

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

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Abstract

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. Our study aims to identify the spectrum of abnormalities in brain magnetic resonance imaging in children with developmental delay. To correlate the MRI features of Cerebral Palsy with perinatal history, clinical features. **Materials and Methods:** Our study is a retrospective descriptive study which involves the evaluation of children presenting with developmental delay to the Department of Radio diagnosis, Tirunelveli Medical College Hospital between July 2022 and January 2023. After explaining the nature of study, oral consent will be obtained from parents. The children are evaluated with a standard MRI protocol. Imaging will be performed on 1.5 T SEIMENS MRI with conventional T2W axial, FLAIR, T2W coronal, T1W sagittal, DWI and SWI, MPR sequences. **Results:** The prevalence of abnormal MRI findings was 78% among the evaluated children. Our study showed predominant involvement of the white matter (35%), ventricles (20%) and corpus callosum (15%). 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%). **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. Hence, appropriate diagnosis on MRI helps in guiding the clinician to plan further patient management.

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 stigma 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. The evaluation of developmental delay is complex and involves various modalities including cytogenetic testing, biochemical and hormonal assays, enzyme assays, electroencephalography (EEG) and neuroimaging. MRI 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.^[2] 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.^[3,4]

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.^[5]

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.^[6]

The sylvian fissure is usually present upon imaging the fetus in the fourth gestational month. During the fifth month the parietooccipital, calcarine and cingulate sulci appear. By the end of the sixth month the central, superior temporal and interparietal sulci appear. The precentral, postcentral, superior frontal and middle temporal sulci appear during the seventh gestational month.^[7]

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.^[8]

T1 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. [Figure 1]



Figure 1: 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 2]

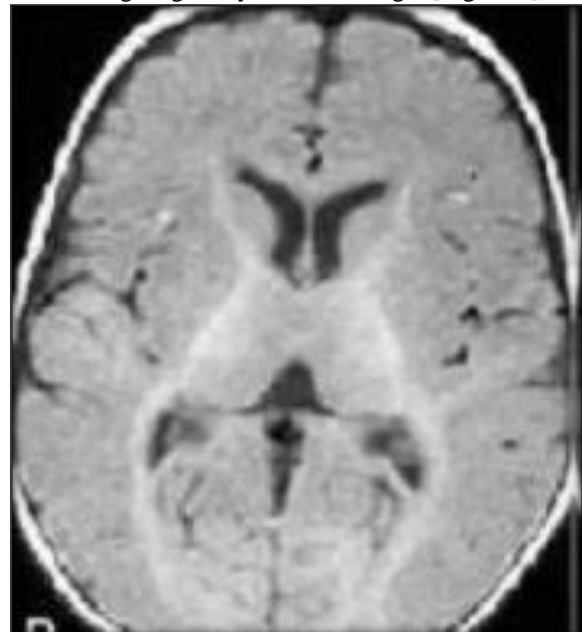


Figure 2: Axial T1 weighted image in a normal 4-month old infant showing myelination of the anterior limb of internal capsule.

T2 weighted images

The ventral brainstem becomes of similar low signal intensity as the dorsal brain stem by the fifth postnatal month. 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".

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 3]

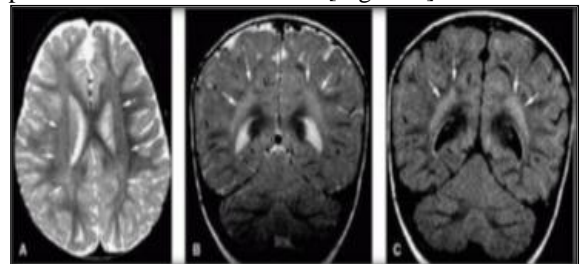


Figure 3: A-C: Axial T2 (A) and coronal T2 (B) weighted and coronal FLAIR (C) images showing increased signal intensity around the trigones representing the "terminal zones" of myelination (arrows).

There are a huge myriad of causes of developmental delay. The causes can be congenital or acquired. The List of the commonly encountered causes of developmental delay are:

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
10. Megalencephaly
11. Cortical dysgenesis with abnormal cell proliferation.

MATERIALS AND METHODS

Our study is a retrospective descriptive study which involves the evaluation of 20 children presenting with developmental delay to the Department of Radio diagnosis, Tirunelveli Medical College Hospital between July 2022 and January 2023. After explaining the nature of study, oral consent will be obtained from parents. The children are evaluated with a standard MRI protocol. Imaging will be performed on 1.5 T SEIMENS MRI with conventional T2W axial, FLAIR, T2W coronal, T1W sagittal, DWI and SWI, MPR sequences.

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

- Children younger than 6 months and older than 10 years of age.
- Children with recognized syndromes including chromosomal disorders.
- iii) The MRI studies which did not fulfill the given protocol (T2W axial, FLAIR, T2W coronal, T1W sagittal, DWI and SWI sequences) were excluded from this study.
- Children with contraindications for MRI was excluded from the study

RESULTS

1. Age

Our study involved the evaluation of 20 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 7. This was followed by 4 children in the age group of 6-8 years followed by 4 children in the age group of 1-2 years. The other subgroups had relatively lesser number of children presenting with developmental delay. Age-wise distribution of the children presenting with developmental delay is depicted in [Chart 1].



Chart 1: Age-wise distribution of the children presenting with developmental Delay

2. Sex

Our study evaluated a total of 20 children among which 11 were males and 9 were females. sex-wise distribution of the children presenting with developmental delay is depicted in [Chart 2].

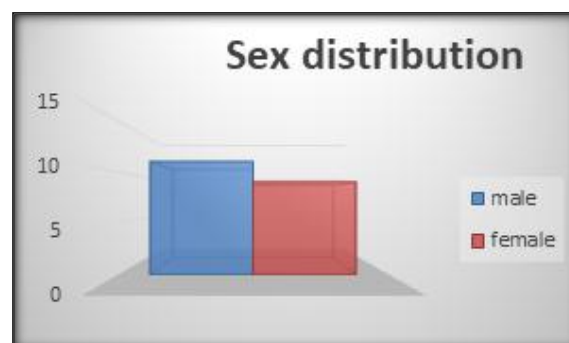


Chart 2: Sex-wise distribution of the children presenting with developmental Delay

3. Gestational Age

The children were divided on the basis of gestational age into preterm, term and late preterm. Among the 20 children evaluated, 8 were preterm while 6 were late preterm. Around 6 of the evaluated children were term. [Table 1 and Chart 3] demonstrating the distribution of children on the basis of gestational age.

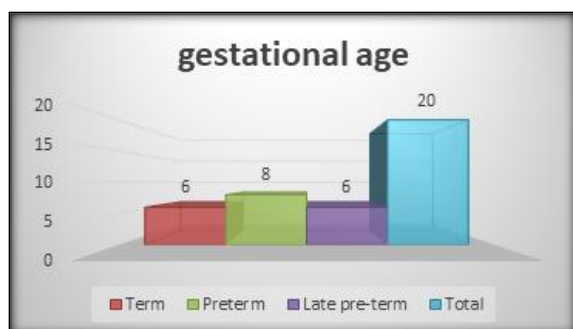


Chart 3: chart demonstrating the distribution of children on the basis of gestational age.

4. Clinical Associations

Relevant clinical associations were elicited and summarised. It was noted that among the 20 children evaluated in our study, 61% had associated seizures. [Chart 4] showing the prevalence of seizures among the evaluated children.



Chart 4: chart showing the prevalence of seizures among the evaluated children.

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"). [Table 2 and Chart 5] depicting the relative frequencies of the involved brain structures on MRI.

6. Categorization of MRI Findings

The prevalence of abnormal MRI findings was 78% among the evaluated children. Among the children with abnormal MRI findings 22% had nonspecific imaging findings as mentioned above. Chart 6-

showing the prevalence of normal and abnormal MRI findings.

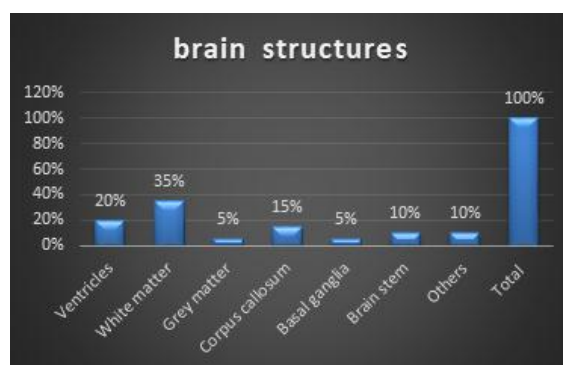


Chart 5: Bar diagram showing the relative frequencies of the involved brain structures on MRI.

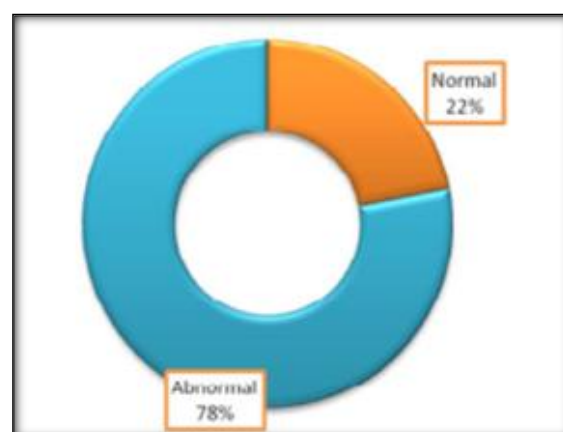


Chart 6: showing the prevalence of normal and abnormal MRI findings.

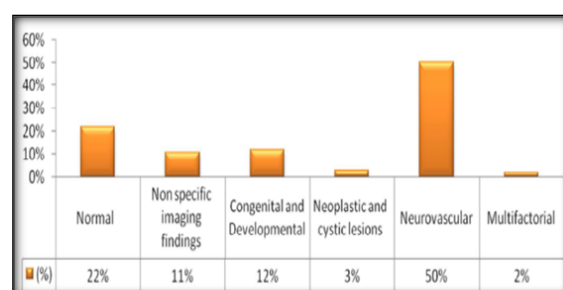


Chart 7: Bar diagram showing the categorization of various MRI findings

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. The remaining 78% cases with an abnormal MRI were further categorized, of which 50 % cases had findings consistent with Neurovascular diseases. The proportion of children with Congenital and developmental disorders, Neoplastic and cystic lesions and nonspecific imaging findings were 12%, 3% and 11% respectively. 2% showed a combined or multifactorial etiology. [Chart 7] showing Bar diagram of categorization of various MRI findings

Table 1: Table demonstrating the distribution of children on the basis of gestational age

Gestational age	Number
Term	6
Preterm	8
Late pre-term	6
Total	20

Table 2: Table showing the relative frequencies of the involved brain structures on MRI

INVOLVED BRAIN STRUCTURES	Number	Percentage %
Ventricles	4	20%
White matter	7	35%
Grey matter	1	5%
Corpus callosum	3	15%
Basal ganglia	1	5%
Brain stem	2	10%
Others	2	10%
Total	20	100%

DISCUSSION

Sample Case 1: 5-year-old, late preterm male child presenting with seizures and developmental delay.

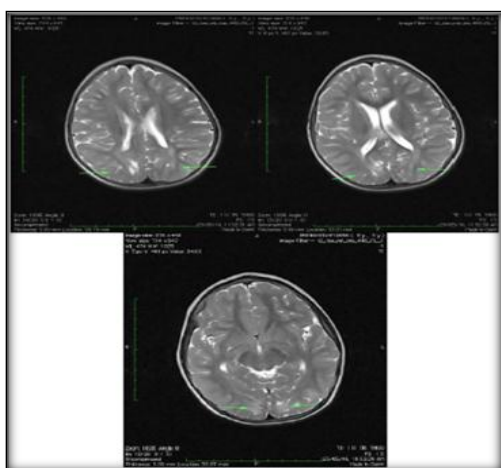


Figure 4: Axial T2 weighted MR images showing paucity of bilateral parietoccipital periventricular white matter with gyral thinning (periventricular leukomalacia) in a case of hypoxic ischemic injury.

Sample Case 2: 10-year-old, preterm male child presenting with developmental delay.



Figure 5: Sagittal T1 weighted MR image shows thinning of posterior body and splenium of corpus callosum (arrows) as a sequelae of hypoxic ischemic injury.

Sample Case 3: 2-year-old, preterm male child, known case of congenital heart disease came with developmental delay.

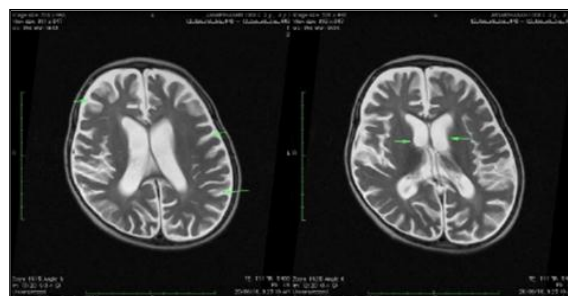


Figure 6: Axial T2 weighted MR image showing prominent sulci and ventricles in bilateral cerebral hemispheres -cerebral atrophy.

Sample Case 4: 2 year old, term male child with developmental delay.

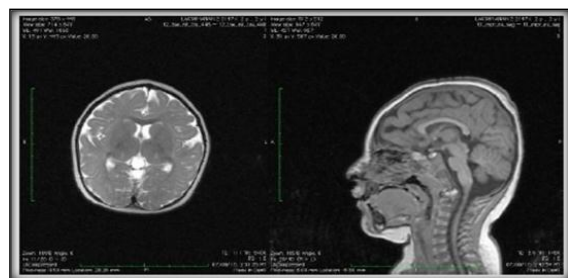


Figure 7: Axial T2 weighted (left) and sagittal T1 weighted image shows a small cranial vault suggestive of microcephaly. Also note that the body of bilateral lateral ventricles are prominent.

The current study was undertaken to evaluate the spectrum of abnormalities on MRI in children with developmental delay. Out of the 20 children evaluated in our study around 7 children were in the age group 3-5 years. The children were categorized based on gestational age with 70% 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.

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.

The various involved brain structures were also studied systematically. The white matter (35%), ventricles (20%) and corpus callosum (15%) 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 with an increased incidence in the age group 3-5 years. Most of the cases were a sequel to hypoxic ischemic injury.

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.

Sample Case 5: 1-year-old, term male child, with developmental delay, seizures and hypotonia

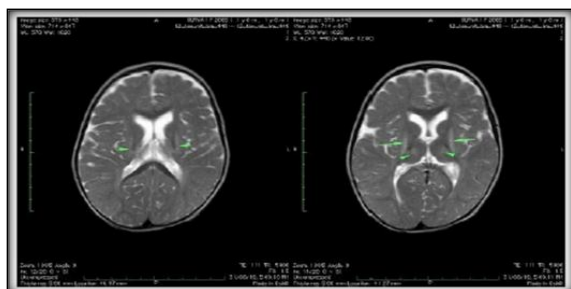


Figure 8: Axial T2 weighted MR images showing hyperintensity in bilateral lentiform nucleus, anterolateral thalami and corona radiata suggestive of "Profound hypoxic ischemic injury".

Sample Case 6: 4-year-old, term female child with developmental delay.

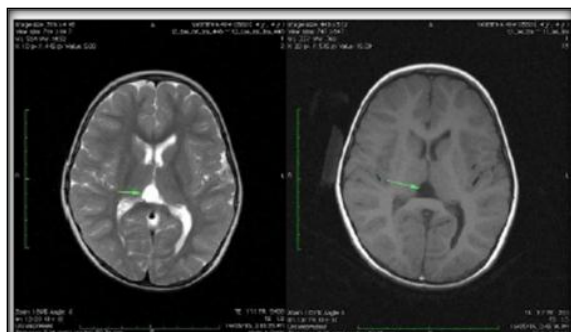


Figure 9: Axial T2 (left) and T1 (right) weighted MR image shows a CSF intensity lesion seen in the floor of the III ventricle (arrows). The lesion showed no restricted diffusion. Features consistent with "Arachnoid cyst".

Sample Case 7: 1 year old, late preterm female child, with developmental delay and spasticity.

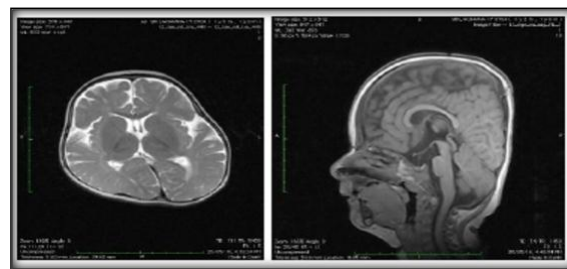


Figure 10: Axial T2 weighted (left) and sagittal T1 weighted (right) MR image shows features of brachycephaly (craniosynostosis).

Sample Case 8: 9-year-old, late preterm male child, with developmental delay.

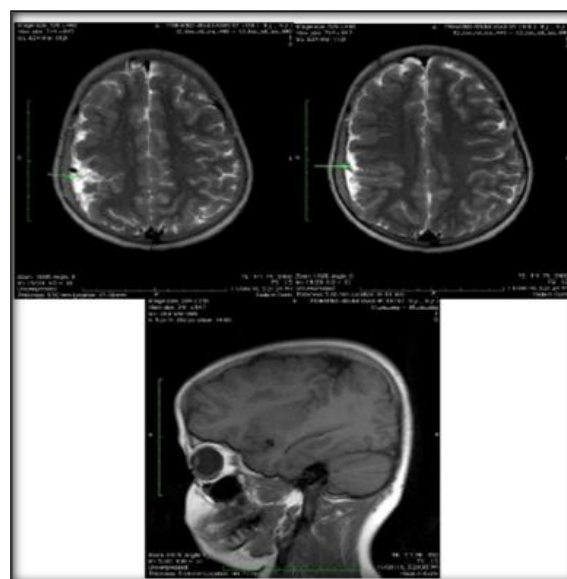


Figure 11: Axial T2 (top row) and sagittal T1 weighted (bottom) MR image shows irregular cortex with multiple shallow gyri with mild cortical thickening and irregular cortical-white matter interface noted in the right frontoparietal region suggestive of Polymicrogyria (PMG).

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. Hence, appropriate diagnosis on MRI helps in guiding the clinician to plan further patient management.

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 20 children with developmental delay who were referred to the Department of Radio

diagnosis, Tirunelveli Medical College Hospital, Tirunelveli. 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 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.

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