Brain Magnetic Resonance Imaging in Developmentally Delayed Children- A Cross Sectional Study

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ABSTRACT

BACKGROUND

Developmental disorders mean the lack of ability in children, to acquire various motor and cognitive milestones at expected maturational age. Neuroimaging, especially brain MRI, has proved to be one of the most reliable methods for evaluating developmentally delayed children, by providing information regarding brain tissue structures and anomalies.

METHODS

In this cross-sectional observational study, MRI features and clinical data of 60 children aged between 6 months to 12 years, who had been diagnosed with developmental delay using Denver developmental screening test were carefully evaluated and statistically analysed. Clinically diagnosed cases of cerebral palsy, neurodegenerative diseases, and syndromes were excluded. Ethical permission and written informed parental consent were obtained.

RESULTS

A total 60 children including 32(53.3%) male children and 28(46.7%) female children were studied. Out of them 45 children (75%) had abnormal magnetic resonance imaging findings-20(62.5%) male and 25(89.9%) female children. Abnormal brain magnetic resonance imaging findings included changes of hypoxic ischemic encephalopathy (60%), nonspecific findings (8.33%) and cerebral malformations (6.67%) No case due to metabolic cause was identified. Out of a total of 60 cases, 26.6% of children were born preterm and among the preterm babies, 93.7% had abnormal magnetic resonance imaging findings. In this study group, 24 patients (40%) had neonatal hypoglycaemia and out of them 23, (95.83%) had abnormal MRI findings.

CONCLUSIONS

This study showed that 75% of children without any clinically obvious cause for developmental delay, had abnormal MRI findings. The most common abnormality observed was hypoxic ischemic encephalopathy (HIE). Predisposing factors like birth asphyxia, neonatal hypoglycaemia, preterm delivery and low birth weight had significant correlation with abnormal MRI findings. Hence, MRI can be a useful tool in the diagnosis, management, and also for evaluation of prognosis in children without any evident cause for the developmental delay.

KEYWORDS

Magnetic Resonance Imaging, Developmental Delay, Hypoxic Ischemic Encephalopathy, Neonatal Hypoglycaemia

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DOI: 10.18410/jebmh/2020/228

Financial or Other Competing Interests: None.

How to Cite This Article:
Mathew A, Brahmadathan MN, Parvathi R. Brain magnetic resonance imaging in developmentally delayed children- a cross sectional study. J. Evid. Based Med. Healthc. 2020; 7(22), 1053-1057. DOI: 10.18410/jebmh/2020/228

Submission 12-03-2020,
Peer Review 06-04-2020,
Acceptance 27-04-2020,
Published 27-05-2020.

BACKGROUND

A large number of children are born each year with biological and environmental risks which carry increased risk of developmental disability. The important biological risk factors are low birth weight, intra uterine infection, neonatal meningitis, seizure etc. Environment risk factors are substance abuse, low socio economic status etc.,[1] There is considerable overlap of risk factors. The most common presentation of developmental disability is failure to achieve age appropriate developmental skills.[2] Developmental delay is defined as a significant delay in motor skills (gross motor and fine motor) or their language milestones affecting their speech and communication or strain in social skills which in turn could interrupt their emotional & behavioural attitude. When one or more of the above developmental domain is affected, a child should be evaluated for developmental delay.[3]

There are various methods to evaluate these development skills, among which, the modified form of Denver Developmental Screening Test II (DDSTII) is most widely accepted.[4]

Neuroimaging, especially brain MRI, has proved to be one of the most reliable methods for evaluating developmentally delayed children, by providing information regarding brain tissue structures and anomalies. Compared to computerised tomogram scan there is also no radiation risk involved in magnetic resonance imaging. M. Shevell et al recommended Routine neuroimaging, with MRI preferred to CT, particularly if abnormalities are found on physical examination.[5]

Standard MRI sequences such as axial T2-W, coronal FLAIR, and coronal and sagittal T1-W images were taken. Midline structures are better identified in sagittal sections. Children under 2 years of age, dual-echo axial STIR sequence can be used. T2*-W gradient-echo sequence can be used to identify haemoglobin breakdown products.[6] The MRI findings can be normal in many cases A.R. Hart et al have broadly classified the abnormal magnetic resonance imaging findings into hypoxic ischemic injury, brain malformation, metabolic causes and nonspecific abnormalities.[7] Barkovich et al have mentioned that the most sensitive and specific imaging technique for examining infants with suspected hypoxic-ischemic brain injury is MR imaging.[8] The earliest imaging findings in term infants who have suffered a severe anoxic ischemic events may be very subtle but can be seen as early as the first day of life on MR images.[9,10]

So there is a need to analyse the prevalence of abnormal findings in MRI in patients with developmental delay. This may be useful in helping parents, clinicians, and others involved in the care of children with developmental delay to understand the nature of the child's condition and to predict their needs in the future.

In hospitals, large number of patients comes to the Paediatrics Department for evaluation of developmental delay. The cause for this is not always identified by clinical examination. Many of these patients are referred for brain magnetic resonance imaging to the Department of Radio diagnosis. So we decided on a cross sectional observational study of the brain magnetic resonance imaging findings of those children aged between 6 months to 12 yrs. in whom a clinical diagnosis was not obvious.

Objectives

1. To observe the neurological findings in brain magnetic resonance imaging of developmentally delayed children without obvious clinical diagnosis.
2. To find association between magnetic resonance imaging findings with predisposing factors for developmental delay.

METHODS

Study was conducted in department of radiodiagnosis Government medical college Thrissur from Jan 2013 to Dec 2013 for period of one year. In this study, 60 children aged between 6 months to 12 years of age who had been diagnosed with developmental delay using Denver developmental screening test referred from the Department of Paediatrics, was assigned to be evaluated using brain MRI. Ethical permission and written informed parental consent were obtained. .An interview questionnaire with the parents provided information about family history and prenatal, pregnancy, and birth information were carefully noted. Gestational diabetes mellitus (GDM), Pregnancy induced hypertension and also history of any perinatal infection such as fever with rash, urinary tract infection, respiratory tract infection was noted. In children, history of neonatal jaundice, seizure, neonatal hypoglycaemia, and neonatal meningitis was considered. Birth asphyxia was considered if the APGAR score at the 10th minute was less than 5. Magnetic resonance imaging was taken using a Signa HDxt 1.5T machine GE healthcare. Standard MRI sequences such as axial T2-W, coronal FLAIR, and coronal and sagittal T1-W images were taken. Midline structures are better identified in sagittal sections. Children under 2 years of age, dual-echo axial STIR sequence can be used. T2*-W gradient-echo sequence can be used to identify haemoglobin breakdown products.

Brain magnetic resonance imaging findings were categorised as normal and abnormal findings. Abnormal findings can be findings suggestive of hypoxic ischemic encephalopathy, cerebral malformations, metabolic diseases and nonspecific findings. Metabolic disease includes Canavan's disease, leucodystrophies, mucopolysaccharidoses and others.[11] Nonspecific findings include cavum septum pellucidum, cavum vergae, and ventriculomegaly, enlarged subarachnoid spaces, and delayed myelination.

Inclusion Criteria

Children aged 6 months to 12 years with development delay referred for MRI Imaging were considered.

Exclusion Criteria

Children with clinically diagnosed cases of cerebral palsy, neurodegenerative diseases, and syndromes were excluded.

Statistical Analysis

The data was entered in Microsoft Excel and descriptive statistics on the population of interest were generated from the data obtained. Statistical analysis was done using Epi info 7. Chi-square test (χ^2 test) was used to find association between predisposing factors and abnormal MRI findings. The statistical significance level was for a p value <0.05.

RESULTS

In this study, 60 children with developmental disorders were studied in a comprehensive manner. Of them 32(53.3%) were males and 28(46.67%) were females. Brain MRI findings of 15 children showed normal imaging findings while the remaining 45, 20 males and 25 females had abnormal pattern The majority of children were less than 2 years (46.6%) followed by 22 children (36.67%) between 2-5 years of age. Only 10(16.67%) children were above 5 years. In the under 2 group, 20(71.4%) had abnormal MRI. In the 2-5 year group 19(86.6%) out of 22 had abnormal MRI and in those above 5 years, 60% of had abnormal MRI findings.

Among 45 patients with abnormal MRI findings, majority had hypoxic ischemic encephalopathy changes (75%) in MRI. There were 4 cerebral malformations - 8.8% among those with abnormal findings. Out of these 4 cases, 3had corpus callosal agenesis (75%) and one was a case of Dandy walker malformation .No cases of metabolic disease was picked up in this study group. Nonspecific findings were seen in 5 (8.33%)and this included 2 cases with prominent Virchow robins space, a case of subdural hygroma, a case with cavum septum pellucidum and 1 case with white matter volume loss. When perinatal history was studied, it was found that 12 (20%) mothers had perinatal infections and among them 11(91.6%) children had abnormal MRI findings. Out of the 15 children born to mothers with GDM, 13 (86.6%) had abnormal MRI findings. Of the 11 mothers with pregnancy induced hypertension, 10 (90.9%) had abnormal MRI findings. According to the presence of neonatal risk factors, this study showed statistically significant association with neonatal hypoglycaemia, as, 23 of 24(95.83%) patients with neonatal hypoglycaemia showed abnormal MRI findings (p value- 0.002).

	MRI		
Asphyxia	**Abnormal**	**Normal**	**Total**
Present	21	2	23
Absent	24	13	37
Total	45	15	60

Table 1. Birth Asphyxia and MRI

	MRI		
Hypoglycaemia	**Abnormal**	**Normal**	**Total**
Present	23	1	24
Absent	22	14	36
Total	45	15	60

Table 2. Neonatal Hypoglycaemia and MRI

Maternal Related Factors	%	χ^2 value	P Value
GDM	25	1.4	0.2
PIH	18.3	1.8	0.17
Infection	20	2.2	0.13
Infant Related Factors			
Jaundice	43.3	0.8	0.3
Seizures	50	0.09	0.7
Hypoglycaemia	40	9.2	0.002
Asphyxia	38.3	5.3	0.02
Preterm	26.6	4	0.04
Low Birth weight	58.3	5.1	0.02
Caesarean section	40	0.37	0.5

Table 3. Predisposing Factors and Statistical Values

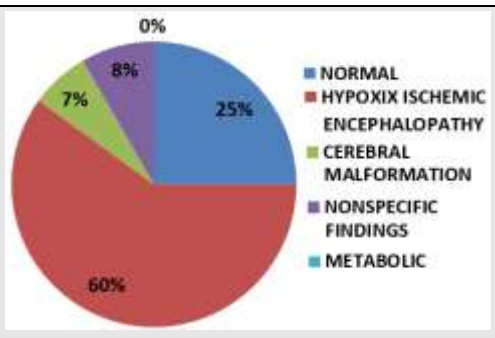

Figure 1. Brain MRI Findings

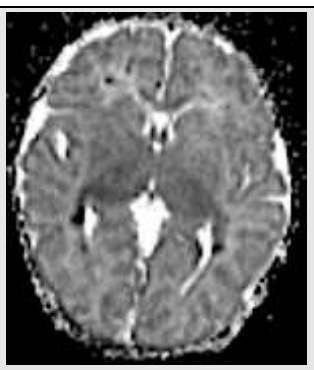

Image 1. Hypoxic Ischemic Encephalopathy- Restricted Diffusion in Thalamus

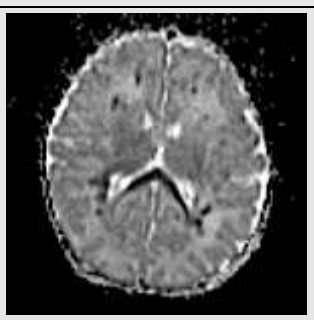

Image 2. Hypoxic Ischemic Encephalopathy- Restricted Diffusion in Splenium

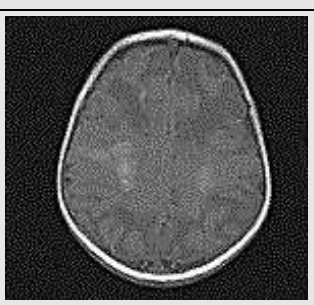

Image 3. Hypoxic Ischemic Encephalopathy- T1 Hyperintensity in Bilateral Deep White Matter

This study also found that, out of the 26 children with neonatal jaundice, 18 (69.23%) had abnormal MRI findings, and 23 of 30 children with seizures (76.7%) showed abnormal MRI findings. Among the 23 children with history of birth asphyxia, 21 (91.3%) had abnormal MRI findings.

Out of the 37 without asphyxia 24 had abnormal MRI findings. This observed difference appears to be statistically significant when χ^2 test was done (p value- 0.02).

In this study group of 60, 16 (26.67%) were preterm deliveries and 44 (73.33%) were term deliveries. Of the 16 preterm cases 15 (93.7%) had abnormal MRI findings and out of the 44 term cases 30 (68.2%) had abnormal MRI findings. The observed difference was found to have statistical significance when χ^2 test was done for preterm deliveries (χ^2 value - 4, p value- 0.04). The minimum birth weight seen in this study was 1000 gm and maximum birth weight was 3200. Only 2 children had very Low Birth Weight (VLBW) birth weight less than 1500 gm. and both had abnormal MRI findings. 33 had moderate low birth weight (LBW) and 25 had normal birth weight. So total 35 children had low birth weight and among them 30 had abnormal MRI findings. 25 children had normal birth weight and among them 15 had abnormal MRI findings. The observed difference was found to be statistically significant when χ^2 test was done (χ^2 value - 5.1, p value- 0.02).

DISCUSSION

There is no doubt that neuroimaging studies are necessary in neonates in whom brain abnormalities are suspected. At the present time, MRI is the most accurate way to examine the brain and an essential tool for assessing changes within it, especially in children without clinically obvious cause for developmental delay.

We studied 60 children with developmental delay, we also studied their history and physical examination findings that could be important. There were 32(53.3%) male children and 28 (46.7%) female children. Out of these 45 children who had abnormal magnetic resonance imaging findings - 20 (62.5%) were males and 25(89.9%) were female children. There was statistical significance between the gender and abnormal MRI findings. The age of presentation ranged from 6 months to 11 years. The median age was 3 years. In a study conducted in Iran out of 580 children 57.4% were male and 42.6% were females.[11] In another study done in United Kingdom median age was 3 years with 60.6% males and 39.4% females.[7] A study conducted in India at AIIMS showed a male female ratio of 2:1 and mean age at presentation - 23.6 months.12 From the above studies, the mean and median age results were found to be similar as our study. Also, a male sex predominance is seen.

Our study showed, maternal age at conception was found to be maximum between 21 to 34 years (88.33%) and out of these deliveries 73.5% had abnormal MRI findings. no statistical significance was observed between the parity and abnormal MRI findings. In a study by S. Nguefack et al, majority of mothers were less than 30 years of age at conception and 45.8% were primiparous.[13] Tikaria et al had 7% mothers above 35 years.[12]

On evaluating neonatal associated disorders, 75% of neonates had abnormal brain magnetic resonance imaging findings and majority of them had hypoxic ischemic encephalopathy changes (60%), and also nonspecific findings (8.33%), cerebral malformations (6.67%) were seen. No cases of metabolic causes were identified. 25% of children had normal MRI in this study. Findings similar to this were seen in a study by Jing Lim Moon et al from Korea. 23.5% of children had normal MRI findings in their study. Major abnormal findings in his study were periventricular leukomalacia, focal infarcts and corpus callosal dysgenesis.[14]

A similar study in Iran by Ali Akbar Momen et al in 2011 was done on 580 children described neurovascular causes as the most common abnormal finding (37.6%). Other findings were nonspecific findings (6.6%), cerebral malformations (6.7%), and metabolic causes (7.2%).[11] S. Nguefack et al had 41.8% of hypoxic ischemic encephalopathy and cerebral malformations 3.3%.[13] Another study in Iran by Fayyazi et al in 198 children with developmental delay had hypoxic ischemic encephalopathy as the cause in 22.6%.[15] In study by Bouhadiba et al cerebral malformations were the most common abnormal magnetic resonance imaging findings (50.4%).[16] In A R Hart et al's study congenital brain malformation was the most common abnormal finding accounting for more than half the findings.7 This was not similar to our study where hypoxic ischemic encephalopathy(HIE) was the most common finding. HIE was the most common abnormal magnetic resonance imaging finding in most of the studies from developing countries though their percentages varied from study to study.

Among the antenatal predisposing factors for developmental delay, 25% of mothers had gestational diabetes mellitus, 18.33% had pregnancy induced hypertension, 20% had perinatal infection. No case of multiple gestations was noted. The observed values did not show a statistically significant association between these maternal risk factors and abnormal magnetic resonance imaging findings. Among the neonatal factors neonatal jaundice was in 43.3%, seizures in 50%, neonatal hypoglycaemia in 40%, birth asphyxia in 38.3%, meningitis in 6.67%. The observed values were statistically significant between abnormal magnetic resonance imaging findings and neonatal hypoglycaemia (p-0.002) and birth asphyxia (0.02). Ali Akbar Momen et al had similar findings- 30.4% cases had neonatal jaundice, 52.8% had neonatal seizures. No correlation between neonatal jaundice and abnormal MRI findings was seen in that study.[11] In Tikaria et al's study from India, birth asphyxia was seen in 20% cases, seizures in 14% cases, neonatal jaundice in 12% cases.[12] Similar to this study S. Nguefack et al had 44.4% cases with perinatal asphyxia and it was the most frequent perinatal factor.[13]

Out of total 60 cases, 26.6% were preterm deliveries and among the babies born preterm 93.7% had abnormal magnetic resonance imaging findings. Our study found statistical significance between preterm delivery and abnormal MRI findings.

In this study 60% had normal delivery and 40% had caesarean section. Statistical significance was not seen between mode of delivery and abnormal MRI findings.

58.3% babies had low birth weight. Out of that 3.3% had very low birth weight and 55% had moderate low birth weight. The observed values between low birth weight and abnormal findings were statistically significant. Tikaria et al found low birth weight in 46% of cases similar to this study, but preterm deliveries were seen in 13% cases and caesarean section in 20% which were less when compared with this study.[12] In S. Nguefack et al study, there were only 4.8% preterm births which were not similar with this study.[13] Diana et al described that apparently well very low birth weight children were consistently at greater risk for both moderate and severe measures of delay.[17]

CONCLUSIONS

Developmental delay is a major health problem in paediatric neurology. This study found that 75% of children without any clinically obvious cause for developmental delay had abnormal MRI findings. So, MRI can be used as a useful investigation in the evaluation of these cases. The most common abnormality observed was hypoxic ischemic encephalopathy. Predisposing factors like birth asphyxia, neonatal hypoglycaemia, preterm delivery, and low birth weight had significant correlation with abnormal MRI findings. Birth asphyxia and neonatal hypoglycaemia are the preventable perinatal predisposing factors. Thus, prevention of these perinatal risk factors and the proper management of neonates at risk needs to be reinforced.

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