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Original Article

Radiology Section

Magnetic Resonance Imaging of Brain Patterns in Children with Cerebral Palsy- A Hospital Based Indian Study

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ABSTRACT

Introduction: Magnetic Resonance Imaging (MRI) of brain is recommended as a standard evaluation in children with Cerebral Palsy (CP).

Aim: To investigate the MRI brain abnormality patterns and its frequency in children with CP and to find the association between the gestational ages, CP clinical types, and the MRI findings.

Materials and Methods: The retrospective observational study was done in a clinically diagnosed cohort of CP with MRI scans performed between November 2016 to July 2019 at Vydehi Hospital, Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore, India. MRI brain scans of 63 children with the clinical diagnosis of CP (term 41, preterm 22), aged between 1 month to 15 years were studied. Births with unknown gestational age and postnatally acquired CP cases were excluded from the study. MRI scans were performed on a Philips Achieva 1.5 T Scanner. MR images of all cases were comprehensively evaluated by a single senior MRI radiologist and split into normal and abnormal categories. Statistical analysis was done by using SPSS version 22 software. A Chi-square test was used as a test of significance for qualitative data and to find the association between the gestational ages, clinical type of CP and MRI findings. p-value of <0.05 was considered as statistically significant.

Results: MRI brain abnormalities were documented in 74.6% of cases. White Matter Injury (WMI) was the most common type (50.8%) followed by gray matter (9.5% superficial + deep), focal vascular insults (6.3%), cerebral malformations (6.3%) and intra cranial haemorrhage (1.6%). Normal MRI findings were observed in 25.4% of cases. The study group consisted of 88.8% of spastic motor type CP of which 31.7% had quadriplegic and hemiplegic CP and 25.4% had diplegic, respectively. The nonspastic type consisted of ataxia or hypotonia (6.3%) and dyskinesia or athetosis (4.8%). MRI abnormal findings were most likely to be identified in children with spastic hemiplegia (90%) and less likely to be in nonspastic motor (50%) types. Deep gray matter injury was more common in dyskinetic type and cerebral malformations were more associated with spastic diplegic CP (p-value -0.014*). In both the term and preterm births, White Matter (WM) abnormality was the most common type (58.5% in term and 36.4% in preterm) but Focal vascular insults were significantly associated with preterm compared to term births (13.6% vs 2.4%, p=0.028).

Conclusion: MRI was useful in revealing underlying brain abnormalities in children with CP. Specific MRI findings in children with CP were found to be associated with neurological subtype and gestational age at birth.

Keywords: Grey Matter Injury, Intra Cranial Hemorrhage, White Matter Injury

INTRODUCTION

William Little and Sigmund Freud first described the clinical syndrome CP in the later half of the 19th century [1] defined as a group of "permanent disorders of movement and posture development that cause limitation of activity attributable to non progressive disturbances in the development of fetal or infant brain, that may be accompanied by a seizure disorder or by disturbance of sensation, cognition, communications, and or behaviour" [1,2]. Incidence of CP is 1.5-2.5 children per 1000 live births and is considered as the most common cause of childhood physical disability [3,4]. CP consists of a different aetiological pathway, pathogenic mechanisms, and clinical manifestations. MRI provides a detailed examination of brain structure and plays an important role in the identification of the most likely pathogenic mechanism [5]. Robinson MN et al., (Victorian CP study) evaluated MRI findings in 154 children with CP and found abnormalities in 84% of children [6].

The most common MRI abnormality was periventricular WMI (31.2%). Ashwal S et al., studied 644 children of CP with MRI brain and found abnormalities in 89% of cases [7]. Pathological abnormality was dependent on the type of CP present, gestational age at birth, or due to an insult occurring later in the life. Bax M et al., study evaluated 351 children with CP, of which 88.3% had an abnormal MRI [8]. Yin R et al., reviewed the MRI brain scans of 42 children (12 premature, 30 full term), found that MRI was useful in revealing underlying brain abnormalities, most of which were due to events in the third trimester or the perinatal period [9]. Truwit CL et al., conducted a study on 40 cases and found that CP in 29 term infants was due to the result of prenatal factors, and less commonly related to the perinatal period [10]. Steinlin M et al., examined the MRI findings of 33 children with congenital hemiplegia and their data suggested a prenatal origin in 20 to 40% of cases [11]. Krageloh-Mann I et al., studied a group of 56 cases with bilateral spastic CP and observed that prenatal aetiology is predominant in term children [12].

Early diagnosis is the key to a speedy aetiologic assessment and prompt referral for early intervention to prevent secondary complications like orthopedic abnormalities, exaggerated sedentary lifestyles, lower fitness and musculoskeletal fragility etc., [13] and optimise functional outcomes. As stated in the practice guidelines issued in 2004 by the American Academy of Neurology [7] MRI is an important part of the initial diagnostic evaluation, even though CP is ultimately a clinical diagnosis. MRI studies of children with CP have the potential to improve our comprehension of an individual's CP, by providing insight into its pathogenesis, aetiology, timing and to estimate the severity of the underlying disease in affected

Individuals [14-18]. In this study, we aim to investigate the MRI brain abnormality patterns and frequency in children with CP and to find the association between the gestational ages, CP clinical types, and the MRI findings.

MATERIALS AND METHODS

A retrospective observational study was done in a clinically diagnosed cohort of children with CP at Vydehi Hospital, Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore; India. MRI brain scans performed between November 2016 to July 2019 were reviewed. Total of 63 children with the clinical diagnosis of CP (boys and girls), aged between 1 month to 15 years were included. Clinical information was obtained from paediatric medical records. Births with unknown gestational age, postnatally acquired CP cases and cases with secondary causes like metabolic and genetic were excluded from the study. Sample size was calculated by using the proportion of CP children with abnormal MRI findings as 71.67% from the study by Sharma N and Dhande R [14]. Using the above values at 99% confidence level a minimum sample size of 60 subjects with CP will be required, present study included 63 children. The study was approved by the Ethics Committee of the Institute (EC Reg NO: ECR/747/Inst/KA/2015/RR -18) and taken permission from appropriate authority. MRI scans were performed on a Philips Achieva 1.5T Scanner. Routine MRI Sequences obtained were axial T1 Fast Spin-Echo (FSE), T2 axial and coronal FSE, axial Fluid-Attenuated Inversion Recovery (FLAIR), Three-Dimensional Spoiled Gradient Recalled (3D-SPGR) and Diffusion-Weighted Imaging (DWI). MRI scans were evaluated by a single senior radiologist, who was blind to the clinical information.

MRI findings were classified into 7 categories, WMI, superficial Gray matter injury, deep Gray matter injury, focal vascular insults, intracranial haemorrhage, cerebral malformations, and normal findings. The MRI classification system was adapted from these studies [3,5,6]. Classifications used for the European CP Study [8] and Arielle Springer A et al., were also considered into account [17]. Definitions used for each MRI pattern in present study were described in [Table/Fig-1].

Classification	Description
Normal	No abnormality
White matter injury	Bilateral signal abnormality and/or volume loss in the periventricular or deep/sub cortical white matter (WM), scalloping of the ventricles, Ventricular dilation and cysts may also be present. Symmetric or asymmetric.
Superficial Gray matter injury	Signal abnormality and /or volume loss predominantly involving the cortical-subcortical grey matter.
Deep Gray matter injury	Signal abnormality or volume loss in deep Gray matter structures (i.e., basal ganglia and thalami).
Focal vascular insult	Infarction in a specifically defined vascular territory.
Intracranial haemorrhage	Epidural, subdural, intracranial or intraparenchymal haemorrhage.
Brain malformations	Abnormal formation of the brain, including polymicrogyria, lissencephaly, pachygyria, heterotopias, schizencephaly, polymicrogyria, cerebellar hypoplasia/atrophy or dysgenesis, holoprosencephaly, hydranencephaly, hydrocephalus, and agenesis of the corpus callosum.
Miscellaneous	Abnormalities unable to be classified into one of the above patterns include, isolated myelination abnormalities, isolated calcifications, infections without specific malformations, and isolated brainstem or cerebellar findings.

[Table/Fig-1]: Definitions for Magnetic Resonance Imaging (MRI) patterns in our study.

All the cases in the study were classified according to two variables, gestation age at birth and clinical type of CP. MRI patterns and frequency of distribution were analysed in these two variables.

Preterm-children who were born at less than 37 weeks gestation and term -children who were born after 37 weeks. CP types were determined by paediatricians and were classified into spastic hemiplegia, spastic tri/quadriplegia, spastic diplegia and ataxic/hypotonic and dyskinetic CP, in concordance with a predetermined classification scheme [19].

STATISTICAL ANALYSIS

Data were entered into Microsoft excel sheet and was analysed using SPSS version 22 software (IBM SPSS Statistics, Somers NY, USA). Categorical data was represented in the form of frequencies and proportions. A Chi-square test was used as a test of significance for qualitative data and used to find the association between the gestational ages, type of CP and MRI findings). The p-value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

Of the 63 patients in the study 63.5% (n=40) were males and 36.5% (n=23) were females. A total of 79.4% (n=50) of cases were between 1 to 10 years age group [Table/Fig-2]. Our study consisted of 88.8% (n=56) of spastic motor type and 11.2% (n=7) of nonspastic type. Spastic quadriplegic type (31.7%) (n=20) was the most common clinical CP [Table/Fig-3].

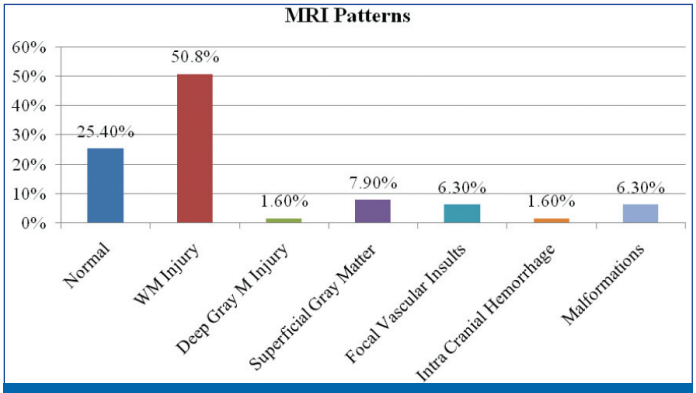
		Count	%
Age	<1 year	6	9.5%
	1 to 5 years	31	49.2%
	6 to 10 years	19	30.2%
	>10 years	7	11.1%
Sex	Female	23	36.5%
	Male	40	63.5%
Gestational age	Term	41	65.1%
	Preterm	22	34.9%

[Table/Fig-2]: General profile of CP subjects in the study.

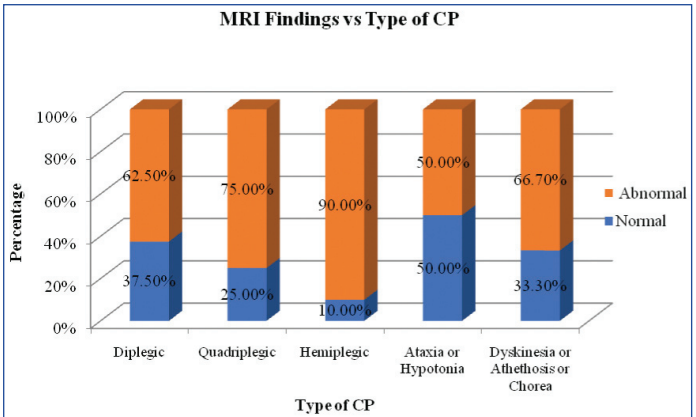
		Count	%
Type of CP	Diplegic	16	25.4%
	Quadriplegic	20	31.7%
	Hemiplegic	20	31.7%
	Ataxia or Hypotonia	4	6.3%
	Dyskinesia or Athetosis	3	4.8%

[Table/Fig-3]: Type of CP distribution.

MRI brain abnormalities were documented in 74.6% of cases. WMI was the most common type (50.8%). Normal MRI findings were present in 25.4% of cases [Table/Fig-4]. MRI abnormal findings were mostly identified in children with spastic hemiplegia (90%) and spastic quadriplegia (75%) compared to spastic diplegic (62.5%) and nonspastic motor types [Table/Fig-5]. In present study there was significant association of deep gray matter injury with dyskinesia



[Table/Fig-4]: MRI findings among CP subjects.



[Table/Fig-5]: Comparison of MRI findings with type of CP. (p=0.275, NS, non-significant).

or athetosis or chorea type (33.3%, p=0.034) and malformations with the diplegic type (25%, p=0.014) [Table/Fig-6]. Focal vascular insults were significantly associated with preterm compared to term births (13.6% vs 2.4%, p=0.028) [Table/Fig-7].

DISCUSSION

MRI brain abnormalities were found in 74.6% of the children in our study. Normal MRI [Table/Fig-8a] results were found in 25.4% (n=16) children in our study. This is comparable with the other population-based studies reported by Towsley K et al., (86.9%), Robinson MN et al., (84%) and Bax M et al., (88.3%) CP studies [3,6,8]. The distribution of cerebral abnormalities in our cohort was lower than that found in Towsley K et al., and Robinson MN et al., CP studies [3,6] and similar to the Sharma N and Dhande R, study (71%) [14]. The frequency of preterm births in our study (34.9%) was similar to that of the Towsley K et al., (39%) and Robinson MN et al., (34%) studies (3,6), but differs with the Sharma N and Dhande R, (68.33%) and Aggarwal A et al., (22.2%) studies [14,15]. There are variations between the classification schemes utilised for these studies, so it is difficult to determine if actual population variations exist.

White Matter

WM abnormality (50.8%) was the most common MRI abnormality in present study, significantly higher than the Towsley K et al., (22.2%), Robinson MN et al., (31.1%), Bax M et al., (42.5%), Sharma N and Dhande R, (46.67%) and Aggarwal A et al., (34%) studies [3,6,8,14,15]. The higher proportion of WM abnormalities in our study might be attributed to the inclusion of cystic leukomalacia and diffuse encephalopathy with WM predominance pattern. The most common WMI (mild and moderate injury) was the involvement of posterior greater than anterior periventricular WM followed by deep WM and subcortical WM [Table/Fig-8a-c]. Severe cases of WMI included cystic leukomalacia in the above-mentioned distribution [Table/Fig-8d].

High risk for WMI was between 23- and 32-weeks' gestation. In present study, WMI makes the higher proportion in term infants (58.5%) than preterm infants (36.4%) [Table/Fig-7] which is comparable with the Robinson MN et al., (60%) [6], however different from the Towsley K et al., (12%) and the Bax M et al., (36%) CP studies [3,8]. The reason for these differences is not known and is only in part likely to be attributable to the variation in the proportion of preterm infants included in each study. Variation in frequency of WMI between studies and the unexpected high incidences of WMI among term children in several studies [6,9,20] indicate that further research and more uniform MR classification of WMI is needed.

Gray Matter Injury

Gray matter injury was found in 9.5% of the patients in our study, of which, 7.9% had superficial gray matter injury (cortical and subcortical) and 1.6% had deep gray matter injury (basal ganglia, thalami, and midbrain) [Table/Fig-8e]. The overall frequency pattern is comparable with that of the Robinson MN et al., (14.3%) study [6]. Variations in classification schemes in different studies make direct comparisons of the frequency of the gray matter injury observed difficult. In our study, superficial Gray matter injury was more frequently associated with both preterm and term births. Deep Gray matter injury was more common in term infants (2.4%) [Table/Fig-7] which is comparable with the Canadian study (5.5%) [3].

Focal Vascular Insults

The frequency of Focal vascular insults in present study (6.3%) was slightly lower than that found by the Towsley K et al., (8.7%) and similar with the Bax M et al., study (7.4%) [3,8].

Similar to these studies, we found that Focal vascular insult was significantly associated with a diagnosis of spastic hemiplegic CP (15%) [Table/Fig-6]. Middle Cerebral Artery (MCA) was the most common territory followed by MCA-PCA watershed territory [Table/Fig-8f]. Surprisingly, our study also found that one patient of ataxia and hypotonia group was with focal infarct in PCA territory.

Intracerebral Haemorrhage

One child had periventricular haemorrhage (1.6%) (preterm hemiplegic) in our study. The frequency of appearance was similar to that of Towsley K et al., (1.6%) study where it is more commonly seen in preterm hemiplegic and term quadriplegic children [3].

Brain Malformations

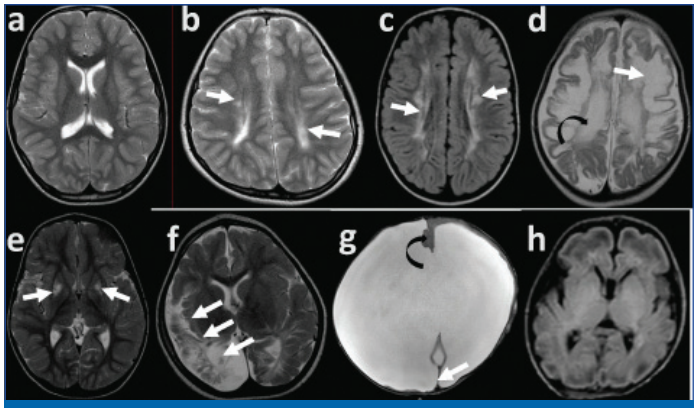
Brain malformations were found in 6.3% of the study cohort which is comparable with the Bax M et al., and Sharma N et al., CP studies [8,14]. In present study, brain malformations were more likely found in preterm (13.6%) children with spastic diplegic type

		Type of CP												p-value
		Diplegic (n=16)		Quadriplegic (n=20)		Hemiplegic (n=20)		Ataxia or hypotonia (n=4)		Dyskinesia or Athetosis or chorea (n=3)		Total		
		Count	%	Count	%	Count	%	Count	%	Count	%	Count	%	
MRI	Normal	6	37.5%	5	25.0%	2	10.0%	2	50.0%	1	33.3%	16	25.4%	0.275
	White Matter Injury	5	31.2%	12	60.0%	13	65.0%	1	25.0%	1	33.3%	32	50.8%	0.072
	Deep Gray Matter Injury	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	33.3%	1	1.6%	**0.034***
	Superficial Gray Matter	1	6.2%	3	15.0%	1	5.0%	0	0.0%	0	0.0%	5	7.9%	0.687
	Focal Vascular Insults	0	0.0%	0	0.0%	3	15.0%	1	25.0%	0	0.0%	4	6.3%	0.287
	Intra cranial haemorrhage	0	0.0%	0	0.0%	1	5.0%	0	0.0%	0	0.0%	1	1.6%	0.702
	Malformations	4	25.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	4	6.3%	**0.014***
	Total	16	100.0%	20	100.0%	20	100.0%	4	100.0%	3	100.0%	63	100.0%	

[Table/Fig-6]: Frequency and distribution of MRI findings with respect to the CP type.
* (Significant)

	Gestational Period				p-value
	Term (n=41)		Preterm (n=22)		
	Count	%	Count	%	
Normal	10	24.4%	6	27.3%	0.802
White Matter Injury	24	58.5%	8	36.4%	0.465
Deep Gray Matter Injury	1	2.4%	0	0.0%	0.649
Superficial Gray Matter	4	9.8%	1	4.5%	0.466
Focal Vascular Insults	1	2.4%	3	13.6%	**0.028***
Intra Cranial Haemorrhage	0	0.0%	1	4.5%	0.169
Malformations	1	2.4%	3	13.6%	0.082

[Table/Fig-7]: MRI brain findings by term or preterm gestational age. The results represent absolute numbers and percentage.
*Significant



[Table/Fig-8]: MRI Brain findings in children with CP.
a): Unremarkable T2W axial image of a seven-year-old child. Mild WMI (b): T2W images of a 10-year-old spastic diplegic child demonstrating mildly increased signal intensities in the centrum semi ovale and posterior periventricular white matter (solid white arrows). Moderate WMI (c): FLAIR axial image of four-year old quadriplegic child demonstrating moderately increased signal intensities in the bilateral periventricular white matter extending to corona radiate (solid white arrows). Severe WMI (d): T2W axial image of a spastic quadriplegic child demonstrating cystic leukoencephalomalacia with near complete loss of white matter (solid white arrow) and ventricular dilatation (curved black arrow). Deep Gray matter injury (e): T2W axial image of a four-year-old child with dyskinetic CP demonstrating increased signal intensities in the bilateral putamen (solid white arrows). Focal vascular insult (f): T2W axial image of the two-year-old hemiplegic child showing an infarct in the right temporal and occipital lobes in MCA and MCA-PCA watershed territories (solid white arrows) with mild atrophy of the right cerebral hemisphere. Cerebral malformations (g,h): T2W axial image of a seven-month-old term child showing Hydranencephaly -completely fluid-filled brain with islands of cortical tissue (curved black arrow) with intact falx (solid white arrow) (g), FLAIR axial images of a 1-month old preterm child showing Pachygyria - smooth cortical surface of the supratentorial brain parenchyma with subtle sulcation in inferior frontal and temporal lobes (h).
CP: Cerebral palsy; T2W: T2-Weighted; WMI: White matter injury; MCA: Middle cerebral artery; PCA: Posterior cerebral artery

(25%, p=0.014*) which is unexpected and different from the Towsley K et al., and Robinson MN et al., studies [3,6]. In present study, four children were found to have cerebral malformations. Hydranencephaly (term diplegic) [Table/Fig-8g], pachygyria (preterm diplegic) [Table/Fig-8h], cerebellar dysgenesis (preterm diplegic) and corpus callosal agenesis (preterm diplegic). Corpus callosal thinning was not included in the malformation due to the frequent association with the WMI.

Nonspecific or Miscellaneous Findings

MRI findings that did not fit into the aforementioned abnormalities and were labelled as miscellaneous [Table/Fig-1]. The miscellaneous group was not included in our study because we didn't find such type of abnormalities in our study. But it constitutes a significant proportion in Towsley K et al., (18.8%), Robinson MN et al., (7.8%) and Bax M et al., (7.1%) CP studies [3,6,8]. This may be related to the significantly high proportions of WMI and normal MRI findings in our study; however, this factor alone is insufficient to entirely explain the absent miscellaneous findings.

Comparison of MRI patterns in all CP types among different CP studies is represented in the [Table/Fig-9].

MRI Pattern	Present study (%)	Towsley K et al., (%) [3]	Robinson MN et al., (%) [6]	Bax M et al., % [8]	Sharma N and Dhande R., (%) [14]
Normal	25.4	11.1	16.2	11.7	28.33
White matter injury	50.8	22.2	31.2	42.5	46.67
Deep gray matter injury	1.6	4.8	14.3	12.8	13.33
Superficial gray matter	7.9	2.4		9.4	
Focal vascular insults	6.3	8.7	16.2	7.4	-
Intra cranial haemorrhage	1.6	1.6		-	-
Malformations	6.3	16.7	12.3	9.1	8.33
Miscellaneous	-	18.3	9.8	7.1	3.33

[Table/Fig-9]: Comparison of MRI patterns in all CP types among different CP studies (Single lesion only) [3,6,8,14].

Limitation(s)

Small sample size-of this study resulted in limited ability to comment on MRI findings in less common motor types and preterm births. Lack of consistency in collection methods and MRI classification systems limit the meaningful comparisons that can be made amongst neuroimaging results from various other published CP studies. Cerebral WMI may be missed on 1.5T MRI with conventional MR sequences, which may be better delineated on 3T MRI with novel sequences like Diffusion Tractography Imaging (DTI) in CP cases. A 3T MRI allows acquisition of thinner slices and improved delineation of smaller structures, making it possible to demonstrate the site and extent of WM abnormalities, intracranial haemorrhage, infarction, posterior fossa abnormalities and maturational changes in the brain [21].

CONCLUSION(S)

Despite the above limitations, our study showed some associations between MRI brain findings and neurological subtypes. Because of the assessment of recurrence risk, counselling of families and potential implementation of prevention strategies, all children with CP should have age-appropriate MRI of the brain.

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- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

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