year-based hospital study from August 2023 to July 2024.

Sample Size:

According to the reference article, Himmelmann K et al. Neuroimaging patterns and function in Cerebral Palsy-application of an MRI classification, prevalence (p) is 48.7%. Considering that, the sample size is 41 and is derived as follows;

The formula used for sample size calculation is,

$$n = \frac{N \times \{Z_{1-\alpha}^2 \times p \times (100-p)\}}{d^2 \times (N-1) + \{Z_{1-\alpha}^2 \times p \times (100-p)\}}$$

where N is the estimated population, p is the prevalence and d is the error.

On an average 60 patients under 5 years with cerebral palsy with p= 48.7% [proportion of white matter lesion] and d= 15% of p comes out to be 7.30[0.15 x 48.7]

For α=10%, $Z_{1-\alpha}$=1.645, p=48.7, q=51.3

$$n = \frac{60 \times (1.645)^2 \times 48.7 \times 51.3}{(7.3)^2 \times (60-1) + \{(1.645)^2 \times 48.7 \times 51.3\}}$$

$$n = 41$$

Hence, the minimum sample size required is 41. As the sample size increases, the accuracy of result also increases.

Sampling Technique:

Universal sampling method

Inclusion Criteria:

1. Children below five years of age with clinical suspicion of Cerebral Palsy
2. Children below five years of age diagnosed with Cerebral palsy

Exclusion Criteria:

1. Children who are not in a stable respiratory and circulatory condition

Data collection procedure:

After obtaining the ethical clearance, patients were recruited based on the above-mentioned inclusion criteria. Written, informed consent was taken after explaining to the patient's parents/guardians about the protocol in their understandable language.

Detailed history of the presenting complaints was taken by face-to-face interview.

MRI imaging of the brain was performed as soon as the children were in a stable respiratory and circulatory condition. The referring physician and anaesthetist were consulted for the type of anaesthesia.

The patients were positioned headfirst in supine position with a head coil and imaging was performed using 3.0 Tesla MR Equipment (Siemens Magnetom Spectra).

The heart rate, oxygen saturation was continuously monitored.

The images were acquired with a 210 x 448 matrix, a field of view of 18 to 23 cm a section thickness of 4 mm.

MRI sequences obtained:

1. T1 Weighted Image
2. T2 Weighted Image
3. Diffusion Weighted Image
4. Fluid attenuation Inversion recovery
5. Susceptibility Weighted Image
6. Magnetic resonance spectroscopy (if needed)

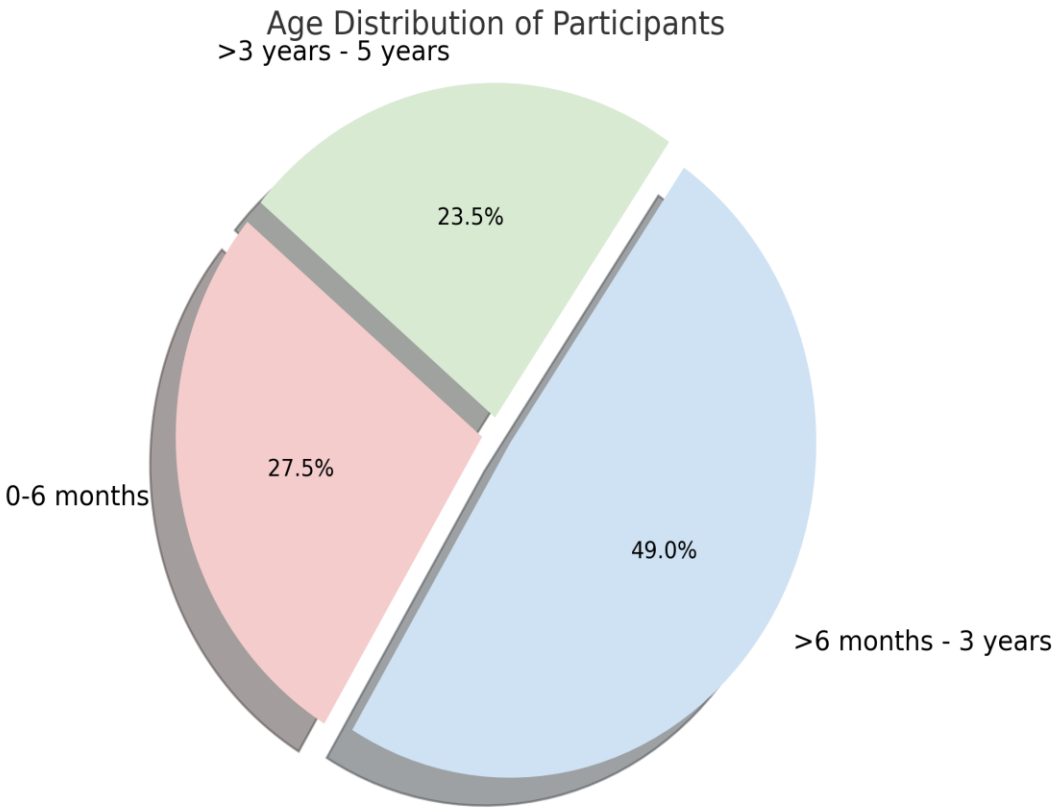
Data processing and analysis/statistical analysis:

Data is analysed using statistical software R version 4.2.2 and Microsoft Excel. Categorical variables were represented by frequency and percentage. Continuous variables were represented by Mean ± SD / Median (Min, Max) form.

[Note: As per the objective, there was no need of any comparison].

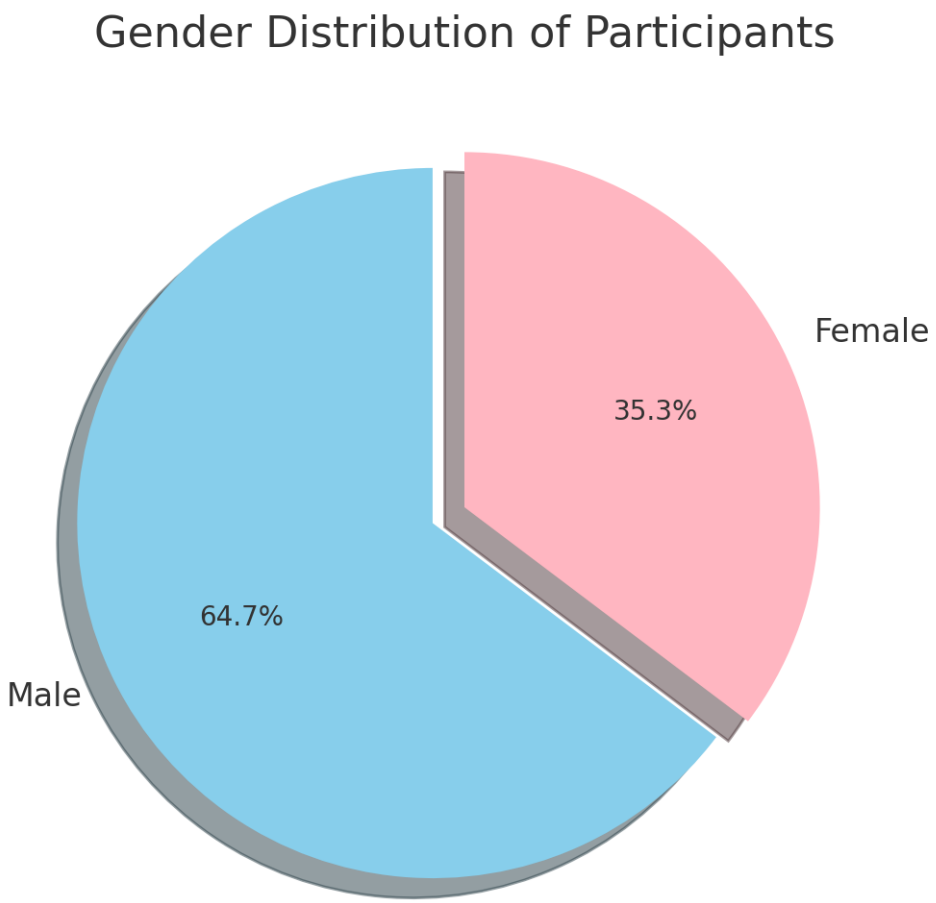
RESULTS

We have included 51 children below the age of 5 years for the purpose of the study. The mean (SD) age was 18.6 months with the minimum of 1 month and maximum of 5 years.



Pie Chart 1: Age Distribution of Participants

This pie chart illustrates the age distribution of **51 participants** categorized into three groups. **14 participants (27.5%)** belong to the **0-6 months** category, **25 participants (49.0%)** fall in the **>6 months - 3 years** group, and **12 participants (23.5%)** are in the **>3 years - 5 years** category. The majority of participants were in the **>6 months - 3 years** group.



Pie chart 2: Gender Distribution of Participants

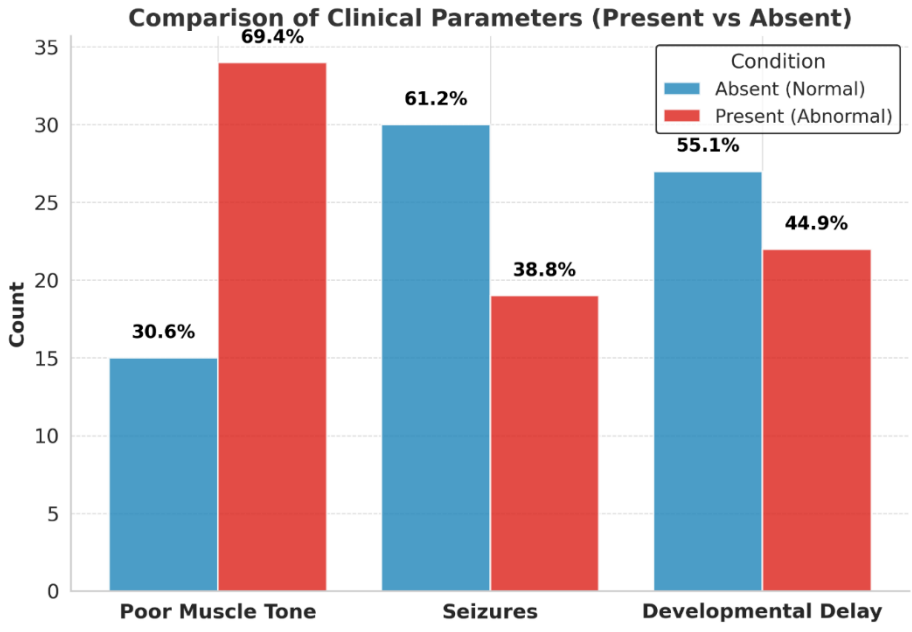
The pie chart illustrates the gender distribution of the **51** participants in the study. Among them, **33 participants (64.7%)** are male, while **18 participants (35.3%)** are female. This indicates a higher proportion of male participants compared to females.

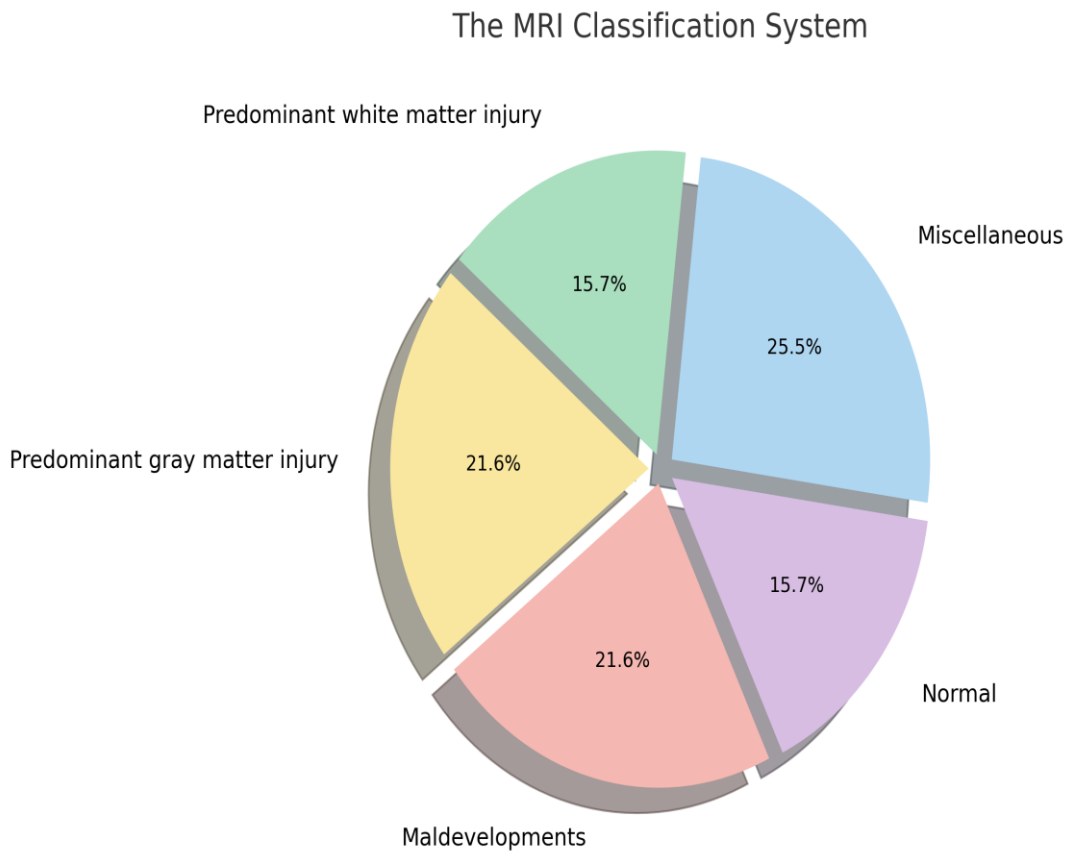
Parameter	Normal (Count, %)	Abnormal (Count, %)
Poor Muscle Tone	Absent: 15 (30.6%)	Present: 34 (69.4%)
Seizures	Absent: 30 (61.2%)	Present: 19 (38.8%)
Developmental Delay	Normal: 27 (55.1%)	Delayed: 22 (44.9%)

Table 1: Summary of Clinical Parameters

Overview of the distribution of poor muscle tone, seizures, and developmental delay. Poor muscle tone was present in **69.4%** of cases, while it was absent in **30.6%**. Seizures were absent in the majority (**61.2%**) of cases, with **38.8%** experiencing seizures. Developmental delay was observed in **44.9%** of cases, whereas **55.1%** had normal developmental progression

Graph 3: Summary of Clinical Parameters





Pie Chart 4: Distribution under MRI Classification System

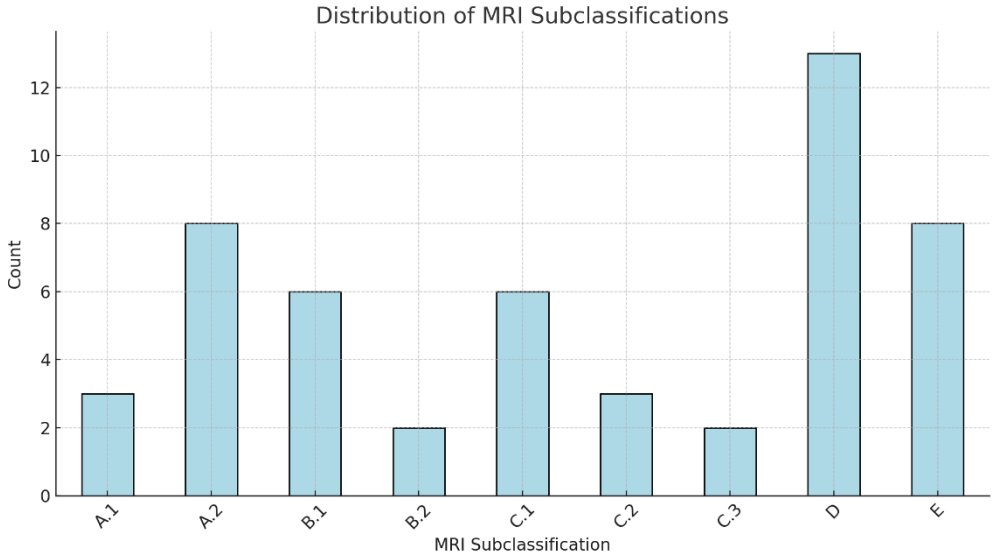
The pie chart represents the distribution of studied cases under different MRI classification categories based on the results:

- **Maldevelopments** account for **21.6%** of the cases, including disorders of cortical formation and other malformations.
- **Predominant white matter injury** represents **15.7%**, covering periventricular leukomalacia (PVL) and sequelae of intraventricular hemorrhage (IVH).
- **Predominant gray matter injury** comprises **21.6%**, involving basal ganglia/thalamus lesions, cortico-subcortical lesions, and arterial infarctions.

- **Miscellaneous cases** make up the largest portion at **25.5%**, which included cerebellar atrophy, cerebral atrophy, delayed myelination, and other conditions.
- **Normal cases** constitute **15.7%**, representing scans without significant MRI abnormalities.

Category	MRICS	Count	Percentage
A	Maldevelopments	11	21.6%
B	Predominant white matter injury	8	15.7%
C	Predominant gray matter injury	11	21.6%
D	Miscellaneous	13	25.5%
E	Normal	8	15.7%

Table 2: Distribution under MRI Classification System



Bar graph 5: Distribution under MRICS (sub-classification)

Bar graph representing the distribution of studied cases under different MRI classification categories based on the results:

- **Maldevelopments** account for **21.6%** (n=11) of the cases, with disorders of cortical formation accounting for 3 of the 11 cased and other maldevelopments being 8 of the total 11 cases
- **Predominant white matter injury** represents **15.7%** (n=8) with PVL being 6 of the 8 cases and sequalae of IVH or PVHI being 2 of the 8 cases
- **Predominant gray matter injury** comprises **21.6%** (n=11) with 6 out of 11 belonging to thalami/ basal ganglia lesions, 3 to cortico & subcortico lesions and 2 being arterial infarctions
- **Miscellaneous cases** make up the largest portion at **25.5%** (n=13)
- **Normal cases** constitute **15.7%** (n=8) representing scans without significant MRI abnormalities.

DISCUSSION

51 children below the age of 5 years were included for the purpose of this study. The mean (SD) age was 18.6 months with the minimum of 1 month and maximum of 5 years with maximum number of cases between 6 months-3 years of age.

This study indicates a higher proportion of male participants [33 (64.7%)] compared to female participants [18 (35.3%)] in our study similar to the study by Nagy E et al [83]

Among 51 patients included in the group, total 43 patients had positive MRI findings (84.6%) which is on par with other studies by R Yin, et al [84] and others [85-88]

Among the clinical parameters studied, poor muscle tone was present in majority of the of cases (n=29) with positive MRI findings followed by presence of developmental delay (n=20) and lastly seizures (n=19).

Patients with positive MRI findings were grouped majorly into Miscellaneous classification (D) being 25.5% of the total cases with maldevelopments (A) and predominant gray matter injury (C) comprising 21.6%, lastly predominant white matter injury (B) and normal (E) group comprising 15.7%.

This is unlike the study conducted by Marnie N Robinson, et al [15] & Sanja Lovrić Kojundžić, et al [89] where predominantly white matter injuries were observed on MRI.

Among MRICS sub-classification,

Disorders of cortical formation accounted for 3 of the 11 cased and other maldevelopments being 8 of the total 11 cases in **MRICS- A**

PVL accounted for 6 of the 8 cases and sequalae of IVH or PVHI accounted for 2 of the 8 cases in **MRICS-B**

6 out of 11 cases in **MRICS-C** belonged to thalami/ basal ganglia lesions, 3 to cortico & subcortico lesions and 2 accounting to arterial infarctions

SUMMARY

- Based on the available data, cerebral palsy in smaller age group is a concerning because it presents with wide range of medical symptoms and diplomatic outcomes are seen.

  Also, etiological spectrum is variable depending on studied population by various research scholars. The changes in MRI will help us to analyse associated abnormalities.

- In this prospective observational study for one year, 51 cases were included who presented with multiple symptoms raising suspicion/ proven cases of Cerebral palsy and were analysed for the variations that were seen on MRI brain imaging.

- Out of 51 children below 5 years of age were taken for the purpose of the study with mean age was 18.6 months

- Based on the available data, the study holds well with the other studies in male predominance for cerebral palsy and positive MRI findings in 84.6% while 15.6% showing no significant findings on MRI.

- This study also showed that poor muscle tone predominant clinical feature in majority of the participants with positive MRI findings followed by developmental delay and seizures.

- Predominance for white matter injury was reported in other studies while our study showed miscellaneous lesions predominance according to MRICS for cerebral palsy.

LIMITATIONS OF THE STUDY

1. Challenges in Interpreting Neonatal MRI

- Interpreting MRI results in neonates is inherently complex due to the ongoing developmental stage of their brains. Distinguishing between normal developmental changes and abnormal ischemic damage can be particularly challenging.
- Misinterpretation of neonatal brain scans may lead to incorrect diagnoses or inappropriate treatment strategies. This complexity underscores the need for highly specialized expertise, which may not always be readily available in all clinical settings.

2. Patient Movement and Need for Anaesthesia

- Neonates, especially those with hypoxic-ischemic encephalopathy (HIE), often require sedation or anaesthesia to remain still during MRI scans. However, this introduces potential risks, such as respiratory complications or adverse reactions to sedatives.
- The necessity for anaesthesia adds complexity to the imaging process. If anaesthesia is either unsafe or insufficient, it can result in lower-quality images or, in some cases, prevent the scan from being performed altogether.

3. Challenges in Predicting Long-Term Outcomes

- While MRI can provide valuable insights into the extent of brain injury, it is not always a reliable predictor of long-term developmental and neurological outcomes.
- MRI findings alone may not provide sufficient information to accurately predict a neonate's future development or recovery potential. This limitation can complicate family counselling and the formulation of prognostic decisions.

4. Additional Challenges:

- Cost of the Study: MRI scans can be expensive, which may limit accessibility for some patients.
- Portability Limitations: MRI equipment is not easily portable, restricting its use to specialized facilities.
- Lack of Control Group: The absence of a control group in the study limits the ability to draw definitive conclusions.

- Uncertainty of Injury Timing: In most cases, the exact timing of the brain injury was unknown, which complicates the interpretation of MRI findings and their correlation with clinical outcomes.

STRENGTH OF OUR STUDY

Of all the observed cases with changes in MRI, has been analysed for the commonest findings which would be one of the reliable pieces of evidence for the further clinical evaluations.

CONCLUSION

In a sample size of 51 for our study, male predominance (overall) with poor muscle tone as major clinical feature was observed in cases with positive findings on MRI in 84.6% of observed participants. Miscellaneous lesions predominance (MRICS-D) was observed followed by predominant gray matter injury and maldevelopments

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ANNEXURE I

INFORMED CONSENT FORM (FROM PARENT/GUARDIAN)

"ROLE OF MAGNETIC RESONANCE IMAGING CLASSIFICATION SYSTEM (MRICS) IN EVALUATION OF CEREBRAL PALSY IN CHILDREN UNDER FIVE YEARS OF AGE: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

Introduction: Cerebral palsy (CP) is the commonest neurodevelopmental disorder of childhood because of a non-progressive damage to the brain, which leads to various activity limitations caused by progressive postural and movement disturbances. Different prenatal, perinatal, and postnatal complications can lead to impairments such as motor dysfunctions, sensory disturbances, perception, intellectual problems, behavior issues, epilepsy, and secondary musculoskeletal problems.

Neuroimaging in children with (suspected) cerebral palsy is useful for contributing to or corroborating the diagnosis, clarifying the etiology and the "timing" of the underlying brain lesion, establishing a prognosis and, in some cases, as a basis for genetic counseling. Therefore, each child with cerebral palsy should undergo at least one neuroimaging procedure.

While cranial ultrasound is often the first and least invasive technique applied in newborns and infants, and computed tomography is beneficial especially in emergency situations, the "gold standard" technique for imaging children with cerebral palsy is magnetic resonance imaging, ideally performed after the age of 2 years [1].

Although not part of the cerebral palsy definition, magnetic resonance imaging (MRI) sheds light on the localization, nature, and severity of brain compromise. The MRI classification system (MRICS), developed by the Surveillance of Cerebral Palsy in Europe (SCPE), describes the typical MRI patterns associated with specific timing of vulnerability in different areas of the brain. The classification has proven to be reliable and easy to use [2].

Globally published literature has reported that the range of CP from 1.5 to 4 per 1000 live births but the prevalence range reported for India is higher ranging from 2.08 to 3.88 per 1000 live births [3]. This study has not been done in our Institution hence this study is done and aims to shed light on different MRICS patterns in cerebral palsy in children.

Withdrawal from participation in the study: Participation in this study in voluntary. You will be free to decide whether your child/ ward should participate in this study or continue participation once enrolled. In case you decide to withdraw your child's/ ward's participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: The participant will not get any benefits by participating in this study. The data gathered will help population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected will be coded, to prevent any identification. The identity will never be revealed. The data collected will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You or your child/ ward will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purpose and/ or presented to scientific groups. However, your or your child's/ward's identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: **Reg No. BS0122014** If you have any question or complaints with regard to your right as study participant, you may contact **The Chairperson,** Ethical committee of JNMC.

Legal rights: By signing this consent form, we are not waving any of your legal rights

CONSENT STATEMENT (FROM PARENT/ GUARDIAN)

I am making a voluntary decision to allow my child/ ward to participate in the study **"ROLE OF MAGNETIC RESONANCE IMAGING CLASSIFICATION SYSTEM (MRICS) IN EVALUATION OF CEREBRAL PALSY IN CHILDREN UNDER FIVE YEARS OF AGE: A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"**. My signature below indicates that I have decided to allow my child/ ward to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator: BS0122014

Signature of the investigator:

ANNEXURE II

PROFORMA

THE MRI CLASSIFICATION SYSTEM

A. Maldevelopments

A.1. Disorders of cortical formation (proliferation and/or migration and/or organization)

A.2. Other maldevelopments (examples: holoprosencephaly, Dandy Walker malformation, corpus callosum agenesis, cerebellar hypoplasia)

B. Predominant white matter injury

B.1. Periventricular leucomalacia, PVL (mild/severe)

B.2. Sequelae of intraventricular hemorrhage (IVH) or periventricular hemorrhagic
infarction (PVHI)

B.3. Combination of PVL and IVH sequelae

C. Predominant gray matter injury

C.1. Basal ganglia/thalamus lesions (mild/moderate/severe)

C.2. Cortico subcortical lesions only (watershed lesions in parasagittal distribution/multicystic encephalomalacia) not covered under C3

C.3. arterial infarctions (middle cerebral artery/other)

D. Miscellaneous

(Examples: cerebellar atrophy, cerebral atrophy, delayed myelination, ventriculomegaly not covered under B, hemorrhage not covered under B, brainstem lesions, calcifications)

E. Normal

Name of Child: -

Age/Sex: -

IP/OP NO: -

Name of Parent/Guardian: -

Age/Sex: -

Vitals	**Baseline**
1. Blood pressure	
2. Temperature	
3. Heart Rate	
4. Oxygen saturation	

- **H/O Seizures-**
- **Muscle tone-**
- **Developmental delay-**

MRI Findings: -

Diagnosis: -

ANNEXURE III

IMAGES

Fig 1- 3.0 Tesla Siemens MRI Machine (Magnetom Spectra)

CASE I

5-month-old girl child presented with history of poor muscle tone and developmental delay since childhood with no history of seizure

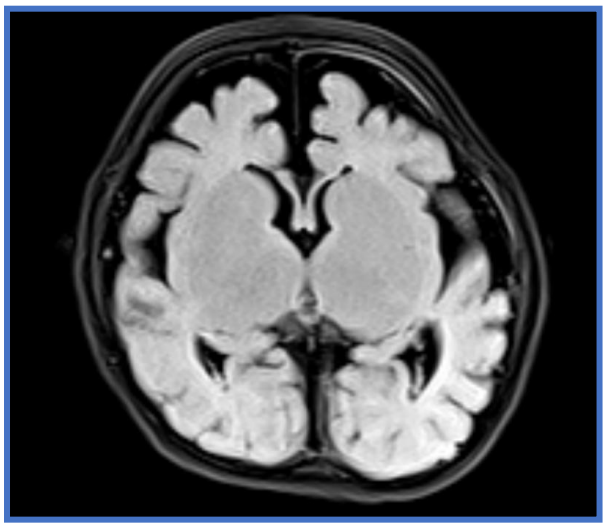

Fig 2

FLAIR Axial WI shows broadening gyri of bilateral insular cortex likely Pachygyria

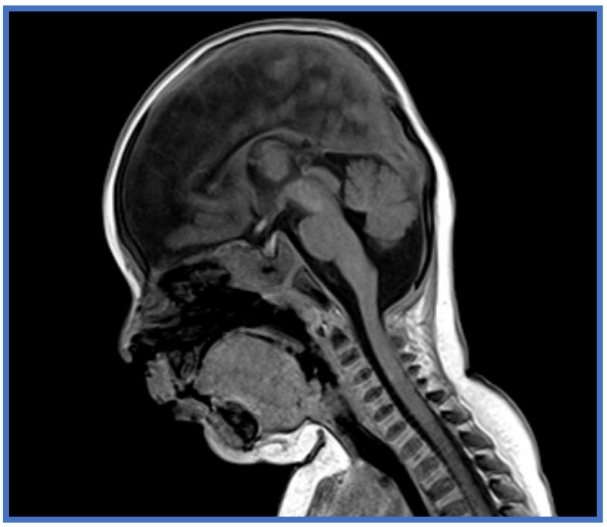

Fig 3

T1 Sagittal WI shows thinning of corpus callosum in its entirety with atrophy

CASE II

7-month-old girl child presented with history of poor muscle tone, seizure (2 episodes) and developmental delay since childhood. History of similar episodes in first born child

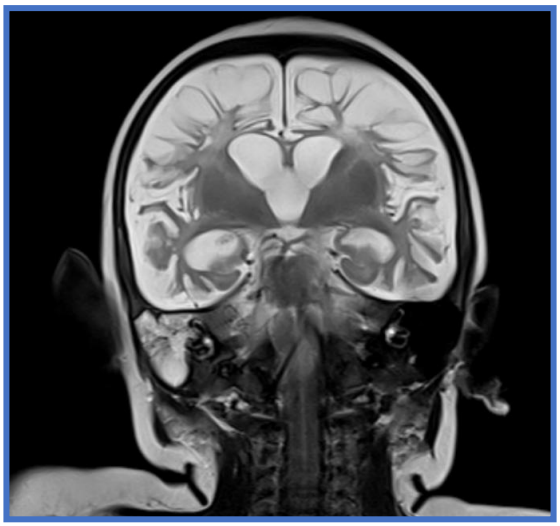

Fig 4

T2 Coronal WI shows Gliosis in bilateral fronto-parieto-temporal region

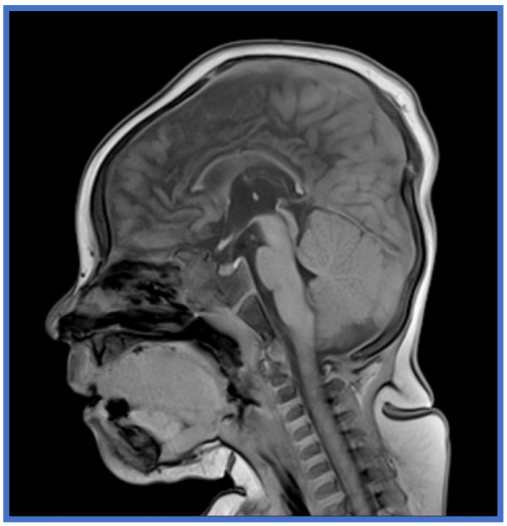

Fig 5

T1 Sagittal WI shows thinning of corpus callosum with atrophy

CASE III

10-month-old boy presented with history of poor muscle tone and seizures since birth with ICU admission.

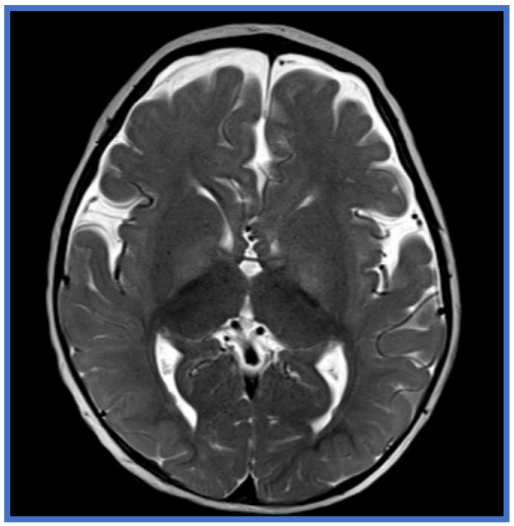

Fig 6

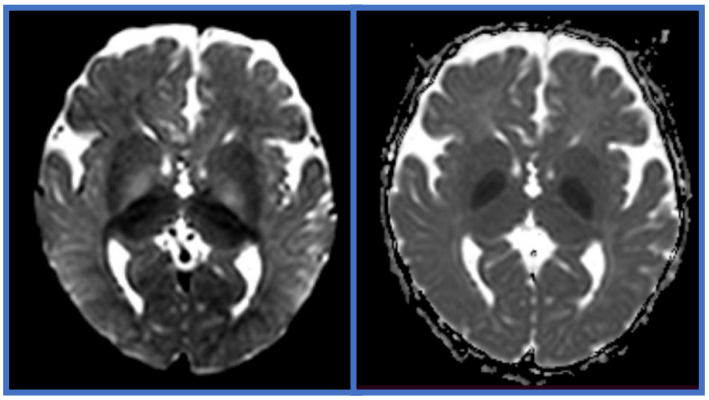

Fig 7

T2 Axial WI shows hyperintensities in bilateral globus pallidi with diffusion restriction on DWI with prominent subdural spaces.

CASE IV

3-month-old girl child presented with history of poor muscle tone with suspicion of cerebral palsy.

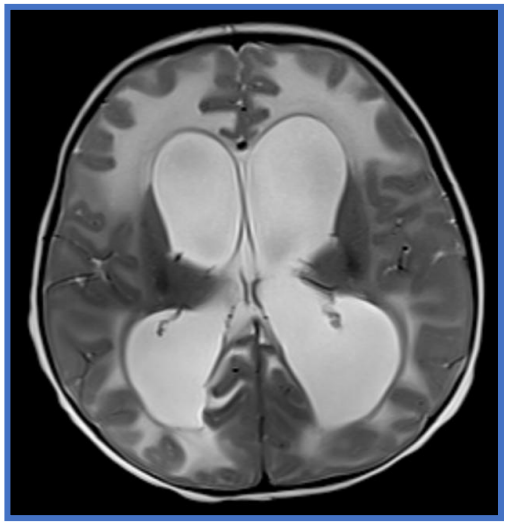

Fig 8

T2 Axial WI shows dilated bilateral lateral ventricles with periventricular seepage

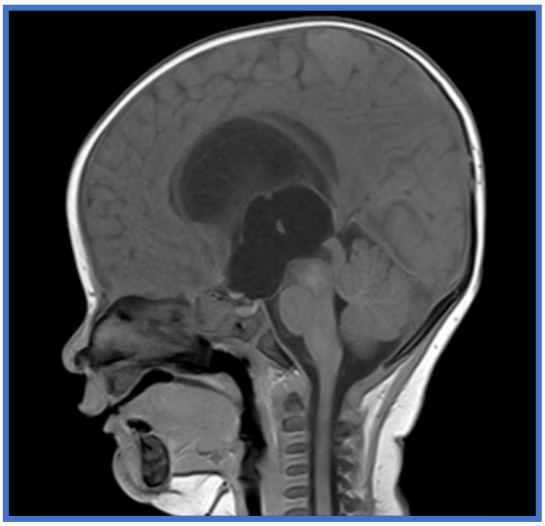

Fig 9

T1 Sagittal WI shows dilated 3rd ventricle with normal appearing 4th ventricle

CASE V

4-month-old boy presented with history of poor muscle tone.

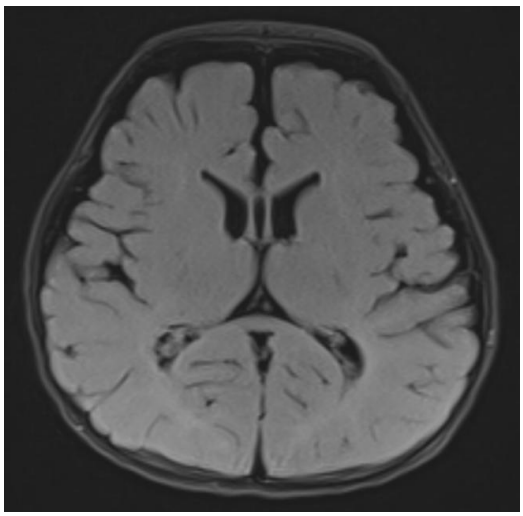

Fig 10

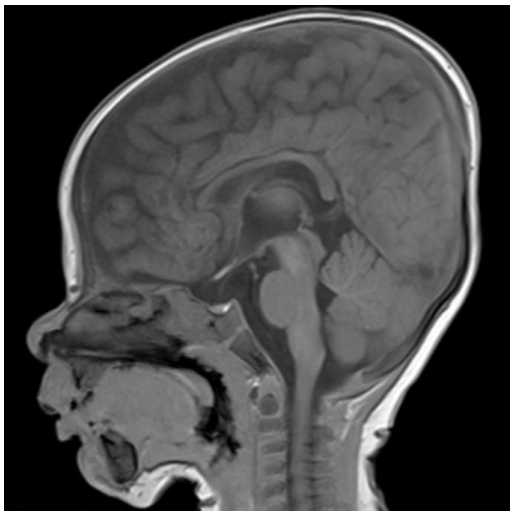

Fig 11

FLAIR Axial WI and T1 sagittal images reveal normal Brain MR anatomy with no significant pathology detected

ANNEXURE IV

KEY TO MASTERCHART

M	**Male**
F	Female
P	Present
A	Absent

A. Maldevelopments

A.1. Disorders of cortical formation (proliferation and/or migration and/or organization).

A.2. Other maldevelopments (examples: holoprosencephaly, Dandy-Walker malformation, corpus callosum agenesis, cerebellar hypoplasia).

B. Predominant White Matter Injury

B.1. Periventricular leukomalacia (PVL) (mild/severe).

B.2. Sequelae of intraventricular hemorrhage (IVH) or periventricular hemorrhagic infarction (PVHI).

B.3. Combination of PVL and IVH sequelae.

C. Predominant Gray Matter Injury

C.1. Basal ganglia/thalamus lesions (mild/moderate/severe).

C.2. Cortico-subcortical lesions only (watershed lesions in parasagittal distribution/multicystic encephalomalacia) not covered under C.3.

C.3. Arterial infarctions (middle cerebral artery/other).

D. Miscellaneous

(Examples: cerebellar atrophy, cerebral atrophy, delayed myelination, ventriculomegaly not covered under B, hemorrhage not covered under B, brainstem lesions, calcifications).

E. Normal

AGE	SEX	POOR MUSCLE TONE	SEIZURES	DEVELOPMENTAL DELAY	MRI CLASSIFICATION SYSTEM	MRI SUB-CLASSIFICATION
5 MONTHS	F	P	No	Delayed	A	A.2
9 MONTHS	F	P	Yes	Delayed	C	C.2
12 MONTHS	M	P	Yes	Delayed	B	B.2
7 MONTHS	F	P	Yes	Delayed	B	B.2
6 MONTHS	M	A	Yes	Normal	A	A.2
1 YEAR	M	A	No	Normal	C	C.2
4 MONTHS	M	P	Yes	Delayed	D	D
13 MONTHS	F	P	Yes	Delayed	B	B.1
8 MONTHS	M	P	Yes	Severely Delayed	D	D
3 MONTHS	F	P	No	Normal	D	D
4 MONTHS	M	P	No	Normal	E	E
2 YEARS	M	A	No	Normal	E	E
10 MONTHS	M	P	No	Normal	E	E
10 MONTHS	M	P	No	Delayed	E	E
6 MONTHS	M	A	No	Normal	D	D
7 MONTHS	M	P	No	Normal	D	D
7 MONTHS	M	P	No	Normal	A	A.2
5 YEARS	F	P	No	Delayed	D	D
7 MONTHS	M	P	No	Normal	A	A.2
3 YEARS	F	P	No	Normal	E	E
5 YEARS	M	P	No	Normal	D	D
3 MONTHS	F	A	No	Normal	A	A.2
15 MONTHS	M	P	No	Normal	E	E
3 YEARS	M	P	No	Normal	A	A.1
5 MONTHS	F	P	No	Normal	E	E
5 YEARS	M	P	No	Normal	C	C.1
7 MONTHS	F	P	No	Normal	C	C.1
12 MONTHS	F	P	No	Delayed	B	B.1
1 MONTH	F	P	No	Severely Delayed	C	C.2
3 MONTHS	M	P	No	Delayed	D	D
11 MONTHS	F	A	No	Delayed	D	D
3 MONTHS	F	P	No	Normal	A	A.2
4 MONTHS	M	P	No	Normal	E	E
4 YEARS	M	P	Yes	Normal	A	A.2
10 MONTHS	F	A	YES	Normal	B	B.1
1.5 YEARS	M	P	Yes	Delayed	B	B.1
10 MONTHS	M	P	Yes	Normal	C	C.1
4 YEARS	F	A	No	Delayed	C	C.1
2 YEARS	M	A	Yes	Delayed	C	C.3
4 YEARS	F	P	Yes	Normal	C	C.3
9 MONTHS	M	A	Yes	Delayed	D	D
7 MONTHS	M	P	No	Delayed	D	D
3 YEARS	M	P	Yes	Normal	C	C.1
11 MONTH	M	P	No	Delayed	B	B.1
4 YEARS	M	A	Yes	Delayed	A	A.1
5 MONTHS	M	P	No	Delayed	C	C.1
3 MONTHS	M	A	Yes	Normal	A	A.1
2 YEARS	M	A	Yes	Delayed	B	B.1
4 YEARS	F	A	Yes	Normal	D	D
2 YEARS	M	P	Yes	Normal	D	D
5 YEARS	M	A	No	Delayed	A	A.2