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Original Research Article

Radiological evaluation of children with developmental delay using magnetic resonance imaging and proton MR spectroscopy

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ABSTRACT

Background: Several factors like environmental, genetic, nutritional and chronic diseases affect the process as well as can have adverse effects on it in the form of delays in developmental milestones. The milestone delay can be evaluated using four domains of gross motor, fine motor, social and language skills. Developmental delay is defined as significant delay (more than two standard deviations below the mean) in one or more developmental domains. Global developmental delay is defined as significant delay in two or more developmental domains. Brain MRI is one of the major investigations of these patients. MRI is also used to examine the usual brain myelination patterns. Investigators have also used proton MR spectroscopy, an emerging MR imaging modality, in children to study neurodegenerative disorders, epilepsy, metabolic disorders, and pediatric neuropsychiatric disorders.
Methods: This prospective observational study involved 100 children aged 6 months to 10 years with developmental delay, referred for brain MRI at a tertiary care center. MRI was performed on a 1.5-T system, and proton MRS was used to calculate N-acetyl aspartate (NAA), choline (Cho), and creatine (Cr) ratios in children with normal MRI findings. Children with progressive neurodevelopmental disorders, recognized syndromes, and CNS infections were excluded.
Results: MRI findings were abnormal in 81% of the children, with neurovascular/traumatic lesions accounting for 59% and congenital/developmental anomalies for 15%. The most common findings involved white matter abnormalities (63%). MRS revealed abnormal neuro-metabolite ratios in 68% of children with normal MRI, indicating metabolic changes.
Conclusions: MRI, combined with proton MRS, significantly improves diagnostic accuracy in children with developmental delay. While structural abnormalities were observed in 81% of children, MRS added value by detecting metabolic abnormalities in children with normal MRI findings.

Keywords: Developmental delay, Children, Magnetic resonance imaging, Neurovascular diseases, Magnetic resonance spectroscopy

INTRODUCTION

Developmental delay is a common pediatric condition, affecting 5-10% of children worldwide. It can manifest in various domains, including motor, language, and cognitive development. Early and accurate diagnosis is crucial for management and intervention. Magnetic resonance imaging (MRI) is a widely used tool for identifying structural abnormalities in the brain that may underlie developmental delay. However, many children

with mild neurodevelopmental disorders have normal brain MRIs, highlighting the need for additional diagnostic tools. Proton magnetic resonance spectroscopy (MRS) allows for the evaluation of neuro-metabolite concentrations, providing insights into neuronal health and metabolic status even when structural MRI appears normal.[1,3]

Aims and objectives

This study aimed to identify the spectrum of MRI abnormalities in children with developmental delay and assess the utility of proton MRS in children with normal brain MRI findings.

METHODS

Study design

This prospective observational study was conducted at the Department of Radiodiagnosis, LLRM Medical College, Meerut, India, from January 2022 to December 2022. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from the parents or legal guardians of all participants.

Inclusion criteria

Children aged 6 months to 10 years presenting with developmental delay were included.

Exclusion criteria

Exclusion criteria were progressive neurodevelopmental disorders, recognized syndromes (e.g., Down syndrome), CNS infections, meningitis, and encephalitis.

Imaging protocol

MRI was performed using a 1.5-T Philips Achieva system. Sequences included T1-weighted, T2-weighted, FLAIR, and diffusion-weighted imaging. Children with normal MRI findings underwent proton MRS with multivoxel techniques. Voxels were placed in bilateral frontal and parieto-occipital subcortical white matter.

MRS analysis

Neuro-metabolite ratios, including NAA/Cr, Cho/Cr, and Lipid/Lactate, were calculated. Proton MRS was performed in 13 children with normal MRI findings to evaluate for neurometabolic abnormalities.

Statistical analysis

Data were analyzed using SPSS v21.0. Categorical variables were compared using the Chi-square test, and continuous variables were compared using the t-test. A p value of <0.05 was considered statistically significant.

RESULTS

Demographic data

A total of 100 children (56 boys, 44 girls) with developmental delay were included. The mean age was 3.40±3.14 years, with the majority of children (30%) in the 3–5-year age group.

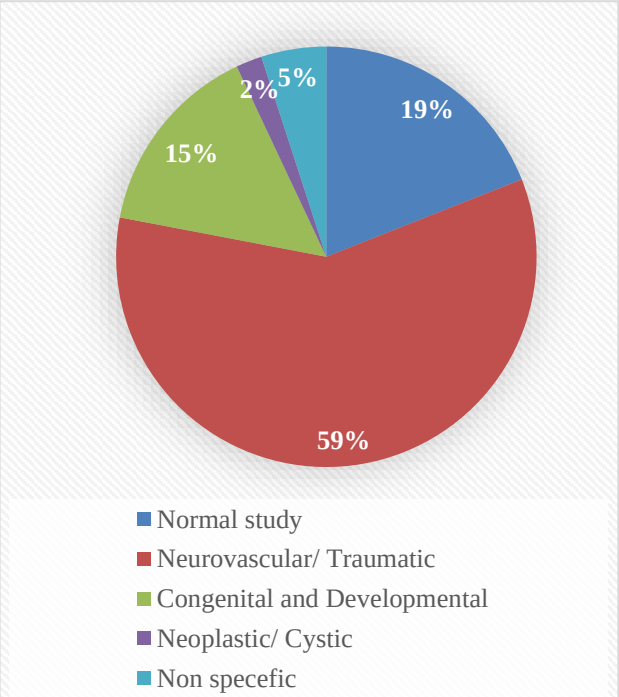

Figure 1: Prevalence of normal and abnormal (categorized) MRI findings.

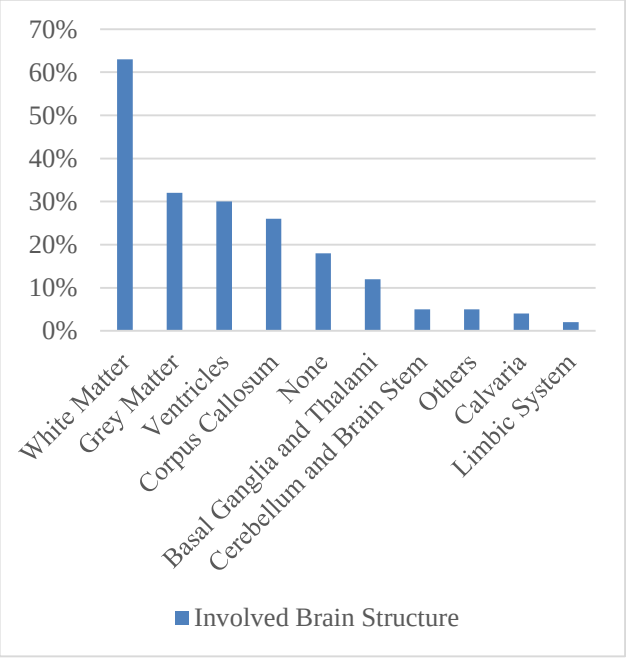

Figure 2: Relative frequencies of the involved brain structures on MRI.

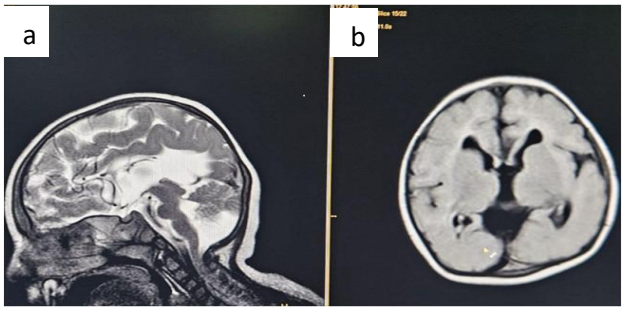

Figure 3 (a and b): Corpus callosal agenesis-race car sign.

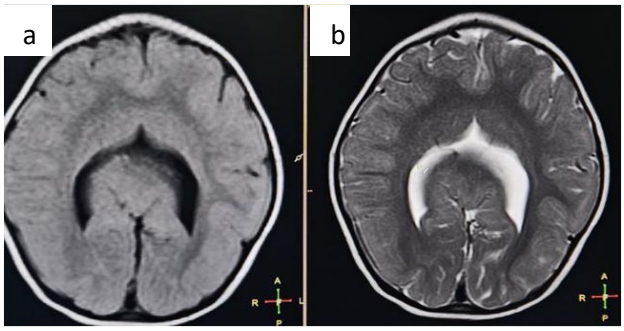

Figure 4 (a and b): Semi-lobar holoprosencephaly.

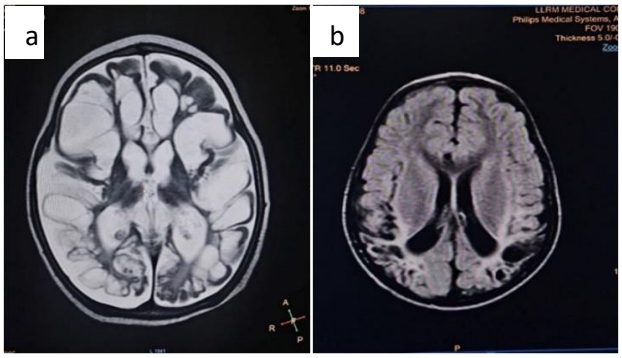

Figure 5 (a and b): Diffuse cystic encephalomalacia (left) and parietooccipital and periventricular gliosis-sequelae to hypoxic ischemic injury.

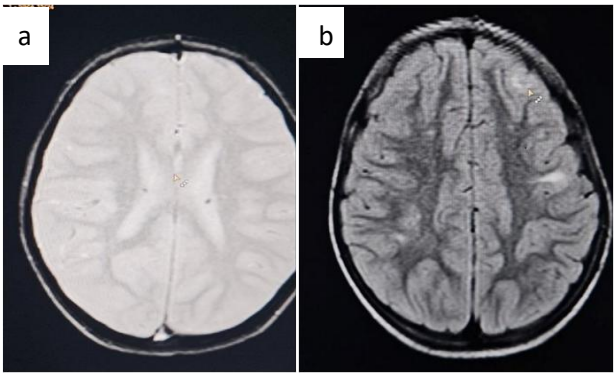

Figure 6: (a, b) Tuberous sclerosis cortical tubers and subependymal calcified nodules (seen as blooming on GRE).

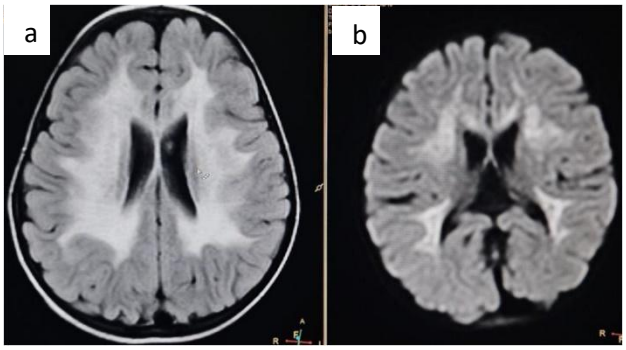

Figure 7 (a and b): Metachromatic leukodystrophy with characteristic-tigroid pattern.

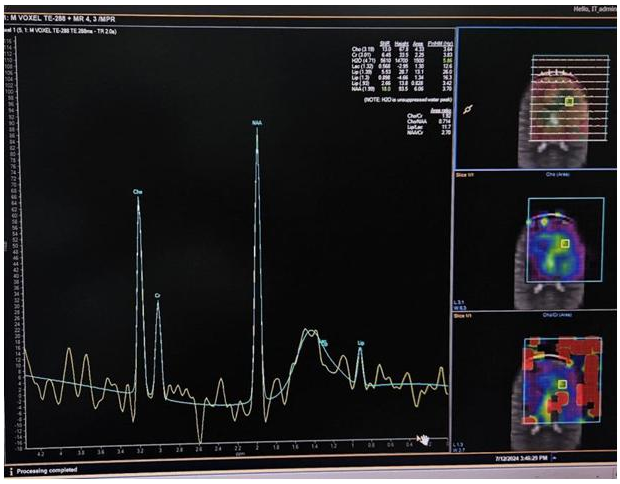

Figure 8: MRI was normal. MR spectroscopy showed elevated Cho/Cr ratio.

MRI findings

Abnormal MRI findings were observed in 81% of the children, neurovascular/traumatic lesions: 59%, congenital and developmental abnormalities: 15%, neoplastic/cystic lesions: 2%, non-specific findings: 5%

A large number of participants answered 14 injections 46 (31.9%) followed by 7 injections 22 (15.2%), 5 injections 28 (19.4%). Similarly, about the site of administration for the vaccine to be given was abdomen 91 (65.9%), buttocks 22 (15.9%), shoulder 18 (13.04%), thigh 2 (1.4%), don't know 5 (3.6%).

White matter abnormalities were most prevalent (63%), followed by gray matter (32%), ventricles (30%), and corpus callosum (26%).

MRS findings

Of the 19 children with normal MRI findings, 13 underwent proton MRS. Abnormal neuro-metabolite ratios were observed in 68% of these children, indicating possible underlying metabolic abnormalities. The following patterns were noted.

NAA/Cr

A significant reduction in the NAA/Cr ratio was seen, indicating reduced neuronal integrity or neuronal loss.

Cho/Cr

An elevated Cho/Cr ratio was observed, suggesting increased cellular turnover or gliosis.

Lipid/lactate peaks

Abnormal peaks, suggestive of mitochondrial dysfunction, were seen in 3 children. These findings demonstrate that MRS can detect metabolic changes even when structural abnormalities are absent on MRI.

Table 1: Summary of basic demographic details.

Age (in years)	**3.40±3.14 Mean±SD||2.00 (1.00-5.25) Median (IQR)**
Age group	
<1	23 (23.0%)
1-2	22 (22.0%)
3-5	30 (30.0%)
6-10	25 (25.0%)
Gender	
Male	56 (56.0%)
Female	44 (44.0%)
Gestational age	
Extreme pre-term	2 (2.0%)
Very pre-term	2 (2.0%)
Moderate-late pre-term	24 (24.0%)
Term	69 (69.0%)
Post-Term	3 (3.0%)
MRI abnormalities (present)	81 (81.0%)

Table 2: Clinical association in patients.

Clinical associations	
None	44 (44.0%)
Seizures	36 (36.0%)
Neurological deficit	19 (19.0%)
Others	13 (13.0%)
Respiratory and cardiac disease	4 (4.0%)

DISCUSSION

Our study highlights the utility of MRI and proton MRS in evaluating children with developmental delay. The high rate of abnormal MRI findings (81%) aligns with prior studies, such as those by Pandey et al, Widjaja et al, Momen et al, Shevell et al, Koul et al, and Battaglia et al who reported abnormal MRI results in up to 63.8%, 84%, 58.6%, 65.5%, 71.8%, and 80.8% of children with developmental delay respectively.[2,4-8]

The majority of these abnormalities involved white matter, consistent with the findings of Bouhadiba et al, who described periventricular leukomalacia and delayed myelination as common contributors to neurodevelopmental deficits.[9]

Neurovascular/traumatic lesions were the most common MRI findings (59%), underlining the significance of perinatal hypoxic-ischemic events and traumatic injuries in developmental delay. This is corroborated by the findings of Pandey et al, who also reported a high prevalence of neurovascular anomalies in children with unexplained developmental delay.[2]

Proton MRS added diagnostic value in children with normal MRI findings by identifying abnormal neuro-metabolite ratios, primarily involving reductions in NAA and elevations in Cho. These results are in line with those of Filippi et al, who found that proton MRS can reveal metabolic abnormalities even in children with normal MRI, emphasizing the importance of metabolic assessments in unexplained developmental delay.[3]

Abnormal lactate peaks, seen in 3 children, raise the possibility of mitochondrial dysfunction, an important consideration in the differential diagnosis of developmental delay. This mirrors findings from studies such as those by Garcia et al, who identified abnormal lactate peaks in children with suspected mitochondrial disorders.[10] MR imaging plays a significant role in comprehensive evaluation of children who present with development delay, and can easily detect many specific etiological and pathophysiological conditions leading to developmental delay.[11-15]

Our study was conducted at a single center, and the relatively small sample size limits the generalizability of our findings. Additionally, proton MRS was only performed on a subset of children due to the technical challenges and the need for patient cooperation.

Larger multicenter studies are needed to validate our findings and to further explore the role of proton MRS in diagnosing metabolic causes of developmental delay. Future research should also focus on the long-term outcomes of children with abnormal MRS findings but normal MRI.

CONCLUSION

MRI remains a vital tool in the evaluation of children with developmental delay, with the majority of affected children showing neurovascular, traumatic, or congenital abnormalities. However, proton MRS provides additional diagnostic value, especially in cases where MRI findings are normal. By detecting metabolic abnormalities such as reduced NAA/Cr and elevated Cho/Cr ratios, MRS can

uncover neurometabolic dysfunctions that may be missed with structural imaging alone.

Recommendations

The integration of MRI and proton MRS significantly enhances diagnostic accuracy and should be considered in the comprehensive evaluation of children with developmental delay. Future studies should aim to establish standardized protocols for the use of MRS in pediatric neuroimaging.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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