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A COHORT STUDY ON THE EVALUATION OF THE BRAIN BY MAGNETIC RESONANCE IMAGING IN PAEDIATRIC PATIENTS WITH DEVELOPMENTAL DELAY

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ABSTRACT

Introduction

One major neuromorbidity that affects children and may have long-term effects on quality of life is developmental delay (DD). Magnetic resonance imaging (MRI) has become a key tool in evaluating these patients. This study aimed to assess DD in pediatric patients by utilizing magnetic resonance imaging (MRI) to identify underlying brain abnormalities that may contribute to the condition.

Methods

This hospital-based prospective observational study included 100 pediatric patients referred for MRI brain evaluation due to developmental delay between January 2021 and July 2022. MRI scans were performed using 1.5 Tesla superconducting MRI machines (GE Optima MR360, Optima MR450W GEM, and SIGNA Artist) with appropriate sequences and planes, using sedation, when necessary, under anesthetist guidance. The brain's anatomical structures were assessed systematically for normalcy and maldevelopment, and the findings were categorized into different etiological groups.

Results

Normal MRI findings were observed in 13% of participants, while 87% showed abnormal results. The most commonly affected anatomical areas were the white matter (52.87%) and the ventricles (44.83%). Of the abnormal cases, 53% were attributed to neurovascular etiologies, such as hypoxic-ischemic encephalopathy (HIE), followed by 14% for congenital and developmental etiology, 13% for metabolic and neurodegenerative disorders, 4% for nonspecific findings, 2% for neoplastic lesions, and 1% for multifactorial causes.

Conclusion:

Clinical examination and analysis are the first steps in diagnosing developmental delay, but brain imaging should be done to rule out any causes and provide appropriate management. Due to its great soft tissue resolution, the MRI brain is the best imaging modality.

Recommendations

MRI should be standard in assessing pediatric developmental delay due to its high sensitivity and specificity in detecting abnormalities. It aids in early diagnosis and guides targeted treatment. Larger studies are needed to refine diagnostic criteria and better understand MRI's role.

Keywords: *Developmental delay, Paediatric patients, MRI Brain, Hypoxic-Ischemic Encephalopathy, Corpus Callosum.*
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INTRODUCTION

Developmental Delay (DD) refers to a condition in which a child exhibits a significant lag in achieving age-appropriate developmental milestones, typically by two or more standard deviations below the mean for children of the same age. It can affect various domains, including motor skills, speech and language, cognitive abilities, and social or emotional development. The term is generally used for children under 5 when delays are identified in one or more developmental areas. DD can be a transient condition, but it

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may also be an early indication of a more persistent or specific neurological or developmental disorder. The World Health Organisation [1] estimates that the prevalence of DD or impairment in children under the age of 14 is roughly 5% worldwide. Gross and fine motor capabilities, social and personal skills, speech and language skills, and cognitive abilities are among the domains that may be impacted [2].

Although precise data is scarce, the prevalence of DD in children reporting to outpatient departments is estimated to be around 5-10% [3]. Developmental delays become apparent during infancy and early childhood, becoming more evident in the early school years, where it is often diagnosed [1].

Various tests and methods are used to assess a child's development. The Denver Developmental Screening Test (DDST) and its modified version, the Denver Developmental Screening Test II (DDSTII), are commonly used tools [1]. Diagnosing the underlying reasons for developmental delay often requires a combination of clinical history, physical examination, and various investigations such as serological, genetic, metabolic, and neuroimaging studies. Neuroimaging, particularly brain MRI, provides significant insights into prior injuries or specific abnormalities indicative of certain diseases [4, 5].

Brain ultrasonography (USG) plays an important role in detecting and managing diseases affecting preterm neonates and term infants, particularly for identifying intracerebral hemorrhage and hypoxic-ischemic changes. However, its limitations include operator dependence and the inability to use it after the fontanelles have closed [3]. Computed Tomography (CT) scans effectively assess cranial or facial abnormalities but have the drawback of exposing patients to harmful radiation [6].

For all age groups, magnetic resonance imaging (MRI) is the preferred imaging technique for studying the brain. When identifying brain anomalies in infants with developmental delays, offers comprehensive anatomical information with high sensitivity and specificity [1, 4]. MRI can identify several pathophysiological and etiological diseases, such as atrophic alterations, white matter disorders, hypoxic-ischemic changes, and congenital anomalies, that lead to developmental delay [3]. Because MRI provides a strong contrast between grey and white matter, it is particularly useful for diagnosing complicated anomalies of the central nervous system (CNS), such as dorsal induction disorders (such as Chiari II malformation) or ventral induction disorders (such as holoprosencephaly) [2]. MRI has the highest sensitivity for identifying hypoxic brain injury in babies and aids in the differentiation of myelinated from unmyelinated white matter.

Thus, for infants or children with DD, MRI is the preferred imaging modality. It enables the identification of specific abnormalities and provides crucial information for diagnosis, treatment, and parental counseling.

This study aimed to assess DD in Indian children to facilitate early diagnosis, aiding physicians in providing targeted treatment and parental counseling.

METHODOLOGY

Study design

A hospital-based prospective cohort observational study.

Study setting

The study took place at the Department of Radiodiagnosis, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India, from January 2021 to July 2022.

Participants

The study was done on 100 patients referred for assessment of patients with DD. Informed consent was taken from the patient's parents.

Inclusion and exclusion criteria

The study included children who showed signs of developmental delay and were between the ages of three months and fourteen years. Children with recognized hereditary conditions, like Down syndrome, Turner syndrome, etc., linked to delayed developmental milestones, a history of head trauma, uncooperative patients, and conditions that make magnetic resonance imaging unfeasible, like claustrophobia or cochlear implants were excluded.

Bias

The bias encountered during the study was referral bias, as the sample was drawn from patients referred specifically for MRI evaluation at a single hospital, potentially limiting the generalizability of the findings.

Data Collection and Procedure

After putting the child to sleep, sedation, or anesthesia, the child's brain was imaged using a 1.5 Tesla superconducting MRI machine (GE make Model Optima MR360) and a 1.5 Tesla superconducting MRI machine (GE-built Model Optima MR450W GEM and SIGNA Artist system) using the proper sequences and planes. Before imaging a baby or young child, Syrup Triclofos (Syp predictory) 50 mg/kg was used to sedate them. Older children who were very cooperative during the imaging process were not sedated when they were imaged. The heads of the patients were firmly positioned inside the receiver coil while they were in the supine posture. In the workstation, the scan was carried out under the direction of a licensed radiologist.

The sequences used are: Axial T1WI, Axial T2WI, Axial T2FLAIR, Axial DWI, Sagittal T2WI, Coronal T2WI, Thin

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slice 3D T1WI (BRAVO), Axial T1FS, Axial T1FS+Contrast, Coronal T1FS+Contrast, Sagittal T1FS+Contrast, Thin slice 3D T1FS+ Contrast. Intravenous Injection of Gadopentetate Dimeglumine contrast was used (Dose- 0.02mL/kg body wt or 0.01 mmol/kg body wt).

Based on the study by [7], several brain structures were systematically evaluated, including the ventricles, corpus callosum, gray and white matter, basal ganglia, brain stem, and cerebellum. The ventricles were assessed for their size and morphology, while the corpus callosum was examined for its thickness and morphology. The gray and white matter were evaluated for sulcation and gyration in line with normal MR brain anatomy. The basal ganglia, brain stem, and cerebellum were all examined for morphological abnormalities.

The study recorded the proportion of patients with normal MRI findings and categorized abnormal findings into five groups, as outlined by [8]: Normal, Traumatic/Neurovascular Diseases, Congenital & DevelopmentalDisorders, Metabolic and Neurodegenerative Diseases, Neoplastic Diseases, and Nonspecific Findings. The latter category included conditions such as ventriculomegaly, enlarged subarachnoid spaces, delayed myelination, and Virchow-Robin spaces.

Statistical analysis

Systematic analysis of the data was conducted, and pertinent findings were made. The data was analyzed using the SPSS, version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used in the statistical analysis, and frequencies and percentages for each parameter in each study group were determined. It computed the mean and standard deviation. The significance level for correlations was set at p-value <0.05.

Ethical considerations

The study protocol was approved by the Ethics Committee (IRB no.-1931/IEC/IGIMS/2020) and written informed consent was received from all the participants.

RESULT

Thirty-one females and 69 males made up the total of 100 patients. The age group of 1-2 years accounted for the largest number of cases in both genders. A statistically significant variation was found between the genders concerning age groups using chi-square statistical analysis ($p<0.05$).

The majority of patients in both the normal and abnormal findings were males. A statistically significant variation ($p<0.05$) was found between the gender-related MRI data according to chi-square statistical analysis.

It was observed that in normal MRI findings, maximum patients (69.23%) were term subjects and 30.77% of patients were preterm subjects. 54% of the abnormal MRI findings were preterm and 44% were term babies. Chi-square statistical analysis demonstrated a statistically significant variation ($p<0.05$) among the MRI findings about gestational age.

With detailed clinical history, it was seen that 39% of patients presented with DD whereas 61% of the patients presented with developmental delay plus and had other clinical associations. Seizure was seen in 35% of all the cases, followed by cerebral palsy seen in 13% of cases, 10% of all the cases presented with ataxia, and 8% with respiratory distress.

It was observed that in abnormal MRI findings, a maximum of 62.1% of patients presented with developmental delay plus and 37.9% of subjects presented with developmental delay. Chi-square statistical analysis showed a statistically significant difference (p-value<0.05) between the MRI findings about clinical findings.

Table 1: Association of Clinical Findings with MRI findings

Clinical Findings	NORMAL		ABNORMAL		TOTAL	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Developmental delay	6	46.15	33	37.9	39	39.0
Developmental delay plus	7	53.85	54	62.1	61	61.0
TOTAL	13	100	87	100.0	100	100
CHI SQUARE	1.880					
p-value	0.045*					

p-value<0.05 is significant

The most commonly affected anatomical structures were white matter (52.87%) followed by ventricles (44.83%), corpus callosum (41.37%), grey matter (33.33%), cerebellum (18.4%) and brainstem (11.5%).

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Table 2: shows the percentage of involved brain structures

Brain structure	ABNORMAL	
	Frequency (n)	Percentage (%)
White matter	46	52.87
Grey matter	29	33.33
Corpus callosum	36	41.37
Ventricles	39	44.83
Brain stem	10	11.5
Cerebellum	16	18.4
TOTAL	87	100

Based on the aetiological criteria, an analysis of 100 cases revealed that 13 cases (32%), had normal MR characteristics. After 87 instances with abnormal MRI scans were further divided into smaller groups, it was shown that Traumatic/Neurovascular Diseases, such as Hypoxic Ischaemic Encephalopathy (HIE), accounted for 53% of the most frequent abnormalities in the current study. As indicated in Table 4, the percentage of children with congenital & developmental, metabolic and neurodegenerative, non-specific, neoplastic, and multifactorial conditions was 14%, 13%, 4%, 2%, and 1%, respectively.

Table 3: Distribution of study subjects according to MRI findings

MRI findings	Frequency (n)	Percentage (%)
Normal	13	13
Non-specific imaging findings	4	4
Congenital and developmental	14	14
Neoplastic lesions	2	2
Traumatic/Neurovascular (HIE)	53	53
Metabolic and neurodegenerative	13	13
Multifactorial	1	1
TOTAL	100	100

Hypoxic ischemic injury in the neonates results in hypoxic ischemic encephalopathy which can be either mild to moderate and severe (Figure 1). This was the most common abnormality encountered in 53% of the cases in the study.

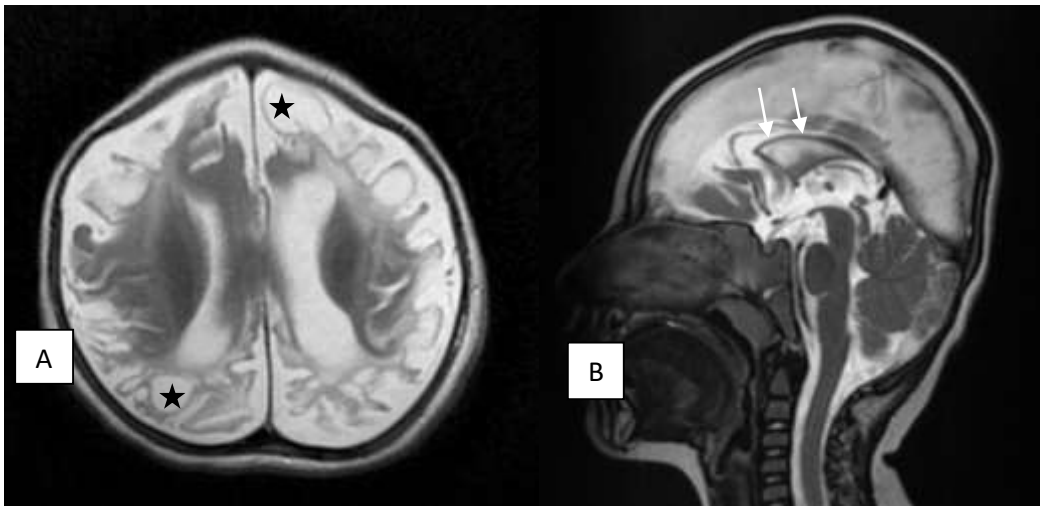

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Figure 1: T2WI in axial (Fig 1A) and sagittal (Fig 1B) planes show diffuse cerebral atrophy, multiple cystic encephalomalacic changes (black star) in bilateral frontoparietal lobes with diffuse thinning of corpus callosum (white arrows)- Severe HIE Sequelae.

Congenital and developmental abnormalities were seen in 14% of the cases which included 2 cases of Joubert Syndrome (Figure 2A), 2 cases of Dandy walker malformation, 1 case of Polymicrogyria, 3 cases of lissencephaly spectrum (Figure 2B), 2 cases of agenesis of corpus callosum, 2 cases of schizencephaly (Figure 2C), 1 case of grey matter heterotopias (Figure 2D), and 1 case of Hemimegalencephaly with cortical dysplasia.

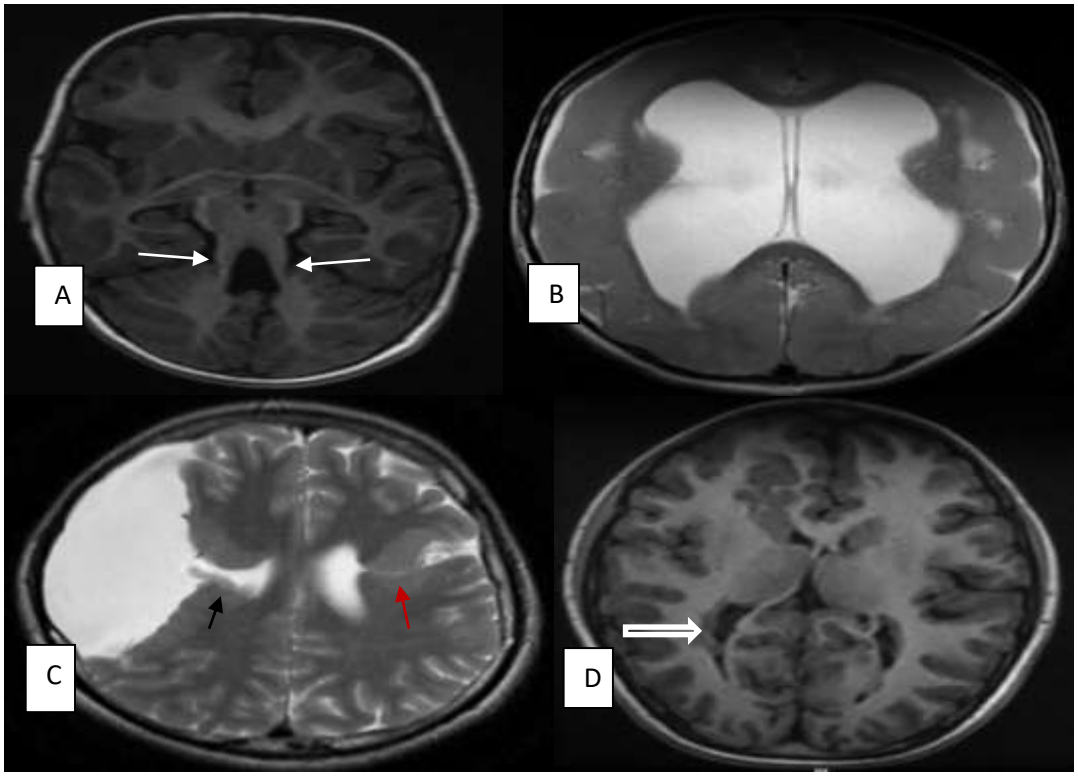

Figure 2: Figure 2A shows mild atrophy of inferior cerebellar vermis and bilateral cerebellar tonsils with thin elongated bilateral superior cerebellar peduncles (white arrows)- Features consistent with Joubert syndrome.

Figure 2B shows features of pachygyria- agyria complex- Lissencephaly (thick and less sulcation) in bilateral cerebral hemispheres, predominantly frontal and parietal lobes with dilated ventricles with periventricular patchy T2 hyperintensity.

Figure 2C shows bilateral schizencephaly, open lip on the right (black arrow) and closed lip on the left (red arrow).

Figure 2D shows small nodules of grey matter along the ependymal lining in the region of occipital horns of bilateral lateral ventricles (block arrow) with adjacent normal white matter with large focal areas of grey matter in bilateral frontal subcortical region - Features suggestive of cortical malformation in the form of periventricular nodular and subcortical heterotopia.

Metabolic and neurodegenerative abnormalities were found in 13% of the patients including 1 case of Dyke-Davidoff-Masson syndrome, 2 cases of Rasmussen encephalitis, 1 case of Alexander disease, 2 cases of Leigh syndrome, 3 cases of Metachromatic leukodystrophy (Figure 3), 1 case of Adrenoleukodystrophy, 1 case of Glutaric aciduria, 1 case of Chronic bilirubin encephalopathy and 1 case of Canavan disease (Figure 4).

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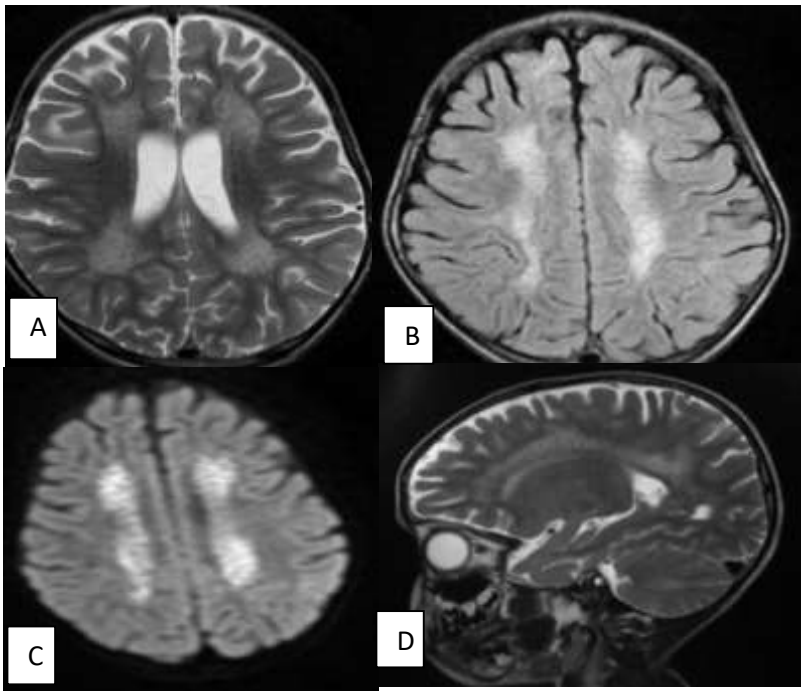

Figure 3: Bilateral symmetrical confluent areas T2 (Figure 3A) and FLAIR (Figure 3B) hyperintensities showing diffusion restriction in the periventricular deep white matter (Figure 3C) with sparing of perivenular white matter giving tigroid pattern (Figure 3D) and subcortical U-fibres -S/o Dysmyelinating disorder – Metachromatic Leukodystrophy.

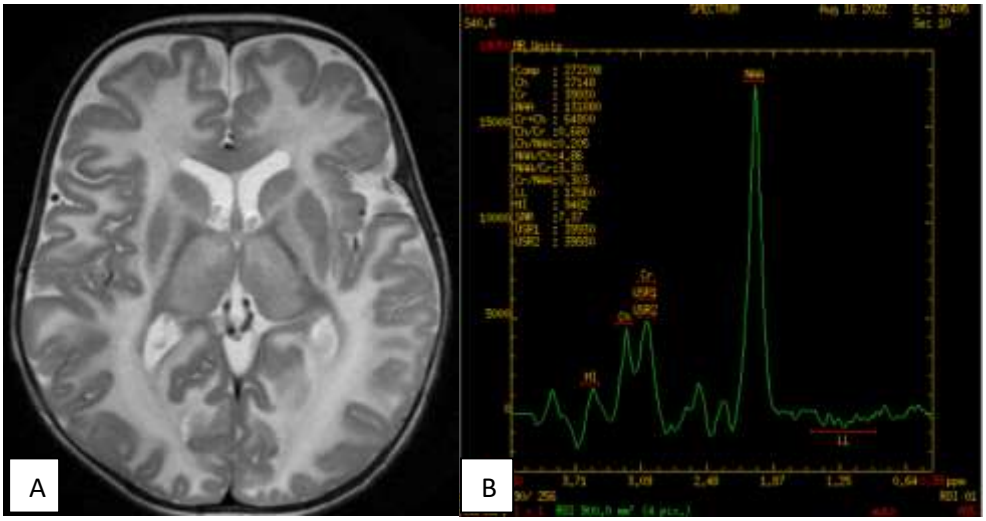

Figure 4: Areas of T2 high signal intensity involving subcortical and periventricular white matter, bilateral thalami, midbrain, and cerebellum with sparing of the corpus callosum, caudate nucleus, and putamen (Figure 4A) with raised NAA peak on MRS (Figure 4B)- Findings consistent with Canavan disease.

Non-specific findings were seen in 4 cases comprising enlarged subarachnoid spaces (2 cases), prominent virchow robin spaces (1 case), and cavum septum pellucidum (1 case).

Neoplastic etiology was seen in 2 cases in which one case had an Atypical infantile CP angle embryonal tumor and the other had a choroid plexus cyst.

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Multifactorial etiology including both HIE and Dandy walker variant was seen in 1 case.

DISCUSSION

Evaluation of DD was done in 100 pediatric patients referred to the department for an MRI Brain from the Department of Paediatrics. A detailed clinical history including the domain affected and the routine blood investigations and biochemical assay were assessed for further correlation.

The current study found that 69 of the 100 patients were males and 31 were females. The majority of patients, both males and females, were between the ages of 1-2 years. The average age of all patients was 3.66 years, 3.22 years for females, and 3.86 years for males, with a minimum age of 7 months and a maximum age of 13 years. Male to female ratio was 1.2:1, according to research by [9, 10] that revealed similar age of presentation and sex incidence.

Of the 100 individuals, it was discovered that 49 patients were term and 51 patients were preterm. It was shown that the majority of patients (69.23%) with normal MRI results were term subjects, while 30.77% of patients had preterm abnormalities. Preterm newborns made up 54% of the aberrant MRI results, whereas term babies made up 44%. A statistically significant variation ($p<0.05$) in the MRI results about gestational age was found using chi-square statistical analysis. A study discovered that preterm children frequently experienced developmental delays [10].

Of the 100 individuals in the study, a maximum of 61% had developmental delay and 39% had developmental delay. A maximum of 62.1% of patients with aberrant MRI findings showed signs of developmental delay, and 37.9% of individuals showed signs of developmental delay alone. A statistically significant variation ($p<0.05$) was found between the MRI results and the clinical findings according to chi-square statistical analysis. According to a study, the distribution of patients with developmental delays based on their clinical features showed that 63 patients (60.58%) had DDs along with other components, such as seizures and neurological abnormalities, while 41 patients (39.42%) had developmental delays alone. Structural anomaly, genetic or metabolic [10].

In the present study, it was observed that white matter was affected in 52.87% of all the cases, followed by ventricles affected in 44.8% of cases, corpus callosum in 41.3% of cases, grey matter in 33.33% of cases, cerebellum in 18% cases and brain stem in 11.5% cases.

In the analysis of 100 cases, the percentage of children with abnormal MRI results yielded an 87% accuracy rate for definite diagnosis. [7, 9, 11–15] have reported similar MRI yields, with yields of 58.6%, 65.5%, 63.8%, 71.8%, 68%, 80.8, and 84%, respectively. The broad range of these results could be explained by the criteria used to choose patients and the general awareness of the need to look into these children in different demographic groups.

The aetiological classification of abnormal MRI Brain findings showed that 53% of cases were of neurovascular etiology, followed by 14% of congenital and developmental etiology, 13% of metabolic and neurodegenerative etiology, 4% with nonspecific findings, 2% with neoplastic lesions and 1% with multifactorial etiology. According to the research, [10] found that congenital or developmental abnormalities were the second most common cause of aberrant MRI results in children, with traumatic or neurovascular etiology accounting for the majority of cases. In the categories of normal, traumatic/neurovascular, congenital/developmental, metabolic/degenerative, and nonspecific etiological, there were 41 (39.42%), 31 (29.81%), 24 (23.08%), 6 (5.77%), and 2 (1.92%) patients, respectively. [14] states that 32% of MRI scans had normal findings, but the other 31% had aberrant findings, including those related to traumatic and neurovascular diseases, prenatal and developmental disorders, metabolic and degenerative conditions, neoplastic conditions, and nonspecific conditions.

MRI imaging is therefore a crucial part of the thorough assessment of children who have developmental delays. It is simple to identify males' distinct pathophysiologic and aetiological disorders that lead to developmental delay.

Generalizability

The generalizability of this study may be limited due to its hospital-based design, which primarily included pediatric patients referred specifically for MRI evaluation of developmental delay. This selection could introduce referral bias, as the sample may not represent the broader population of children with developmental delays in the community. Additionally, the study was conducted at a single institution in India, which may limit the applicability of the findings to different geographical locations or healthcare settings. Consequently, while the results provide valuable insights into the role of MRI in assessing developmental delay, further research with larger, more diverse populations across multiple centers is needed to enhance the generalizability of the findings.

CONCLUSION

It is concluded that the best modality with a high yield for diagnosing DD aetiologies is brain imaging with magnetic resonance imaging (MRI). Furthermore, there should be other outcomes in addition to the developmental delay's clinical diagnosis. An accurate diagnosis, which results in suitable treatment and parent counseling, is made possible by an MRI Brain. The likelihood of improving the yield of diagnosis grows with not only MRI brain imaging but also additional imaging advancements like Functional MRI, MR Spectroscopy, Diffusion Tensor Imaging, and Tractography, particularly in these children's structurally normal brains.

Limitations of the study

1. The present study was conducted with a limited sample size. Future studies are required to be conducted on more number of patients.
2. The main limitation of the study was its hospital-based nature, which predisposes to the referral bias.

Recommendations

MRI evaluation should be a standard component in the assessment of pediatric patients with DD. Given its high sensitivity and specificity in detecting various etiological factors, MRI can significantly aid in the early diagnosis and categorization of abnormalities, thereby guiding more targeted treatment plans and improving patient outcomes. Further studies with larger sample sizes are encouraged to refine diagnostic criteria and enhance the understanding of MRI's role in developmental delay.

Acknowledgment

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List of abbreviations

DD: Developmental Delay
DD Plus: Developmental Delay Plus
MRI: Magnetic Resonance Imaging
HIE: Hypoxic-Ischemic Encephalopathy
CNS: Central Nervous System
CT: Computed Tomography
USG: Ultrasonography

Source of funding

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Conflict of interest

The authors have no conflicting interests to declare.

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