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Research Article

Assessment of Clinico-Radiological Profile of Brain in Children with Developmental Delay

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Abstract: ***Background:*** Developmental delay denotes an extensive delay in one or more developmental domains. It has an estimated occurrence of 1-3% worldwide. Magnetic resonance imaging of the child's brain appears to be the most assuring neuroimaging technique in the evaluation and diagnosis of patients with the developmental delay disorders. ***Aims and Objectives:*** Our aim was to identify the spectrum of abnormalities in the brain by using MR imaging in children with developmental delay and also categorize all the morphological abnormalities. Secondly, the role of MR spectroscopy (MRS) to evaluate the severity and magnitude of different neurometabolite ratios in children with normal brain imaging were also studied. ***Materials and Methods:*** Our study involves the examination of 120 children presenting with developmental delay to the Department of Radiodiagnosis, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, between July 2018 to June 2019. The children were examined with a standard MRI protocol. Clinical and demographic features and parameters were noted. The different brain structures involved were studied systematically, and the morphological abnormalities were categorized. ***Results:*** The occurrence of abnormal MRI findings was 78% among the evaluated children. Our study showed predominant involvement of the ventricles, white matter and corpus callosum. The marginal proportion of various morphologic abnormalities was Non-specific findings (11%), Neoplastic and cystic lesions (3%), Neurovascular diseases (50%), Congenital and developmental (12%) and combined aetiology (2%). Ten children with a normal MRI were subjected to MR Spectroscopy which revealed no significant difference in the neurometabolite ratios among the patients. ***Conclusion:*** MR imaging has good specificity and sensitivity in diagnosing various disorders of developmental delay. Careful evaluation of the MRI helps to identify the probable aetiology in most of the cases. Proton MR Spectroscopy is an advanced technique in evaluating children with developmental delay and should be incorporated in the standard MRI protocol in cases where it is feasible. Hence, appropriate diagnosis on MRI helps in guiding the physician to plan further patient management.

Keywords: Developmental Delay, Children, Magnetic Resonance Imaging, Neurovascular Diseases, Magnetic Resonance Spectroscopy.

INTRODUCTION

Child development and growth is a continuous process which begins from conception and continues throughout an individual's life. Developmental delay denotes a significant delay in one or more developmental domains. It poses a social stigma upon the child and his or her family. The developmental delay has an estimated prevalence of 1-3% worldwide (Momen, A. A. *et al.*, 2011). Developmental delay needs careful evaluation to ascertain the aetiology, which is evident in around 50-70% of the cases.

Child development, in its broadest sense, encompasses not only physical but also mental growth which leads to the anatomical, physiological, cognitive and behavioural changes that occur throughout the duration of childhood. As per the paediatricians, child development related to the changes in children's ability to perform fine movements with their hands, move, communicates, learns new knowledge, self-care and interact with others.

Child development is a dynamic process that is determined by the interaction of genetic, biological and environmental factors. Child developmental delay is defined as a significant delay (more than two standard deviations below the average value) in one or more developmental domains (Battaglia, A., & Carey, J. C. 2003, February). Behavioural, cognitive and motor development observed in infants and children is a reflection of postnatal brain development. Myelination

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and synaptogenesis are considered the biological correlates of this developmental process and have been studied extensively. Any delay in neurodevelopment is likely to have a biological correlate. Brain MRI is one of the major investigations of these patients, and based on previous studies, about 60% of cases have abnormal findings in MRI (Shevell, M. I. *et al.*, 2003).

Prevalence of developmental delay in children has been reported at 5-10%. MR imaging is an important part of the comprehensive evaluation of children with developmental delay, as many specific etiologic and pathophysiologic conditions that lead to developmental delay can be detected easily (McDonald, L. A., & Rennie, A. C. 2011).

The evaluation of developmental delay is complex and involves various modalities including cytogenetic testing, biochemical and hormonal assays, enzyme assays, electroencephalography (EEG) and neuroimaging. Magnetic resonance imaging has evolved over the years as one of the most sensitive modalities in imaging a child with developmental delay. Around 60% of the children with developmental delay have an abnormal MRI (Petersen, M. C. *et al.*, 1998, March; Pandey, A. *et al.*, 2004; & Koul, R. *et al.*, 2012).

Further, MRI provides a detailed anatomical evaluation of the brain and also provides information on the extent of myelination and its associated microstructural 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 properly categorizing the patients, this has a significant impact on patient management (Koul, R. *et al.*, 2012; & Battaglia, A. *et al.*, 1999).

A complete study will provide important information about the patient, the rate and type of brain abnormalities. It helps to identify these diseases and their prognosis, preventing the recurrence and parent counselling. Aim of the study is to know the most common MRI brain findings in children with global developmental delay and prevalence of normal and abnormal findings in patients in global developmental delay.

The present study was undertaken prospectively in 120 consecutive patients presenting to the Paediatric OPD of a tertiary hospital for evaluation of developmental delay.

METHODOLOGY

This is a prospective, descriptive study involving a sample size of 120 children presenting with developmental delay. The children are referred to the Department of Radiodiagnosis, Mamata Academy of Medical Sciences, Bachupally, Hyderabad, between July 2018 to June 2019 for neuroimaging as a part of their evaluation.

Subject recruitments: 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. However, the children younger than 6 months and older than 10 years of age, children with progressive neuro developmental disorders, children with congenital CNS infections, meningitis and encephalitis, children with recognised syndromes including chromosomal disorders were excluded from this study.

Primary Screening: The children presenting with developmental delay were evaluated clinically by a paediatrician with expertise in developmental paediatrics and were referred for brain Magnetic Resonance Imaging to the Department of Radiodiagnosis.

The commonly used scales to assess developmental delay include DENVER II (revision of the Denver Developmental Screening Test, DDST) and Trivandrum Developmental Screening Chart was used, and the clinical and demographic details of the patient were noted down. Informed consent for neuroimaging was obtained from the parents or legal guardian of the child.

Sedation: Infants and younger children were sedated using Syrup Triclofos (Syppedicloryl) 50 mg/kg just before imaging the child. In children, inadequately sedated with the above drug, IV midazolam 0.1 mg/kg/dose under strict clinical supervision and monitoring was used for sedation. Older children who were well cooperative for the imaging procedure were imaged unsedated. Necessary emergency equipment and drugs were made available in the MRI room.

MRI Procedure: All patients will be evaluated using a 1.5 Tesla MRI system (MagnetomSymphony, Siemens Healthcare) [Insert Name of the MRI machine available in your college]. The patients were categorised depending on their symptoms and examined in the supine position, and the head was placed securely in the receiver coil. The scan was performed under the supervision of a qualified Radiologist in the workstation.

Statistical analysis: The collected research data was compiled and analysed with SPSS software.

RESULT

In this study, the evaluation of 120 children between 6 months and 10 years of age, who presented with developmental delay. The study revealed a significant number of children presenting with the

developmental delay between the age group of 3-6 years. The number of children presenting with developmental delay in the below-mentioned age group was 36. The other subgroups had relatively lesser number of children presenting with developmental delay.

Table 1: Gender and Age-wise distribution of the children presenting with developmental delay

Age	Gender		Total
	Female	Male	
<1	5	3	8
1- 2	7	2	9
3-4	20	17	37
5-6	16	15	31
7-8	11	7	18
8-9	8	4	12
9-10	3	2	5
Total	70	50	120

Further, the association of positive MRI findings prevailing among various age groups was studied. It was noted that among the 68 children in the age group 3-5 years, 37had abnormal brain MRI findings. It was noted and statistically analysed that there was a significant association between the age of presentation and abnormal MRI findings ($p<0.05$)

Table 2: Tabular Association of Age with MRI findings

6Age	MRI findings		Total
	Normal	Abnormal	
<1	1	7	8
1- 2	2	7	9
3-4	11	26	37
5-6	8	23	31
7-8	4	14	18
8-9	1	11	12
9-10	0	5	5
Total	27	93	120

Out of the 87 developmentally delayed children associated with seizures, 67 had an abnormal MRI. Further, it was noted that among the 27 children with a normal MRI, only 7 were associated with seizures. Hence, it was inferred that the children with associated seizures had a larger proportion of abnormal MRI ($p<0.001$)

Table 3: Tabular representation of association of Seizures with MRI findings

Seizures	MRI findings		Total
	Normal	Abnormal	
Without Seizures	20	26	33
With Seizures	7	67	87
Total	27	93	120

It was observed that among the 26 children presenting with "only" developmental delay, 15 had normal MRI findings. This was in contrast to the children who presented with developmental delay "plus" syndromes. Out of 94 children displaying with additional clinical features along with developmental delay, 82 had an abnormal MRI. Hence, the presence of additional clinical features in children with developmental delay was associated with abnormalities in the brain MRI ($p<0.001$), which could reflect graver clinical prognosis.

Table 4: The Clinical presentation of study population with normal and abnormal MRI findings

Clinical presentations	MRI findings		Total
	Normal	Abnormal	
Only Developmental Delay	15	11	26
Developmental Delay Plus	12	82	94
Total	27	93	120

The various MRI findings were categorized into one or more of the below-mentioned categories revealed that normal brain MRI in 27 cases (22.5%). The remaining cases with an abnormal MRI were further categorized, of which 56 cases (46.67%) had findings consistent with Neurovascular diseases. The proportion of children with Congenital and developmental disorders, Neoplastic and cystic lesions and non-specific imaging findings were 16 cases (13.33%), 7 cases (5.83%) and 11 cases (9.17%) respectively. 3 cases (2.5%) showed a combined or multifactorial aetiology.

Table 5: Tabular Categorization of MRI findings (N=120) in patients

Categories	Number (N)	Percentage (%)
Normal	27	22.5
Congenital and Developmental	16	13.33
Neoplastic and cystic lesions	7	5.83
Neurovascular	56	46.67
Multifactorial	3	2.5
Non-specific imaging findings	11	9.17
Total	120	100

Further, the neurovascular category was evaluated based on the age of the patients. It was noted that around 67.86% of the patients in the category were in the age group of 3-6 years. Rest of the age groups showed the nearly equal incidence of the neurovascular aetiology with a relatively lower incidence in the older age group (9-10 years).

Table 6: Tabular representation of Age wise distribution of the Neurovascular aetiology

Age	Neurovascular Number	Percentage (%)
<1	4	7.14
1- 2	2	3.57
3-4	21	37.5
5-6	17	30.36
7-8	7	12.5
8-9	4	7.14
9-10	1	1.79
Total	56	100

DISCUSSION

Neuroimaging by MRI has an imperative role in examining and diagnosis of a child with developmental and growth delay, and the aetiological yield can be raised if other associated clinical and neurological signs and symptoms are taken into the considerations (Widjaja, E. *et al.*, 2008; & Patel, S., & Barkovich, A. J. 2002). Many of the children with abnormal MRI findings in our study were in gender-wise males (57%) were more in number than females (43%) and as per the age group of three to 12 months (38%) compared with the next peak at the age group of one to two years (24%). Similar age of presentation and gender incidences was observed in the study carried out by Momen, A. A. *et al.*, (2011).

The 55 cases with abnormal MRI were examined for the involvement of different and multiple anatomical structures. Abnormalities of ventricles mainly the corpus callosum, white matter were most commonly seen in 62% and 58% cases respectively. Widjaja *et al.*,., [9] observed that 90 such children and noted that Ventricles (48%) and Corpus Callosum (44%) were the most typically involved structures, while the other structures involved were almost similar to the present study. Based on these MRI findings, we could classify MR features into various aetiologies.

Momen, A. A. *et al.*, (2011) have classified their MRI findings into aetiological categories; in which Traumatic/Neurovascular Diseases (Hypoxic-Ischemic Brain Injury) ranked the topmost while other categories were almost as similar to our study with one except for congenital and developmental anomalies these cases were slightly lesser than what we have encountered. The congenital and developmental anomalies have characteristic clinical and radiological findings, and their identification is essential in order to prevent recurrence and helps in parent counselling (Williams, H.J. 2004; Rivkin, M. J. 2000; Moes, P. *et al.*, 2009; & McDonald, L. *et al.*, 2006).

In our study we have found 14 such cases (17%); which exactly fit into this classification; whereas Momen, A. A. *et al.*, (2011) published the

study in which a slightly more incidence of not terminating the pregnancy which could be explained by the religious beliefs that these patients follow in case of antenatally diagnosed abnormality.

Prevalence of developmental delay in children has been reported at 5-10%. The determination of cause is vital for a number of reasons including prognostication, surveillance and prevention of secondary disability, potential treatment, and appropriate genetic counselling (McDonald, L. A., & Rennie, A. C. 2011; Harbord, M. G. *et al.*, 1990; Shevell, M. I. *et al.*, 2003; Walters, A. V. 2010; & Widjaja, E. *et al.*, 2008).

Apart from clinical history, physical examination, chromosomal analysis and biochemical testing, neuroimaging plays a vital role in the etiologic profiling of these developmentally delayed children (Patel, S., & Barkovich, A. J. 2002; & Williams, H. J. 2004). Neuroimaging, as a second-line investigation in patients with developmental delay, yields a high variable result from 9-80%. However, the yield of the result increases with specific problems such as microcephaly, focal neurological deficit, seizure disorder (McDonald, L. *et al.*, 2006; Moes, P. *et al.*, 2009; & Harbord, M. G. *et al.*, 1990).

MR imaging is an essential tool of the extensive evaluation of children with developmental delay, as many specific aetiologic and pathophysiologic conditions that lead to developmental delay can be detected easily.

CONCLUSION

This study was carried out to investigate and diagnose the spectrum of abnormalities on MRI in children with developmental delay. The role of MR Spectroscopy in children with normal MRI was also studied.

It was inferred that the children with associated seizures had a more significant proportion of abnormal MRI. 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 (developmental delay "plus").

MR Spectroscopy in children with normal MRI, revealed no significant difference in the neurometabolite ratios among the children evaluated. Since MR Spectroscopy adds to the time period of the conventional MR protocol and is by far dependant on the patient being motionless for the entire duration of the study, this limits its use in younger children and infants due to motion artefacts and risk of prolonged sedation.

MRI has good sensitivity in diagnosing various disorders associated with developmental delay. Careful evaluation of the MRI helps to identify the probable aetiology in most if not all cases. Additional clinical variables also add to the diagnostic accuracy of MRI.

MR Spectroscopy is a transpiring technique in evaluating children with developmental delay. Proton MR Spectroscopy should be included in the standard imaging protocol while evaluating older children with developmental delay.

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 role of MR Spectroscopy in imaging a child with developmental delay was also evaluated.

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 counselling.

LIMITATIONS

Lack of an etiological diagnosis in a few cases of developmental delay. Longitudinal studies in the form of follow up imaging will be more helpful to establish a relationship between the abnormalities on MR imaging and the long-term prognosis of the child.

Limitations of MRI such as long imaging time, adequate patient immobilization and claustrophobia are few of the other limitations of the study. Further, MR Spectroscopy has various limitations like contamination from surrounding tissues, lack of information of the metabolites from other regions of the brain and lack of precise measurement of absolute metabolite values.

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