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AN OBSERVATIONAL STUDY ON MRI IMAGING FEATURES IN THE EVALUATION OF GLOBAL DEVELOPMENTAL DELAY IN PAEDIATRIC AGE GROUP

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Abstract:

Global developmental delay (GDD) is a significant challenge faced by the pediatric population. Early identification and intervention are crucial for a better outcome. Magnetic resonance imaging (MRI) is a non-invasive imaging modality that can be used to evaluate children with GDD. This paper aims to review the role of MRI in the evaluation of children with GDD.

Aim: This study aimed to evaluate MRI imaging features in children with developmental delay. The current study was a cross-sectional study conducted in the Department of Radio-diagnosis at SMS Hospital, Jaipur, Rajasthan.

Results: In our study, a total of 80 children who were clinically suspected of global development delay were evaluated between the age group of 3 months to 18 years using 3T MRI It was found that 71% of cases had abnormal MRI findings. This study provides a systematic approach to the causes of developmental delay in children and the importance of MRI investigation.

Conclusion: We conclude from our study that MRI is the most useful investigation in patients clinically suspicious of developmental delay and can help in diagnosing the underlying aetiology.

Keywords: Global developmental delay, MRI, pediatrics, neuroimaging, brain malformations.

Introduction:

Developmental delay is diagnosed when there is a significant delay in two or more of the following domains: gross motor, fine motor, speech and language, cognition and social/personal development.[1]

It has a negative social impact on the child and his or her family. The global prevalence of developmental delay is estimated to be 1-3%.[2] Developmental delay requires careful evaluation to determine the aetiology, which is evident in 50-70% of cases.

Although comprehensive data for the Indian population is not available, studies from other countries have shown that about 15% of children have some developmental disability, and according to WHO estimates of the global disease burden, approximately 5% of all children under the age of 14 have some developmental disability. Furthermore, GDD has been reported in 1%-3% of the paediatric population aged five and under.[3-5]

Aetiology varies from specific diseases to sequelae of perinatal ischemic insult. Developmental delay may become evident during infancy or early childhood but becomes more apparent & therefore more often diagnosed in early school years.[6]

Neurometabolic disorders can present with developmental delay and regression and the symptoms can appear at any age from newborns into adulthood. In patients with developmental delay or regression, with or without a seizure, abnormal neurologic exam along with a positive family history of a similar disorder in close relative or parents and abnormal brain imaging with specific patterns, a neurometabolic disorder should be considered as one of the important treatable diseases.[2] Hypoxic-ischemic injury in preterm neonates causes ~50% of all cases of cerebral palsy.

The developmental delay may appear throughout infancy or early childhood, but it is more noticeable and thus more frequently diagnosed during the early school years [7]. Having a diagnosis allows clinicians to specify treatment options, monitor for known consequences, and provide prognosis and condition-specific family support (including family-planning choices). This assures that the child and his or her family have the best possible outcomes [8]. A diagnosis can offer parents a reason and a sense of closure or acceptance; it also prevents professionals from proceeding with potentially more costly and invasive investigations [9-11].

Evaluation of developmental delay is a multifaceted process involving cytogenetic testing, biochemical and hormonal assays, enzyme assays, electroencephalography (EEG), and neuroimaging, among others. Over the years, magnetic resonance imaging has become one of the most sensitive imaging modalities for children with developmental delays. Approximately sixty per cent of children with developmental delay have an abnormal MRI.

The main causes of delay in development include a range of various diseases from which a large number associate with specific findings in brain MRI. Magnetic resonance imaging is the modality of choice in investigating infants and children with developmental delays.[12]

The MRI of the brain is one of the most important tests for these patients.

In addition, MRI gives a detailed evaluation of the brain's anatomy as well as information on the degree of myelination and accompanying microstructural alterations. Appropriate categorisation of patients based on neuroimaging supports clinicians in further evaluation of the kid, allowing them to reach a diagnosis more quickly and easily.

This study provides a systematic approach to the causes of developmental delay and the importance of its rigorous investigation. It particularly highlights practical aspects relevant to neurological practice. A complete study provides important information about the patient, the rate and the type of brain abnormalities. It helps to identify these diseases and their prognosis, preventing the recurrence and also help in parent counselling.

MATERIALS AND METHODS

STUDY AREA:
Department of Radio-diagnosis, Department of Paediatrics, SMS Hospital, Jaipur, Rajasthan

STUDY TYPE:
Qualitative study

STUDY DESIGN:
Descriptive type of observational study

STUDY DURATION:
Data collection for the study was started after approval from the institutional research and review board, up to November 2022. Then it took another 2 months to process the data and write the thesis.

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STUDY TOOL:
Pre-tested, pre-designed proforma was used to collect data.

EQUIPMENT:
GE SIGNA ARCHITECT 3T MRI Machine

SAMPLE SIZE:
A sample of 80 cases was calculated at 95% confidence and 80% power to verify the expected proportion of 72.3% of abnormality in MRI of Children with Global Developmental Delay As per the seed article. (DOI: 10.7860/IJARS/2016/20141.2140)

SAMPLING TECHNIQUE:
Every eligible case was included in the study.

STATISTICAL ANALYSIS:
Qualitative data were analysed in terms of percentage and proportion.
The difference in proportion was analysed with the Chi-Square test and the mean difference will be analysed with the unpaired 'T-test.
For significance, a P value less than 0.05 will be considered significant.

STUDY UNIVERSE:
Patients with Developmental Delay were referred to the Department of Radio-diagnosis and Modern Imaging for MRI SCAN at SMS Medical College & Hospital, Jaipur.

STUDY POPULATION:
Patients fulfilling inclusion and exclusion criteria

INCLUSION CRITERIA
- Children who were referred for brain MRI with developmental delay, aged between 3 months to 18 years, admitted for the first time to diagnose the cause of delay was included in the study.
- Parents willing to give informed written consent.

EXCLUSION CRITERIA
- Children with a known genetic disorder, such as Down's syndrome, Turner's syndrome, etc., associated with delayed developmental milestones
- History of head injury and non-cooperative sick children.
- Patients <3 months and >18 years of age.
- General Contraindication to magnetic resonance imaging-claustrophobia, cochlear implant, pacemaker.
- Refusal to consent for the study.

Results and discussion:
Current study was a cross-sectional study conducted in the Radio-diagnosis, Department of Paediatrics, SMS Hospital, Jaipur, Rajasthan. This study aimed to evaluate MRI imaging features in children with developmental delay. A total of 80 participants were included in the study. 57 out of 80 patients had Abnormal Brain MRI findings which were categorised into the following groups

I. Normal
II. Neurovascular disease
III. Recognisable syndromes
IV. Congenital/ Structural malformations.

V. Metabolic and degenerative
VI. Non-specific findings: ventriculomegaly, hypoplasia of corpus callosum, delayed myelination, persistent cavum septum verge etc.

Group II: 31 (54%) out of 57 patients belonged to this group which includes neurovascular disease and constituted the largest group. Among them most common findings were hypoxic-ischemic encephalopathy (10 cases), cystic encephalomalacia (7 cases) and periventricular leucomalacia (5 cases) with associated findings of thinning of the corpus callosum, delayed myelination was noted.
Group III: Includes children with recognizable syndromes. 2 (3%) out of 57 patients presented with developmental delay had tuberous sclerosis and Sturge weber syndrome.
Group IV: Includes patients with congenital/ structural malformation. 8 (14%) out of 57 cases had congenital malformation. Among them 3 patients in the age group of <1 yrs had lissencephaly spectrum which includes agyria, pachygyria and band heterotopia, another 2 patients in the age group of <1 yrs, one had holoprosencephaly and another had Dandy walker malformation, 2 patients in the age group of 1-5yrs had corpus callosum agenesis, 2 patients in the age group of 6-10yrs had malformation secondary to abnormal post migrational development of the brain which includes polymicrogyria and schizencephaly, 1 patient had Dyke Davidoff Masson syndrome.
Group V: Includes patient with metabolic diseases which has specific findings on brain MRI. 9 (22.5%) out of 57 patients had metabolic diseases. Among them 2 patients in the age group of <1yr had findings of Leigh's syndrome, another 1 patient in the age of <1yr had features of hypomyelination, 5 patients in the age group of 1- 5yrs had 1 patient with features suggesting giant axonal neuropathy and other patient has metachromatic leukodystrophy, krabbes disease and vanishing white matter disease.
Group VI: Non-specific findings were found in 7 (12%) out of 57 cases of which 2 patients had delayed myelination, 1 patient had Arnold Chiari II malformation, 1 patient had craniosynostosis, 1 patient had hypoplasia of corpus callosum, 2 patients had ventriculomegaly

BASELINE CHARACTERISTICS:
In our study, the mean age of study participants was 5.1±3.9 years and out of the 80 participants, a maximum of 31 (38.8%) belonged to age 1-5 years followed by 23 (28.7%) in age of 5-10 years. In our study, out of the 80 participants, 40 (50%) were male and 40 (50%) were female.

A similar kind of study was done by Randhawa HS et al [46] and enrolled 60 pediatric patients (three months to 12 years). In this study, most of the patients 21 out of 60 were in the age of <2 years followed by 15 in the age of 2-5 years. In this study, male participants were 33 and female participants were 27.
Habibullah H et al [45] also did a similar study and 170 children aged 3 months to 12 years presenting with developmental delay were enrolled in the study. In this study most of the children in age 2-5 years i.e. 50 and 93 were male and 77 were female.

CLINICAL VARIABLES:
The proportion of children with associated seizures in a study by Widjaja et al[16] was 26% wherein 90 children with developmental delay were evaluated with a brain MRI. The percentage of children with seizures in a study by Momen et al [13] and Koul et al [14] was 53% and 43% respectively.

COMPARISON OF NORMAL VERSUS ABNORMAL MRI FINDINGS:
In our study, out of the 80 participants, 57 (71.3%) had abnormal MRI findings.

This was compared with other similar studies in the literature. In the study by Ali et al [15], the proportion of children with an abnormal MRI was 68%. Other studies including Momen et al [13],

Widjaja et al [16] and Koul et al [14] 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).

COMPARISON OF THE INVOLVED BRAIN STRUCTURES:

In our study, out of the 80 participants, 29 (36.3%) had abnormal grey matter, 50 (62.5%) had abnormal white matter, 14 (17.5%) had abnormal corpus callosum, 38 (47.5%) had abnormal ventricles, 7 (8.8%) had abnormal cerebellum, 25 (31.3%) had abnormal myelination.

In a study by Widjaja et al [38], the white matter was abnormal in 26% of the children. The corpus callosum, ventricles, grey 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. In a study by Ali et al [15], white matter and corpus callosum were abnormal in 58% and 16% of children which was higher than the figures obtained in our study.

COMPARISON OF VARIOUS CATEGORIES:

In our study, out of the 80 participants, 57 (71.3%) had abnormal MRI findings and a maximum of 31 (38.8%) belongs to group II, followed by 23 (28.7%) belongs to group I.

In a study by Ali et al [15], the most common abnormality encountered was Neurovascular diseases like hypoxic-ischemic encephalopathy (31%).

In a study by Momen et al [13], the most common categorical abnormality was neurovascular diseases which accounted for nearly 38% of the total cases.

Table 1: Distribution of participants according to age group

Age group	Frequency	Percent
≤1 years	17	21.3
1-5 years	31	38.8
5-10 years	23	28.7
>10 years	9	11.3
Total	**80**	**100.0**

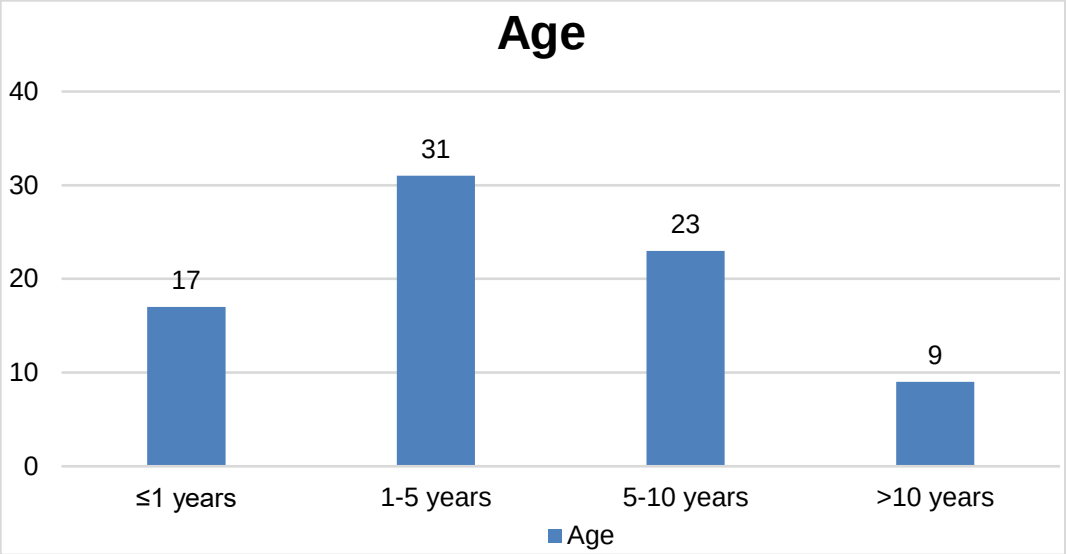

Table 2: Distribution of participants according to seizure history

Seizure History	Frequency	Percent
Absent	45	56.3
Present	35	43.8
Total	**80**	**100.0**

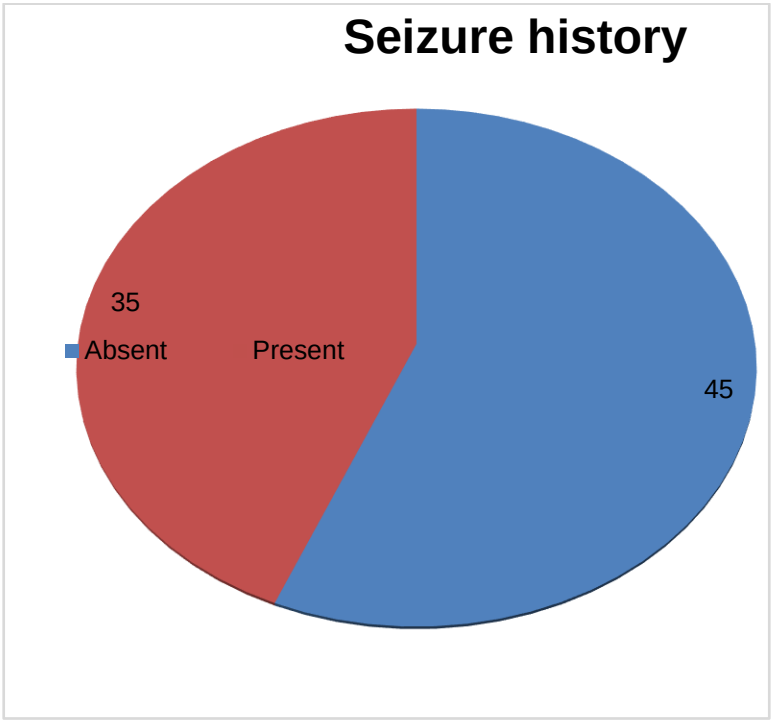

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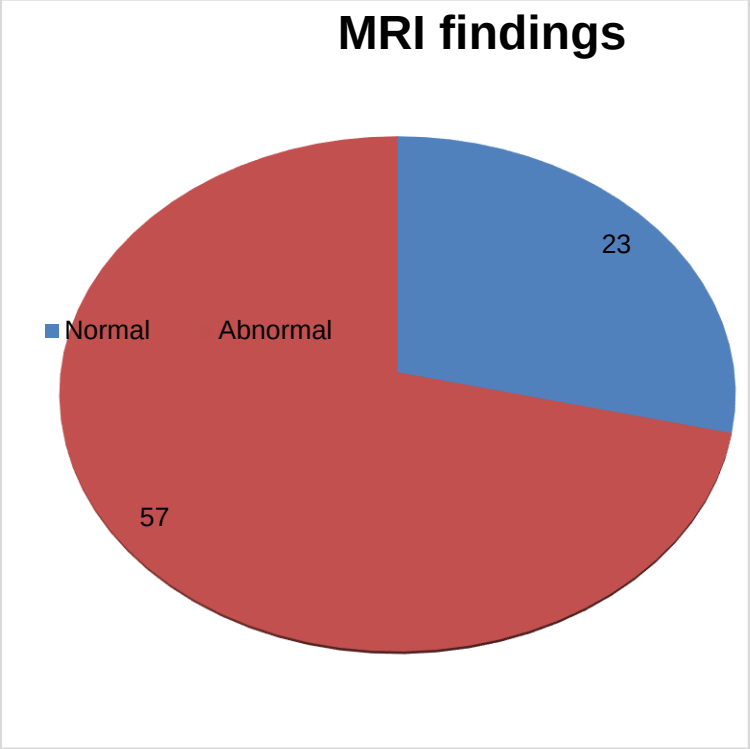
Table 3: Distribution of participants according to MRI findings

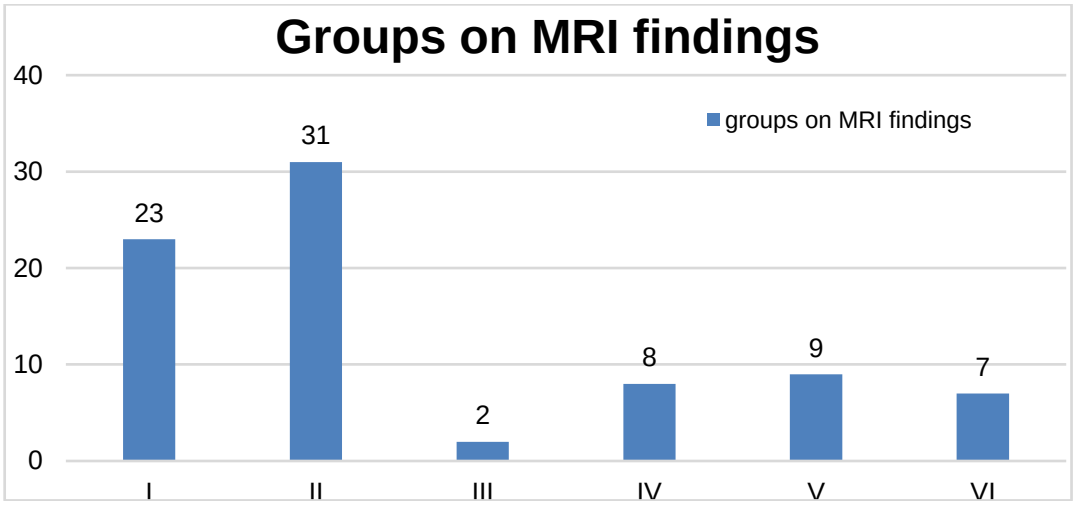
MRI findings	Frequency	Percent
Normal	23	28.7
Abnormal	57	71.3
Total	**80**	**100.0**



In our study, out of the 80 participants, 57(71.3%) cases had abnormal MRI findings.

Table 4: Distribution of participants according to groups on MRI findings

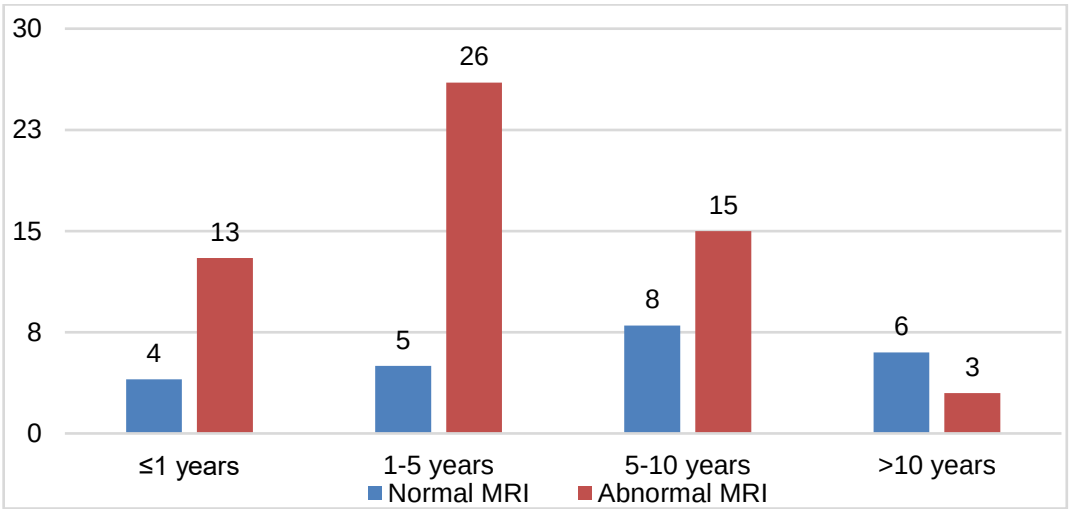
MRI findings	Frequency	Percent
I	23	28.7
II	31	38.8
III	2	2.5
IV	8	10.0
V	9	11.3
VI	7	8.8
Total	**80**	**100.0**



In our study, out of the 80 participants, a maximum of 31(38.8%) cases belong to group II, followed by 23(28.7%) cases belonging to group I.

Table 5: Comparison of MRI findings with age

Age	MRI findings				p-value
	Normal		Abnormal		
	Count	%	Count	%	
≤1 years	4	17.4%	13	22.8%	0.025
1-5 years	5	21.7%	26	45.6%	
5-10 years	8	34.8%	15	26.3%	
>10 years	6	26.1%	3	5.3%	
Total	**23**	**100.0%**	**57**	**100.0%**	



In our study, a statistically significant association was found between age and abnormal MRI findings. Abnormal findings were found to be high among the 1-5 years age group.

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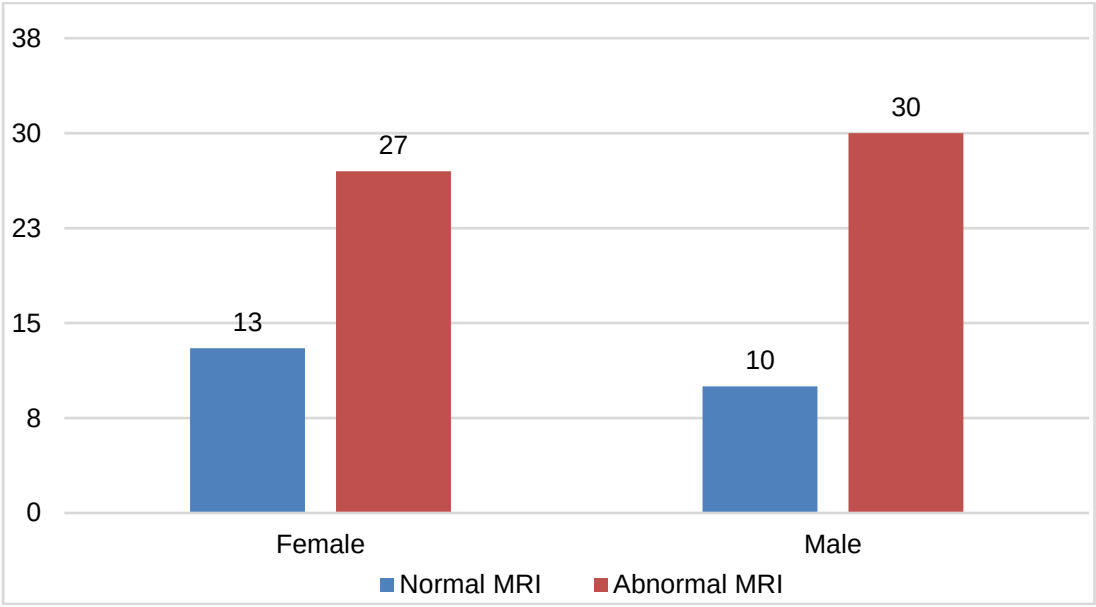
Table 6: Comparison of MRI findings with gender

Gender	MRI findings				p-value
	Normal		Abnormal		
	Count	%	Count	%	
Female	13	56.5%	27	47.4%	0.459
Male	10	43.5%	30	52.6%	
Total	**23**	**100.0%**	**57**	**100.0%**	



In our study, no statistically significant association was found between gender and MRI findings.

Conclusion:

MRI is a valuable tool in the evaluation of children with GDD. MRI can help identify structural abnormalities and provide information about the timing of brain injury, which can aid in the identification of the underlying etiology of GDD. MRI should be considered as part of the diagnostic workup for children with GDD, particularly when other diagnostic tests have failed to identify an underlying cause. Further research is needed to better understand the role of MRI in the evaluation of children with GDD and to identify the most effective imaging protocols for this population.

Conflict of the study

There was no conflict of interest in study.

LIMITATIONS OF THE STUDY

1) Smaller sample size and shorter period
2) Follow-up of the cases could not be done due to a shorter period
3) We did not include trauma and neoplastic cases in our study
4) We did not correlate abnormal MRI findings with electroencephalographic studies.
5) Few of the older patients were referred from the peripheral centres which should have been investigated earlier

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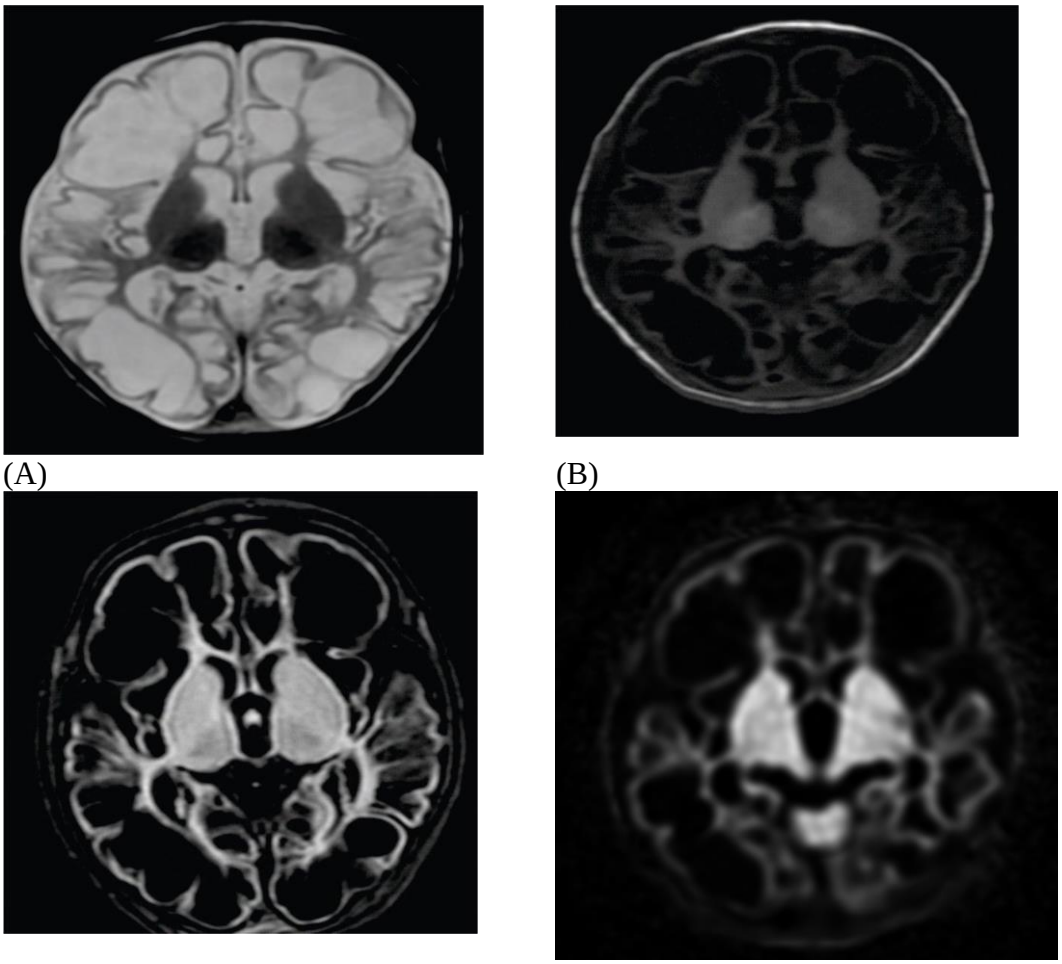
Case illustration:

CASE 1: DIFFUSE HYPOXIC-ISCHEMIC INSULT WITH MULTI-CYSTIC ENCEPHALOMALACIA

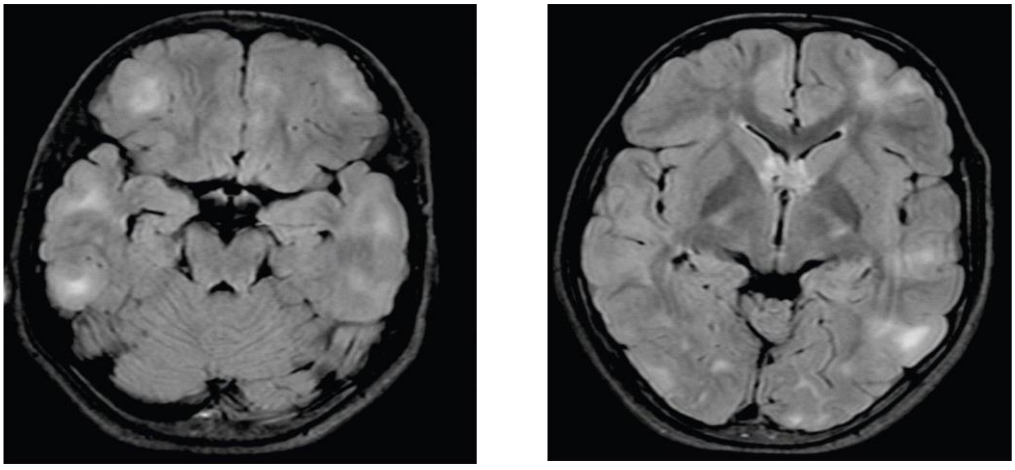


(A) (B)

(C) (D)

T2W axial (A) T1W axial (B) , T2 FLAIR axial (C) images shows cystic encephalomalacia in bilateral cerebral hemisphere with paucity of underlying white matter. Bilateral basal ganglia shows diffusion restriction on DWI images (D)

CASE 2: TUBEROUS SCLEROSIS



(A) (B)

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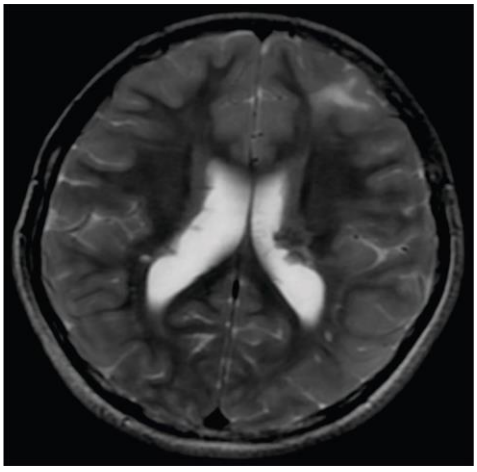
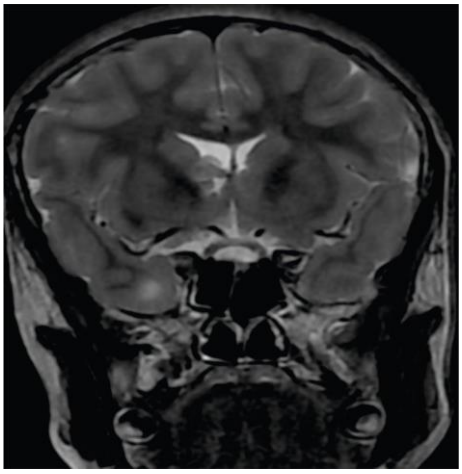
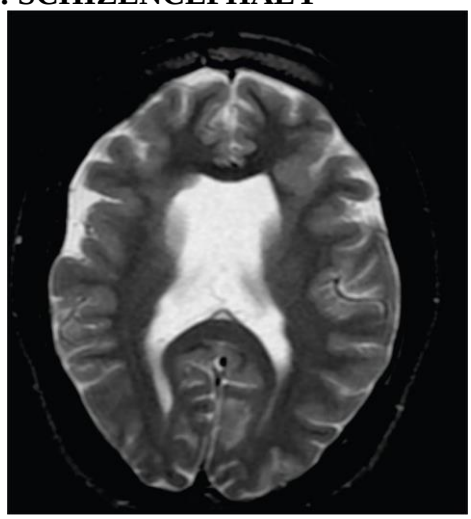
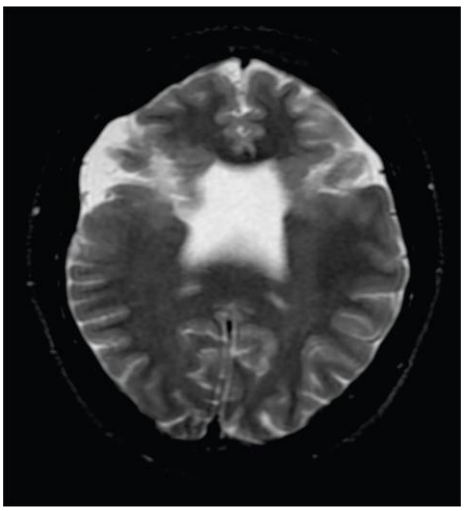



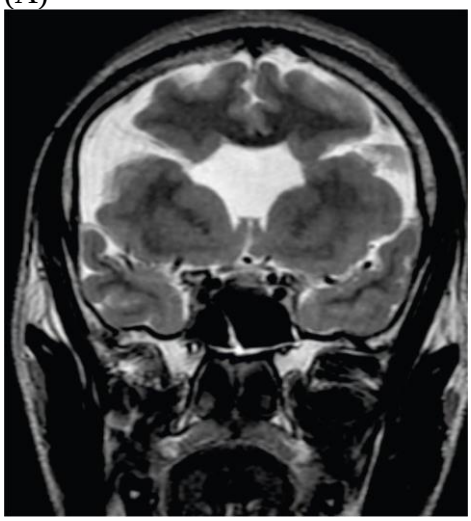
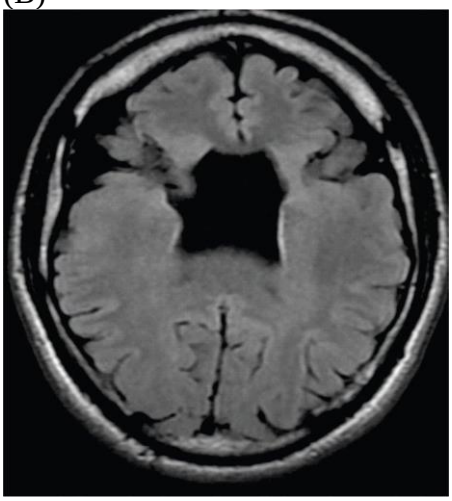
(C) (D)

T2FLAIR axial (A&B) ,T2 axial (C) and T2 coronal (C) images showing multiple subependymal nodules and cortical tubers with white matter hyperintesities.

CASE 3: SCHIZENCEPHALY

(A) (B)

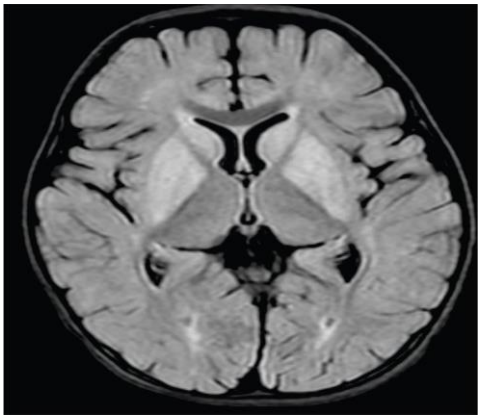



(C) (D)

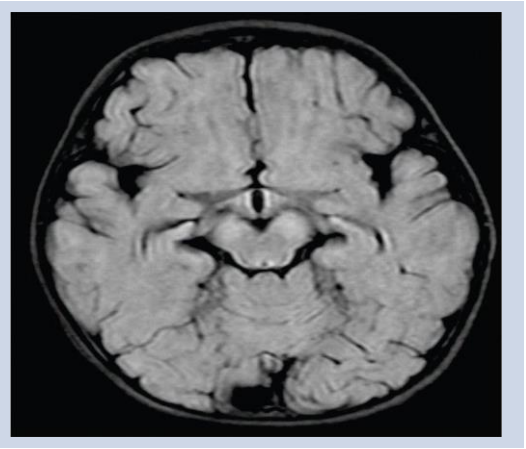
T2 axial (A&B) ,T2 coronal (C) &T2 FLAIR axial (D) images showing extra axial CSF attenuating collection along right frontal convexity which is communicating with frontal horn of right lateral ventricle, communications tract

is lined by grey matter- open lip schizencephaly. left side closed lip schizencephaly with absent septum pellucidum.

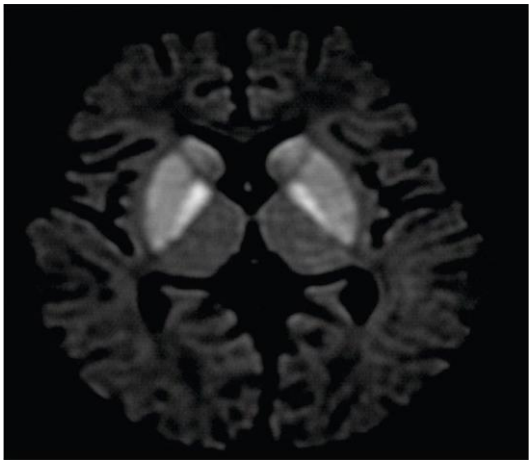
CASE 4: LEIGH'S SYNDROME



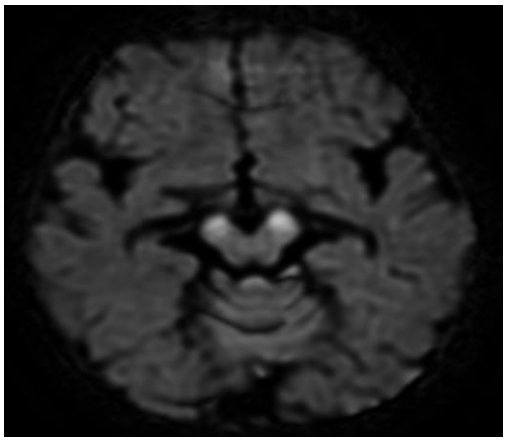
(A)



(B)



(C)



(D)

T2 FLAIR axial (A&B) sections shows bilateral symmetrical hyper-intensity in corpus striatum & crus cerebri of midbrain showing diffusion restriction on DWI images(C&D) - leigh's syndrome

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