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Original Research Article

Neuroimaging in paediatric patients with developmental delay

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ABSTRACT

Background: Aim and objectives of the study were to radiologically evaluate paediatric patients with developmental delay (DD), assess the relative prevalence of abnormal brain MRI, further categorize them based on the abnormal imaging findings and structures affected. The purpose of this study is to diagnose the underlying etiology that helps in early treatment and amelioration of the condition, parental counselling regarding the outcome of the child, providing an estimate of child's developmental potential and the recurrence risk in siblings.
Methods: 135 paediatric patients of the age 3 months to 15 years with DD referred to department of radiology were investigated with MRI scans of the brain via 1.5T Siemens scanner after making the child sleep or sedated. The sequences used were: axial T1, axial T2, axial FLAIR, axial DWI, axial ADC, axial SWI, axial PHASE, sagittal T1 and coronal FLAIR. CT scan of the brain was done only when indicated on 128 slice Siemens Somatom perspective scanner. Informed consent shall be taken from patient's parents. Clinical and demographic details of the enrolled patients were noted in the Performa. Data collected was analysed using descriptive and inferential statistics.
Results: Out of 135 children with DD, 69.1% (n=92) were male and 31.9% (n=43) were female. Majority of these children belonged to 3 months to 1 year and 2 to 5 years of age group. About 81.4% (n=110) of children with DD had abnormal findings in MRI. Among children with abnormal MRI findings, 42.9% had hypoxic ischemic changes, 6.6% had congenital malformations and non-specific causes, respectively 4.4% had neurodegenerative and occlusive neurovascular conditions, respectively 3.7% had CSF disorders and neoplasms, respectively 2.9% had infection associated changes and non-traumatic intracranial bleed, respectively 2.2% had metabolic disorders and 0.7% had demyelination. Majority of cases had ventricular abnormality, followed by the corpus callosum.
Conclusions: DD presents with a wide spectrum of etiologies, clinical findings and MRI features ranging from completely normal to abnormal. The present study could establish the various morphological appearances of DD on MRI and further categorize them into various subgroups be effective in diagnosis, management and prognosis determination processes.

Keywords: DD, Paediatric neuroimaging, MRI brain

INTRODUCTION

Development is a complex and continuous process of maturity, parallel to the growth of child, which can affect many aspects and begins from conception and continues until maturity. The rate of development varies from a child to another and depends on genetic factors, environmental aspects and chronic diseases.[1]

DD is defined as delay in attaining developmental milestones at expected age that is a frequently encountered problem in paediatric neurology.[2,3]

Global DD (GDD) is a subset of developmental disorders that is defined as a significant delay or below the appropriate standard in two or more developmental domains. It may occur due to static or progressive disorders of the central nervous system. In these patients,

regression, stability, or disease progression may develop.[4,5] The term GDD generally applies to younger children (usually <5 years), whereas the term mental retardation applies to older children when IQ testing is more valid and reliable.[4,6-8]

Significant DD is diagnosed when performance is 2 SD or more below the mean on developmental tests, or there is a discrepancy of 25% or more from the expected rate in 1 or more domains of development.[3,9,10]

There are wide range of etiologies which include genetic, metabolic, endocrine, vascular, malformation syndromes, traumatic, infections, toxins and environmental causes. In some, clinical findings can lead to diagnosis but in most of the cases, neuroimaging is necessary to visualise the abnormality leading towards the accurate diagnosis which further helps clinician to provide appropriate treatment.[11]

All cases of delayed milestones should undergo neuroimaging as recommended by the American academy of neurology. MRI is more preferred, compared to computed tomography. MRI aids in visualising structural abnormality and aetiological causes of delayed development.[12]

Computed tomography (CT) is the modality of choice in acute or emergent presentations which aids in detecting intracranial haemorrhage, cerebral edema, hypoxic-ischemic injury, infarction, hydrocephalus/shunt dysfunction, neoplasm, intracranial calcifications or abnormal collections.[12]

METHODS

This cross-sectional observational study was conducted in the department of radiodiagnosis, RajaRajeswari medical college and hospital during period June 2020 to September 2022. Neuroimaging of all patients was done after proper history and examination. This included history of delayed milestones, epilepsy, mental retardation, neurological deficit, birth history related to antenatal, intra-natal and postnatal events, maternal medical history, antenatal history of drug intake, alcohol/ smoking exposure. Intra-natal history included complications during delivery, birth weight and cry at birth. Postnatal history included duration of postnatal hospital stay and neonatal intensive care unit (NICU) stay.

The 135 paediatric patients of the age 3 months to 15 years with DD were investigated with MRI scans of the brain via 1.5T Siemens after making the child sleep or sedated. The sequences used were: axial T1, axial T2, axial FLAIR, axial DWI, axial ADC, axial SWI, axial PHASE, sagittal T1 and coronal FLAIR. CT scan of the brain was done when indicated on 128 slice Somatom perspective Siemens. Informed consent was taken from patient's parents. Clinical and demographic details of the enrolled patients were noted in the Performa. Data collected was analysed using descriptive and inferential statistics.

Neuroimaging

MRI images were analyzed with axial, sagittal and coronal images studied together.

Patients categorized based on age group, gender, clinical features, anatomical structures involved and aetiology.

Abnormal brain MRI cases divided into 10 groups based on aetiology: Congenital disorders, CSF disorders, demyelination, infection, metabolic conditions, neoplasms, neuro-degenerative diseases, trauma-neurovascular, occlusive neuro-vascular and non-specific findings.

Following Widjaja et al protocol structures were systematically evaluated[17]-1. Ventricles: Size and morphology. 2. Corpus callosum: thickness and morphology. 3. Grey and white matter. 4. Basal ganglia: morphology. 5. Brain stem: Morphology and 6. Cerebellum: morphology.

Statistical analysis

Data collected was analysed using descriptive and inferential statistics and the software used for analysis was MS excel spreadsheet and statistical package for social sciences (SPSS) version 26.0.

RESULTS

In this study, 135 children with developmental disorders were studied of which 92 (69.14%) were male and 43 (31.85%) were female. The ratio was 2.1:1 between males and females (Table 1).

Table 1: Age and gender distribution of children with DD.

Variables	N	Percentage (%)
Age (Years)		
3 months-1 year	41	30.37
>1-2	9	6.66
>2-5	41	30.37
>5-8	18	13.33
>8-12	14	10.37
>12-15	12	8.88
Gender		
Male	92	69.14
Female	43	31.85

Patients are divided into six age groups: 3 months to 1 year, 1 to 2 years, 2 to 5 years, 5 to 8 years, 8 to 12 years and 12 to 15 years. 41 patients (30.37%) were in the age range of 3 months to 1 year, 9 patients (6.6%) were 1 to 2 years, 41 patients (30.37%) were 2 to 5 years, 18 patients

(13.33%) were 5 to 8 years, 14 patients (10.37%) were 8 to 12 years and 12 patients (8.8%) were 12 to 15 years. Most of the children with abnormal MRI findings were in the age group of 3 months to 1 year and 2-5 years (30.3%) (Table 1).

Distribution according to clinical features of DD, there were 49 (36.2%) patients with isolated DD, whereas 86 (63.7%) presented with DD and additional features such as epilepsy, neurological deficits, abnormalities of head size, facial dysmorphism, cleft lip/palate, visual and auditory disturbances, gait disturbances, motor disturbances, social and cognitive problems, consanguinity/ bad obstetric history (Table 2).

Table 2: Distribution of children with DD based on clinical features.

Clinical features	N	Percentage (%)
Isolated DD	49	36.2
DD plus (with additional features of seizures, short stature, abnormal head circumference, neurological defects, motor delay, language/ speech delay, social / emotional delay and cognitive impairment resp.)	86	63.7
Total	135	100

Brain MRI findings in 25 cases (18.5%) reported normal and in the rest 110 cases (81.48%) showed abnormal pattern. About the gender relation between normal and abnormal MRI, results showed that both male and female groups have abnormal MRI, meaning from 92 males, 73 cases (79.34%) and from 43 females, 37 cases (86.0%) showed abnormal MRI.

The 110 abnormal cases were further subgrouped based on the aetiological factors; of which 58 cases (42.96%) had findings consistent with traumatic-neurovascular diseases. The proportion of children with congenital, CSF disorders, demyelination, infection, metabolic, neoplastic, neurodegenerative, occlusive neurovascular, non-traumatic intracranial bleed and non-specific were 9 cases (6.6%), 5 cases (3.7%), 1 case (0.7%), 4 cases (2.9%), 3 cases (2.2%), 5 cases (3.7%), 6 cases (4.4%), 6 cases (4.4%), 4 cases (2.9%) and 9 cases (6.6%), respectively as shown in (Table 3).

The most common abnormality encountered in present study was traumatic neurovascular diseases like hypoxic ischemic encephalopathy (HIE). Majority of these children belonged to 3 months to 1 year and 2 to 5 years of age group and 60.3% of them were males and 39.7% were female children.

Distribution of the MRI finding based on structural morphology, there were 59 (43.7%), 46 (34.07%), 32 (23.1%), 14 (10.37%), 16 (11.85%) and 6 (4.44%) patients with abnormal MRI findings in ventricles, corpus callosum, white matter, grey matter, cerebellum, brainstem respectively (Table 4).

Table 3: Classification of children with DD based on radiological diagnosis.

MRI brain findings	N	Percentage (%)
Congenital	9	6.66
CSF disorders	5	3.70
Demyelination	1	0.74
Infection	4	2.96
Metabolic	3	2.22
Neoplasm	5	3.70
Neurodegenerative	6	4.44
Occlusive neurovascular	6	4.44
HIE (trauma and neurovascular)	58	42.96
Non-traumatic intracranial bleed	4	2.96
Non specific	9	6.66
Normal	25	18.51
Total	135	100

Table 4: Classification of children with DD based on structural morphology.

Morphological features	N	Percentage (%)
Ventricles	59	43.7
Corpus callosum	46	34.07
White matter	32	23.1
Grey matter	14	10.37
Cerebellum	16	11.85
Brainstem	6	4.44

DISCUSSION

DD presents a broad spectrum of etiologies, clinical findings and MRI features ranging from utterly normal to abnormal.

In our present study of 135 patients distribution according to gender was 92 (69.14%) males and 43 (31.85%) females. Males slightly more in number than females.

Palve et al 2016 reported that "30 were males, while 20 were female patients,"[13] Ali et al said in his research, males (57%) were slightly more in number than the females (43%), although there is no considerable difference.[14] Jauhari et al, Shevell et al also reported male gender preponderance in their studies for which no plausible mechanism has been proposed.[15,16]

Distribution according to the clinical features of DD, 49 (36.2%) patients with isolated DD, whereas 86 (63.7%) had a DD with other components, i.e., seizures and other

neurological defects, motor (fine and gross) delay, language / speech delay, social / emotional delay and cognitive impairment.

Ali et al reported that "out of 81 patients, isolated DD was present in 8 patients, and DD plus other clinical features such as seizures, neurological deficit, a structural abnormality was seen in 73 patients; hence, the majority of patients had DD plus other symptoms." [14]

In our study, 25 (18.5%) patients had normal MRI findings, whereas 110 cases (81.48%) had abnormal MRI findings. Similar MRI results reported by Momen et al, Shevell et al, Pandey et al, Koul et al, Battaglia et al, and Widjaja et al, i.e., 58.6%, 65.5%, 63.8%, 71.8%, 80.8% and 84% respectively.[4,17,18,20-22] This wide range could be due to differences in patient selection criteria.

Similar results were shown by Ali et al they reported "that out of 81 children with DD only 32% (26 cases) had normal MRI findings and they were advised further evaluation to diagnose the idiopathic cause of DD. Abnormal findings were seen in remaining 68% (55 cases).[14]

In our study, distribution of the MRI finding based on structural morphology were 59 (43.7%), 46 (34.07%), 32 (23.1%), 14 (10.37%), 16 (11.85%), and 6 (4.44%) patients with abnormal findings in ventricles, corpus callosum, white matter, grey matter, cerebellum, brainstem respectively. The majority of cases had a ventricular abnormality, followed by the corpus callosum.

Widjaja et al studied 90 such children and found that ventricles (48%) and corpus callosum (44%) were the most commonly involved structures, while the other structures involved were almost similar to present study.[17] Similar findings were seen in these studies. Palve et al showed that corpus callosum abnormalities and ventricles were seen in 10 patients out of 42 patients.[13]

In our study, there were 25 (18.5%), 58 (42.96%), 9 (6.66%), 6 (4.44%), 6 (4.44%), 5 (3.7%), 5 (3.7%), 4 (2.96%), 4 (2.96%), 3 (2.22%), 1 (0.74%) and 6 (5.77%) patients in the etiological category of normal, traumatic neurovascular, congenital, neurodegenerative, occlusive neurovascular, CSF disorders, neoplastic, infectious, nontraumatic intracranial bleed, demyelination, metabolic and nonspecific respectively. The majority of children with abnormal MRI findings in a traumatic neurovascular category, followed by congenital anomalies.

Palve et al reported that "out of 42 patients, there were 8 patients with traumatic neurovascular diseases followed by congenital and developmental anomalies".[13] Ali et al reported that "normal were 32% and abnormal findings of which traumatic and neuro-vascular diseases, congenital and developmental, metabolic and degenerative, neoplastic and nonspecific 31%, 17%, 10%, 2.5% and 7.5% respectively."[14]

Congenital abnormalities of brain found in 9 cases as: Lissencephaly-pachygyria spectrum (Figure 1), pontocerebellar hypoplasia (Figure 1), pituitary interruption syndrome (Figure 4), dysgenesis of corpus callosum with colpocephaly (Figure 3), Struge Weber syndrome (Figure 2), microcephaly with cerebellar atrophy, absent posterior pituitary bright spot with inferior cerebellar vermian hypoplasia, Leigh syndrome.

Infection associated changes (n=4) included are tuberculoma, subdural empyema and cerebellar encephalitis; three cases of hypoglycemic encephalopathy were included under metabolic causes. Five children had CSF disorders (cistern magna, communicating hydrocephalus, aqueduct stenosis).

Five cases presenting with DD had neoplastic origin (pilocytic astrocytoma, tectal glioma, intramedullary astrocytoma, PNET and multiple gliomas in a case of neurofibromatosis 1). Nonspecific cases included delayed myelination, neuroglial cyst, BESSI, persistent cavum septum pellucidum and encephalocele.

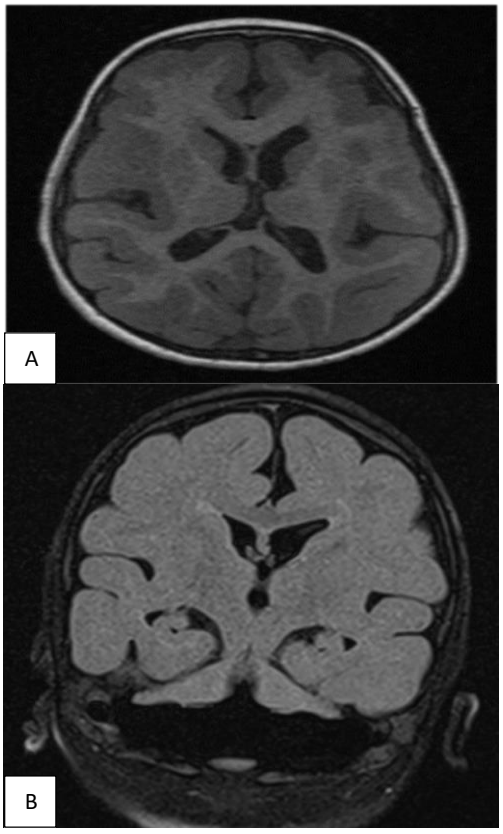

Figure 1 (A and B): Pontocerebellar hypoplasia with lissencephaly-pachygyria spectrum in a four-year-old male child presenting with global DD. T1W axial MR image showing sparse cortical sulci with wide gyri in bilateral cerebral hemispheres and thickened cerebral cortex. FLAIR coronal MR image showing markedly hypoplastic bilateral cerebellar hemispheres and absent caudal part of the vermis cerebelli ("dragon fly appearance"), leaving most of posterior fossa empty.

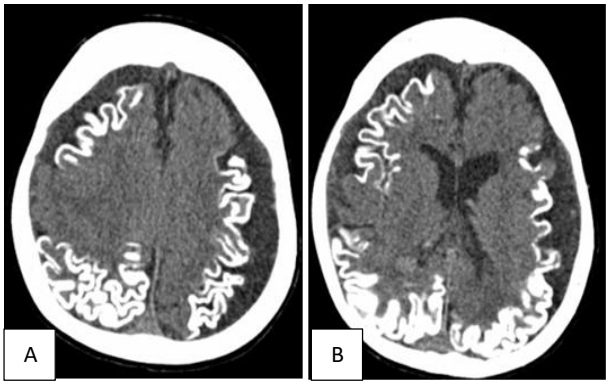

Figure 2 (A and B): Struge Weber syndrome in a 9-year-old male patient presenting with recurrent seizures, glaucoma and DD. MDCT brain axial images showing gyriform cortico-subcortical calcifications in bilateral cerebral hemispheres, enlarged bilateral choroid plexus, left cerebral hemiatrophy and diffuse calvarial thickening.

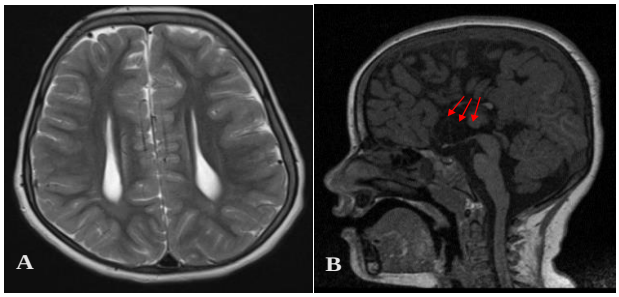

Figure 3 (A and B): Dysgenesis of corpus callosum with colpocephaly in a 6-year-old female preterm born child presenting with global DD. T2W axial MR image showing widely spaced parallelly oriented bodies of bilateral lateral ventricle ("racing car sign") and dilated trigones. T1W sagittal MR image showing absent genu and rostrum of corpus callosum with markedly hypoplastic body and splenium.

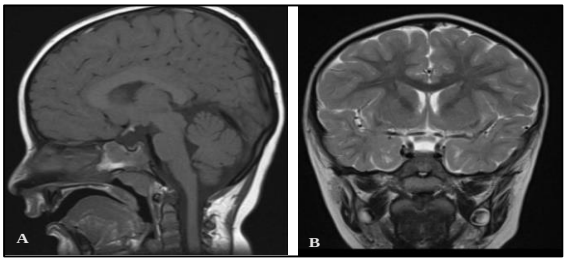

Figure 4 (A and B): Pituitary stalk interruption syndrome in a 6-year-old male child presenting with hypoglycemia, short stature, seizures and DD. T1W sagittal MR image showing posterior pituitary bright spot in the region of hypothalamus, abutting the optic chiasma (ectopic) and anterior pituitary is small in size measuring 2.4 mm craniocaudally and volume of 43 cc. T2W coronal MR image showing absent pituitary stalk.

CONCLUSION

DD presents with a wide spectrum of etiologies, clinical findings and MRI features ranging from completely normal to abnormal. MRI evaluation of the brain contributes to the diagnosis of etiologies of DD. Further serial and sequential MRI may be necessary to ascertain disease progression. The present study could establish the various morphological appearances of DD on MRI and further categorize them into various subgroups. This method is effective in diagnosis, management, prognosis determination processes and parent counselling with regard to outcomes and the risk of recurrence in siblings and subsequent generations.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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