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Research Article

Magnetic Resonance Imaging of the Brain in Pediatric Patients with Global Developmental Delay

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Abstract

Background: Global developmental delay (GDD) is defined as a significant delay in one or more of the developmental domains [1,2]. The causes for GDD vary extensively making systematic evaluation crucial. Although in some cases a definite diagnosis may not be reached by imaging, MRI plays a significant role in assessing patients with developmental delay [2,3].

Aims and Objectives: This study aims to analyze the spectrum of MRI findings in pediatric patients with developmental delay.

Materials and Methods: A retrospective, observational study was conducted over five years four months (April 2018-August 2023) on 128 pediatric patients referred for MRI with a diagnosis of GDD. The MRI findings were evaluated and classified into eight categories.

Results: Of the 128 cases, 37 (28.9%) had normal MRI findings while 91 (71%) presented abnormalities. Out of the 91 abnormal cases, the most common abnormalities were delayed myelination (28.6%) and neurovascular abnormalities (27.5%). There was no significant difference in the prevalence of abnormal MRI when classified by presentation as isolated GDD and GDD with other associated conditions.

Conclusion and Key Message:

- The causes of GDD are many and varied and the treatment of these patients is complex and multidimensional.
- MRI serves as a valuable tool for evaluate patients with the clinical diagnosis of developmental delay, aiding in the diagnosis, prognostication, treatment and parental counseling [11].

Keywords: *MRI-Magnetic Resonance Imaging; GDD-Global Developmental Delay; VR Spaces-Virchow Robin Spaces; PVL-Periventricular Leukomalacia; HIE-Hypoxic Ischemic Encephalopathy*

Introduction

Developmental delay is defined as a delay in attaining the expected milestones for age. GDD is a subset of developmental disabilities and is defined as a delay in 2 or more of the following domains: gross/fine motor, speech/language, cognition, social/personal, and activities of daily living. Significant delay is defined as performance two standard deviations or more below the mean on age-appropriate, standardized norm referenced testing [2,3,9].

The prevalence of GDD is estimated to be approximately 5% to 10% [4].

The multifaceted and diverse causes for developmental delay pose challenges in patient evaluation. In the presence of specific history such as birth asphyxia/seizures/physical findings of dysmorphic features, the clinician may be able to identify the cause for GDD. However, in the majority of cases, the GDD may be unexplained, making systematic evaluation important.

Neuroimaging with MRI is recommended whenever available for comprehensive evaluation of patients with GDD [3]. MRI imaging in these cases not only helps in diagnosis but also offers prognostic insights and guides future treatment or rehabilitation strategies [4,5].

Materials and Methods

This retrospective observational study analyzed brain MRI findings in 128 pediatric patients who were referred to the department of Radiology of Bangalore Baptist Hospital with a clinical diagnosis of GDD. The study was conducted over a period of 5 yrs and 4 months from April 2018 - August 2023. The MRI images of these patients were evaluated by a paediatric radiologist with 12 yrs experience, and the MRI reports were categorized into 8 groups namely: (a) Normal, (b) Nonspecific, (c) Delayed myelination, (d) Neurovascular/traumatic, (e) Metabolic/neurodegenerative, (f) Congenital and developmental, (g) Neoplastic, (h) Recognizable syndromes [3-5].

Bangalore Baptist Hospital Institutional Research Board approval was obtained for the study for waiver of consent, the approval number being BBH/IRB/2024/035.

Inclusion and exclusion criteria: Patients referred with a clinical diagnosis of GDD aged from 3 months to 14 yrs were included in the study.

Patients with known syndromes (e.g. Down syndrome, Turners' syndrome), autism, and ongoing infective conditions like meningitis were excluded from the study.

The MRI scans were conducted on a 1.5 T Seimens Avanto Tim and Dot system. The basic MRI sequences performed were Axial T1TSE, Axial T2TSE, Axial T2 FLAIR, Axial diffusion, SWI, Axial T1IR, Coronal T2TSE, and Sagittal T1TSE. In patients with history of seizures, seizure protocol was performed with additional T2 and FLAIR oblique coronal scans through the mesial temporal lobes and hippocampus. Post contrast imaging and spectroscopy was performed in few of the cases based on the pre-contrast MRI findings.

Most of the scans were done under general anesthesia while few were conducted with oral sedation.

Data and statistical analysis

The needed information such as age, gender, clinical data and MRI findings were collected from the patients' records and analyzed using Microsoft Excel.

Results

Of the 128 cases, 72 were male and 56 were female. Abnormal MRI findings were present in 91 cases (71%), while 37 cases (28.9%) showed normal MRI results (Table 1).

	Normal (n = 37)		Abnormal (n = 91)		Total (n = 128)
Age	**Number**	**%**	**Number**	**%**	**Number (%)**
3 months - 1 year	4	10.8	22	24.2	26 (20.3%)
1 - 2 years	11	29.7	23	25.3	34 (26.6%)
2 - 5 years	13	35.1	21	23.1	34 (26.6%)
5 - 8 years	07	18.9	15	16.5	22 (17.2%)
8 - 12 years	02	5.5	08	8.8	10 (7.8%)
12 - 15 Years	00	0.0	02	2.1	02 (1.5%)
Sex					
Male	22	59.4	50	54.9	72(56.3%)
Female	15	40.6	41	45.1	56(43.7%)

Table 1: *Age and sex distribution of the study population with normal and abnormal MRI.*

The abnormal MRI cases were classified into seven categories (Table 2 and figure 1).

MRI findings	Number (n = 128)	Percentage
Normal	37	28.9
Nonspecific	21	16.4
Delayed myelination	26	20.3
Neurovascular/traumatic	25	19.6
Metabolic/neurodegenerative disease	8	6.2
Congenital and developmental	9	7.0
Neoplastic	1	.8
Syndrome	1	.8

Table 2: *Etiological classification based on MRI findings.*

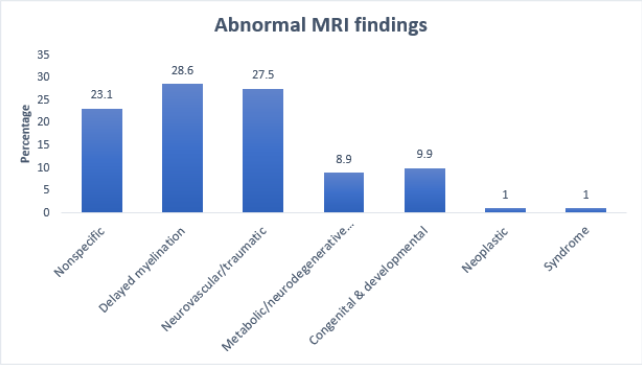

Figure 1: *Bar graph showing classification of MRI findings in the 91cases with abnormal MRI.*

Delayed myelination was the most prevalent abnormality in our study followed by neurovascular/traumatic abnormalities. Among the 25 cases (27.5%) classified as neurovascular/traumatic abnormalities, 19 patients had periventricular leukomalacia while six patients had cystic encephalomalacia.

Nonspecific findings which accounted for 21 cases (23.1%) included findings such as terminal zone hyperintensity, T2 and FLAIR white matter hyperintense foci, diffusely thin corpus callosum with no other features of PVL, mild prominence of CSF spaces and ventricles and prominent VR spaces. Notably, nonspecific T2 and FLAIR white matter hyperintensities were the most common findings within this category.

Eight patients had MRI findings suggestive of metabolic/neurodegenerative conditions, of which one patient was diagnosed with pyruvate dehydrogenase deficiency (Figure 2), one patient, had encephalopathy with reversible myelin vacuolization due to MYRF mutation, one patient had mesial temporal sclerosis and two patients had sequalae of hypoglycemia. The remaining three patients had MRI features suggestive of metabolic disorder, however declined further evaluation.

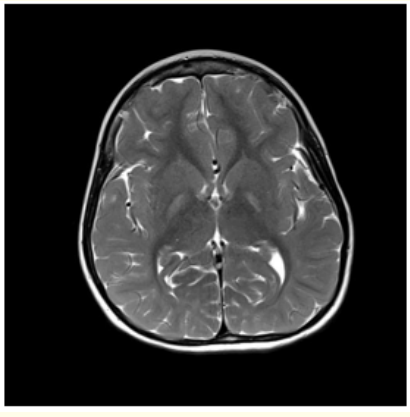

Figure 2: *10 year old with pyruvate dehydrogenase deficiency. T2 axial image shows hyperintensity of bilateral globus pallidus.*

The category of congenital/developmental disorders included nine patients which consisted of I case each of arachnoid cyst, polymicrogyria, pachygyria (Figure 3), focal cortical dysplasia, nodular heterotopias, Pelizaeus Merzbacher syndrome, Aqueductal stenosis and two cases of microcephaly.

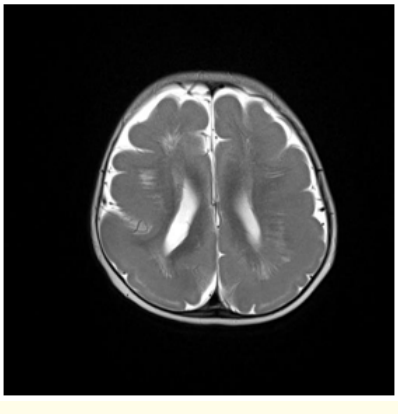

Figure 3: *1 year old with pachygyria. T2 axial image showing gross reduction of gyri and marked thickening of the cortex with posterior predominance.*

There was one case of posterior fossa epidermoid cyst presenting in the category of neoplastic conditions and one case of Joubert syndrome was diagnosed (Figure 4).

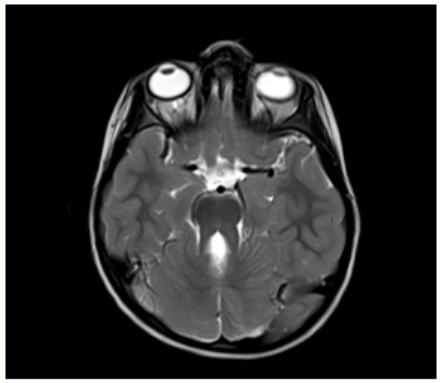

Figure 4: *4 year old with Joubert Syndrome. T2 axial image shows thickened and elongated superior cerebellar peduncles with 'Molar tooth' sign.*

Out of the 128 patients, 58 were diagnosed with isolated GDD, 30 with GDD and seizures, and 40 with GDD alongside other conditions such as hypotonia, dystonia, hearing impairment, and microcephaly (Table 3a).

	Normal (n = 37)		Abnormal (n = 91)		Total (n = 128)
Clinical presentation	**Number**	**%**	**Number (%)**	**%**	**Number (%)**
Only GDD	21	56.8	37	40.7	58 (45.3%)
GDD + Seizures	08	21.6	22	24.1	30 (23.4%)
GDD+ other condition	08	21.6	32	35.2	40 (31.3%)

Table 3a: *Clinical presentation of the study population with normal and abnormal MR.*

Among the 91 patients with abnormal MRI, 40.7% had isolated GDD, 24.1% had GDD and seizures, and 35.2% had GDD with other clinical conditions. The combined occurrence of GDD with associated clinical conditions accounted for 59.3% of the abnormal MRIs. However, the association between GDD with other clinical conditions and abnormal MRI was not statistically significant in our study (Chi-square test, p = 0.09) (Table 3b).

	Normal (n = 37)		Abnormal (n = 91)		Chi square	p-value
Clinical presentation	**Number**	**%**	**Number (%)**	**%**	2.751	0.09
Only GDD	21	56.8	37	40.7		
GDD + other	16	43.2	54	24.1		

Table 3b: *Chi square test to evaluate for statistical significance between clinical presentation and abnormal MRI.*

Discussion

Our study which focused on evaluating pediatric patients with Global Developmental Delay (GDD) using MRI, underscores the complexities in diagnosing and categorizing developmental delays. GDD, characterized by delays in multiple developmental domains, poses diagnostic challenges due to its diverse etiologies [1,2].

Our findings affirm the pivotal role of neuroimaging, specifically MRI, in comprehensively assessing GDD [3,12]. MRI not only aids in diagnosis but also assists in prognosis and devising tailored treatment strategies [4,5]. The observed abnormalities in our study encompassed a spectrum of etiologies, substantiating the varied nature of GDD.

In our study of 128 patients 72 (56.3%) were males and 56 (43.7%) were females. Abhineya G., *et al*. [6] in their study also had more number of males amounting to 69.1%.

Out of 128 cases, 28.9% had normal MRI while 71% had abnormal MRI. This is comparable with Althaf Ali., *et al*. [8] who in their study of 81cases reported 68% and Koul R., *et al*. [16] who reported 71.8% of cases with abnormal MRI findings. A higher percentage of abnormal MRIs were reported by Dittekavi LVPP., *et al.* [5], Abhineya G., *et al*. [6] and Naaila., *et al.* [15] namely 87.5%, 81.4% and 82% respectively. Hafiz Habibulla., *et al.* in their study reported a lower number abnormal MRI in 54.7% of cases [9].

In our study we further classified the MRI abnormalities into seven categories. (Figure 1). This method of classification is similar to the studies conducted by Abhineya G., *et al*, Althaf Ali., *et al*, Rini Palve., *et al.* and Konde S R., *et al.* [6,8,10,17] however delayed myelination was not included as a category in the above-mentioned studies. Dattekavi LVPP., *et al.* [5] and Abhineya G., *et al.* [6] included infective etiology as a category. In our study, however we did not have any cases showing MRI features of infection. Widjala E., *et al.* [13] in their study followed a different approach of classifying abnormalities depending on the anatomic site of involvement and concluded that ventricular abnormalities were the most common finding.

The commonest abnormality encountered in our study was delayed myelination seen in 28.6% followed by neurovascular and traumatic abnormalities accounting for 27.5%. The commonest MRI abnormality detected shows considerable variation from study to study with Dittekavi., *et al.* [5] reporting metabolic and degenerative abnormalities as the most common finding in their study while Abhineya G., *et al.* [6] reported hypoxic ischemic encephalopathy and Althaf Ali., *et al.* [8] and Pranay D I., *et al.* [15] reported neurodegenerative/ traumatic as their most common findings respectively. The high prevalence of delayed myelination in our study emphasizes the need for serial MRIs to determine the progression of myelination in these patients.

Nonspecific findings were seen in 23.1% of abnormal MRIs in our study, which is significantly higher than Althal Ali., *et al.* [8] who reported 7.5% nonspecific MRI findings. Hafiz Habibullah., *et al.* [9] in their study reported 60% cases showing nonspecific findings. Nonspecific findings, though challenging to interpret, constituted a considerable portion of abnormal MRIs, warranting further follow up.

Congenital and developmental abnormalities accounted for 9.9% in our study, similar to Abhineya., *et al.* [6] who reported 6.6%. Dittekavi LVPP., *et al.* [5] and Althaf Ali., *et al.* [8] reported higher percentage of congenital abnormalities, 37.5% and 17% respectively.

In our study the patients who presented with GDD and seizures and GDD with conditions such as hypotonia, dysmorphic features, hearing/visual impairment accounted for 59.3% of abnormal MRIs collectively as compared to patients with patients with isolated GDD who accounted for 40.7%. This is comparable to the study by Abhineya G., *et al.* [6] who reported 63.7% abnormal MRIs in patients presenting with GDD and other associated conditions. Hart Antony., *et al.* [7] also reported similar findings with 55.3% abnormal MRIs in cases of GDD with associated conditions.

Interestingly, while a substantial portion of our cohort presented with GDD accompanied by additional clinical conditions, the statistical association between associated clinical conditions and abnormal MRI findings did not reach significance. This suggests that the complexity of GDD etiology extends beyond direct clinical correlations.

Two patients in our study required neurosurgical intervention with a diagnosis of epidermoid cyst of the posterior fossa and arachnoid cyst with features of mass effect. Moreover, two of our patients diagnosed with pyruvate dehydrogenase deficiency and encephalopathy with reversible myelin vacuolization due to MYRF mutation were started on specific treatment for the above mentioned conditions.

Limitations of the Study

Despite its insights, our study encounters limitations that temper the depth of our findings:

- As delayed myelination emerged as the most prevalent abnormality in our study serial MRIs would be ideal for these patients to determine the significance of this finding by assessing the progression of myelination. The absence of follow-up MRIs restricts our understanding of dynamic changes in delayed myelination.
- Notably, few cases exhibited MRI features suggestive of metabolic or neurodegenerative conditions, however, patient non-compliance limited definitive diagnoses in these instances, emphasizing the need for comprehensive patient cooperation.

Conclusion

In conclusion, our study underscores the indispensable role of MRI in delineating the multifaceted etiologies of Global Developmental Delay (GDD). Our study shows that MRI is useful in all cases of GDD irrespective of the presence or absence of associated clinical conditions. In this study we were able to classify the abnormalities into distinct categories which not only aided in the diagnosis and treatment but also helped in facilitating informed decision-making, prognosis, and parent counseling which are integral to the management of GDD.

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Conflict of Interest

Nil.

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