A Dissertation on

A STUDY OF MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY OF BRAIN IN CHILDREN WITH DEVELOPMENTAL DELAY

Dissertation Submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY CHENNAI - 600 032

With partial fulfillment of the regulations for the award of the degree of

M.D. RADIO DIAGNOSIS

BRANCH VIII

COIMBATORE MEDICAL COLLEGE, COIMBATORE

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CERTIFICATE

This dissertation titled "**MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY OF BRAIN IN CHILDREN WITH DEVELOPMENTAL DELAY"** is submitted to The Tamilnadu Dr. M.G.R Medical University, Chennai, in partial fulfillment of regulations for the award of M.D. Degree in Radio Diagnosis in the examinations to be held during April 2017.

This dissertation is a record of fresh work done by the candidate **Dr. NAINA SURESH**, during the course of the study (2014 - 2017).

This work was carried out by the candidate herself under my supervision.

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The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted / ~~Not accepted~~ and you are permitted / ~~Not permitted~~ to proceed with the above Study.

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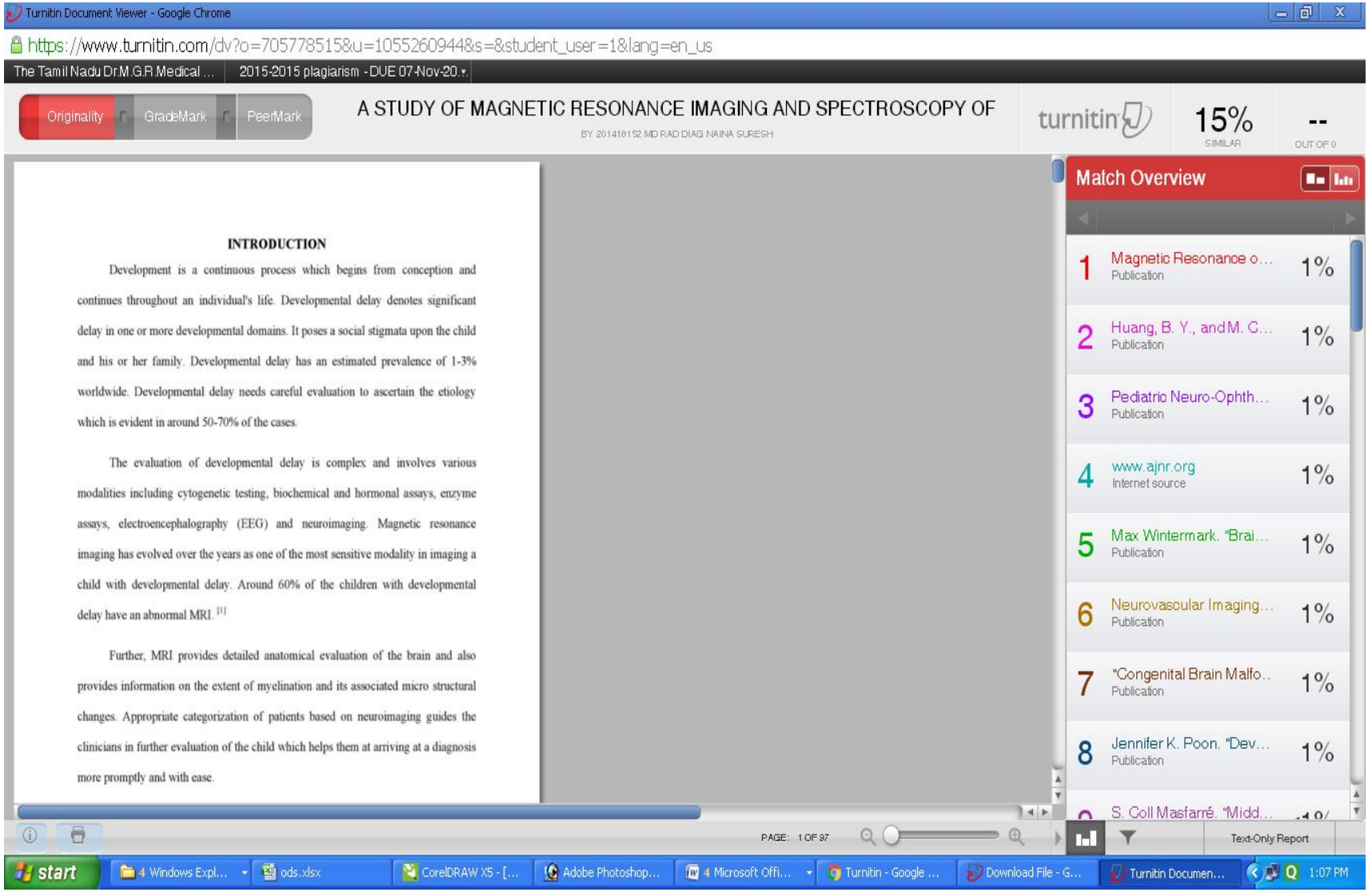
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INTRODUCTION
Development is a continuous process which begins from conception and continues throughout an individual's life. Developmental delay denotes significant delay in one or more developmental domains. It poses a social stigmata upon the child and his or her family. Developmental delay has an estimated prevalence of 1-3% worldwide. Developmental delay needs careful evaluation to ascertain the etiology which is evident in around 50-70% of the cases.
The evaluation of developmental delay is complex and involves various modalities including cytogenetic testing, biochemical and hormonal assays, enzyme assays, electroencephalography (EEG) and neuroimaging. Magnetic resonance imaging has evolved over the years as one of the most sensitive modality in imaging a child with developmental delay. Around 60% of the children with developmental delay have an abnormal MRI. [1]
Further, MRI provides detailed anatomical evaluation of the brain and also provides information on the extent of myelination and its associated micro structural changes. Appropriate categorization of patients based on neuroimaging guides the clinicians in further evaluation of the child which helps them at arriving at a diagnosis more promptly and with ease.
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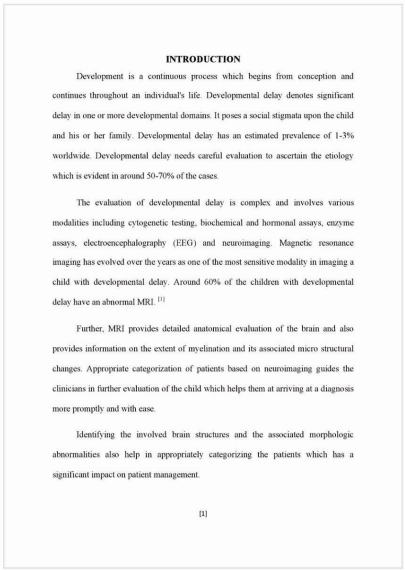

INTRODUCTION

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Identifying the involved brain structures and the associated morphologic abnormalities also help in appropriately categorizing the patients which has a significant impact on patient management.

[1]

DECLARATION

I, **Dr. Naina Suresh** solemnly declare that the dissertation titled **" MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY OF BRAIN IN CHILDREN WITH DEVELOPMENTAL DELAY "** was done by me at Coimbatore Medical College, during the period from July 2015 to July 2016 under the guidance and supervision of **Dr. N. Sundari, M.D.RD,** Professor, Department of Radio Diagnosis, Coimbatore Medical College, Coimbatore. This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch -) in Radio Diagnosis.

I have not submitted this dissertation on any previous occasion to any University for the award of any degree.

Place:

Date: **Dr. Naina Suresh**

ACKNOWLEDGEMENT

I express my sincere gratitude to our respected Dean, **Dr. A. EDWIN JOE, MD., BL.,** Coimbatore Medical College Hospital, Coimbatore for permitting me to conduct this study.

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I would grossly fail in my duty, if I do not mention my gratitude to my **subjects** who have volunteered to participate in the study.

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Last but not the least, I would thank the **Almighty** for His blessings and kindness.

LIST OF ABBREVIATIONS

MRI	-	Magnetic Resonance Imaging
TR	-	Time to repeat
TE	-	Time to echo
FOV	-	Field of view
DF	-	Distance factor
FLAIR	-	Fluid attenuation inversion recovery
NAA	-	N-acetylaspartate
Cr	-	Creatine
Cho	-	Choline
mI	-	Myoinositol
GRE	-	Gradient echo sequence
DWI	-	Diffusion weighted imaging
ADC	-	Apparent diffusion coefficient
WHO	-	World Health Organization
CT	-	Computed Tomography
NMDA	-	N-methyl-D-aspartate
HII	-	Hypoxic ischemic injury
PVL	-	Periventricular leukomalacia
CTEV	-	Congenital Talipes Equinovarus
cLIS	-	Classic lissencephaly

ABSTRACT

A STUDY OF MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY OF BRAIN IN CHILDREN WITH DEVELOPMENTAL DELAY

BACKGROUND:

Developmental delay denotes significant delay in one or more developmental domains. It has an estimated prevalence of 1-3% worldwide. Brain magnetic resonance imaging appears to be the most promising neuroimaging technique in the evaluation of patients with developmental delay.

AIMS AND OBJECTIVES:

Our study aims to identify the spectrum of abnormalities in brain magnetic resonance imaging in children with developmental delay and categorize the morphologic abnormalities. Secondly, the role of Proton Magnetic Resonance Spectroscopy (MRS) to ascertain the magnitude and severity of various neurometabolite ratios in children with normal brain imaging will also be studied.

MATERIALS AND METHODS:

Our study involves the evaluation of 100 children presenting with developmental delay to the Department of Radio diagnosis, Coimbatore Medical College Hospital between July 2015 and July 2016. The children were evaluated with a standard MRI protocol. Clinical and demographic parameters were noted. The various involved brain structures were studied systematically and the morphologic abnormalities were categorized.

RESULTS:

The prevalence of abnormal MRI findings was 78% among the evaluated children. Our study showed predominant involvement of the white matter (50%), ventricles (37%) and corpus callosum (24%). The relative proportion of various morphologic abnormalities was Neurovascular diseases (50%), Congenital and developmental (12%), Non-specific findings (11%), Neoplastic and cystic lesions (3%) and combined etiology (2%). 10 children with a normal MRI were subjected to MR Spectroscopy which revealed no significant differance in the neurometabolite ratios amomg the patients.

CONCLUSION:

MR imaging has good sensitivity in diagnosing various disorders of developmental delay. Careful evaluation of the MRI helps identifying the probable etiology in most if not all cases. Proton MR Spectroscopy is an emerging technique in evaluating children with developmental delay and should be incorporated in the standard MRI protocol in cases where it is feasible. Hence, appropriate diagnosis on MRI helps in guiding the physician to plan further patient management.

KEY WORDS :

Developmental delay, children, magnetic resonance imaging, neurovascular diseases, magnetic resonance spectroscopy.

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INTRODUCTION

Development is a continuous process which begins from conception and continues throughout an individual's life. Developmental delay denotes significant delay in one or more developmental domains. It poses a social stigmata upon the child and his or her family. Developmental delay has an estimated prevalence of 1-3% worldwide [1]. Developmental delay needs careful evaluation to ascertain the etiology which is evident in around 50-70% of the cases.

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Further, MRI provides detailed anatomical evaluation of the brain and also provides information on the extent of myelination and its associated micro structural changes. Appropriate categorization of patients based on neuroimaging guides the clinicians in further evaluation of the child which helps them at arriving at a diagnosis more promptly and with ease.

Identifying the involved brain structures and the associated morphologic abnormalities also help in appropriately categorizing the patients which has a significant impact on patient management.

OBJECTIVES

1. To identify the spectrum of abnormalities in brain Magnetic Resonance Imaging (MRI) in children with developmental delay and categorize the morphologic abnormalities.
2. Role of Proton Magnetic Resonance Spectroscopy (MRS) to ascertain the magnitude and severity of various neurometabolite ratios in children with normal brain imaging

METHODOLOGY

STUDY DESIGN:

This is a prospective, descriptive study involving a sample size of 100 children presenting with developmental delay. The children are referred to the **Department of Radio diagnosis, Coimbatore Medical College Hospital** for neuroimaging as a part of their evaluation.

STUDY PERIOD:

Between July 2015 and July 2016.

STUDY DURATION:

One year.

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA:

Children with developmental delay aged between 6 months and 10 years, referred to our department for Brain Magnetic Resonance Imaging to evaluate the cause of developmental delay.

EXCLUSION CRITERIA:

i) Children younger than 6 months and older than 10 years of age.

ii) Children with progressive neurodevelopmental disorders.

iii) Children with congenital CNS infections, meningitis and encephalitis.

iv) Children with recognized syndromes including chromosomal disorders.

STUDY PROTOCOL

PRELIMINARY SCREENING:

The children presenting with developmental delay will be evaluated clinically by a paediatrician with expertise in developmental paediatrics and will be referred for brain Magnetic Resonance Imaging to the Department of Radiodiagnosis.

The commonly used scales to assess developmental delay include **DENVER II (revision of the Denver Developmental Screening Test, DDST)** and **Trivandrum Developmental Screening Chart.**

The clinical and demographic details of the patient were noted down. Informed consent for neuroimaging will be obtained from the parents or legal guardian of the child.

SEDATION:

Infants and younger children will be sedated using Syrup Triclofos (Syp pedicloryl) 50 mg/kg just before imaging the child.

In children inadequately sedated with the above drug, IV midazolam 0.1 mg/kg/dose under strict clinical supervision and monitoring will be used for sedation.

Older children who were well cooperative for the imaging procedure were imaged unsedated.

Necessary emergency equipment and drugs were made available in the MRI room.

MRI PROTOCOL

All patients will be evaluated using a 1.5 Tesla MRI system (**Magnetom Symphony, Siemens Healthcare**). The patients were placed in the supine position and the head was placed securely in the receiver coil. The scan was performed under the supervision of a qualified Radiologist in the workstation.

The following sequences will be performed in all patients.

T2 axial	TR/TE 5400ms/111ms, slice thickness 5 mm, slices 20, FOV 230 mm, DF 30%
T2 coronal	TR/TE 3500ms/116ms, slice thickness 3 mm, slices 18, FOV 230 mm, DF 20%
T1 mpr sagittal	TR/TE 1450ms/3.93ms, slice thickness 3 mm, FOV 230 mm, DF 50%
FLAIR axial	TR/TE 8110ms/114ms, slice thickness 5 mm, slices 19, FOV 230 mm, DF 30%
T1 tir coronal	TR/TE 6200ms/70ms, slice thickness 3 mm, slices 18, FOV 230 mm, DF 20%
DWI and ADC map	TR/TE 3600ms/98ms
Gradient echo sequence	TR/TE 540ms/19ms, slice thickness 5 mm, FOV 230 mm, DF 30%, flip angle 20 degrees
T1 axial	TR/TE 310ms/7.7ms, slice thickness 5 mm, slices 19, FOV 230 mm, DF 30%

Table 1: Table showing the various MRI sequences used in the study.

The children with a normal MRI of the brain were subjected to **Proton MR spectroscopy**. Multivoxel MR spectroscopy with the voxels placed in the subcortical white matter of the frontal and parieto-occipital lobes bilaterally

(TR/TE 1400ms/135ms) was performed. The following neurometabolite ratios were calculated.

i. N-acetylaspartate (NAA)/creatine (Cr)

ii. Choline (Cho)/Cr

CATEGORIZATION OF THE PATIENTS

STEP 1:

The children were categorized based on their gestational age into preterm, term and late preterm [2] based on the following table

	Definition
Preterm	Born at 37 weeks gestation or less
Late preterm	Born between 34-0/7 and 36-6/7 weeks of gestation
Term	Born between beginning of week 38 and end of week 41 of gestation

Table 2: Table showing classification of neonates on the basis of gestational age.

STEP 2:

The following brain structures were systematically evaluated based on a study by **Widjaja et al** [3]

i. ventricles
ii. corpus callosum
iii. gray matter
iv. white matter
v. limbic system
vi. basal ganglia
vii. brain stem
viii. cerebellum

ix. cranial vault

STEP 3:

The proportion of patients with a normal MRI were noted. The various abnormal MRI findings and their corresponding diagnosis were categorized based on a study by **Williams et al** [4]. The various morphologic abnormalities were categorized into one or more of the following categories

i. Normal
ii. Non specific findings like cavum septum pellucidum, cavum vergae, ventriculomegaly, prominent Virchow-Robin spaces (VRS), prominent cisterna magna etc.,
iii. Neurovascular including periventricular leukomalacia, hypoxic - ischemic injury, encephalomalacia, atrophy, gliosis etc.,
iv. Congenital and developmental including vascular malformations
v. Neoplastic and cystic lesions
vi. Combined or multifactorial

The results were analyzed systematically and relevant observations were made. All data were analyzed with a statistical software package - Statistical Package for the Social Sciences (**SPSS**), version 16.0 for Windows.

REVIEW OF LITERATURE

Developmental disabilities have a worldwide prevalence of 5-10% in children. Developmental delay is **defined as the process of significant delay in one or more of the developmental domains** [1] (more than two standard deviations below the mean) namely

1) Gross motor
2) Fine Motor & Visual
3) Auditory, speech and language
4) Social and behavioural

Developmental delay can be either **specific or global**. Specific or isolated developmental delay involves delay in a single domain (eg: Motor or speech and language). Global developmental delay implies delay in two or more developmental domains. Global developmental delay has an estimated prevalence of 1-3% in children [5]

Developmental delay needs careful and prompt evaluation to ascertain the etiology which is evident in around 50-70% of the cases. There are a huge myriad of causes of developmental delay. The causes can be congenital or acquired [5]

The below mentioned table gives us a list of the commonly encountered causes of developmental delay.

1.	**Genetic or syndromic**	Trisomy syndromes Neurocutaneous syndromes Fragile X Syndrome Angelman's syndrome
2.	**Metabolic**	Mucopolysaccharidosis Phenylketonuria Urea cycle disorders
3.	**Endocrine**	Congenital hypothyroidism
4.	**Cerebral Malformations**	Neuronal Migration Disorders
5.	**Infections**	Perinatal eg: Rubella, CMV Neonatal eg: Neonatal meningitis
6.	**Toxins**	Fetal : Maternal alcohol or drugs during pregnancy Childhood : Lead toxicity
7.	**Traumatic**	
8.	**Cerebral Palsy**	
9.	**Developmental coordination disorder**	

Table 3: Classification of causes of developmental delay.

The evaluation of a child with developmental delay is crucial and involves a multidisciplinary approach. Detailed antenatal, perinatal and postnatal history is mandatory. A detailed clinical examination including neurological, auditory and visual evaluation also plays a significant role in evaluating a child with developmental delay. Clinical evaluation of the child has to be supplemented with various laboratory investigations including cytogenetic testing, hormonal and biochemical assays, metabolic screening, antibody titres, electroencephalography (EEG) etc.,

The WHO estimates around 5% of the paediatric population worldwide to be suffering from some form of disability. The prevalence of developmental disorders in the United states is around 16-18% in children below18 years of age.

The **prevalence of developmental delay in India** is around **1.5-2.5%** in children under two years of age.

DEVELOPMENTAL SCREENING TOOLS:

There are various screening tests implemented to diagnose developmental delay with a great deal of certainty. The screening tools can be interview based as in the case of the **Parents' Evaluation of Developmental Status (PEDS)** or can be based on a questionnaire, for example the "**Ages and Stages Questionnaire" (ASQ).**

One of the commonly used development screening tools is the **Denver II** formerly called the **Denver Developmental Screening Test (DDST)**. This is a more appropriate surveillance tool in view of its psychometric qualities. The Denver II has a low specificity of around 43% causing over identification of children [6]

Some of the screening tools developed in India include the **Baroda Development Screening Test for Infants** developed from the Bayley scales of Infant Development. **The Developmental Assessment Tool for Aganwadis (DATA)** is also a useful screening tool to diagnose developmental delay in toddlers.

The Trivandrum Developmental Screening Chart (TDSC) is another screening tool developed using the Baroda Norms. Another broad based screening

tool is the **Disability Screening Schedule (DSS)** useful for identification of all major disabilities in children under 6 years of age.

Detailed and careful evaluation and appropriate investigation help in determining a cause in around 50-70% of the cases of developmental delay. Neuroimaging plays an important role in the evaluation of a child with developmental delay [7]

There are various neuroimaging options to choose from in the current imaging scenario ranging from Neurosonography, Computed tomography, Magnetic resonance imaging to more sophisticated techniques like Magnetic resonance spectroscopy (MRS), Diffusion Tensor Imaging (DTI), functional MRI etc.,

MRI appears to be the most promising neuroimaging technique in evaluating children with developmental delay. It provides better anatomic details and hence improved diagnostic accuracy.

Based on previous studies, **around 60 % of the children with developmental delay have an abnormal MRI**. Magnetic resonance imaging permits highly sensitive evaluation of the maturation of gray and white matter, in addition to assessment of micro structural changes secondary to myelination [7]

PRINCIPLES OF BRAIN DEVELOPMENT:

The cerebral hemispheres are formed from the **cerebral vesicles** that appear around 35 days of gestation as outpouchings of the telencephalon from the regions of the foramen of Munro. The cerebral vesicles exhibit marked expansion with the development of the cellular layer's which form the germinal matrices [8]

The cerebral hemispheres eventually develop from the cells in the germinal matrices. The neurons of the cerebral cortex are formed from the ventricular zone of the germinal matrix, while the sub ventricular zone generates the glial cells. The occipital pole begins to develop at around the 43rd gestational day and the temporal pole develops at around the 50th gestational day. The cerebral sulcation also follows an orderly appearance. The sylvian fissure is usually present upon imaging the fetus in the fourth gestational month. During the fifth month the parietooccpital, calcarine and cingulate sulci appear. By the end of the sixth month the central, superior temporal and interparietal sulci apperar. The precentral, postcentral, superior frontal and middle temporal sulci appear during the seventh gestational month.

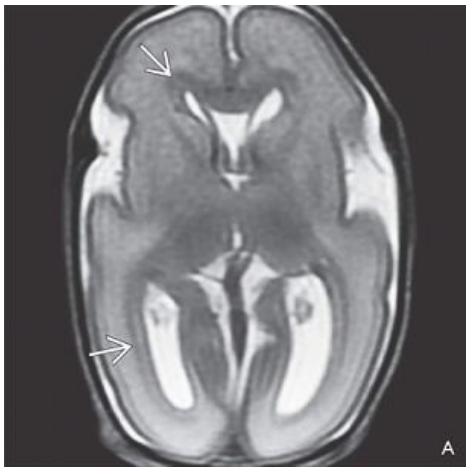

Figure 1: Axial T2 weighted images in a 26 week premature infant. The sylvian fissures are just beginning to form.

IMAGING OF THE PRETERM BRAIN

Transfontanelle ultrasonogram is an useful preliminary screening modality but does not provide information about the myelination pattern. CT due to its low contrast resolution provides suboptimal information on assessment of

myelination. Further, CT also requires the use of ionizing radiation and hence it is seldom used to image the infant brain [9]

The brain is essentially agyric prior to 24 weeks of gestation with the exception of the wide sylvian fissures. On MRI the cortex appears hyperintense with respect to the underlying white matter on T1 weighted images and very hypointense compared to the white matter on T2 weighted images. The last portion of the germinal matrix to involute is the ganglionic eminence at the region of the caudate heads.

Between the germinal zones and cortex is the **"intermediate zone"** or the developing fetal white matter. Between 24-28 weeks, the sulci mentioned above develop. There is also myelination of some of the brain stem structures like the median longitudinal fasciculus, the medial and lateral lemnisci and the superior and inferior cerebellar peduncles [9]. The basal ganglia and thalami are also well seen with a signal intensity similar to the cerebral cortex on both T1- and T2 weighted images.

Around 31- 32 weeks, the myelinated dorsal brain stem is contrasted by the unmyelinated ventral pons. The posterior limb of internal capsule remains hypointense on T1 weighted images upto 38 to 40 weeks [10]

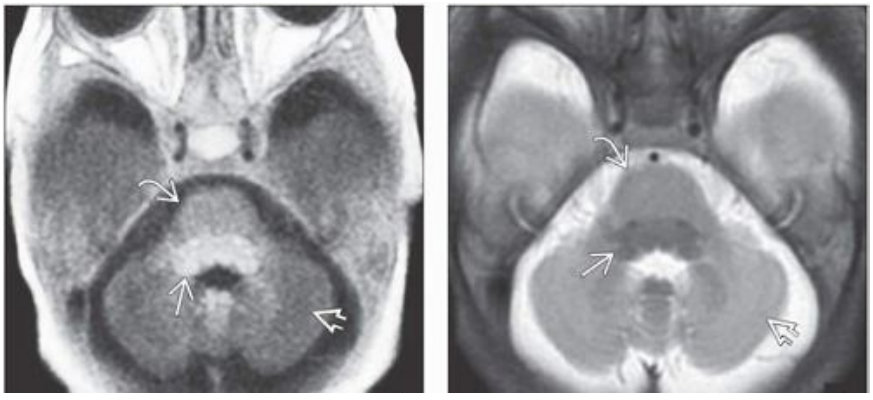

Figure 2: Axial T1 (left) and Axial T2 (right) weighted images showing myelination in the dorsal brainstem (straight arrow). The ventral brainstem (curved arrow) and cerebellar white matter (block arrow) are unmyelinated.

NORMAL POSTNATAL BRAIN DEVELOPMENT:

Myelination of the fetal brain begins around the fifth month and continues throughout life. In general, **myelination progresses from caudal to cephalad and from dorsal to ventral**. Hence the occipital lobes myelinate earlier than the frontal lobes [10]

SPIN ECHO MRI OF POSTNATAL BRAIN:

The general rule of myelination goes by the fact that the changes of white matter maturation are best seen on T1 weighted images during the first 6-8 months of life and on T2 weighted images between 6 to 18 months.

T_1 WEIGHTED IMAGES:

The newborn brain is grossly similar to the adult brain T2 weighted imaging characteristics, in that the white matter has lower signal intensity than the gray matter. The structures exhibiting high signal intensity at birth include the globus pallidus, ventral lateral portion of the thalamus, central portion of the corona radiata and the posterior portion of the posterior limb of the internal capsule. The anterior limb of the internal capsule does not develop high signal upto 2-3 months of age [9].

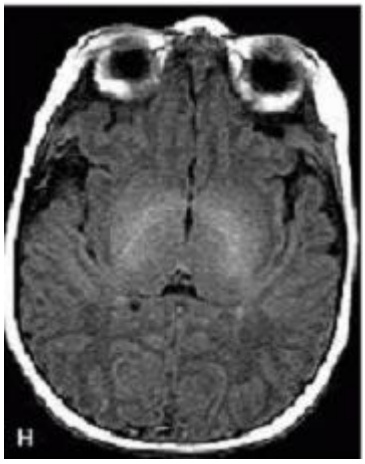

Figure 3: Axial T1 weighted image showing myelination of the posterior limbs of the internal capsule and lateral thalami in a normal 38-40 week infant.

The splenium of the corpus callosum shows high signal intensity in all infants by 4 months. The myelination progress anteriorly, hence the genu exhibits high signal by 6 month of age.

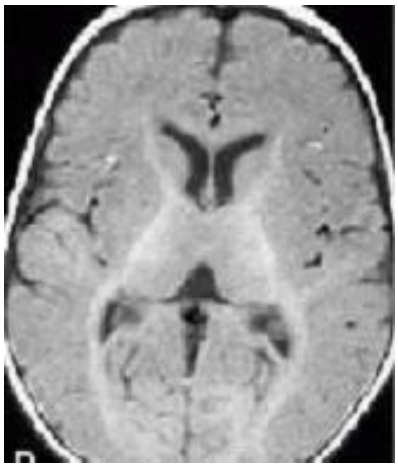

Figure 4: Axial T1 weighted image in a normal 4 month old infant showing myelination of the anterior limb of internal capsule.

T2 WEIGHTED IMAGES:

The ventral brainstem becomes of similar low signal intensity as the dorsal brain stem by the fifth postnatal month[9]. The internal capsule matures in a posterior to anterior manner. The anterior limb starts to become hypointense by

the 7th month and is completely hypointense by the 11th month. The corpus callosum also myelinates in a similar fashion with the splenium exhibiting low signal by 6 months and the genu by 8 months of age.

The subcortical white matter matures last proceeding from posterior to anterior. Hence by the end of the second year of life the white matter myelination is complete with the exception of the "terminal zones" [10].

There are areas of persistent high signal intensity in the white matter lateral to the bodies of the lateral ventricles and more aptly, dorsal and superior to the trigones on T2 weighted images. These regions are called the **"terminal zones" of myelination** and are seen throughout the first decade of life. It is important to differentiate these terminal zones from periventricular leukomalacia.

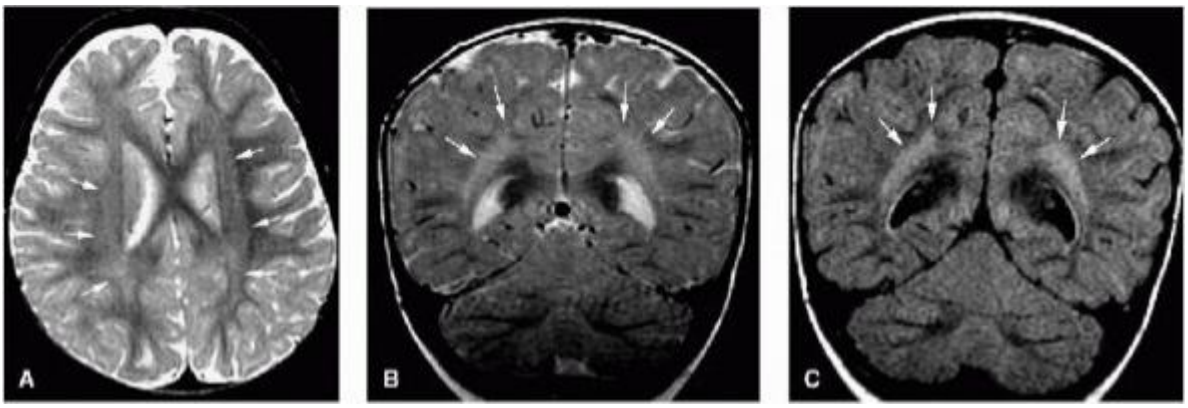

Figure 5: A-C : Axial T2 (A) and coronal T2 (B) weighted and coronal FLAIR (C) images showing increased signal intensity around the trigones representing the "terminal zones" of myelination (arrows).

WHITE MATTER INJURY OF PREMATURITY:

This type of brain injury in premature neonates is called **periventricular leukomalacia** (PVL). It most commonly involves the deep white matter of the

hemispheres. Not all cases of periventricular white matter injury is a result of hypoxic ischemic injury. Infections, hydrocephalus and metabolic diseases are a few causes of periventricular white matter injury[10].

ETIOPATHOGENESIS:

The occurance of white matter injury is related to many different factors such as intrauterine infections, chorioamnionitis, premature rupture of membranes and hypotension with impaired auto regulation. However recent data suggest that the injury results from hypoxic injury to the late oligodendrocyte progenitors, or to the neurons of the subplate, which is a deep transient layer of the cerebral cortex.

The most common location is the posterior periventricular white matter adjacent to the trigone of the lateral ventricles and the frontal white matter adjacent to the foramina of Munro. The incidence of this injury increases with decrease in the gestational age [10].

IMAGING:

On sonographic evaluation, white matter injury most commonly manifests as areas of increased echogenicity (called **periventricular "flare")** which can progress to periventricular cysts and end stage PVL which manifests as ventricular enlargement. However, ultrasonography has a decreased sensitivity and positive predictive value in the diagnosis of newborn white matter injury as the initial ultrasonographic examinations can be normal in neonates who go on develop PVL and, conversely the finding of periventricular "flare" can be seen in many healthy subjects [10].

MRI has better diagnostic accuracy in detecting white matter abnormalities particularly in cases of non cystic white matter injury. On MRI the earliest imaging finding is of periventricular foci of T1 shortening interspersed between larger areas of T2 prolongation seen around 3-4 days of life. Subsequent imaging reveals T2 shortening around 6 – 7 days of life [11].

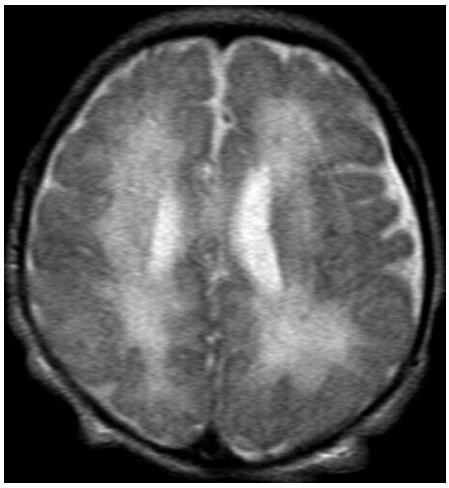

Figure 6: Periventricular leukomalacia in a preterm neonate. Axial T2 weighted image shows hyperintensity in the periventricular white matter.

End stage PVL demonstrates gross reduction of the periventricular white matter with dilatation of the ventricles. Thinning of the corpus callosum particularly the splenium and posterior body can also be demonstrated [11].

SEVERE ASPHYXIA:

The thalami, dorsal brain stem and anterior vermis are most frequently involved. The involvement of the basal ganglia is less severe especially in the neonates born less than 32 weeks of gestation. The perirolandic cortex is spared in preterm neonates.

On MRI, diffusion abnormalities are evident in the thalami around day 1 of life and peak around days 3 -5 after which there is subsequent **“pseudo**

normalization". There is T1 shortening by day 3 and by day 7 this is followed by T2 shortening [11].

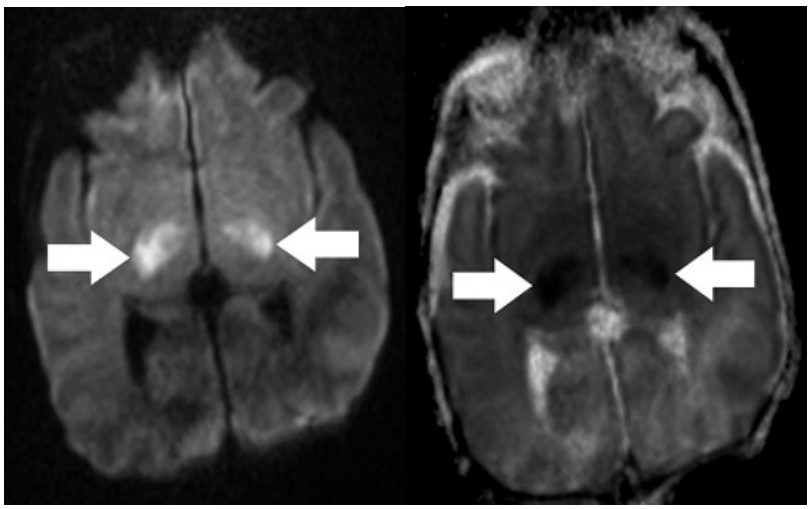

Figure 7: Severe asphyxia in a preterm neonate. Axial diffusion weighted image (left) and corresponding ADC map (right) shows restricted diffusion in bilateral ventrolateral thalami (arrows).

HYPOXIC ISCHEMIC INJURY IN THE TERM NEONATE

The prevalence of hypoxic ischemic injury in term neonates ranges between 2-4/1000 live term births. The imaging characteristics can be divided on the severity of injury into severe and mild to moderate.

SEVERE ASPHYXIA

The severe asphyxial pattern of injury follows a central distribution with involvement of the putamina, thalami, dorsal brainstem, hippocampi and occasionally the perirolandic cortex. These areas are the most susceptible in view of the active myelination or the presence of increased concentration of NMDA receptors.

Cranial ultrasonography has a lower sensitivity (~ 50%) for detection of the abnormalities and hence MR imaging plays a pivotal role. Diffusion weighted

images play an important role in the early diagnosis with signal abnormalities detected as early as 24 hours. The diffusion abnormalities peak around 3 – 5 days and "pseudo normalize" around the end of the first week. However, decreased ADC values persist upto the 2nd week [10].

T1 and T2 weighted images show no demonstrable abnormality on day 1, and hence are less valuable in diagnosing hypoxic injury in the acute setting. The involved areas demonstrate hyperintense signal on both T1 and T2weighted images by day 2. This is followed by T2 shortening in the involved areas, usually by the 2nd week. T1 shortening may however persist for months. The exact pathogenesis responsible for the signal alterations on T1 and T2 weighted images remains controversial. The general consensus favours the fact that conventional T1 and T2 MR images are useful at the end of the first week [11].

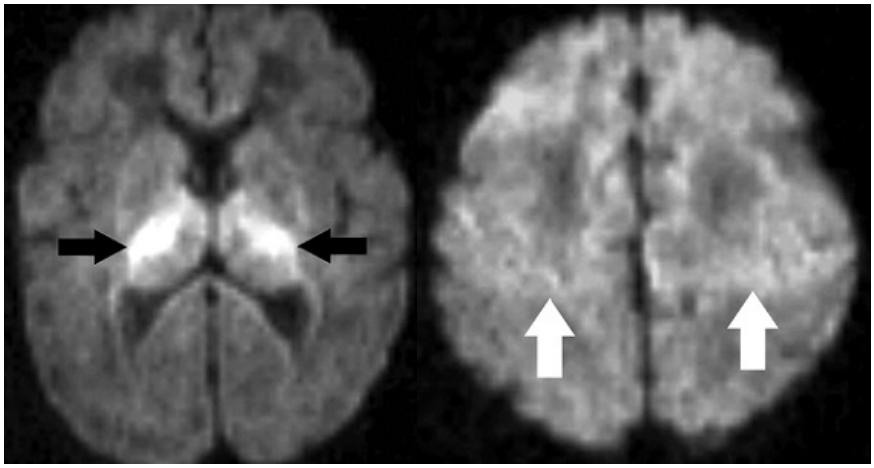

Figure 8: Severe neonatal HII in a term infant. Axial DWI showing high signal intensity in bilateral ventrolateral thalami (black arrows) and perirolandic cortex (white arrows).

PARTIAL ASPHYXIA:

The vital brain structures viz., the brainstem, thalami, based ganglia and hippocampi are generally spared from mild to moderate degrees of hypoxic – ischemic insult. The auto regulatory mechanisms in the brain cause shunting of blood to these vital structures at the expense of metabolically less active regions of the brain like the cortex and white matter.

As a result of shunting of blood, the **water shed or intervascular boundary zones** are involved. Cranial sonography has limited value in the detection of watershed zone injuries, in view of its anatomical limitation. Hence, MRI is the diagnostic modality of choice in these infants. Diffusion weighted imaging has better diagnostic accuracy in the acute setting. Cortical and subcortical white matter restriction in the watershed territories are usually demonstrated in the first 24 hours. However, diffusion weighted images should always be interpreted in conjunction with the corresponding ADC maps [11].

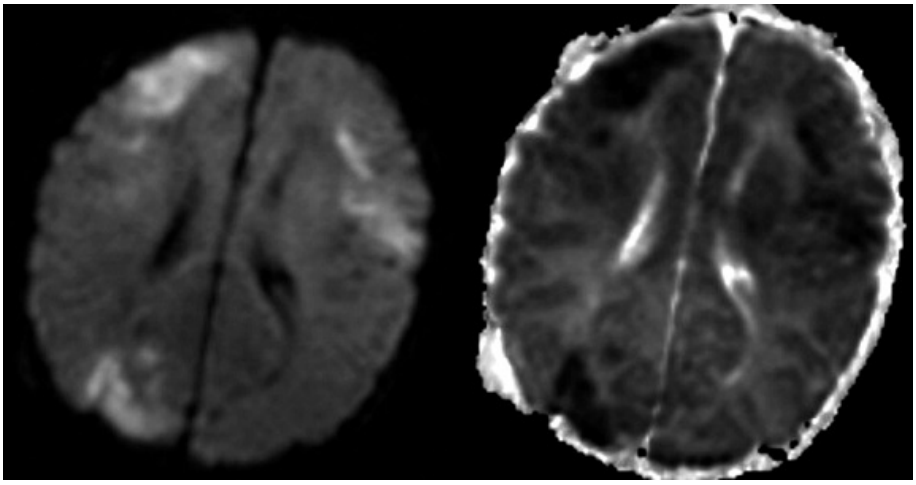

Figure 9: Partial neonatal HII in a term neonate. Axial DWI (left) and corresponding ADC map (right) shows restricted diffusion in the cortex and subcortical white matter in a watershed distribution.

Conventional T1 and T2 weighted images are less useful in the diagnosis of mild to moderate hypoxic ischemic injury especially in the acute setting. Cortical swelling with loss of gray – white matter differentiation and hyperintense signal in the cortex and subcortical regions, predominantly in the watershed territories are seen on T2 weighted images by day 2. Diminished white matter volume with cortical thinning and atrophy are seen in chronic cases.

CONGENITAL MALFORMATIONS OF THE BRAIN:

Abnormal neurodevelopment, leading to a dysplasia or malformation, is a finding commonly encountered in children with developmental delay.

EARLY BRAIN DEVELOPMENT:

Around day 15 of life, the ectodermal cells proliferate along the surface of the embryo forming the **"primitive streak".** The Hensen's node forms at one end of the primitive streak, from which the cells forming the notochord migrate rostrally and form the **"neural plate".** At about day 17, the lateral aspects of the neural plate thicken and bend medially forming the **"neural tube"** [8].

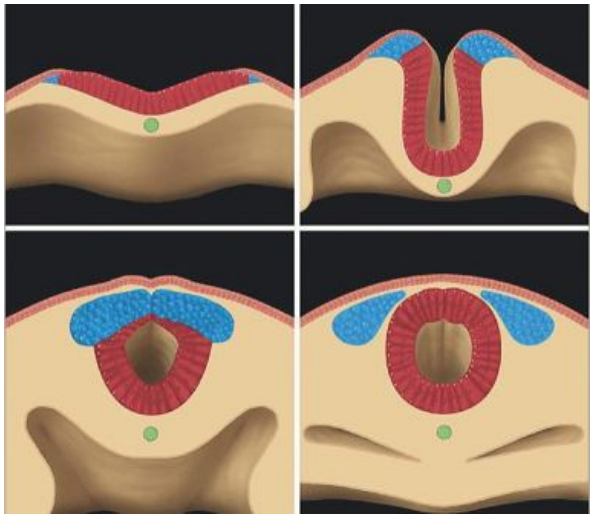

Figure 10: Schematic diagram showing the formation and closure of the neural tube. The neural plate(red) forms, folds and fuses in the midline. The

neural and cutaneous ectoderm then separate. The notochord(green) and neural crest(blue) are shown.

The neural tube closes in a **zipper – like fashion** cranially and caudally. The neural tube closes at the anterior neuropore at the cephalic end at around day 25 of gestation.

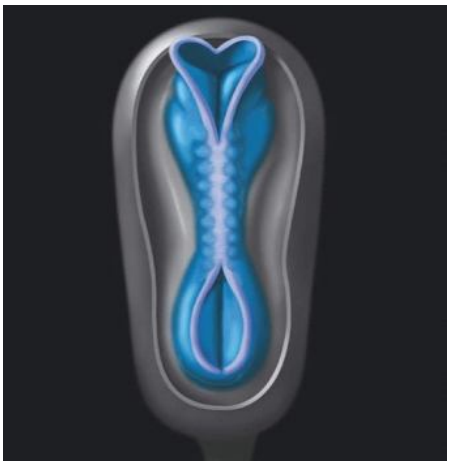

Figure 11: Schematic diagram showing the neural tube which closes in a bidirectional zipper-like manner, starting in the middle and proceeding toward both ends.

Three dilatations or brain vesicles form in the neural tube namely the **forebrain or prosencephalon**, the **midbrain or mesencephalon** and the **hind brain or the rhombencephalon** [8]. The prosencephalon divides into the diencephalon and the telencephalon. The diencephalon is composed of the thalami, hypothalami and globi pallidi. The cerebral hemispheres, putamina and caudate nuclei arise from the telencephalon. The rhombencephalom will divide into the myelencephalon, which forms the pons and medulla, and the metencephalon, which eventually forms the cerebellar hemispheres and vermis [9].

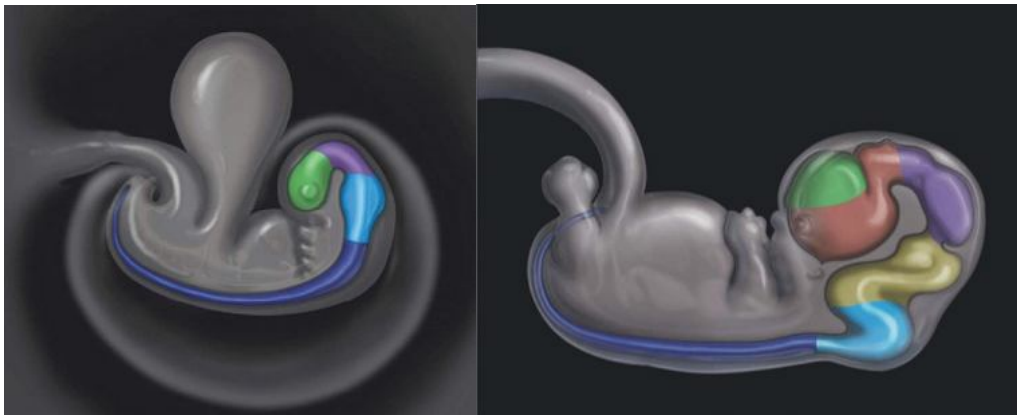

Figure 12: Schematic diagram demonstrating the development of the primary vesicles. The prosencephalon (green) gives rise to the telencephalon (green) and diencephalon (red), the mesencephalon (purple) to the midbrain and the rhombencephalon (light blue) to the metencephalon (yellow) and myelencephalon (light blue) .

ANOMALIES OF THE CEREBRAL COMMISSURES:

The corpus callosum is the largest of the cerebral commissures. It is composed of five parts namely the **rostrum, genu, body, isthumus, and splenium**. The corpus callosum forms in a ventral to dorsal direction. The posterior genu and anterior body form initially followed by the posterior body and anterior genu. The splenium and rostrum form last [9].

SPECTRUM OF CORPUS CALLOSAL ABNORMALITIES:

The corpus callosum may be absent (aplasia) or partially formed (hypoplasia). The portions of the corpus callosum forming earlier in the development sequence will be formed while the later formed portions will not. Exceptions to this “front – to – back” rule occur in a few disorders viz., lobar

holoprosencephaly and syntelencephaly where the splenium may be present despite the absence of the genu/ body [9,10].

IMAGING OF CALLOSAL ANOMALIES:

Corpus callosal agenesis can be detected on axial images, however sagittal and coronal images demonstrate the associated deformities better.

Nonconverging, parallel, widely separated lateral ventricles can be demonstrated on axial images [9]. Other imaging features include **"high – riding" third ventricle** that expands into the interhemispheric fissure, radiating "spoke-wheel" gyral pattern extending perpendicularly to the roof of the third ventricle, upturned pointed corners of the lateral ventricles (**"Viking helmet" or "moose head" appearance)** , prominent white matter tract situated inside the apex of the lateral ventricle called **"Probst bundle"**, and absent septi pellucidi [12].

Corpus callosal hypogenesis show features depending on the segments missing.

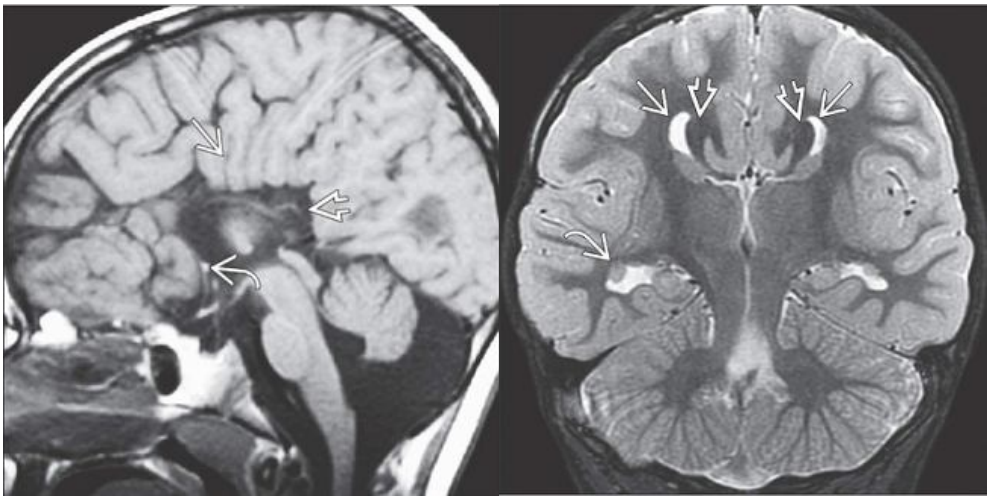

Figure 13: Corpus callosal agenesis. (Left) Sagittal T1 weighted image showing "spoke-wheel" gyri (straight arrow) converge on the third ventricle (block arrow). The anterior commissure is normal (curved arrow). (Right)

Coronal T2 weighted image shows "Viking helmet" appearance with curved, upturned lateral ventricles (straight arrow), Probst bundles (block arrow) and heterotopic gray matter (curved arrow)

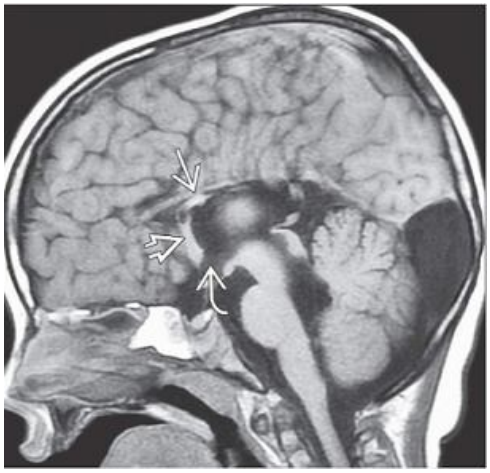

Figure 14: Sagittal T1 weighted image revealing features of corpus callosal hypogenesis. The genu (block arrow), remnant of body (straight arrow) are present. The rostrum (curved arrow) and splenium are absent.

MALFORMATIONS OF CORTICAL DEVELOPMENT:

There represent a broad spectrum of cortical lesions. The three major processes in cerebral cortical development are proliferation, neuronal migration and postmigrational development.

Barkovich et al [9,10] suggested classifying the malformations of cortical development into three primary groups.

GROUP I: MALFORMATIONS SECONDARY TO NEURONAL PROLIFERATION OR APOPTOSIS

1. Microcephaly
2. Megalencephaly
3. Cortical dysgenesis with abnormal cell proliferation
    a. Cortical tubers

b. Focal cortical dysplasia (Taylor type, FCD II b)

GROUP II: MALFORMATIONS SECONDARY TO ABNORMALITIES OF NEURONAL MIGRATION

1. Heterotopia
2. Lissencephaly spectrum
    a. Agyria
    b. Pachygyria
    c. Subcortical band heterotopia
3. Subcortical heterotopia
4. Cobblestone malformations

GROUP III: ABNORMALITIES OF POSTMIGRATIONAL DEVELOPMENT

1. Polymicrogyria
2. Schizencephaly
3. Focal cortical dysplasia (types I and III)

The imaging features of some of the common malformations are described below.

MICRO CEPHALY:

It is defined as a head circumference more than three standard deviations below the mean for age and sex. It can be primary (genetic) or secondary.

Imaging reveals a small cranial vault with overlapping and closely apposed sutures. The craniofacial ratio is reduced (usually ≤ 1.5:1). The cortical surface may appear normal, microlissencephalic or small with simplified gyral pattern [9,10,13].

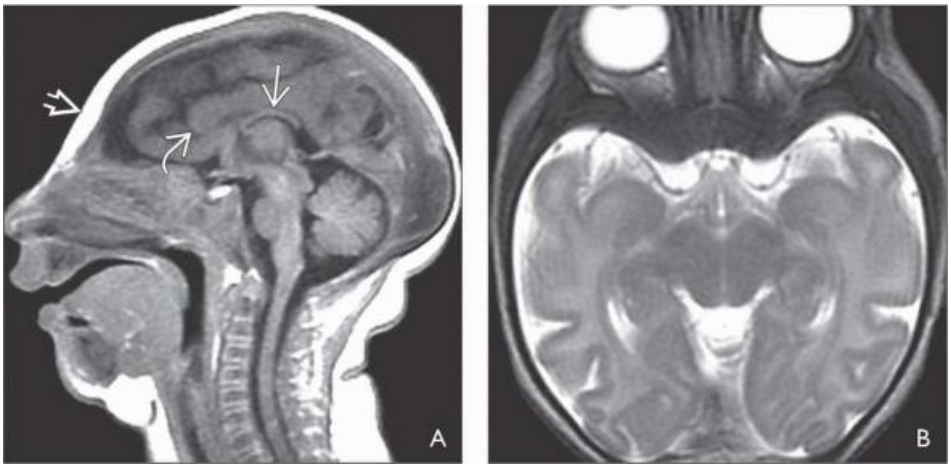

Figure 15: Microcephaly (A) Sagittal T1 weighted image with features of microcephaly. Craniofacial disproportion (ratio of 1.5:1) with a sloping forehead (block arrow) and simplified gyral pattern (curved arrow) noted. The corpus callosum is thin and dysplastic (straight arrow). (B) Axial T2 weighted image shows a simplified gyral pattern with few gyri and shallow appearing sulci.

HEMIMEGALOENCEPHALY:

This is a malformation characterized by enlargement of one cerebral hemisphere. Around 30% of the cases are syndromic and associated with syndromes such as Neurofibromatosis type 1, Klippel – Weber- Trenaunay syndrome etc [10].

Imaging reveals an enlarged, dysplastic appearing cerebral hemisphere with thickened cortex, abnormal gyration and associated abnormalities of the white matter. The lateral ventricle is enlarged and deformed [13].

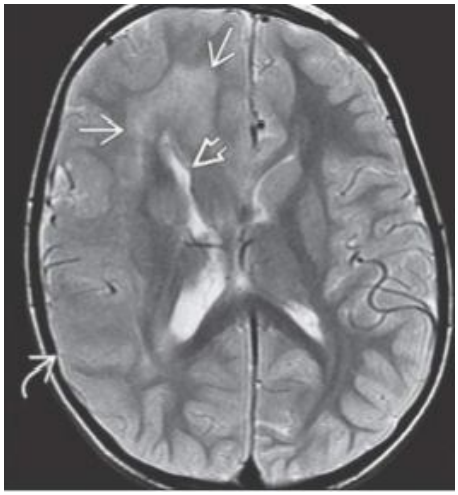

Figure 16: T2 weighted axial image of hemimegaloencephaly. The features demonstrated include enlarged right hemisphere with hyperintense white matter (straight arrow), enlarged and deformed lateral ventricle (block arrow) thickened dysplastic cortex (curved arrow).

LISSENCEPHACY SPECTRUM:

In classic lissencephaly the surface of the brain lacks normal sulcation and gyration.

Agyria is defined as a thickened cortex with gyral absence (“complete” lissencephaly). Classic lissencephaly (cLIS) in characterized by a smooth cortical surface, thick band of deep gray matter demarcated from the underlying white matter. Associated callosal anomalies, most commonly callosal hypogenesis co-exist with cLIS [10,13].

Imaging reveals a smooth cortical surface with a thick band of deep gray matter. There is a thin outer cellular layer that is isointense with gray matter covering a hyperintense "cell-sparse" layer. The white matter is reduced in volume [10,13,14].

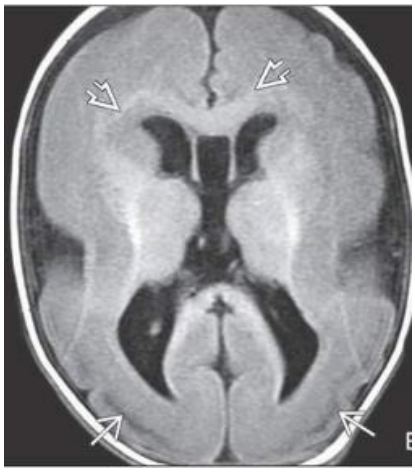

Figure 17: T1 axial image showing features of classic lissencephaly. The brain surface appears smooth, with a few shallow sulci and broad flat gyri. There is a thin outer cortex with a hypointense "cell-sparse" layer (straight arrow). White matter volume is reduced (block arrow).

Band heterotopia or "double cortex" syndrome is a band of gray matter separated from the cortex by a layer of normal white matter [13,14].

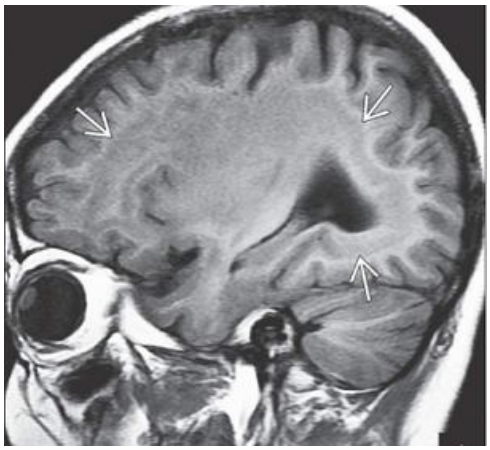

Figure 18: Sagittal T1 weighted image shows band heterotopia with a thin outer cortex, myelinated white matter, band of gray matter (straight arrows) and periventricular white matter ("double cortex").

Pachygyria can be focal or diffuse. When diffuse the parietooccipital regions are more severely involved. Pachygyria is differentiated from

polymicrogyria on thin section, high resolution images by the smooth cortical-white matter junction[14].

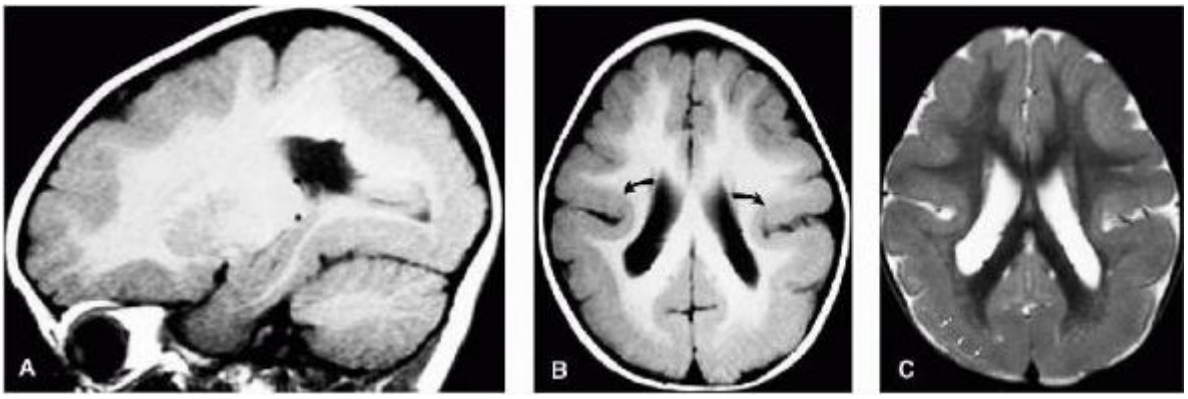

Figure 19: Diffuse pachygyria. A. Parasagittal T1 weighted image showing thickened cortex with relatively few and large gyri and sulci. B. Axial T1 weighted images reveal more severe involvement of the parietal and occipital regions with abnormally vertical sylvian fissures (arrows). C. Axial T2 weighted image reveals hyperintensity (arrows) indicating the "cell sparse" zone in the parietal lobe.

POLYMICROGYRIA:

This malformation is characterized by an irregular cortex with multiple convolutions and shallow sulci. The most common location is bilateral perisylvian polymicrogyria seen in around 61% of the cases. Lesser common locations include frontal, parasagittal parietooccipital and generalized [15].

Imaging reveals an overfolded cortex with nodular surface. The gray – white matter interface is often “stippled”.

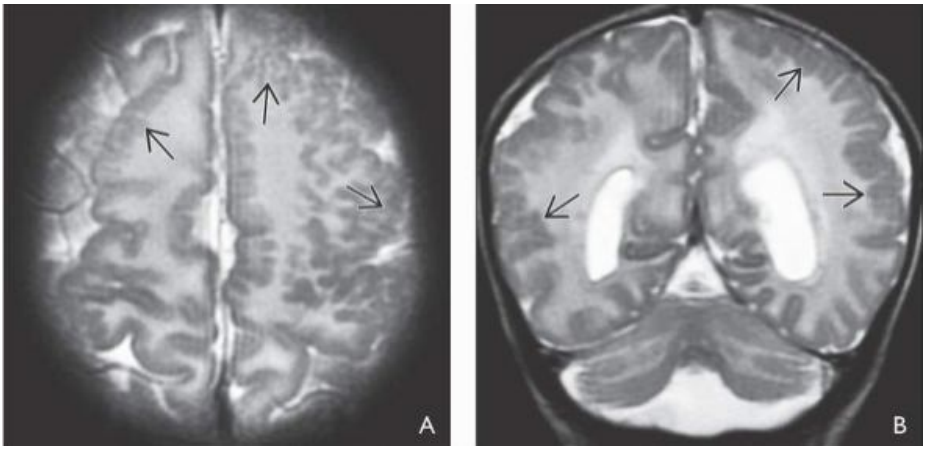

Figure 20: Axial (A) and coronal (B) T2 weighted image shows multiple foci of polymicrogyria (straight arrows).

SCHIZENCEPHALY:

This is characterized by a gray matter lined cleft that extends from the ventricular ependyma to the pial surface of the cortex. The “lips” of the cleft can be fused as in a **“closed lip” schizencephacy** or widely separated as in a **“open lip” schizencephaly.**

Imaging reveals a gray matter lined CSF intensity cleft extending from the ventricular wall to the pial surface. There is a focal V – shaped outpouching or “dimple” of the CSF seen extending from the lateral ventricle [15,16].

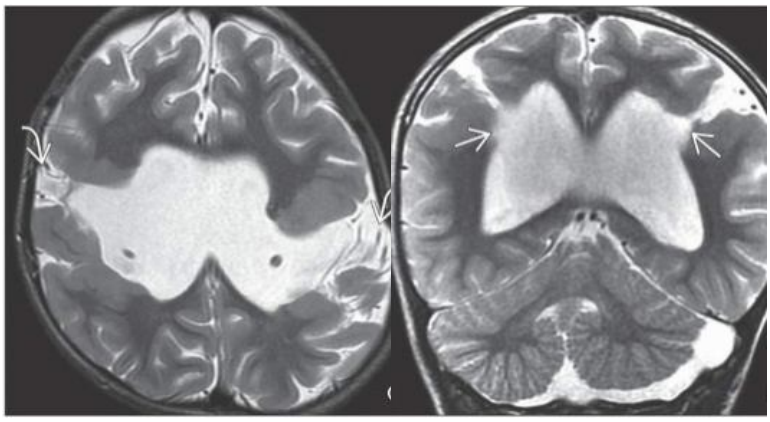

Figure 21: Open lip Schizencephaly. (left) Axial T2 weighted image shows the open "lips" of both clefts containing prominent "flow voids".(right) Coronal T2 weighted image show the pointed "nipples" (straight arrows) of CSF that extend outward from the ventricles into the schizencephalic clefts.

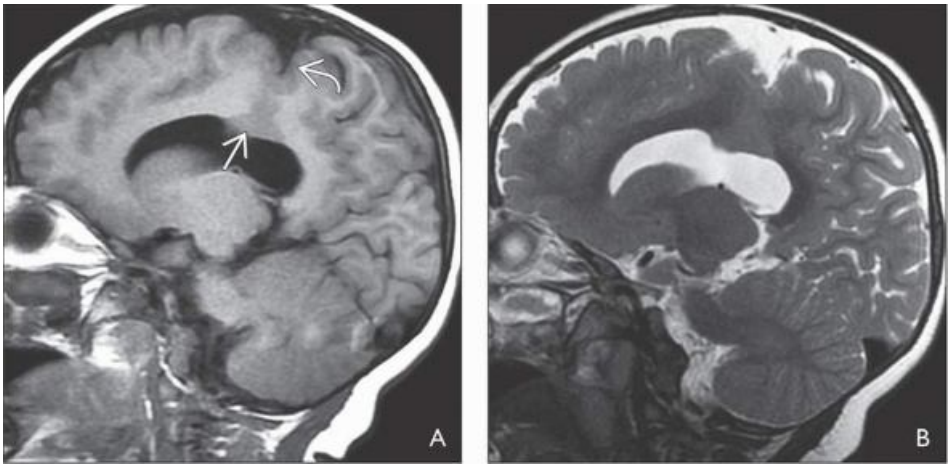

Figure 22: Unilateral "closed lip schizencephaly" A. Sagittal T1 weighted image demonstrating the gray matter extending from the ventricle (straight arrow) to the pial surface (curved arrow) B. Sagittal T2 weighted image shows that the gray matter lining the cleft is the same signal intensity as the cortex.

HOLOPROSENCEPHALIES AND RELATED DISORDERS:

"Holoprosencephaly" are a group of disorders characterized by the failure of differentiation and cleavage of the prosencephalon. It can be caused various genetic factors and teratogens namely maternal diabetes, Patau syndrome, Edwards syndrome etc. It is commonly associated with facial dysmorphism particularly midline facial clefts [9,10].

There are three subcategories as classified by **DeMyer** namely **alobar, semilobar and lobar.**

ALOBAR HOLOPROSENCEPHALY:

Most neonates are stillborn or live a very short life span and this marks the most severe form of holoprosencephaly. On imaging, there is evidence of complete fusion of the brain across the midline without an interhemispheric fissure. The cerebrum is replaced by a “pancake like mass” of tissue. There is a holoventricle continuous with a large dorsal cyst.

SEMILOBAR HOLOPROSENCEPHALY:

The brain is less dysmorphic than in the alobar form. On imaging, the falx and interhemispheric fissure are partially formed in the posterior aspects. The anterior regions of the brain remain fused. The temporal horns are rudimentary. The septum pellucidum is absent. The callosal splenium is present with agenesis of the genu and body of the corpus callosum. The deep cerebral nuclei are partially separated. However, the caudate heads, hypothalami and thalami are partially fused [10].

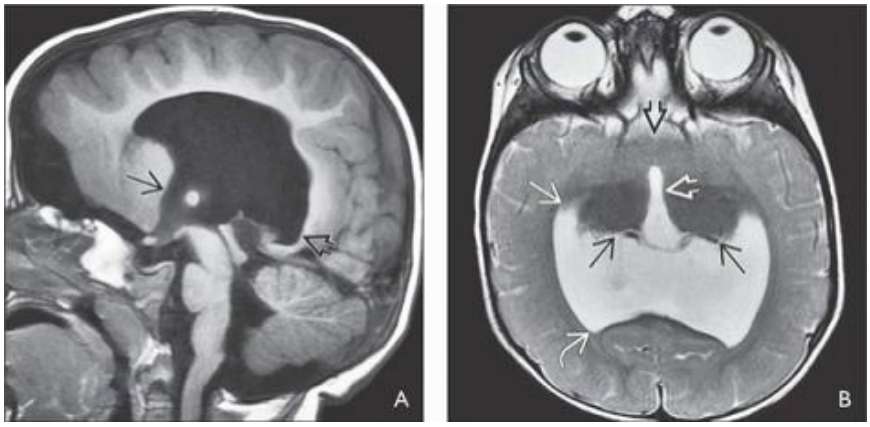

Figure 23: Semilobar holoprosencephaly A. Sagittal T1 weighted image shows partial differentiation of third ventricle (straight arrow), occipital horns (block arrow) B. Axial T2 weighted image shows rudimentary temporal (straight arrow) and occipital (curved arrow) horns. The thalami

are separated (black straight arrow) but the hypothalamus remains fused (black block arrow).

LOBAR HOLOPROSENSEPHALY:

These patients have less severe clinical manifestations. On imaging, the frontal lobes are developed and the frontal horns of the laleral ventricles are present. The basal ganglia and thalami are mostly separated. The septum pellucidum is however, absent. The splenium and posterior body of the corpus callosum is formed [10].

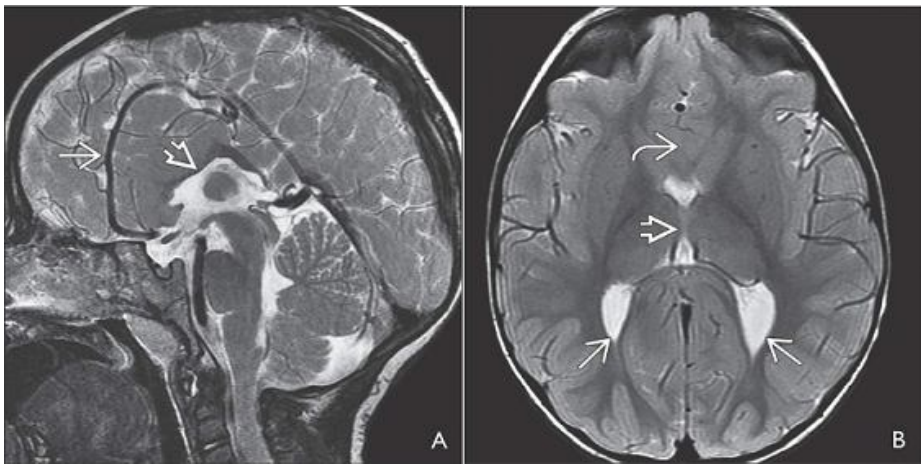

Figure 24: Lobar holoprosencephaly A. Sagittal T2 weighted image shows well differentiated brain, nearly normal appearing third ventricle (block arrow), azygous ACA (straight arrow) B. Axial T2 weighted image shows well developed occipital horns (straight arrow), third ventricle (block arrow), poorly seen frontal horns with minimal anterior midline fusion (curved arrow).

SYNTELENCEPHALY (MIDDLE INTERHEMISPHENIC VARIANT):

This is a variant of holoprosencephaly wherein the interhemispheric fissure is formed anteriorly and posteriorly with fusion of the hemispheres in the posterior frontal and parietal regions.

Imaging reveals absence of the mid section of the interhemispheric fissure and the posterior frontal or parietal lobes fuse across the midline. The genu and splenium of the corpus callosum are formed. The lateral ventricles appear narrow and fused. The third ventricle is well formed however, the septi pellucidi are absent [9,10].

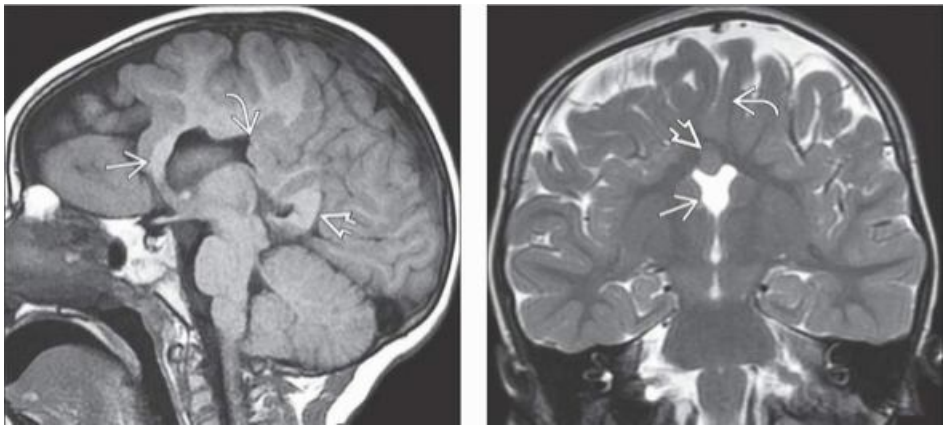

Figure 25: Syntelencephaly A. Sagittal T1 weighted image. Genu (straight arrow) and splenium (block arrow) of the corpus callosum are present without an intervening body. Abnormal appearing gray matter (curved arrow) is seen deforming the lateral ventricle. B. Coronal T2 weighted image shows narrow, non separated lateral ventricles (straight arrow) with a nodule of gray matter (block arrow) perched on top of the fused lateral ventricle. The posterior frontal lobes are continuous across the midline (curved arrow).

POSTERIOR FOSSA MALFORMATIONS:

CHIARI MALFORMATIONS:

Hans Chiari in 1891, described a group of hindbrain malformations associated with hydrocephalus and subdivided then into three types [10].

CHIARI 1 MALFORMATION:

This is defined as caudal cerebellar tonsillar ectopia. Most patients remain asymptomatic (50%). On imaging, there is evidence of tonsillar herniation below the foramen magnum. The criterion for tonsillar ectopia varies with age, however 6 mm should be used as the criterion in the first decade of life. The spine should be screened for syringohydromyelia which is seen in 40 – 80 % of symptomatic patients. The tonsils are “pointed” with vertically oriented folia, and a crowded foramen magnum with obliterated retrocerebellar subarachnoid space [17].

CHIARI 2 MALFORATION:

This is a complex hindbrain malformation associated with myelodysplasia. On imaging, there is a small shallow posterior fossa and a short concave clivus. Other imaging features include an irregular interhemispheric fissure, cervicomeduallary kink, "towering" cerebellum, compression and deformation of the quadrigeminal plate by the superiorly herniated cerebellum leading to a “beaked" tectum, "soda straw" fourth ventricle with absent fastigium, corpus callosal dysgenesis, lacunar skull and associated malformations of cortical development [10,17].

CHIARI 3 MALFORMATION:

This is the rarest of the Chiari malformation. It is characterized by herniation of the posterior fossa contents through a low occipital or upper cervical bony defect. On imaging there are features similar to Chiari 2 with a defect in the ventral chondral portion of the supraoccipital bone with posterior spina bifida at C1-C2 level. MRI best delineates the sac contents which often include the cerebellum and / or brainstem [9,10,17].

DANDY – WALKER SPECTRUM:

This is a generalized disorder of mesenchymal development that affects both the cerebellum and meninges. Dandy walker malformation (DWM) is characterized by an enlarged posterior fossa, superior displacement of the tentorium and accompanying venous sinuses, dilatation of the fourth ventricle and vermian hypoplasia [17].

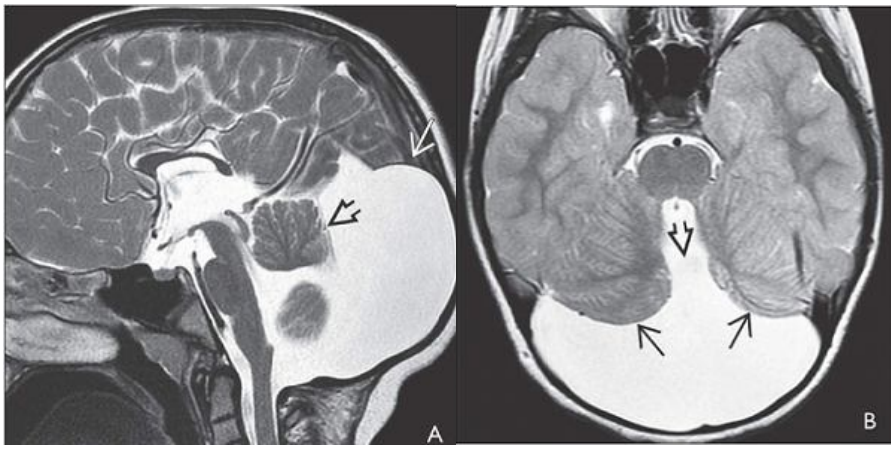

Figure 26: Classic Dandy walker malformation (DWM) A. Sagittal T2 weighted image showing a large posterior fossa cyst elevating the torcular (straight arrow), superiorly rotated vermian remnant (block arrow), small pons and dysgenetic corpus callosum B. Axial T2 weighted image shows the fourth ventricle opening dorsally into the large posterior fossa cyst (block

arrow). The cerebellar hemispheres are small and "winged anteriorly" (straight arrows).

JOUBERT SYNDROME:

This is a complex mid- and hindbrain malformation with the classic **"molar tooth"** sign on imaging. This disorder follows an autosomal recessive inheritance. The clinical presentation is a child with developmental delay, ataxia and respiratory difficulties.

MRI is the cornerstone in diagnosing Joubert's syndrome. The classic imaging features include a small dysmorphic vermis, classic "molar tooth" appearance on axial images due to a foreshortened midbrain with enlarged superior cerebellar peduncles and absence of their decussation surrounding an oblong or diamond shaped fourth ventricle [10,17].

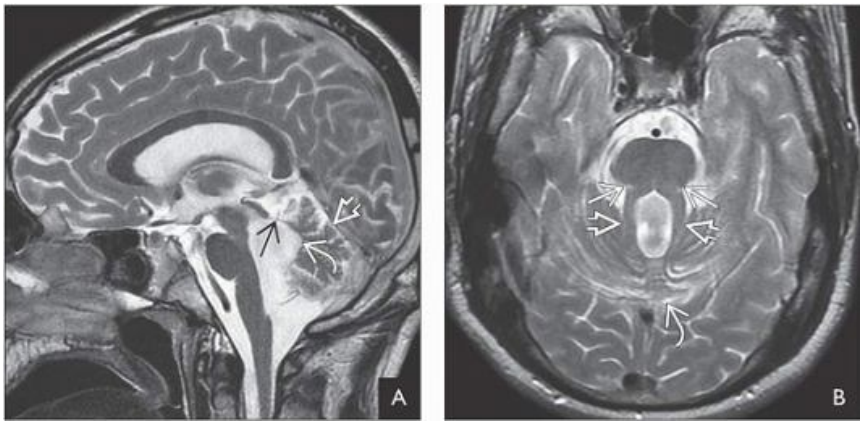

Figure 27: Classic Joubert syndrome A. Sagittal T2 weighted image shows small misshapen vermis (block arrow), upwardly convex superior fourth ventricle (straight arrow) and rounded enlarged fastigial point (curved arrow) B. Axial T2 weighted image shows the classic "molar tooth sign": Foreshortened midbrain with narrow isthmus (straight arrows), thick superior cerebellar peduncles (block arrows) surrounding an elongated fourth ventricle, and disorganized cleft vermis (curved arrow).

INHERITED METABOLIC BRAIN DISORDERS:

These form a diverse group of disorders involving various biochemical alterations. Brain injury and clinical symptoms can be caused by either lack of production of a normal metabolite or accumulation of an abnormal metabolite. There have been several classification systems in the past to classify these disorders. However, the most practical of them is the imaging-based approach elaborated by ***Barkovich et al*** [10]. The approach is based on whether the disorder primarily or exclusively involves

1. White matter
2. Gray matter
3. Both

DISORDERS PREDOMINANTLY AFFECTING WHITE MATTER:

These disorders can be further subdivided into those primarily involving

i. Deep or periventricular white matter
ii. Subcortical white matter

The subsequent discussion includes important imaging features of a few commonly encountered diseases.

METACHROMATIC LEUKODYSTROPHY:

This is a devastating **lysosomal storage disorder** caused by deficiency of **arylsulfatase A** responsible for the degradation of sulfogalactosylceramide. The disease manifests in three clinical forms namely late infantile, juvenile and adult form.

MRI demonstrates confluent, symmetric butterfly-shaped T2/ FLAIR hyperintensity in the deep periventricular white matter with the corpus callosum splenuim and parietooccipital periventricular white matter initially involved. The subcortical fibers are typically spared until late in the disease. High resolution images demonstrate the **"tiger" or "leopard" pattern** with stripes of affected and unaffected myelin extending peripherally from the lateral ventricles [10,19].

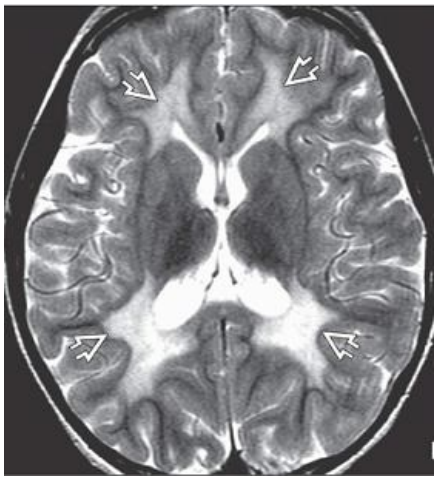

Figure 28: Metachromatic leukodystrophy. T2 weighted image shows the classic "butterfly" pattern of symmetric hyperintensities around the frontal horns and atria of the lateral ventricles (block arrows).

X LINKED ADRENO LEUKODYSTROPHY (XALD):

The classic form is the result of a mutation of the ALD gene resulting in abnormal peroxisome metabolism resulting in **accumulation of very long chain fatty acids (VLCFAs)**. The classic XALD is seen exclusively in boys 5 – 15 years of age.

MRI reveals a **"posterior predominant" pattern** in around 80% of the patients with XALD. There is a T2/FLAIR hyperintense signal in the corpus

callosal splenium and white matter surrounding the atria and occipital horns of the lateral ventricles [18,19].

There are three distinct zones of myelin loss in patients with adrenoleukodystrophy. The innermost zone consists of a necrotic "burned out" core, an intermediate zone of active demyelination and perivascular inflammation and the most peripheral zone of ongoing demyelination without inflammation.

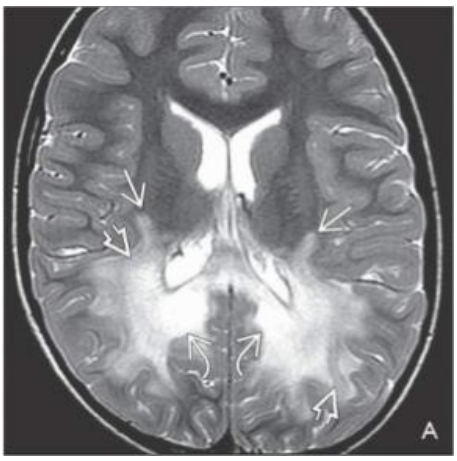

Figure 29: Classic X-Linked Adrenoleukodystrophy. Axial T2 weighted image shows symmetric lesions surrounding the atria. The central hyperintense "burned out" core (curved arrow) is surrounded by a less hyperintense layer of active demyelination (block arrow). The most peripheral zone (straight arrow) shows demyelination without inflammatory changes.

PHENYLKETONURIA (PKU):

This is an autosomal recessive disorder caused by a mutation in the **phenylalanine hydroxylase (PAH) gene**. Untreated cases show severe mental retardation and global developmental delay.

MRI demonstrates T2/FLAIR hyperintensity in the periventricular white matter particularly in the frontal and peritrigonal regions associated with mild

restricted diffusion. Proton MR spectroscopy demonstrates a Phe (phenylalanine) peak at 7.37 ppm [9,10].

SUBCORTICAL WHITE MATTER PREDOMINANCE:

MEGALOENCEPHALIC LEUKODYSTROPHY WITH SUBCORTICAL CYSTS (Van der knaap disease):

This disorder is remarkable for its relatively mild neurologic signs and symptoms in the setting of an abnormal imaging study. MRI reveals diffuse confluent T2/FLAIR hyperintensity in the subcortical white matter. The affected gyri appear swollen. Characteristic subcortical cysts develop in the posterior frontal & temporal lobes [10].

DISORDERS PREDOMINANTLY AFFECTING GRAY MATTER:

These disorders can be subdivided into those that involve the cortex and those that mainly affect the deep gray nuclei.

DISORDERS PREDOMINANTLY INVOLVING THE DEEP GRAY NUCLEI:

PANTOTHENATE KINASE – ASSOCIATED NEURODEGENERATION (HALLERVORDEN – SPATZ DISEASE)

This is a rare metabolic disorder that presents with gait disturbances, choreoathetotic movements and mental deterioration. There is excessive iron deposition in the globus pallidus and substantia nigra due to mutations in the pantothenate kinase gene (PANK2)

MRI reveals marked hypointensity in the globus pallidus and substantia nigra with a small focus of central hyperintensity in the medial aspect of the

globus pallidus due to tissue gliosis and vacuolization **(the classic "eye of tiger" sign)** [9,10]

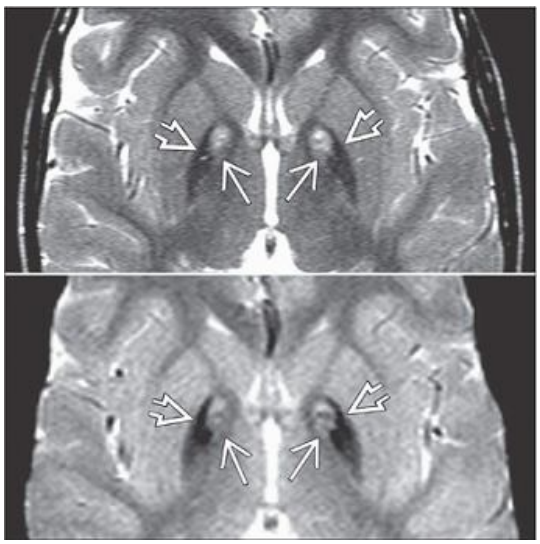

Figure 30: Pantothenate kinase-associated neurodegeneration (PKAN). Axial T2 weighted image (top) and axial GRE image (bottom) show the classic "eye of the tiger" sign with bilateral hyperintense foci (straight arrows) in the medial globi pallidi surrounded by striking hypointensity (block arrows).

DISORDERS PREDOMINANTLY AFFECTING THE CORTEX:

RETT SYNDROME:

This is a progressive neurodevelopmental disorder caused by a mutation in the methyl – CPG – binding protein – 2 gene **(MECP2).** The disorder almost always affects girls. Imaging studies reveals microcephaly with global reduction in gray and white matter volumes more predominant in the frontal and anterior temporal cortex.

DISORDERS AFFECTING BOTH GRAY AND WHITE MATTER

MUCOPOLYSACCHARIDOSIS (MPSs):

These are lysosomal storage disorders characterized by accumulation of **glycosaminoglycans** in various organs. The MPSs are designated as MPSs 1 – 9 with specific enzyme deficiencies.

Imaging studies characteristically reveal macrocephaly, enlarged perivascular spaces predominantly in the posterior cerebral white matter and corpus callosum **("Hurler holes")** and pachymeningopathy [9,19].

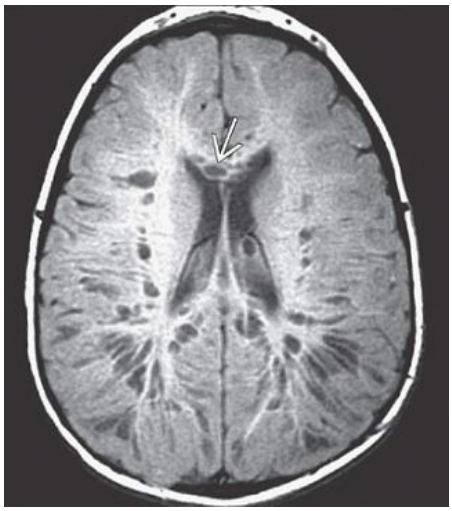

Figure 31: Mucopolysaccharidosis (Hurler disease). Axial T1 weighted image shows markedly enlarged perivascular spaces in the white matter including the corpus callosum (straight arrow).

PROTON MR SPECTROSCOPY:

This is a novel MR imaging modality to evaluate children with developmental delay. Children with mild neurodevelopmental delay generally have normal MRI findings. With the use of MR spectroscopy the normal myelin maturation can be assessed [25].

NAA (N-acetyl aspartate) is the most sensitive neuronal marker of the central nervous system. NAA shows a peak at 2.01 ppm. The levels rise as

myelination progresses. This is due to the process of **dendritic proliferation**. Absolute or relative (to Cr) decrease of this metabolite can be seen in cases of neuronal damage [10]. Although the adult brain shows higher concentrations of NAA in the cortex as compared to the white matter, the concentration of NAA is equal in both gray and white matter in the infant brain. This is because of active lipid synthesis [10,25,27].

Choline (Cho) serves as a precursor molecule for myelination. It is a component of the various cell membranes and its levels indicates **membrane turnover**. Cho peak is observed at 3.21 ppm. There is a significant decline in the Cho/Cr(Creatine) ratio in the first few months of life due to myelination. Because of its association with the structural components of the cell, the Cho peak is enlarged in highly cellular processes like high grade neoplasms and neurodegenerative disorders. In the mature brain, Cho concentration is higher in the white matter than the cortex [25,27].

The ***Creatine (Cr)*** peak is visualized at 3.03 ppm. It has contributions from creatine and phosphocreatine. The levels of creatine remains stable and hence it is used in most cases as an index for comparison with other metabolites.

The absolute concentrations of the metabolites is difficult to determine by MR spectroscopy in vivo. Hence, calculation of metabolite ratios and comparison of the spectral peaks of the various metabolites appears more logical.

REVIEW OF PREVIOUS STUDIES:

In a study by ***Ali et al*** [20], the prevalence of normal and abnormal MR imaging in patients presenting with developmental delay was evaluated. In this

study 81 patients between three months to twelve years were evaluated. 68% of the cases had an abnormal MRI. The patients with an abnormal MRI were further categorized based on the imaging features. 31% of the cases with abnormal neuroimaging were found to have traumatic/neurovascular diseases. The white matter predominantly the corpus callosum and ventricles were the most commonly affected structures.

In a study by ***Widjaja et al*** [3]**,** the prevalence of abnormalities on MRI in patients with idiopathic developmental delay was studied. The study evaluated, the following structures systematically: corpus callosum, gray matter, white matter, basal ganglia, ventricles, cerebellum, brainstem and limbic system. 90 patients were evaluated. 76 patients had abnormal MRI findings. Abnormalities of the ventricles and corpus callosum were identified in 48% and 44% of the cases respectively. Other MRI abnormalities included those involving the white matter (26%), cerebellum (6%), hippocampi (6%) and brainstem (4%).

In a study by ***Griffiths et al,*** the overall detection rate of the relevant pathology by MRI and spectroscopy in developmentally delayed children was studied. The study evaluated 157 children of which 71 % had a normal MRI. The percentage of children with non – specific and specific abnormalities on MRI was 10% and 19% respectively.

In a study by ***Kjos et al*** [21], 76 children with an unknown cause of developmental retardation were evaluated with MRI. 21 children had significant abnormalities on MR imaging of the brain. The most common finding on MRI

was atrophy seen in 9 patients. The other categories of abnormalities on MRI were congenital morphogenetic abnormalities (7 patients), delayed pattern of myelination (6 patents) and T2 hyperintense foci within the brain (4 patients).

In a study by ***Bouhadiba et al*** [22],the diagnostic value of MRI in children with developmental delay was studied. 224 patients were evaluated. 109 cases had an abnormal MRI. Cerebral malformations were present in 55 cases. The other abnormal neuroimaging findings were cerebral atrophy (12 cases), white matter diseases (7 cases), myelination delay (26 cases), increased signal of posterior white matter on T2 weighted images (9 cases), post ischemic lesions (10 cases), phakomatosis (2 cases) and widened Virchow- Robin spaces (3 cases).

In a study by ***Soto – Ares et al*** [23], cerebral MRI of children with mental retardation was reviewed in order to establish a neuroanatomical picture. 30 patients were evaluated out of which 27 had imaging abnormalities. Corpus callosal dysplasia (46%), partially opened septum pellucidum and/or cavum vergae (33%), ventriculomegaly (33%), vermian hypoplasia (33%) and cerebral cortical dysplasia (23%) were the most commonly encountered abnormalities. Other findings included subarachnoid space enlargement (16.6%), white matter anomalies (10%) and disorganized cerebellar foliae (20%).

In a study by ***Momen et al*** [24], brain MRI findings in developmentally delayed children was studied. 580 developmentally delayed children between 2 months and 15 years of age were evaluated. 58.6 % of the cases had an abnormal brain MRI. Majority of the cases belonged to the Neurovascular and trauma group

(37.6%). Other categories demonstrated were congenital and developmental anomalies of brain (6.7%), nonspecific findings (6.6%), metabolic or neuro degenerative diseases (7.2%) and recognisable syndromes (0.5%).

In a study by ***Filippi et al*** [25] , the role of MR spectroscopy in children with developmental delay was studied. The study involved 14 children with developmental delay who had a normal MRI of the brain. The children were divided into two groups. One older than two years and the other aged two years or below with age-matched controls. The study evaluated various neuro metabolite ratios in the subcortical white matter of bilateral frontal and parieto-occipital lobes. NAA/Cr and Cho/Cr ratios were measured and compared with the control groups. It was noted that in children less than two years no significant difference was observed between the study and control group. However, in children above two years, there was a reduction in the NAA/Cr ratio and increase in the Cho/Cr ratio in the above mentioned regions compared to the control group.

In a study by ***Fayed et al*** [26], 12 children with developmental delay were evaluated with MR spectroscopic examination. The study involved children aged between 3 and 12 years, with age matched control groups. The children with an abnormal MRI were excluded. The study involved the voxel placed in the left centrum semiovale. Various ratios were calculated and matched to age specific control groups. There was a significant decrease in the following ratios in children with developmental delay: NAA/Cr, NAA/Ch and NAA/mI.

In a study by ***Kosucu et al*** [27], the role of MR spectroscopy in children with psychomotor delay was studied. The study involved 20 children (mean age

8.65 years) with psychomotor delay. A group of 19 children with no psychomotor delay served as controls. Voxels were placed at bilateral frontal and parietal regions (gray and white matter). The ratios of NAA/Cho , NAA/Cr and Cho/Cr were calculated. There was no significant difference in the neurometabolite ratios in various brain regions among the children with and without psychomotor delay.

In a study by ***Pandey et al*** [28], the yield of neuroimaging in children with developmental delay was studied. The study involved 47 children with no obvious etiological diagnosis. 63.82% children had abnormal neuroimaging. It was further noted that there was a strong correlation between the incidence of positive neuroimaging findings and the severity of developmental retardation. Further the presence of additional neurological deficits in addition to developmental delay had a higher incidence of abnormal imaging.

In a study by ***Koul et al*** [29], 110 children with global developmental delay were studied at a hospital in Oman. The children were aged 5 years or less. MRI was done in 105 children, out of which 81.3% had an abnormal MRI. Abnormal neurological findings were present in 84% of the children with developmental delay.

In a study by ***Zeegers et al*** [30], the radiological findings in children with developmental delay was studied. 45 children were evaluated in the study, out of which 49% had abnormalities on MRI.

In a study by ***Martin et al*** [31], 48 children with unexplained developmental delay aged between 1 month and 13 years were evaluated with MR spectroscopy.

The study also included an age matched control group of 23 children with normal development. The voxels were positioned in the following regions: frontoparietal white matter and/or deep gray matter. Various neuro metabolites and their ratios were calculated: NAA, mI, Cr, Cho, NAA/Cr, mI/Cr and Cho/Cr. The study showed no significant difference in the neuro metabolites and their ratios between the study population and the control group.

OBSERVATION

1. AGE

Our study involved the evaluation of 100 children between 6 months and 10 years of age, who presented with developmental delay. The study revealed a **significant number of children presenting with developmental delay between the age group of 3-5 years**. The number of children presenting with developmental delay in the above mentioned age group was 35. This was followed by 25 children in the age group of 6-8 years followed by 20 children in the age group of 1-2 years. The other subgroups had relatively lesser number of children presenting with developmental delay (15 children in the group <1 year of age and 5 children between 9-10 years of age).

Age Distribution			
	Gender		
Age	Male	Female	Total
<1	9	6	15
1- 2	12	8	20
3 - 5	21	14	35
6 - 8	14	11	25
9 - 10	4	1	5
Total	60	40	100

Table 4: Age-wise distribution of the children presenting with developmental delay

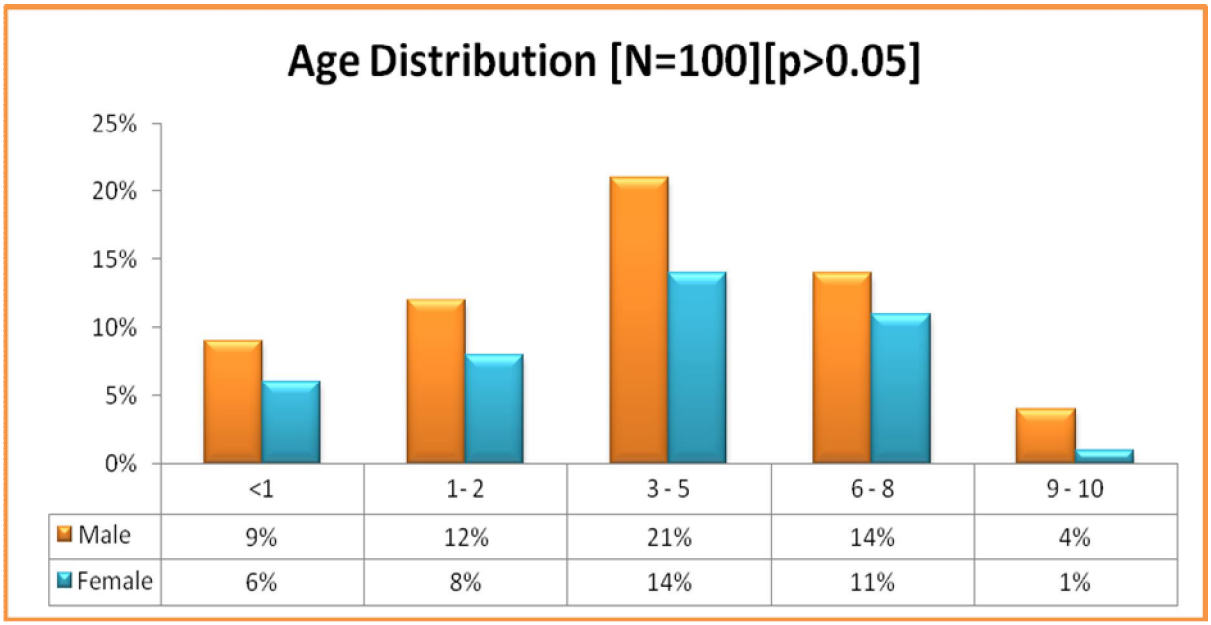

Figure 32 : Diagram demonstrating the age-wise distribution of the children presenting with developmental delay.

Further, the association of positive MRI findings prevailing among various age groups was studied. It was noted that among the 35 children in the age group 3-5 years, 30 had abnormal brain MRI findings. Among the 25 children in the age group 6-8 years, 16 had abnormal brain MRI findings. It was also noted that 14 children in the age group 1-2 years and 13 children in the age group <1 year had an abnormal brain MRI. It was concluded that there was a **significant association between the age of presentation and abnormal MRI findings** ($p<0.05$)

Association of Age with MRI findings			
	MRI Findings		
Age	Normal	Abnormal	Total
<1	2	13	15
1- 2	6	14	20
3 - 5	5	30	35
6 - 8	9	16	25
9 - 10	0	5	5
Total	22	78	100

Table 5: Association of age with MRI findings

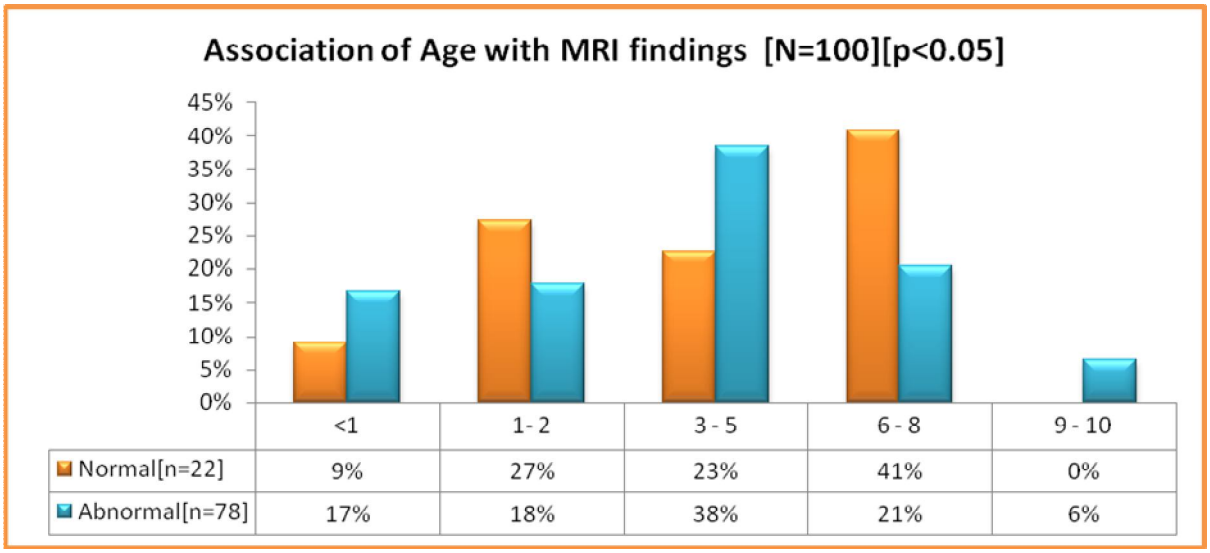

Figure 33: Diagram demonstrating the association of age with MRI findings.

2. SEX

Our study evaluated a total of 100 children among which 60 were males and 40 were females. The mean age was 4.3 for males and 4.0 for females (95% CI for mean).

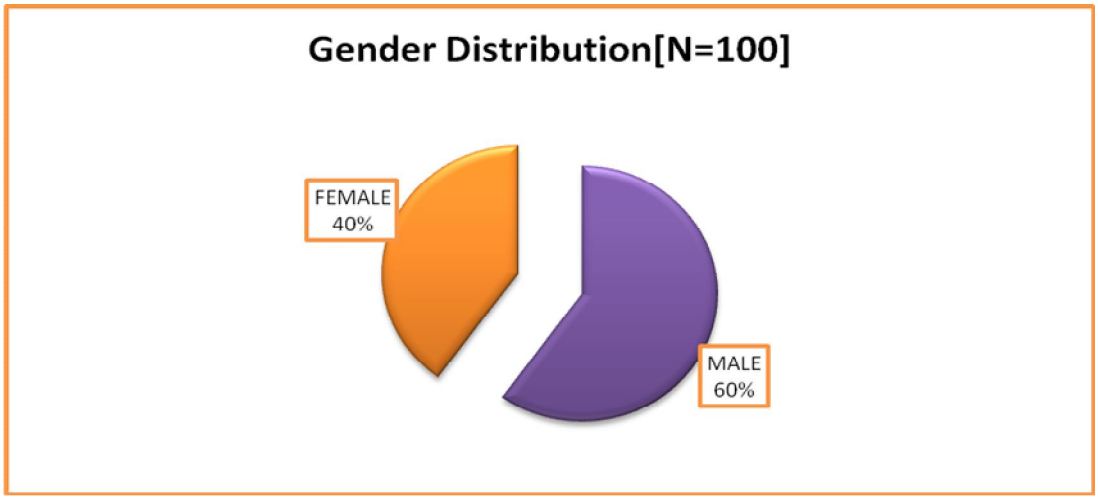

Figure 34 : Pie chart demonstrating the gender distribution (n=100)

Mean Age with Gender							
			95% CI for Mean				
	Mean	SD	Lower	Upper	Minimum	Maximum	Sig
Male	4.3	2.6	3.6	5.0	0.1	10	
Female	4.0	2.4	3.2	4.8	0.6	9	>0.05
Total	4	3	3.656	4.665	0.1	10	

Table 6: Table demonstrating the mean age with gender distribution.

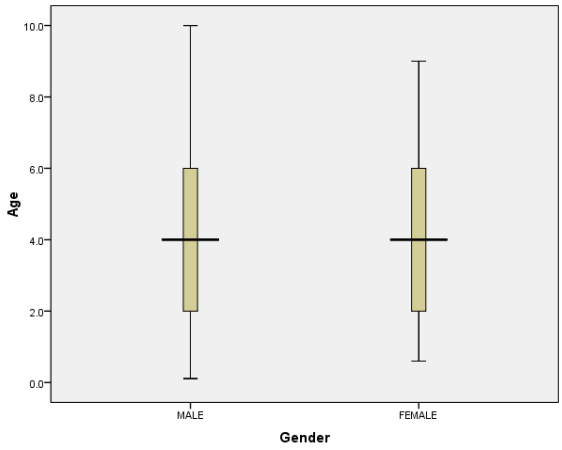

Figure 35: Box plot diagram demonstrating the mean age with gender distribution.

Further, the association of gender with MRI findings was studied. Among the 60 male children evaluated in the study, 45 had abnormal MRI findings. Among the female children evaluated, 33 out of 40 had abnormal MRI findings. The proportion of male children contributing to abnormal MRI findings (n=78) was 58% as compared to 42% in the female population under study. However, **no significance between the gender and MRI findings was observed** (p>0.05).

Association of Gender with MRI findings				
	MRI Findings			
Gender	Normal	Abnormal	Total	
Male	15	45	60	
Female	7	33	40	
Total	22	78	100	

Table 7: Table showing association of gender with MRI findings.

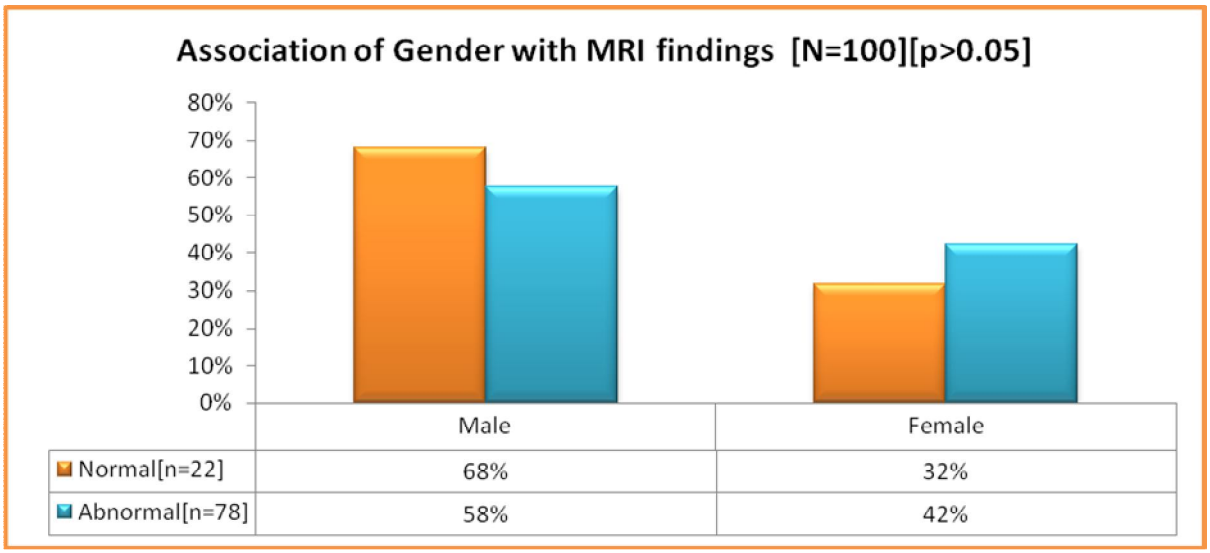

Figure 36: Bar diagram showing showing association of gender with MRI findings.

3. **GESTATIONAL AGE**

The children were divided on the basis of gestational age into preterm, term and late preterm. Among the 100 children evaluated, 39% were preterm while 31% were late preterm. Around 30% of the evaluated children were term.

Gestational Age		
Gestational Age	N	(%)
Term	30	30%
Preterm	39	39%
Late preterm	31	31%
Total	100	100%

Table 8: Table demonstrating the distribution of children on the basis of gestational age.

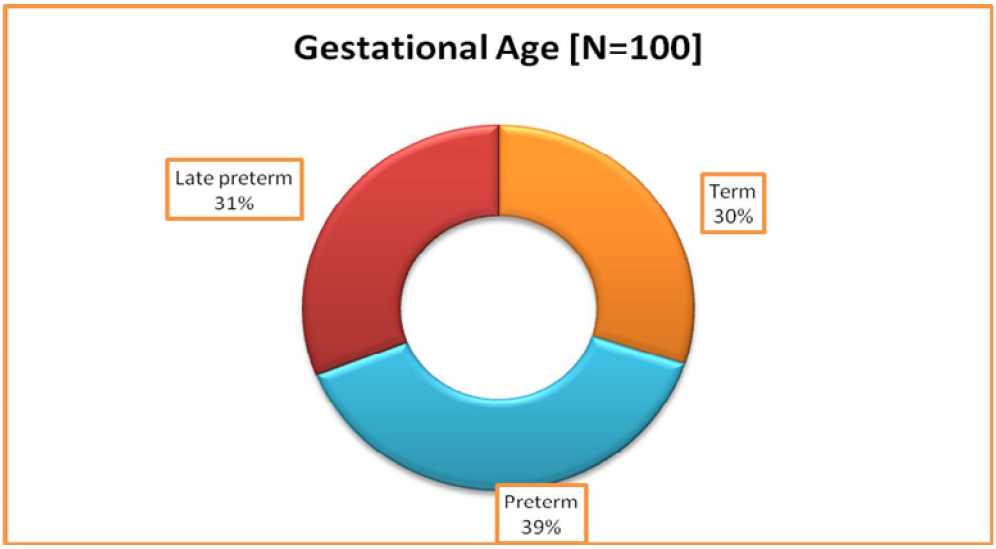

Figure 37: Doughnut chart demonstrating the distribution of children on the basis of gestational age.

It was noted that among the 39 preterm children, 34 had an abnormal MRI. Further, 27 late preterm children were found to have abnormal imaging findings. Hence, the **prevalence of abnormal neuroimaging was more among the preterm and late preterm children**.

Association of Gestational Age with MRI findings			
	MRI Findings		
Gestational Age	Normal	Abnormal	Total
Term	13	17	30
Preterm	5	34	39
Late preterm	4	27	31
Total	22	78	100

Table 9: Table showing the association of gestational age with MRI findings.

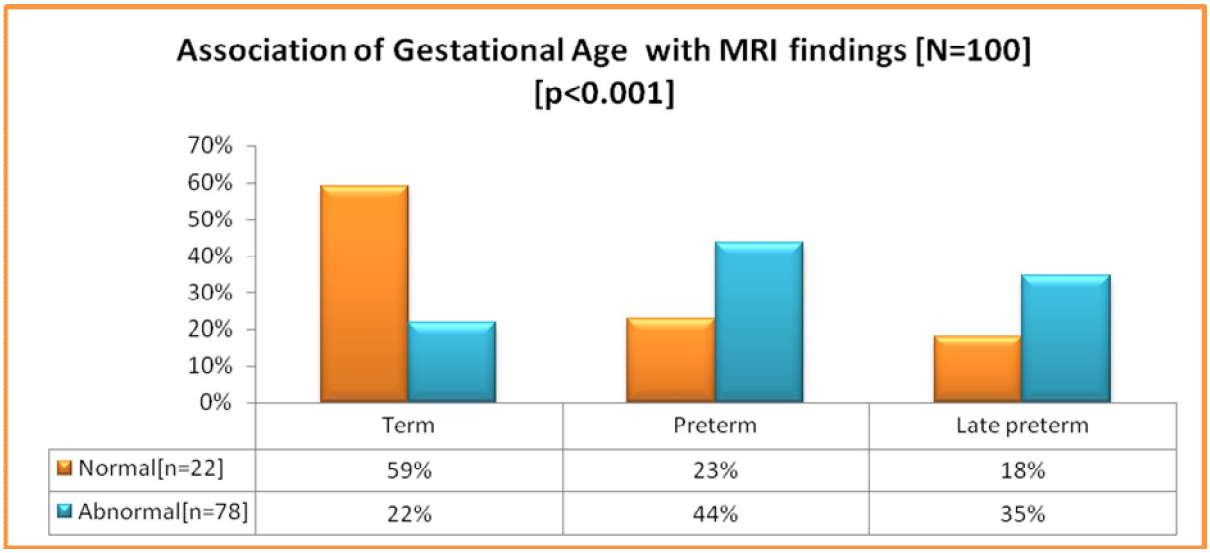

Figure 38: Bar diagram showing the association of gestational age with MRI findings.

4. CLINICAL ASSOCIATIONS

Relevant clinical associations were elicited and summarised. It was noted that among the 100 children evaluated in our study, 61% had associated seizures.

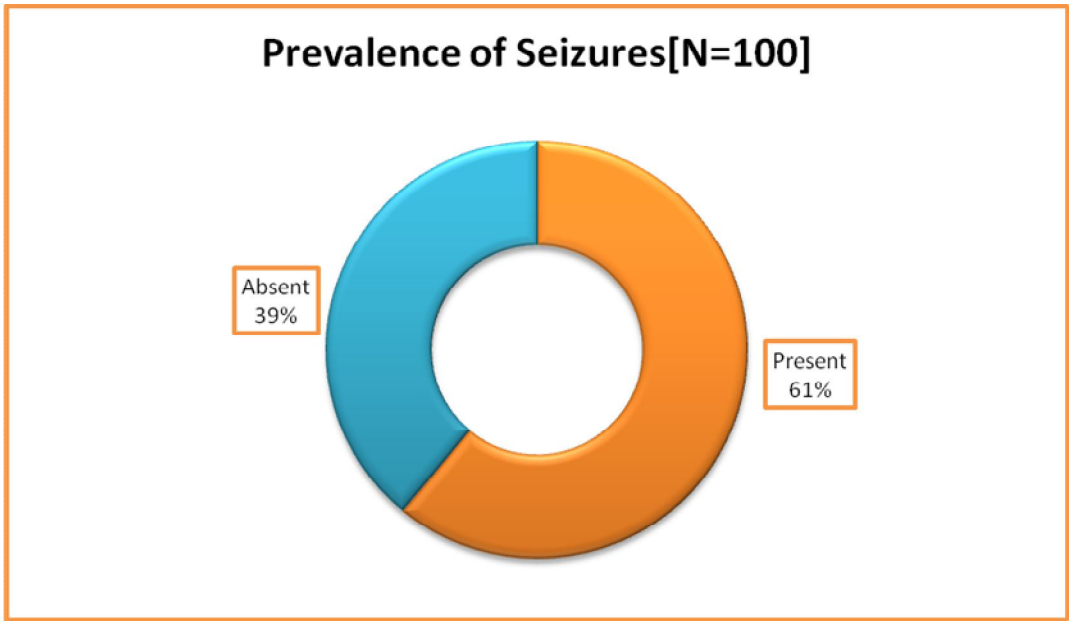

Figure 39: Doughnut chart showing the prevalence of seizures among the evaluated children.

Out of the 61 developmentally delayed children associated with seizures, 56 had an abnormal MRI. Further, it was noted that among the 22 children with a normal MRI only 5 were associated with seizures. Hence, it was inferred that the **children with associated seizures had a larger proportion of abnormal MRI** ($p<0.001$).

Association of Seizures with MRI findings			
	MRI Findings		
Seizures	Normal	Abnormal	Total
With Seizures	5	56	61
Without Seizures	17	22	39
Total	22	78	100

Table 10: Table showing the association of seizures with MRI findings.

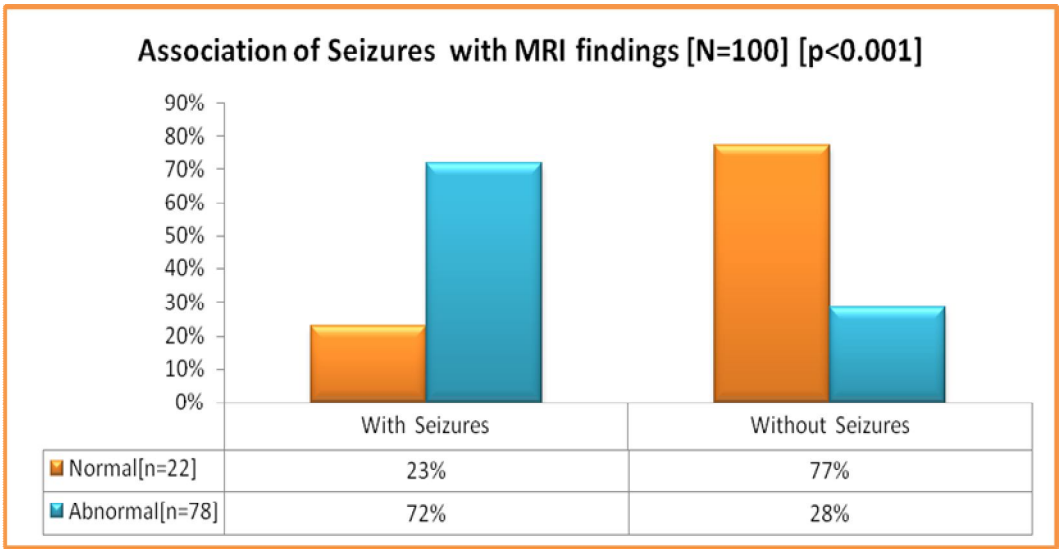

Figure 40: Bar diagram showing the association of seizures with MRI findings.

The spectrum of clinical findings was studied in detail. 61% of the children presenting with developmental delay had associated seizures, 24% had some form of neurological deficits, 8% had respiratory and cardiac disease, 5% had hypothyroidism. No significant clinical association was demonstrated in 20% of the children. A smaller group of children accounting for 8% had associated features lik CTEV, visual disturbances, reduced head circumference etc.,

Spectrum of clinical findings		
Clinical findings	N	(%)
Seizures	61	61%
Neurological deficits	24	24%
Respiratory and cardiac disease	8	8%
Hypothyroidism	5	5%
Others	8	8%
Nil	20	20%

Table 11: Table showing the spectum of clinical findings in percentage (%)

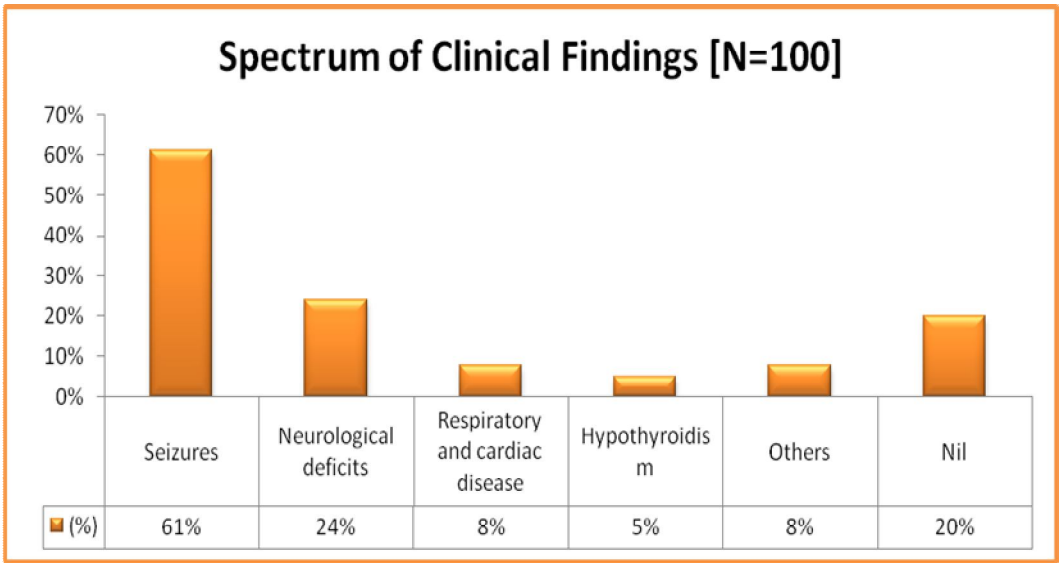

Figure 41: Bar diagram showing the various clinical findings.

Among the children with neurological deficits (24%), 11% had hypotonia and 7% had spasticity. Gait abnormalities were seen in 4% while 2% had associated hemiplegic cerebral palsy.

Prevalence of Neurological Deficits [n=24]		
Neurological Deficits	N	(%)
Hypotonia	11	11%
Spasticity	7	7%
Gait abnormality	4	4%
Hemiplegic cerebral palsy	2	2%
Total	24	24%

Table 12: Table showing the prevalence of various neurological deficits (n=24)

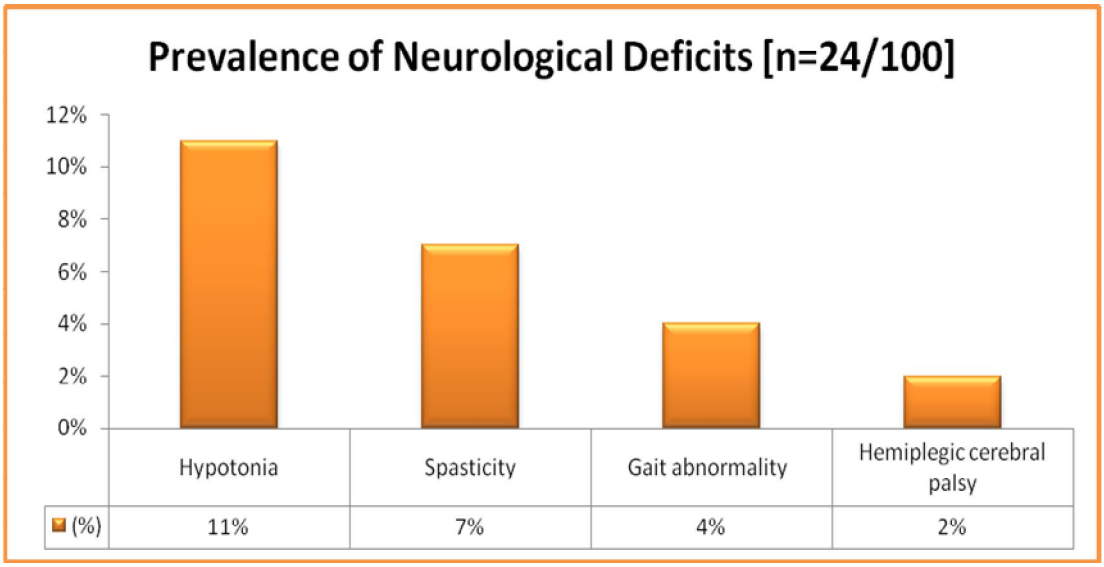

Figure 42: Bar diagram showing the prevalence of various neurological deficits (n=24)

It was noted that among the 20 children presenting with "only" developmental delay, 11 had normal MRI findings. This was in contrast to the children who presented with developmental delay "plus" syndromes. Out of 80 children presenting with additional clinical features along with developmental delay, 69 had an abnormal MRI. Hence, the **presence of additional clinical features in children with developmental delay was associated with abnormalities in the brain MRI** ($p<0.001$) which could reflect graver clinical prognosis.

The Clinical presentation of study population with normal and abnormal MRI findings				
	MRI Findings			
Clinical presentation	Normal	Abnormal	Total	
Only Developmental Delay	11	9	20	
Developmental Delay Plus	11	69	80	
Total	22	78	100	

Table 13: Table showing the clinical presentation of the study population with normal and abnormal MRI.

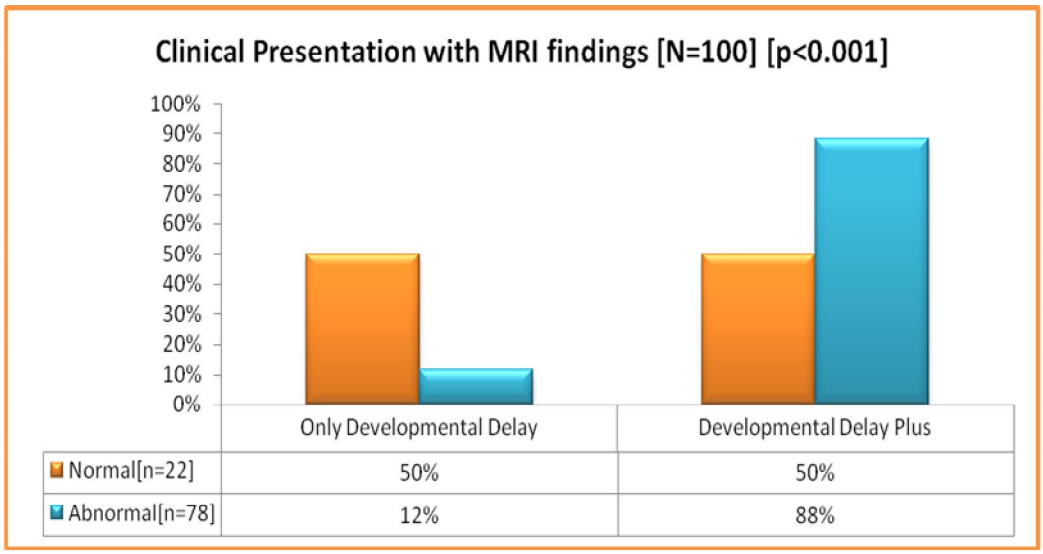

Figure 43: Bar diagram showing the clinical presentation of the study population with normal and abnormal MRI.

5. INVOLVED BRAIN STRUCTURES

The MR images were evaluated in detail with regard to the various structures involved in patients presenting with developmental delay. The following brain structures were systematically evaluated based on a study by **Widjaja et al-** ventricles, corpus callosum, gray matter, white matter, basal ganglia, limbic system, brain stem, cerebellum and cranial vault.

Our study revealed **abnormalities of the white matter in 50% of the patients** with developmental delay**. Ventricular abnormalities were seen in 37% of the patients**. The **corpus callosum was abnormal in 24%** while the gray matter showed abnormalities in 13% of the patients. Abnormalities of the basal ganglia and limbic system were seen in 5% and 3% of the patients respectively. The cranial vault was abnormal in 4% of the patients. Brain stem abnormalities were seen in only 2% of the patients. Around 10% of the patients had involvement of other brain structures like vermis, cerebellar tonsils, subarachnoid spaces and cisterns, choroid plexus etc., (denoted as "Others")

MRI findings - Involved Brain structures				
	Abnormal		Normal	
Involved Brain structures	N	(%)	N	(%)
Ventricles	37	37%	63	63%
White Matter	50	50%	50	50%
Gray matter	13	13%	87	87%
Corpus callosum	24	24%	76	76%
Limbic system	3	3%	97	97%
Basal ganglia	5	5%	95	95%
Brain stem	2	2%	98	98%
Cranial vault	4	4%	94	94%
Others	10	10%	90	90%
Total	100	100%	100	100%

Table 14: Table showing the relative frequencies of the involved brain structures on MRI

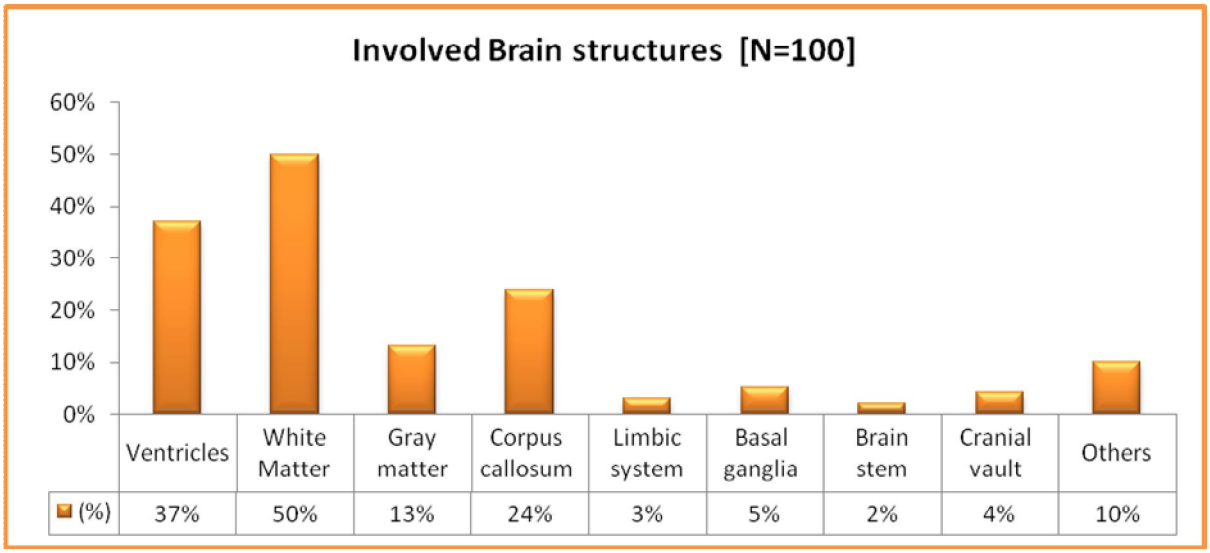

Figure 44: Bar diagram showing the relative frequencies of the involved brain structures on MRI.

6. CATEGORIZATION OF MRI FINDINGS

The various MRI findings and diagnosis were categorized based on a study by **Williams et al**[4] .

The prevalence of abnormal MRI findings was 78% among the evaluated children. Among the children with abnormal MRI findings 11% had non specific imaging findings as mentioned above.

Prevalence of MRI findings		
MRI Findings	n	(%)
Normal	22	22%
Abnormal	78	78%
Total	100	100%

Table 15: Table showing the prevalence of normal and abnormal MRI findings.

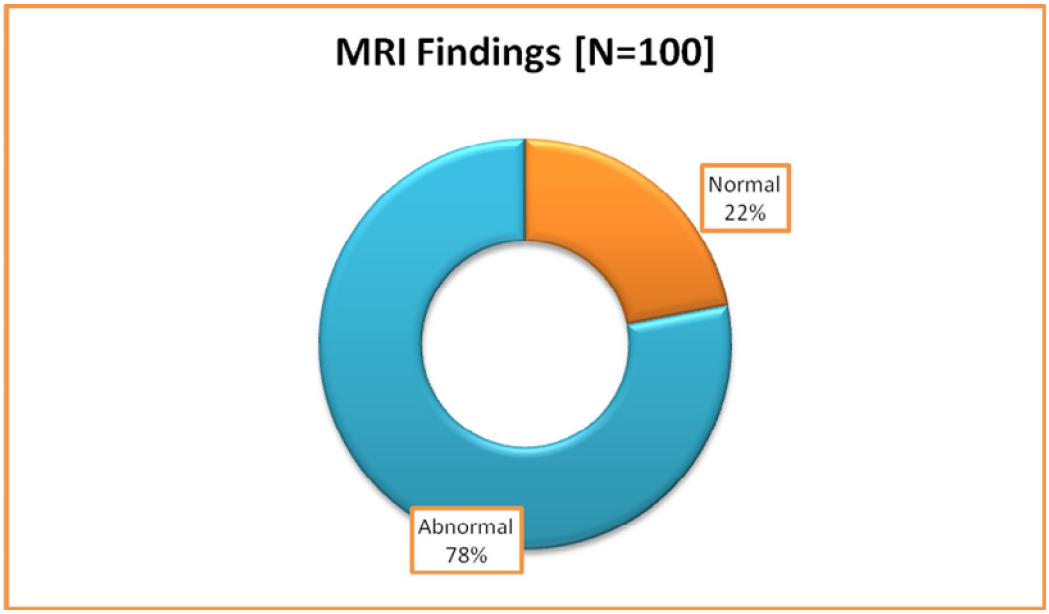

Figure 45: Doughnut diagram showing the prevalence of normal and abnormal MRI findings.

The various MRI findings were categorized into one or more of the above mentioned categories based on a study by Williams et al. Etiological categorization revealed **normal brain MRI in 22 cases** (22%). The remaining 78 cases with an abnormal MRI were further categorized, of which **50 cases (50%) had findings consistent with Neurovascular diseases**. The proportion of children with Congenital and developmental disorders, Neoplastic and cystic lesions and non specific imaging findings were 12 cases (12%), 3 cases (3%) and 11 cases (11%) respectively. 2 cases (2%) showed a combined or multifactorial etiology

Categorization of MRI findings (N=100)		
Categories	N	(%)
Normal	22	22%
Non specific imaging findings	11	11%
Congenital and Developmental	12	12%
Neoplastic and cystic lesions	3	3%
Neurovascular	50	50%
Multifactorial	2	2%
Total	100	100%

Table 16: Table showing the categorization of various MRI findings.

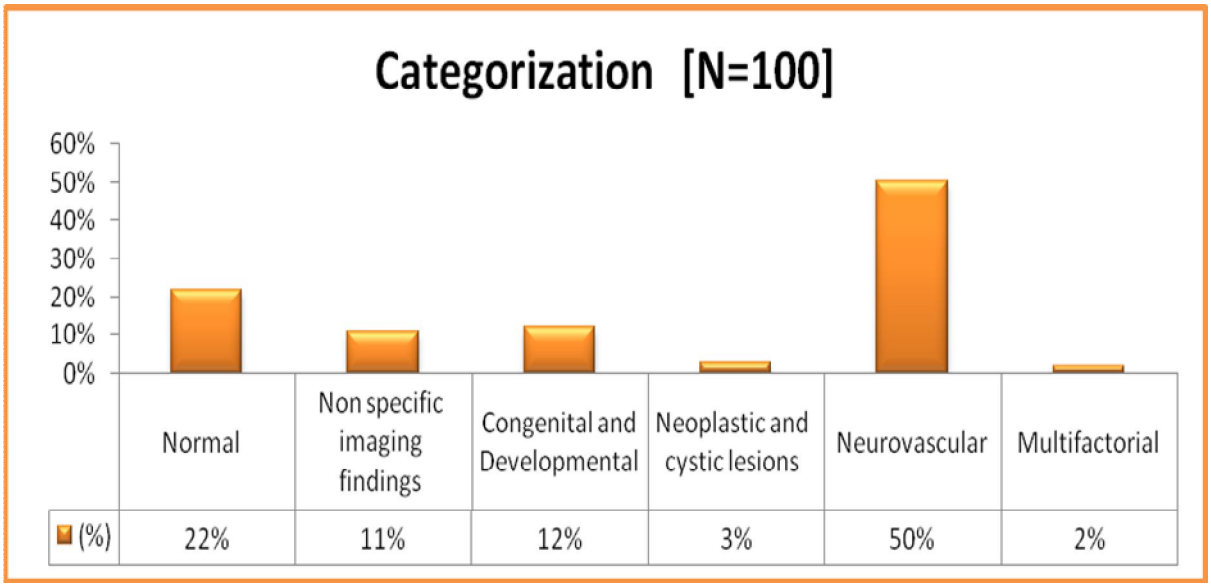

Figure 46: Bar diagram showing the categorization of various MRI findings.

Further, the neurovascular category was evaluated based on the age of the patients. It was noted that around 30% of the patients in the category were in the age group of 3-5 years. Rest of the age groups showed nearly equal incidence of the neurovascular etiology with a relatively lower incidence in the older age group (9-10 years).

Age wise distribution of the Neurovascular etiology			
	Neuro vascular		
Age	N	%	
<1	10	20%	
1- 2	10	20%	
3 - 5	15	30%	
6 - 8	12	24%	
9 - 10	3	6%	
Total	50	100%	

Table 17: Table showing the age wise distribution of the neurovascular etiology.

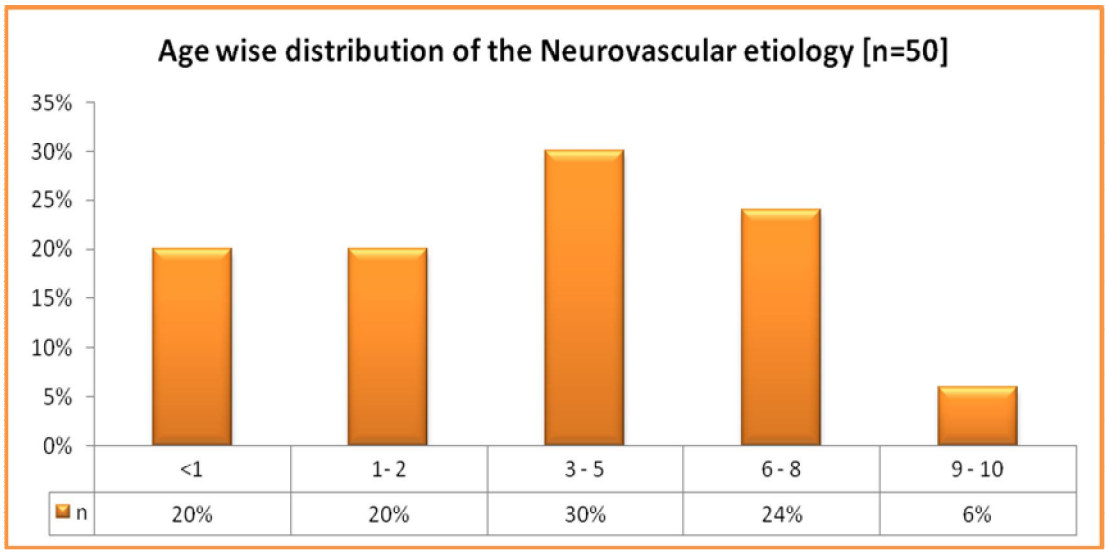

Figure 47: Bar diagram showing the age wise distribution of the neurovascular etiology.

7. MR SPECTROSCOPY:

22 children had a normal MRI in our study. Out of the 22 children, 10 children were subjected to MR Spectroscopic evaluation. Various neurometabolite ratios were calculated using multivoxel MR spectroscopy. Voxels were placed in bilateral frontal and parieto-occipital subcortical white matter. The following metabolite ratios were calculated : NAA/Cr and Cho/Cr.

MR spectroscopy with the multivoxel technique was done in 10 children with normal MRI. This included children with adequate cooperation and with no risk of prolonged sedation. Since the spectroscopic evaluation is done prospectively after evaluating the preliminary MRI, various technical difficulties like motion artefacts due to inadequate cooperation by the child and risk of increased sedation mainly in younger children and infants, limit the use of this technique. Further, the risk versus benefit proportion of the technique should always be gauged.

There was no significant differance in the neurometabolite ratios among the patients in whom MR Spectroscopy was performed. The average metabolite ratios of the children are summarized below.

NAA/Cr	Cho/Cr
2.50	1.37

Table 18: Table showing the average neurometabolite ratios in the children evaluated with MR Spectroscopy.

DISCUSSION

COMPARASION OF CLINICAL VARIABLES WITH OTHER STUDIES:

Out of 100 children presenting with developmental delay in our study, 61% had associated seizures. The proportion of **children with associated seizures in a study by Widjaja et al[3] was 26%** wherein 90 children with developmental delay were evaluated with a brain MRI. The percentage of children with seziures in a study by **Momen et al [24] and Koul et al [29] was 53% and 43%** respectively.

	Current study	Widjaja et al [n=90]	Momen et al [n=580]	Koul et al [n=110]
Clinical findings	(%)	(%)	(%)	(%)
Seizures	61%	26%	53%	43%

Table 19: Table showing comparative analysis of the proportion of children with seziures in various studies.

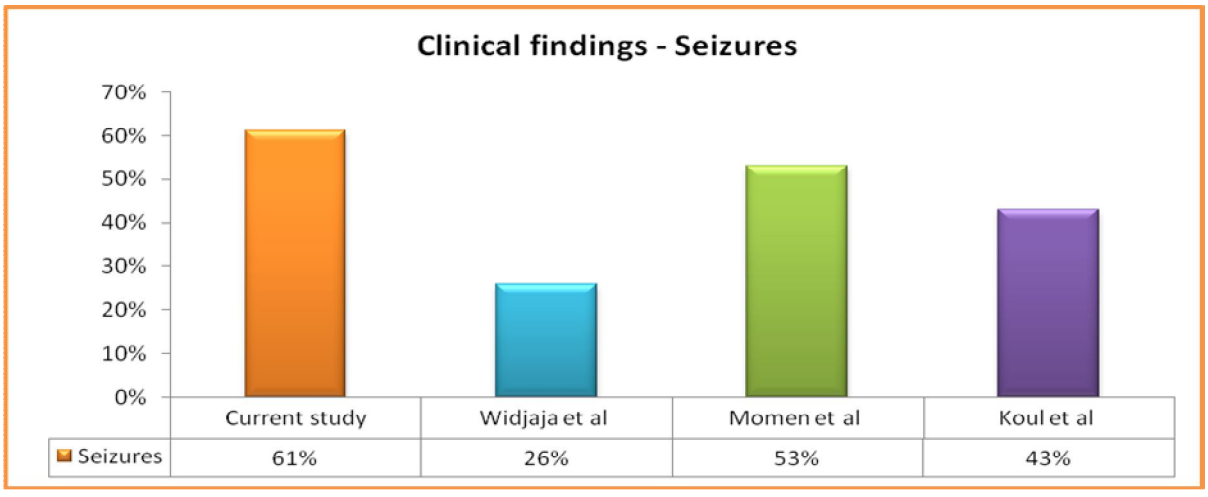

Figure 48: Bar diagram showing comparative analysis of the proportion of children with seizures in various studies.

Hence, the proportion of children with developmental delay associated with seizures was comparable with prior studies (Momen et al, Koul et al).

The proportion of children with an abnormal MRI presenting with developmental delay only was 12% versus **88% of children with developmental delay "plus" associated with an abnormal MRI.** This was compared to other relevant studies. In a **study by Ali et al [20], 89% of children with developmental delay "plus" had an abnormal MRI**. Similarly in a study by Widjaja et al, 88% of children with developmental delay "plus" were associated with abnormal MRI.

This further **emphasizes the association of abnormal MRI in children with developmental delay "plus" disorders**.

Clinical presentation with abnormal MRI findings						
	Current study		Ali et al[n=81]		Widjaja et al [n=90]	
Clinical presentation	(%)		(%)		(%)	
Only Developmental Delay	12%		11%		12%	
Developmental Delay Plus	88%		89%		88%	

Table 20: Table showing comparasion of clinical presentation with abnormal MRI.

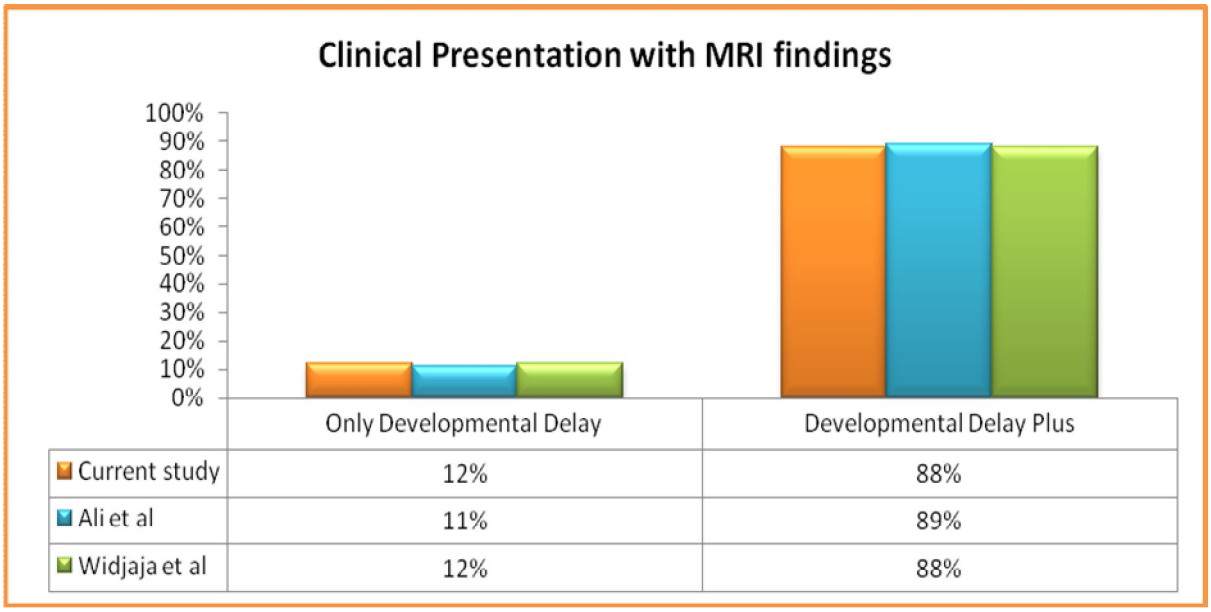

Figure 49: Bar diagram showing comparasion of clinical presentation with abnormal MRI.

COMPARASION OF NORMAL VERSUS ABNORMAL MRI FINDINGS:

The proportion of children with normal and abnormal MRI findings in our study was 22% and 78% respectively. This was compared with other similar studies in literature. In the study by **Ali et al [20] the proportion of children with an abnormal MRI was 68%**. Other studies including Momen et al [24], Widjaja et al [3] and Koul et al [29] had the following percentage of children with an abnormal MRI; 59%, 84% and 81% respectively.

The findings of our study are **comparable to the studies by Ali et al, Koul et al and Widjaja et al.** However, the study by Momen et al showed a larger number of children with a normal MRI as compared to our study (41%). This could be partly due to the relaxation of the upper age limit included in their study (2 months to 15 years) and the larger sample size (n=580).

	MRI Findings	
	Normal	Abnormal
Current study [n=100]	22%	78%
Ali et al[n=81]	32%	68%
Momen et al [n=580]	41%	59%
Widjaja et al [n=90]	16%	84%
Koul et al [n=110]	19%	81%

Table 21: Table showing comparasion of normal and abnormal MRI findings.

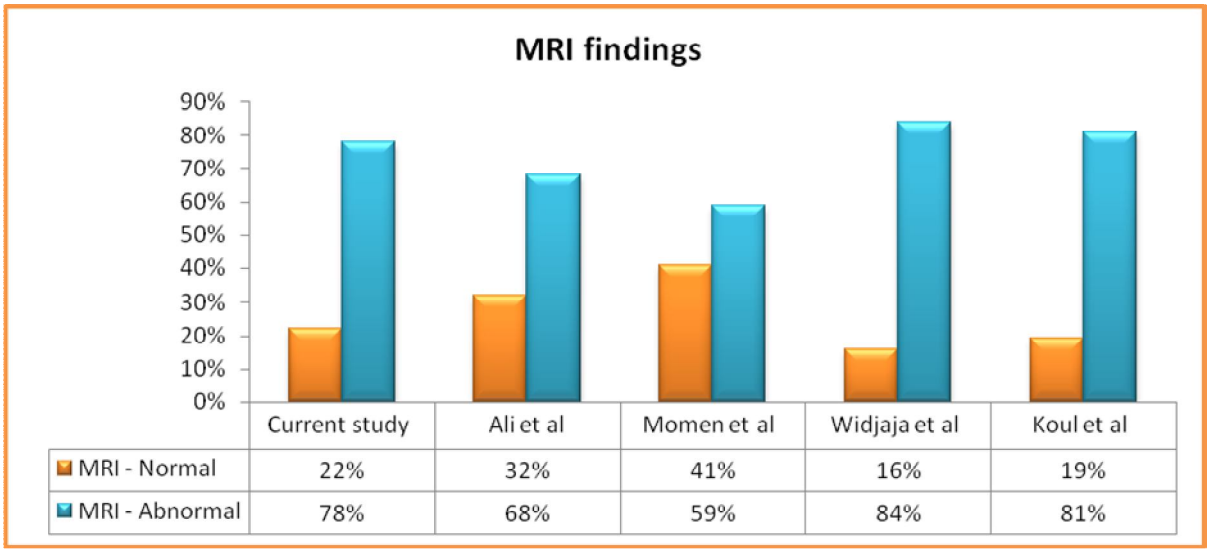

Figure 50: Bar diagram showing comparasion of normal and abnormal MRI findings.

COMPARASION OF THE INVOLVED BRAIN STRUCTURES:

The various involved brain structures were compared with other studies. Our study showed abnormalities of the white matter in 50% of children. The corpus callosum, ventricles, gray matter, basal ganglia, limbic system and brain stem were involved in 24%, 37%, 13%, 5%, 3% and 2% of children respectively. In a study by **Widjaja et al [3], the white matter was abnormal in 26% of the children**. The corpus callosum, ventricles, gray matter, basal ganglia, limbic system and brain stem were involved in 44%, 48%, 4%, 2%, 6% and 4% of children respectively. Our study showed an increased proportion of children with involvement of the white matter compared to the above mentioned study.

MRI findings - Involved Brain structures				
	Current study		Widjaja et al [n=90]	
Involved Brain structures	(%)		(%)	
Ventricles	37%		48%	
White Matter	50%		26%	
Gray matter	13%		4%	
Corpus callosum	24%		44%	
Limbic system	3%		6%	
Basal ganglia	5%		2%	
Brain stem	2%		4%	

Table 22: Table showing comparasion of the various involved brain structures.

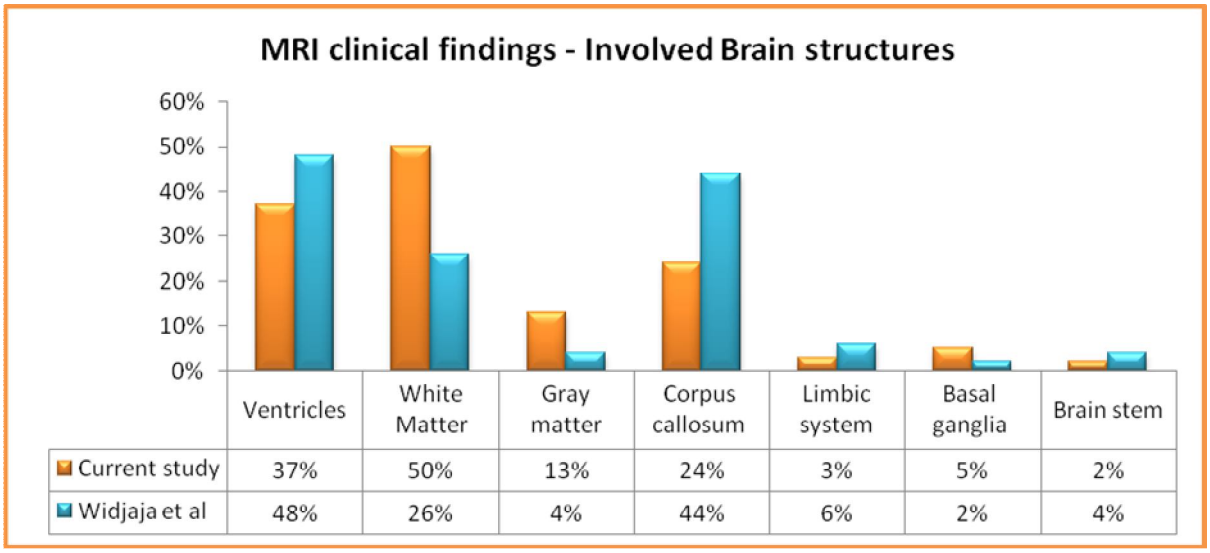

Figure 51: Bar chart showing comparasion of the various involved brain structures.

In a study by **Ali et al [20], white matter and corpus callosum were abnormal in 58% and 16% of children** which was comparable to the figures obtained in our study.

MRI findings - Involved Brain structures			
	Current study	Ali et al[n=81]	
Involved Brain structures	(%)	(%)	
Ventricles	37%	62%	
White Matter	50%	58%	
Gray matter	13%	11%	
Corpus callosum	24%	16%	
Brain stem	2%	9%	

Table 23: Table showing comparasion of the various involved brain structures.

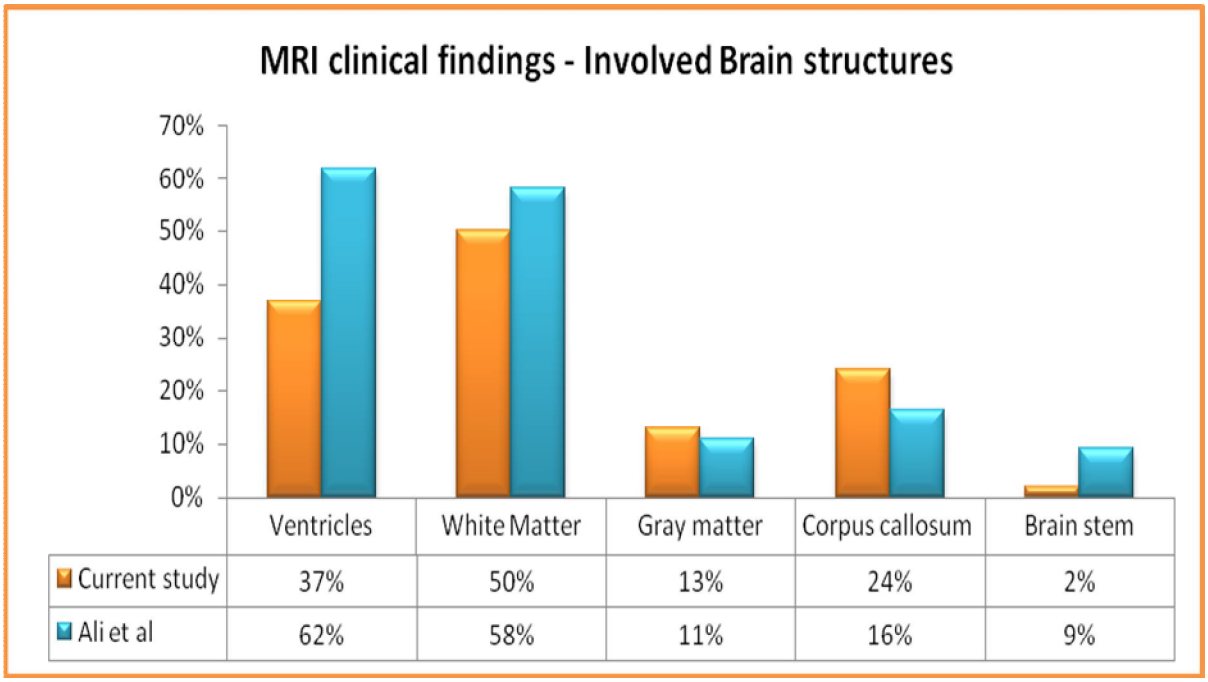

Figure 52: Bar chart showing comparasion of the various involved brain structures.

COMPARASION OF VARIOUS CATEGORIES:

The categories based on the morphologic abnormalities on MRI were compared with the relevant studies. In a **study by Ali et al [20], the most common abnormality encountered was Neurovascular disesaes like hypoxic ischemic encephalopathy** (31%). Our study reported a slightly higher percentage of children in this category (50%). The rest of the categories were comparable to the above mentioned study.

Categorization of MRI findings				
	Current study		Ali et al[n=81]	
Categories	(%)		(%)	
Normal	22%		32%	
Non specific imaging findings	11%		8%	
Congenital and Developmental	12%		17%	
Neoplastic and cystic lesions	3%		3%	
Neurovascular	50%		31%	

Table 24: Table showing comparasion of various categories of abnormalities on MRI.

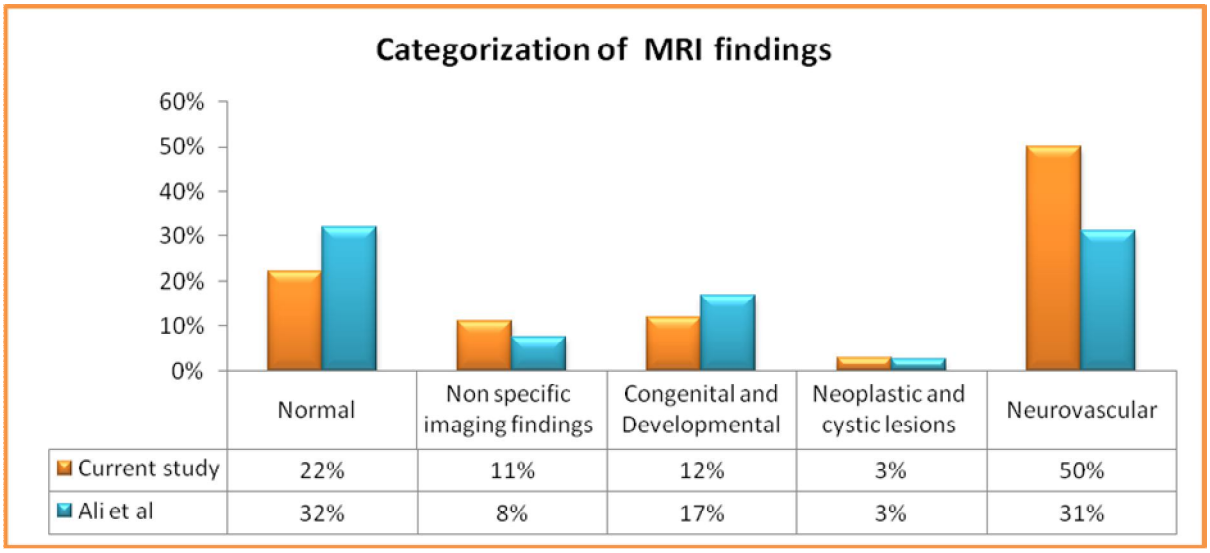

Figure 53: Bar diagram showing comparasion of various categories of abnormalities on MRI.

In a study by **Momen et al [24], the most common categorical abnormality was neurovascular diseases which accounted for nearly 38% of the total cases**. This was comparable to our study. The rest of the compared variables showed similar proportions as obtained in our study.

Categorization of MRI findings				
	Current study		Momen et al [n=580]	
Categorize	(%)		(%)	
Normal	22%		41%	
Non specific imaging findings	11%		7%	
Congenital and Developmental	12%		7%	
Neurovascular	50%		38%	

Table 25: Table showing comparasion of various categories of abnormalities on MRI.

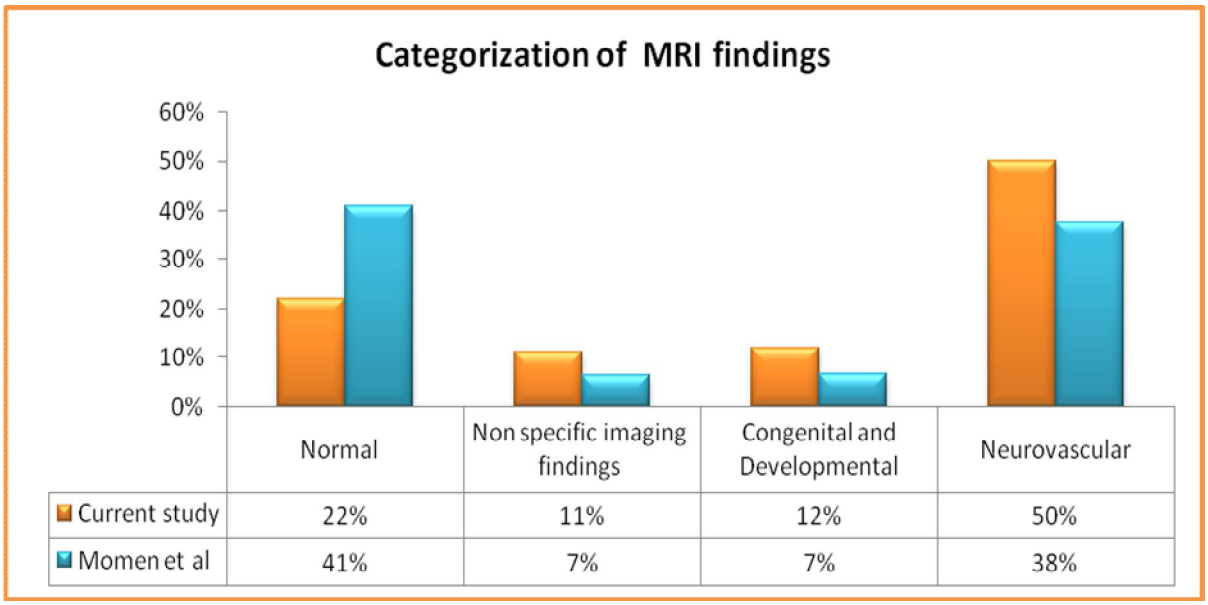

Figure 54: Bar diagram showing comparasion of various categories of abnormalities on MRI.

COMPARASION OF THE MR SPECTROSCOPY FINDINGS:

MR Spectroscopic examination was done in 10 children with a normal MRI of the brain. The average neurometabolite ratios were calculated and it was noted that there was no significant difference among the various patients evaluated.

Our **findings were comparable to those of Filippi et al [25], Kosucu et al [27] and Martin et al** [31] who also demonstrated no significant differance in the neuro metabolite ratios in children with or without developmental delay. However Filippi et al stated a reduction in the metabolite ratios in children above two years of age.

As stated by previous studies like Filippi et al [25] and Kosucu et al [27] the lack of neurometabolite ratio correlation could be attributed to the small sample size of the children undergoin spectroscopic examination.

REPRESENTATIVE CASES

CASE 1:

5 year old, late preterm male child presenting with seizures and developmental delay.

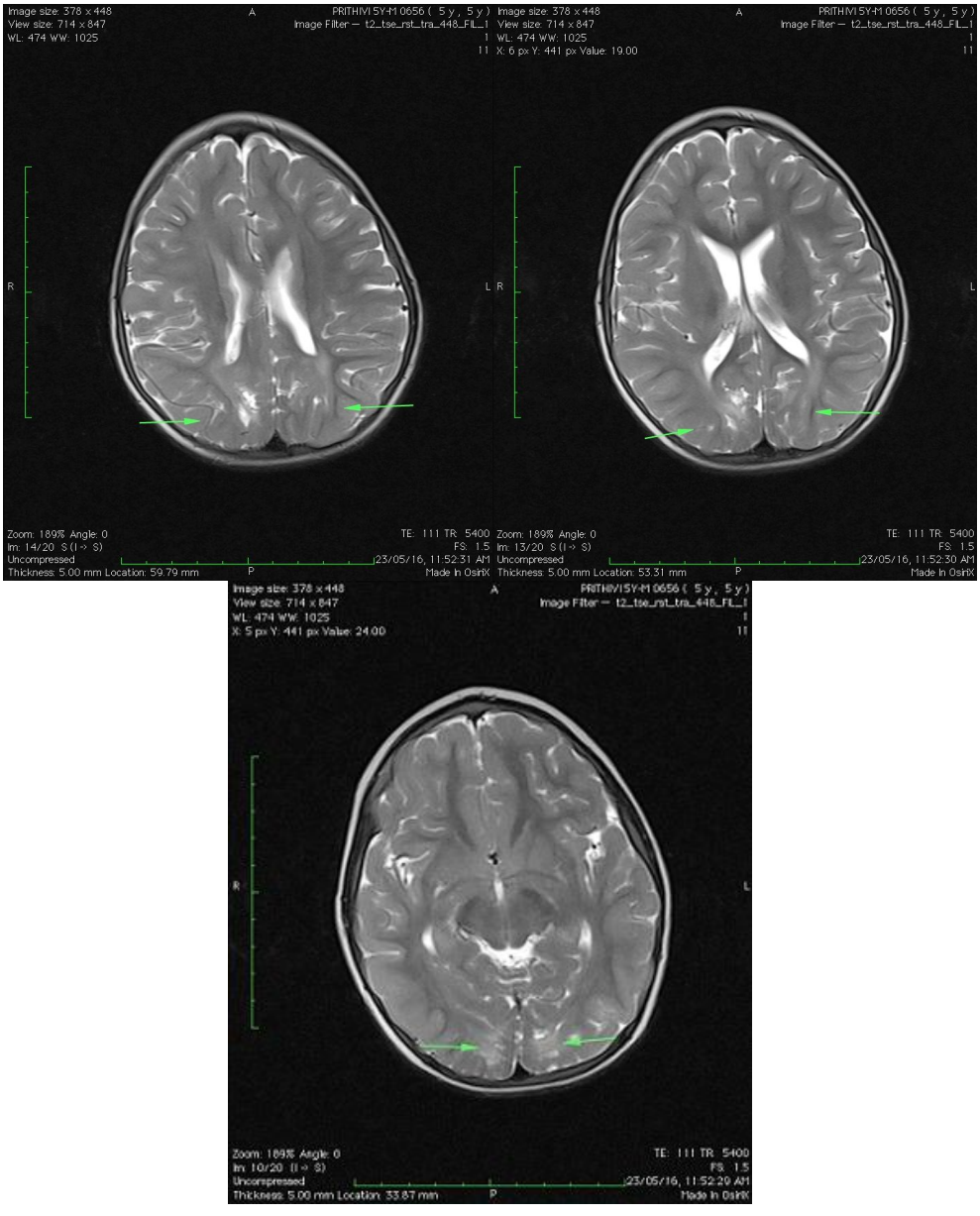

Figure 55 : Axial T2 weighted MR images showing paucity of bilateral parietoccipital periventricular white matter with gyral thinning (periventricular leukomalacia) in a case of hypoxic ischemic injury.

CASE 2:

10 year old, preterm male child presenting with developmental delay.

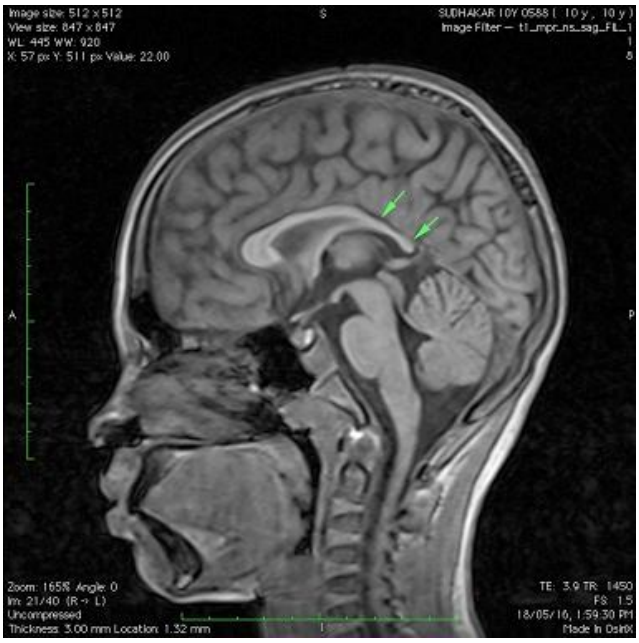

Figure 56: Sagittal T1 weighted MR image shows thinning of posterior body and splenium of corpus callosum (arrows) as a sequalae of hypoxic ischemic injury. Child also had features of periventricular leukomalacia.

CASE 3:

2 year old, preterm male child, known case of congenital heart disease came with developmental delay.

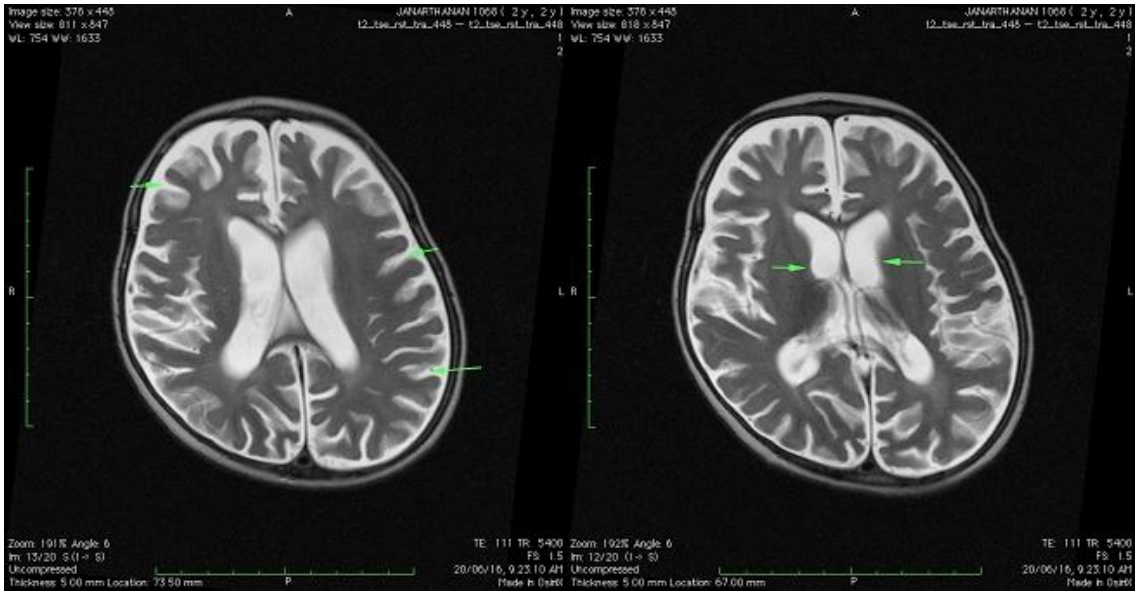

Figure 57: Axial T2 weighted MR image showing prominent sulci and ventricles in bilateral cerebral hemispheres -cerebral atrophy.

CASE 4:

2 year old, term male child with developmental delay.

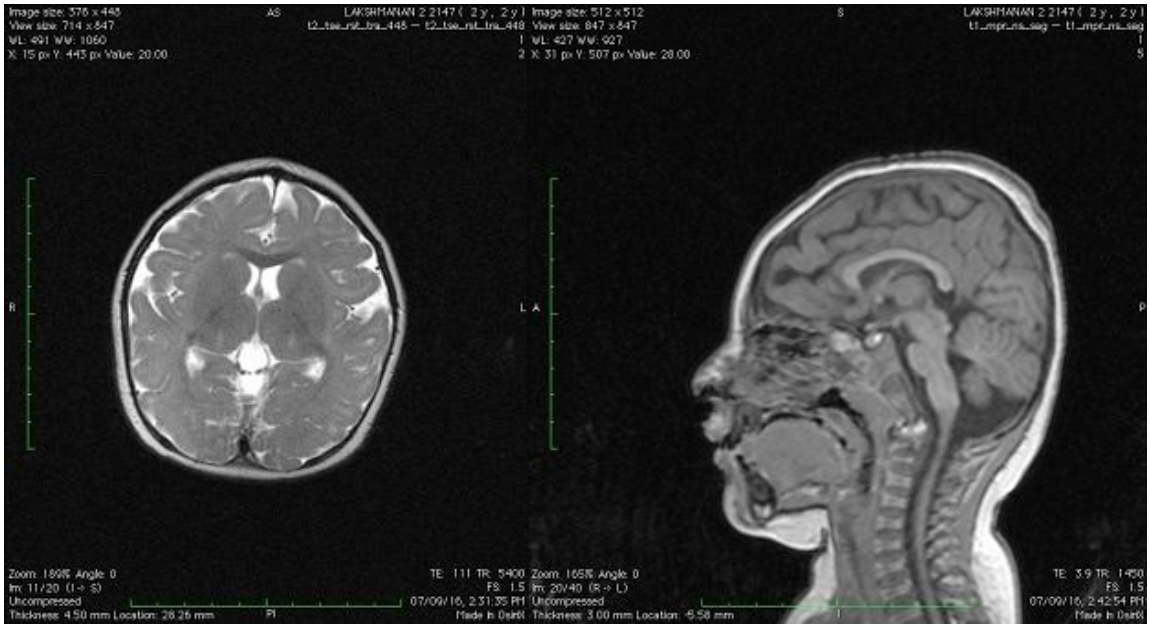

Figure 58: Axial T2 weighted (left) and sagittal T1 weighted image shows a small cranial vault suggestive of microcephaly. Also note that the body of bilateral lateral ventricles are prominent.

CASE 5:

1 year old, term male child, with developmental delay, seizures and hypotonia.

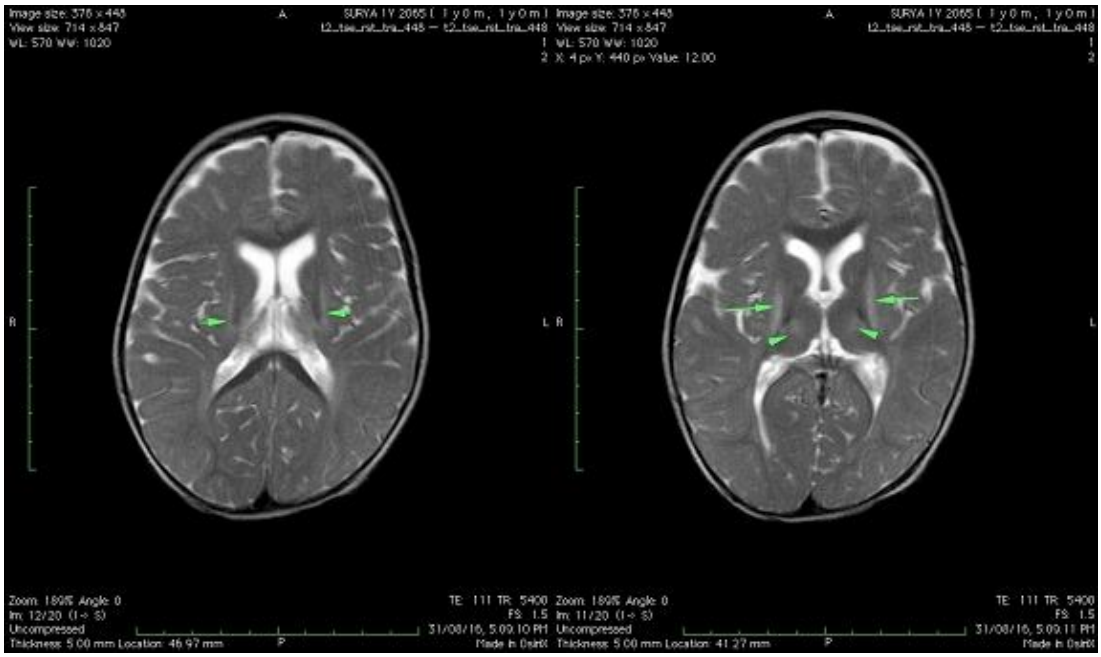

Figure 59: Axial T2 weighted MR images showing hyperintensity in bilateral lentiform nucleus, anterolateral thalami and corona radiata suggestive of "Profound hypoxic ischemic injury".

CASE 6:

4 year old, term female child with developmental delay.

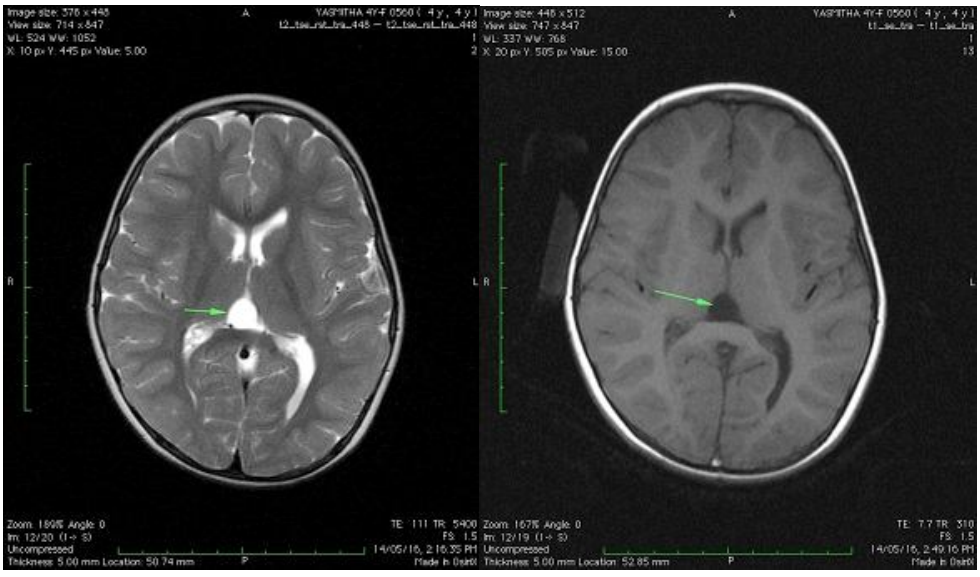

Figure 60: Axial T2 (left) and T1 (right) weighted MR image shows a CSF intensity lesion seen in the floor of the III ventricle (arrows). The lesion showed no restricted diffusion. Features consistent with "Arachnoid cyst".

CASE 7 :

9 year old, late preterm male child, with developmental delay "plus" syndrome.

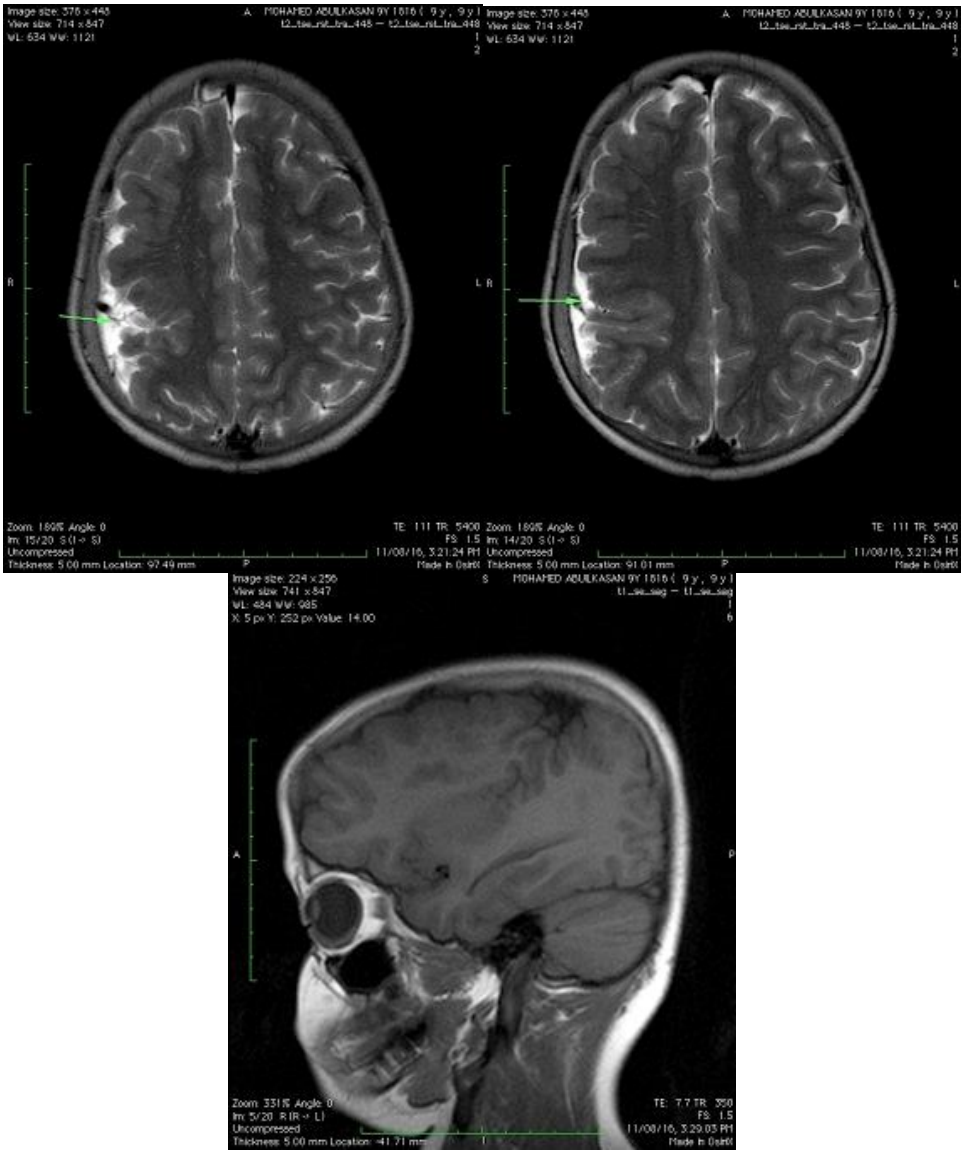

Figure 61: Axial T2 (top row) and sagittal T1 weighted (bottom) MR image shows irregular cortex with multiple shallow gyri with mild cortical thickening and irregular cortical-white matter interface noted in the right frontoparietal region suggestive of Polymicrogyria (PMG).

CASE 8:

8 months old, term male child, presented with lack of attaining head control and seizures.

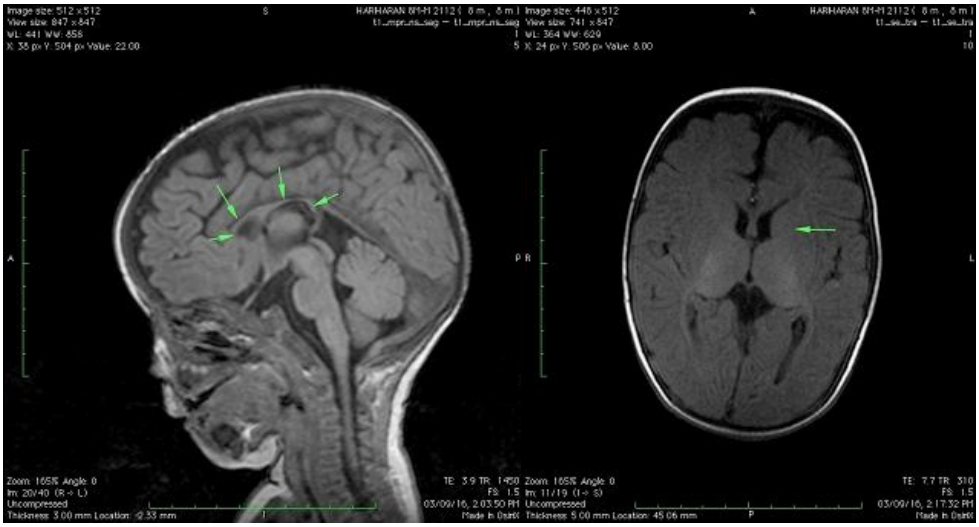

Figure 62: Left : Sagittal T1 weighted MR image showing global thinning of the corpus callosum (arrows). Right : Axial T1 weighted MR image showing delayed myelination (anterior limb of internal capsule and peripheral white matter show lack of hyperintense signal) (arrow). These findings are a result of hypoxic ischemic insult to the brain. The child also had other features of profound hypoxic ischemic injury (hyperintensity of thalami and lentiform nuclei).

CASE 9:

1 year old, late preterm female child, with developmental delay and spasticity.

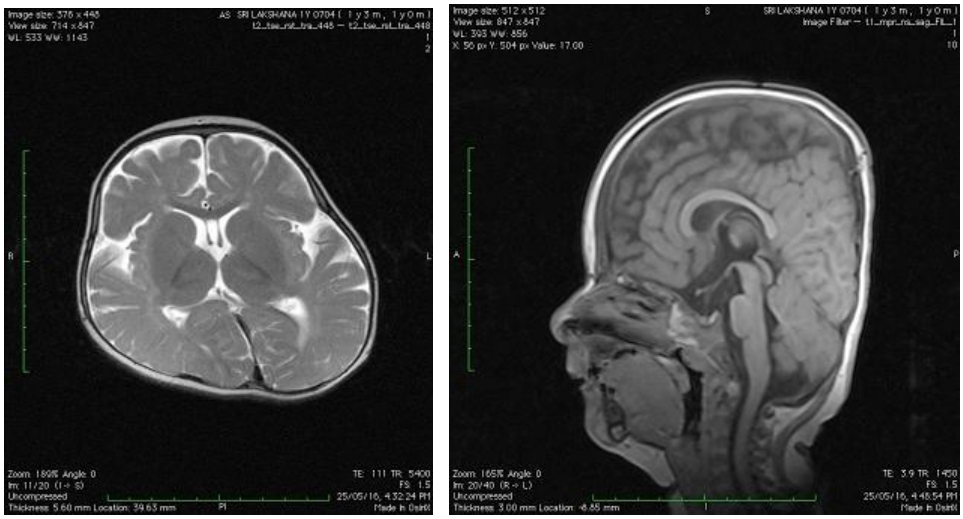

Figure 63: Axial T2 weighted (left) and sagittal T1 weighted (right) MR image shows features of brachycephaly (craniosynostosis).

CASE 10:

3 year old, preterm male child, presenting with developmental delay and seizures.

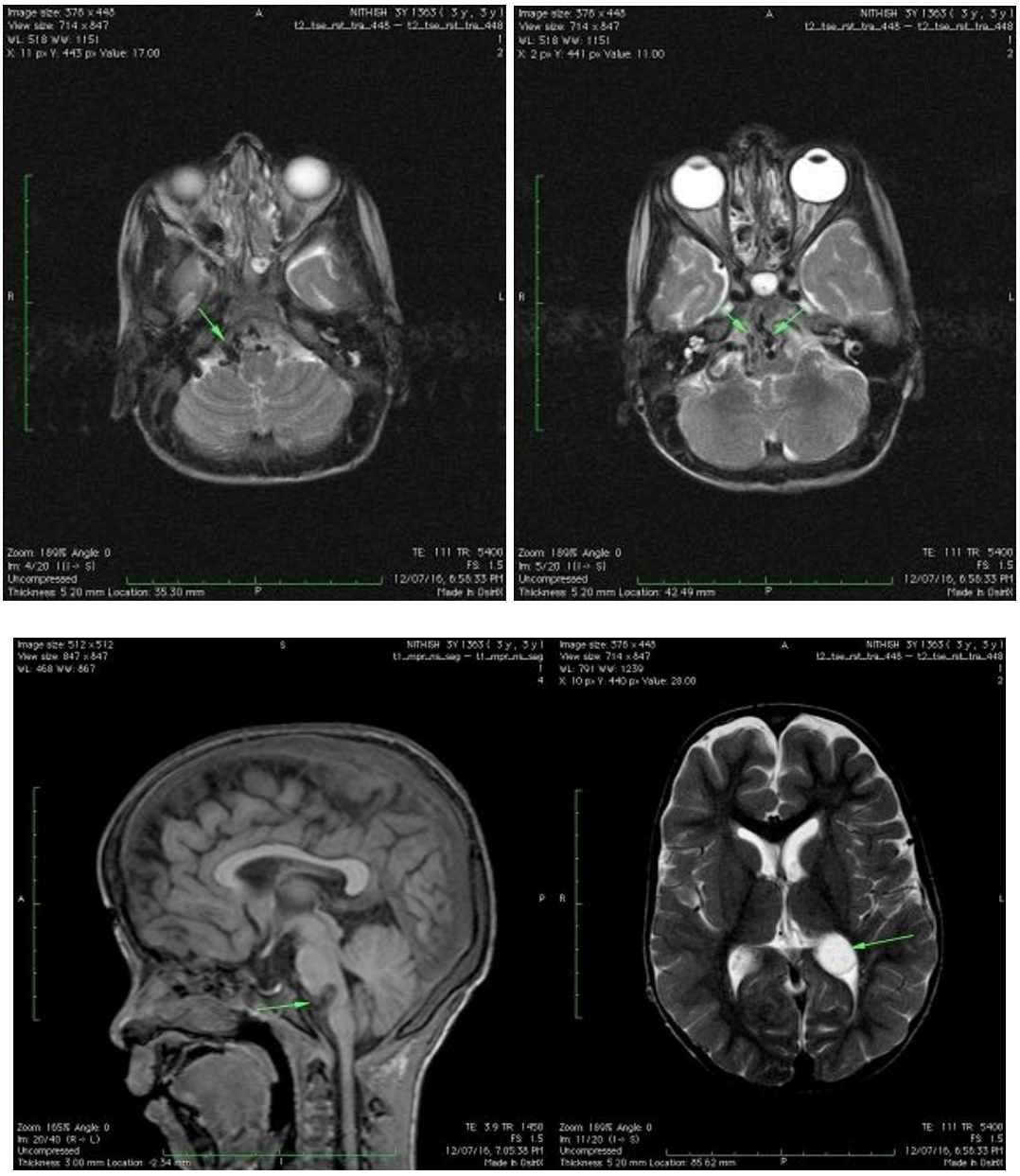

Figure 64: Axial T2 weighted (top) and sagittal T1 weighted (bottom left) MR image showing multiple, tortuous flow voids seen surrounding the ventral brain stem and abutting the basal cisterns (posterior fossa pial arteriovenous malformation). Axial T2 weighted image (bottom right) showing incidental choroid plexus cyst (arrow).

CASE 11:

5 year old, preterm female child with developmental delay. MRI brain within normal limits.

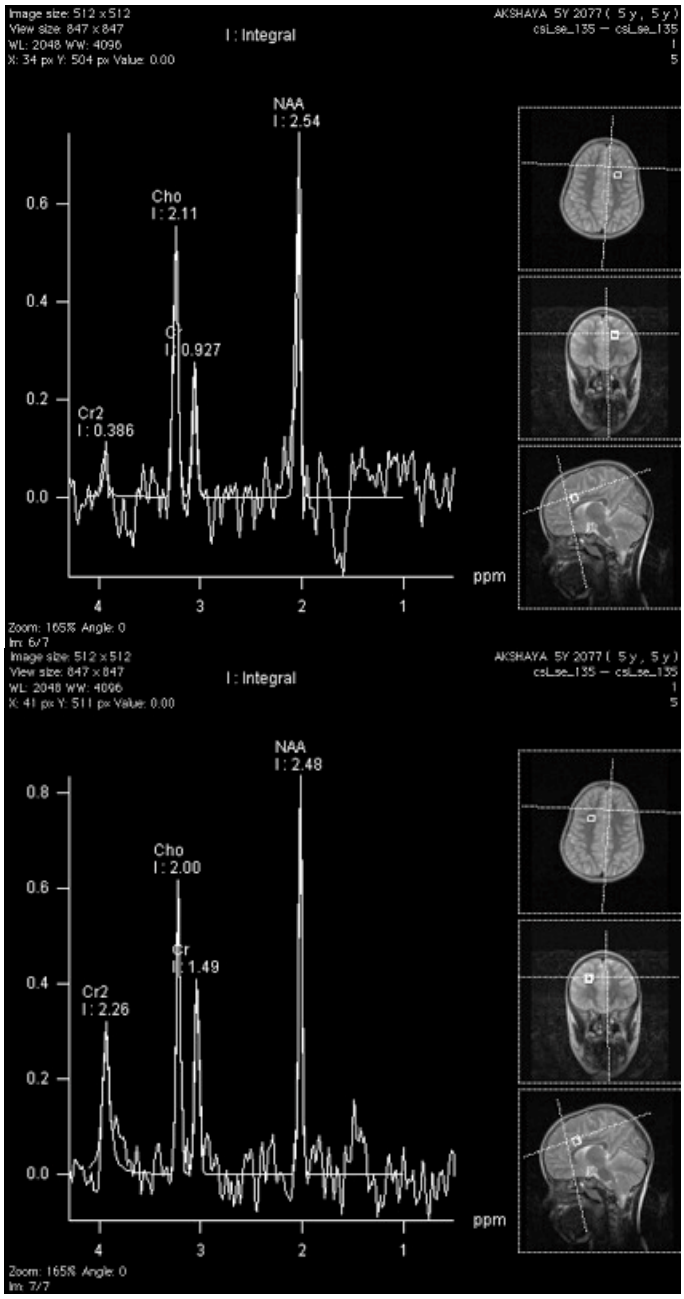

Figure 65: Multivoxel MR Spectroscopy with voxels in bilateral frontal and parieto-occipital white matter (frontal region shown in figures) shows normal neurometabolite ratios.

CONCLUSION

The current study was undertaken to evaluate the spectrum of abnormalities on MRI in children with developmental delay. The role of MR Spectroscopy in children with normal MRI was also studied.

Out of the 100 children evaluated in our study around 35 children were in the age group 3-5 years. The children were categorized based on gestational age with 39% of the children being preterm. Further, these children had an associated abnormal MRI in most cases. It was also noted that 61% of the children had associated seizures. It was inferred that the children with associated seizures had a larger proportion of abnormal MRI (56 out of the 61 children with seizures).

Among the rest of the children, 24% presented with one or more neurological deficits. It was also noted that there existed a significant correlation between the occurrence of an abnormal MRI and the presence of additional clinical features along with developmental delay (developmental delay "plus"). Among the 80 children presenting with developmental delay "plus", 69 had an abnormal MRI.

The various involved brain structures were also studied systematically. The white matter (50%), ventricles (37%) and corpus callosum (24%) were involved in most cases. Around 78% of the children had an abnormal MRI in our study. The various MRI abnormalities were categorized. The category of Neurovascular diseases showed the highest proportion of children in our study (50%) with an increased incidence in the age group 3-5 years. Most of the cases were a sequel to hypoxic ischemic injury.

MR Spectroscopy in children with normal MRI revealed no significant difference in the neurometabolite ratios among the children evaluated. Since MR Spectroscopy adds to the time period of the conventional MR protocol and is by far dependant on the patient being motionless for the entire duration of the study, this limits its use in younger children and infants due to motion artifacts and risk of prolonged sedation.

MRI has good sensitivity in diagnosing various disorders associated with developmental delay. Careful evaluation of the MRI helps identifying the probable etiology in most if not all cases. Additional clinical variables also add to the diagnostic accuracy of MRI.

MR Spectroscopy is an emerging technique in evaluating children with developmental delay. Proton MR Spectroscopy should be included in the standard imaging protocol while evaluating older children with developmental delay.

SUMMARY

Developmental delay has an estimated worldwide prevalence of 1-3% in children. Prompt and careful evaluation yields an etiology in around 50-70% of the cases. Neuroimaging forms an important diagnostic tool in children with developmental delay with around 60 % of the children having an abnormal MRI.

Our study involved 100 children with developmental delay who were referred to the Department of Radio diagnosis, Coimbatore Medical College Hospital, Coimbatore. The clinical and demographic parameters were evaluated. All children were subjected to MR imaging of the brain with standard protocols. The images were scrutinized with great deal of accuracy.

Age and gender specific results were obtained and analyzed. Further, the various involved brain structures were evaluated systematically. The study also elicited the prevalence of normal MRI in children with developmental delay. The various morphologic abnormalities were appropriately categorized. The role of MR Spectroscopy in imaging a child with developmental delay was also evaluated.

The goals of imaging should always focus on combined clinical and radiological variables. Hence, careful evaluation of the MRI helps the physician in further patient management and parent counseling.

LIMITATIONS

Lack of an etiological diagnosis in a few cases of developmental delay. Longitudinal studies in the form of follow up imaging will be more helpful to establish a relationship between the abnormalities on MR imaging and the long term prognosis of the child.

Limitations of MRI such as long imaging time, adequate patient immobilisation and claustrophobia are few of the other limitations of the study. Further, MR Spectroscopy has various limitations like contamination from surrounding tissues, lack of information of the metabolites from other regions of the brain and lack of precise measurement of absolute metabolite values.

CONSENT FORM

Yourself Master/Miss ..... c/o parent/guardian..... are being asked to be a participant in the research study titled **"MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY OF BRAIN IN CHILDREN WITH DEVELOPMENTAL DELAY"** in Coimbatore Medical College Hospital, Coimbatore, conducted by Dr. Naina Suresh, Post Graduate student in the department of Radio diagnosis, Coimbatore Medical College Hospital. You satisfy eligibility as per the inclusion criteria. You / your parent or guardian can ask any queries you may have before agreeing to participate.

PURPOSE OF RESEARCH:

1. To identify the spectrum of abnormalities in brain Magnetic Resonance Imaging (MRI) in children with developmental delay and categorize the morphologic abnormalities.

2. Role of Proton Magnetic Resonance Spectroscopy (MRS)

to ascertain the magnitude and severity of various neurometabolite ratios in children with normal brain imaging

PROCEDURES INVOLVED:

Infants and younger children will be sedated using oral/IV medication just prior to scanning. All patients will be evaluated using a 1.5 Tesla MRI system and routine sequences including MR Spectroscopy will be performed and findings will be recorded and stored on a computer.

PRIVACY AND CONFIDENTIALITY:

Privacy of individuals will be respected and any information provided will be kept confidential.

AUTHORISATION TO PUBLISH RESULTS:

Results of the study may be published for scientific purposes and/or presented to scientific groups; however you will not be identified.

STATEMENT OF CONSENT:

I ..... the parent/guardian of .....voluntarily give my consent to participate in this study. I have read the consent form/it has been read to me. The study has been fully explained to me and I understand that I am entitled to explanations regarding the study as and when necessary.

.....

Signature /Left thumb impression of parent/legal guardian of the child with date

.....

Signature of witness with date

xggpj;gotk;

bry;td;/ bry;tp..... taJ.....
je;ij / jha/ fhgghsh;..... fpH;f;fz;l
tpyhrj;jpy;
trpf;Fk;.....
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muR kUj;Jtf;fy;Y}hp kUj;Jtkidapy;nkwbfhs;sggLk; \is
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je;ij / jha; fhgghsh;bgah; rhl;rpad;bgah;

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Sl.No	Patient Name	Age	Sex(M=Male,F=Female)	Gestational Age	Relevant clinical associations	MR imaging features	Diagnosis	Categorization	Involved brain structures	MR Spectroscopy ratios
1	Anoj Kumar	2 yrs	M	Late preterm	Nil	Nil significant	Normal study	Normal	Nil	…
2	Hadasha	7 mon	F	Preterm	Seizures, hypotonia	Bilateral cerebral hemispheres show prominent sulcal spaces (cerebral atrophy) with thin posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	Gray matter, white matter, corpus callosum	…
3	Baby Fathima	9 mon	F	Preterm	Seizures, CTEV	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
4	Nithin	2 yrs	M	Term	Seizures	Paucity of left parietal deep whitematter	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
5	Hariharan	5 yrs	M	Preterm	Seizures	Volume loss in bilateral medial temporal lobes and hippocampi	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, limbic system	…
6	Mahesh	2 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	…
7	Vishwa	1 yr	M	Preterm	Seizures, hypotonia	Paucity of bilateral white matter , gyri are relatively few and broad with smooth cortical-white matter junction predominantly in bilateral parietal lobes, bilateral prominent ventricles	Sequalae to hypoxic ischemic injury with pachygyria	Neurovascular/Traumatic ; Congenital and developmental	White matter, gray matter, ventricles	…
8	Sri lakshana	1 yr	F	Late preterm	Bilateral visual impairment, spasticity	Brachycephaly, hypomyelination of dorsal brainstem , Pthsis bulbi right eye ,Calcified lens left eye	Brachycephaly(Craniosynostosis) with hypomyelination of brain stem	Congenital and Developmental	Brain stem, cranial vault	…
9	Prithvi	5 yrs	M	Late preterm	Seizures	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
10	Yogeshwaran	8 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.48, Cho/Cr 1.36
11	Hashini	6 yrs	F	Late preterm	Seizures	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	…
12	Hari	1 yr	M	Term	Hypotonia, gait abnormality	Severe paucity of bilateral frontal white matter with prominent ventricles and global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…
13	Vishnu	6 yr	M	Preterm	Seizures, hyotonia	Area of cystic encephalomalacia in right parietotemporal periventricular white matter with dilated lateral ventricle and global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…
14	Dhanadhayalan	1 yr	M	Late preterm	Seizures	Nil significant	Normal study	Normal	Nil	…
15	Sudhakar	10 yrs	M	Preterm	Respiratory tract infections , hypothyroid	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia, thinning of posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…
16	Yashmitha	4 yrs	F	Term	Nil	CSF intensity lesion seen in the floor of III ventricle with no restricted diffusion or surrounding edema	Arachnoid cyst floor of III ventricle	Neoplastic and cystic lesions	Ventricles	…
17	Yuvaraj	9 yrs	M	Late preterm	Nil	Paucity of bilateral parietal periventricular white matter with gyral thinning- Periventricular leukomalacia, thinning of posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, corpus callosum	…
18	Chirangivi	10 yrs	M	Late preterm	Seizures, spasticity	Bilateral gyri are relatively few and broad with smooth cortical-white matter junction	Pachygyria	Congenital and Developmental	Gray matter, white matter	…
19	Deepan	4 yrs	M	Preterm	Nil	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
20	Vignesh	7 yrs	M	Term	Hemiplegic cerebral palsy	Prominent sulci in right frontoparietotemporal region with dilated right lateral ventricle	Right frontoparietotemporal atrophy-?Post ischemic	Neurovascular/Traumatic	White matter, gray matter, ventricles	…
21	Krishnan	7 yrs	M	Preterm	Seizures	Paucity of bilateral parietal deep white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
22	Logasree	5 yrs	F	Late preterm	Seizures, hypotonia	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and dilated ventricles - Periventricular leukomalacia , mild thinning of posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…
23	Rithik	2 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	…
24	Janardhanan	2 yrs	M	Preterm	Congenital acyanotic heart disease	Prominent sulci and ventricles in bilateral cerebral hemispheres -cerebral atrophy with global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, gray matter, ventricles, corpus callosum	…
25	Tharika	18 mon	F	Preterm	Hypothyroid	Nil significant	Normal study	Normal	Nil	…

26	Logavardhini	8 yrs	F	Late preterm	Seizures	Volume loss in bilateral medial temporal lobes and hippocampi with prominent ventricles, thinned splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, limbic system, ventricles, corpus callosum	...
27	Jegan	4 yrs	M	Preterm	Spasticity	Paucity of bilateral parietal periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	...
28	Ragul	2 yrs	M	Term	Seizures	Nil significant	Normal study	Normal	Nil	...
29	Ashmitha Parveen	2 yrs	F	Preterm	Seizures	Paucity of bilateral periventricular white matter with gyral thinning and dilated ventricles - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	...
30	Dhanushree	2 yrs	F	Term	Seizures	Prominent sulci in bilateral frontal lobes - frontal cortical atrophy	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	Gray matter	...
31	Nithish	3 yrs	M	Preterm	Seizures, gait abnormality	Multiple dilated flow voids seen surrounding the ventral brain stem abutting the basal cisterns, dilated intracavernous and supraclinoid portion of intracranial ICA and engorged dural venous sinuses, cysts seen in bilateral	Posterior fossa pial Arteriovenous Malformation(AVM) ; Bilateral choroid plexus cysts	Congenital and Developmental ; Neoplastic and cystic lesions	Brain stem, cerebral vasculature, Choroid plexus	...
32	Md Rifan	1 yr	M	Late preterm	Seizures, respiratory tract infections	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and dilated ventricles - Periventricular leukomalacia , thinning of posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
33	Rishiba	9 yrs	F	Late preterm	Respiratory tract infections	Paucity of bilateral periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	...
34	Abdul Kathar	8 yrs	M	Late preterm	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.51, Cho/Cr 1.39
35	Shalini	9 mon	F	Preterm	Seizures, hypotonia	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and dilated ventricles - Periventricular leukomalacia , global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
36	Sabareeshawaran	6 mon	M	Preterm	Seizures	Global thinning of the corpus calloum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	Corpus callosum	...
37	Vaishnavi	18 mon	F	Preterm	Seizures	Moderate dilatation of bilateral lateral and III ventricles with irregular ventricular margin, IV ventricle not dilated, slyvian aqueduct is narrowed at the level of the superior colliculi, corpus callosum is stretched and thinned out	Congenital aqueductal stenosis	Congenital and Developmental	Ventricles	...
38	Pradeep	11 mon	M	Term	Nil	Nil significant	Normal study	Normal	Nil	...
39	Ashmitha Sri	2 yrs	F	Late preterm	CTEV	Paucity of bilateral frontal periventricular white matter with gyral thinning and dilated ventricles- Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	...
40	Akshaya	3 yrs	F	Preterm	Hypothyroid	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.51, Cho/Cr 1.37
41	Surya	1 yr	M	Term	Seizures, hypotonia	Hyperintensity noted in bilateral lentiform nucleus, anterolateral thalami and corona radiata on T2 weighted images with no restricted diffusion	Profound hypoxic ischemic injury	Neurovascular/Traumatic	Basal ganglia, white matter	...
42	Kavin kumar	4 yrs	M	Term	Seizures	Discrete periventricular T2/FLAIR white matter intensities noted with no restricted diffusion	Non specific periventricular T2/FLAIR white matter hyperintensities	Non specific imaging findings	White matter	...
43	Sridhar	5 yrs	M	Preterm	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.48, Cho/Cr 1.35
44	Kirthiga	7 yrs	F	Late preterm	Seizures, CTEV	Paucity of bilateral parietooccipital white matter with gyral thinning and dilated ventricles - Periventricular leukomalacia , thinning of posterior body of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
45	Hariharan	8 mon	M	Term	Seizures, hypotonia	Hyperintense signal noted in bilateral posterolateral thalami and lentiform nucleus, global thinning of corpus callosum, delayed myelination(anterior limb of internal capsule and peripheral white matter shows delayed myelination as	Profound hypoxic ischemic injury	Neurovascular/Traumatic	Basal ganglia, corpus callosum, white matter	...
46	Farhan	8 yrs	M	Preterm	Seizures	Fetal origin of right posterior cerebral artery(PCA)	Fetal origin of right posterior cerebral artery(PCA)	Non specific imaging findings	Cerebral vasculature	...
47	Lakshmanan	2 yrs	M	Term	Reduced head circumference	Small cranial vault, body of bilateral lateral ventricles are prominent, mega cisterna magna	Microcephaly, Prominent lateral ventricles, mega cisterna magna	Congenital and Developmental	Cranial vault, ventricles	...
48	Mohammad Abulkasan	9 yrs	M	Latepreterm	Seizures, spasticity, gait abnormality	Irregular cortex with multiple shallow gyri with mild cortical thickening and irregular cortical-white matter interface noted in the right frontoparietal region	Polymicrogyria (PMG)	Congenital and Developmental	White matter, gray matter	...
49	Sarvesh	7 yrs	M	Preterm	Seizures	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia, thinning of posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
50	Gowrishri	5 yrs	F	Late preterm	Seizures	Prominent sulci and ventricles in bilateral frontoparietal regions -cerebral atrophy with global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, gray matter, corpus callosum	...
51	Gowtham	6 yrs	M	Late preterm	Congenital acyanotic heart disease	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.47, Cho/Cr 1.38
52	Yogaraj	4 yrs	M	Late preterm	Seizures	Paucity of bilateral parietal periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	...
53	Wasim Abdul	3 yrs	M	Preterm	Nil	Thinning of the posterior body and splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	Corpus callosum	...
54	Amuthavani	8 yrs	F	Term	Seizures	Prominent lateral ventricles	Prominent lateral ventricles	Non specific imaging findings	Ventricles	...
55	Sathish kumar	15 mon	M	Preterm	Seizures, spasticity	Hyperintensity noted in bilateral putamina and anterolateral thalami and on T2 weighted images with no restricted diffusion	Profound hypoxic ischemic injury	Neurovascular/Traumatic	Basal ganglia	...
56	Vanipriya	3 yrs	F	Term	Seizures	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	...
57	Devita	4 yrs	F	Preterm	Nil	Inferior vermian hypoplasia , "key-hole" configuration of the IV ventricle communicating with a large cisterna magna	Dandy-Walker Variant	Congenital and Developmental	Vermis, ventricles, cisterns	...
58	Vigneshwaran	2 yrs	M	Preterm	Seizures, Abnormal cranial vault	Narrow elongated cranial vault - dolichocephaly	Dolichocephaly(Craniosynostosis)	Congenital and Developmental	Cranial vault	...
59	Sowbarnika	3 yrs	F	Preterm	Seizures, spasticity	Paucity of bilateral periventricular white matter with cystic encephalomalacic changes and dilated ventricles	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	...
60	Harikumar	4 yrs	M	Late preterm	Respiratory tract infections, seizures	CSF intensity lesion seen in the right middle cranial fossa widening the ipsilateral slyvian fissure with no restricted diffusion or surrounding edema	Middle cranial fossa arachnoid cyst	Neoplastic and cystic lesions	Subarachnoid space	...
61	Sasikumar	15 mon	M	Preterm	Seizures, hemiplegic cerebral palsy	Prominent sulci in left frontoparietotemporal regions with dilated left lateral ventricle	Left frontoparietotemporal atrophy- ? Post ischemic insult	Neurovascular/Traumatic	White matter, gray matter, ventricles	...
62	Hariharan.S.	5 yrs	M	Late preterm	Seizures	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia, global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
63	Kathir	6 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.48, Cho/Cr 1.39
64	Kevin	4 yrs	M	Term	Gait abnormality	Prominent right lateral ventricle	Prominent right lateral ventricle	Non specific imaging findings	Ventricles	...
65	Firthose	4 yrs	F	Preterm	Seizures	Thinning of posterior body and splenium of corpus callosum with mild paucity of bilateral parietal periventricular white matter	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, corpus callosum	...
66	Banupriya	7 yrs	F	Term	Hypothyroid	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.52, Cho/Cr 1.36
67	Anupriya	1 yr	F	Preterm	CTEV, seizures, hypotonia	Hyperintensity noted in bilateral lentiform nucleus, anterolateral thalami and perieloudic cortex on T2 weighted images with no restricted diffusion	Profound hypoxic ischemic injury	Neurovascular/Traumatic	Basal ganglia, white matter, gray matter	...
68	Irudhayaraj	2 yrs	M	Late preterm	Seizures	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and prominent ventricles- periventricular leukomalacia, global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
69	Chandran	5 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.50, Cho/Cr 1.38
70	Gopal	3 yrs	M	Late preterm	Seizures	Peg like, pointed cerebellar tonsils herniating below the foramen magnum (8 mm below the basion-opisthion line) with a crowded foramen magnum	Chiari 1 malformation	Congenital and Developmental	Cerebellar tonsils	...
71	B/O Soundarya	6 mon	F	Preterm	Seizures, hypotonia	Absence of falx and interhemispheric fissure in the mid section with fusion of the posterior frontal and parietal lobes across the midline, absent septum pellucidum, genu and splenium of the corpus callosum are formed	Syntelencephaly	Congenital and Developmental	Corpus callosum, white and gray matter, ventricles, falx cerebri	...
72	Gowripriya	3 yrs	F	Late preterm	Seizures	Paucity of bilateral parietooccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia, thinning of splenium of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	...
73	Haribalan	2 yrs	M	Late preterm	Respiratory tract infections	Well defined CSF intensity lesion in right parietotemporal lobe lined by white matter communicating with the right lateral ventricle with no restricted diffusion	Porencephalic cyst	Neurovascular/Traumatic	White matter, gray matter, ventricles	...
74	Vanithamani	7 yrs	F	Preterm	Seizures	Parasagittal parietooccipital regions show irregular cortex with shallow gyri and cortical thickening with irregular cortical-white matter interface	Polymicrogyria (PMG)	Congenital and Developmental	Gray matter, white matter	...
75	Navin kumar	8 yrs	M	Term	Nil	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.51, Cho/Cr 1.36

76	Meena	6 yrs	F	Late preterm	Seizures	Paucity of bilateral parietal periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
77	Janaki	4 yrs	F	Term	Congenital acyanotic heart disease	Nil significant	Normal study	Normal	Nil	…
78	Prabhu	5 yrs	M	Late preterm	Seizures	Bilateral gyri are broad and thick and fewer in number with smooth cortical-white matter junction with prominent ventricles	Pachygyria	Congenital and Developmental	Gray matter, white matter	…
79	Harshini	2 yrs	F	Preterm	Reduced head circumference	Small cranial vault	Microcephaly	Congenital and Developmental	Cranial vault	…
80	Thenmalar	6 yrs	F	Preterm	Seizures	Paucity of bilateral posterior frontal and parietal periventricular white matter with gyral thinning - Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter	…
81	Sowkath Ali	4 yrs	M	Late preterm	Nil	Cysts seen in bilateral choroid plexus with no diffusion restriction	Choroid plexus cysts	Neoplastic and cystic lesions	Choroid plexus	…
82	Sowjanya	8 yrs	F	Term	Hypothyroid	Nil significant	Normal study	Normal	Nil	NAA/Cr 2.49, Cho/Cr 1.38
83	Yogarajan	1 yr	M	Late preterm	Seizures	Thinning of splenium and posterior body of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	Corpus callosum	…
84	Kavipriya	18 mon	F	Preterm	Seizures, hypotonia	HIyperintensity noted in bilateral putamina, posterolateral thalami and hippocampi on T2 weighted images with no restricted diffusion	Profound hypoxic ischemic injury	Neurovascular/Traumatic	Basal ganglia, limbic system	…
85	Divya	3 yrs	F	Preterm	Seizures, spasticity	Paucity of bilateral periventricular white matter with diffuse cystic encephalomalacic changes and dilated lateral ventricles	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	…
86	Gowrishankar	4 yrs	M	Term	Nil	Prominent lateral ventricles	Prominent lateral ventricles	Non specific imaging findings	Ventricles	…
87	Fathima	5 yrs	F	Term	Seizures	Mega cisterna magna	Mega cisterna magna	Non specific imaging findings	Cisterns	…
88	Karthick	8 yrs	M	Term	Seizures	Nil significant	Normal study	Normal	Nil	…
89	Kishore	6 yrs	M	Preterm	Seizures, hypotonia, CTEV	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia, thinning of splenium and posterior body of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…
90	Harshini	5 yrs	F	Term	Nil	Cavum septum pellucidum and cavum vergae	Cavum septum pellucidum and cavum vergae	Non specific imaging findings	Ventricles	…
91	Karthikeyan	3 yrs	M	Late preterm	Seizures	Prominent Virchow-Robin(VR) spaces	Prominent Virchow-Robin(VR) spaces	Non specific imaging findings	Nil	…
92	Durga	6 yrs	F	Late preterm	Seizures	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles- periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	…
93	Ashmitha	3 yrs	F	Term	Seizures	Nil significant	Normal study	Normal	Nil	…
94	Hari	4 yrs	M	Preterm	Nil	Prominent left lateral ventricle	Prominent left lateral ventricle	Non specific imaging findings	Ventricles	…
95	Banupriya	2 yrs	F	Preterm	Seizures	Nil significant	Normal study	Normal	Nil	…
96	Abdulkasim	5 yrs	M	Term	Respirtory tract infections	Cavum septum pellucidum	Cavum septum pellucidum	Non specific imaging findings	Ventricles	…
97	Nithin kumar	5 yrs	M	Preterm	Seizures	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles- Periventricular leukomalacia	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles	…
98	Manivel	6 yrs	M	Preterm	Nil	Nil significant	Normal study	Normal	Nil	…
99	Sajitha	6 yrs	F	Term	Seizures	Mega cisterna magna	Mega cisterna magna	Non specific imaging findings	Cisterns	…
100	Sabari	7 yrs	M	Late preterm	Seizures	Paucity of bilateral parietoccipital periventricular white matter with gyral thinning and prominent ventricles- periventricular leukomalacia, global thinning of corpus callosum	Sequalae to hypoxic ischemic injury	Neurovascular/Traumatic	White matter, ventricles, corpus callosum	…