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Original Article

Relationship between gross motor function and magnetic resonance imaging findings in children with cerebral palsy

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Abstract

This cross-sectional study was carried out at the department of Pediatric Neurology, Institute of Pediatric Neurodisorder and Autism, Bangabandhu Sheikh Mujib Medical University, Dhaka with the aim to assess the relationship between gross motor function and MRI findings in children with cerebral palsy. The duration of the study was 12 months. All the cerebral palsy cases who met the selection criteria were enrolled. Detailed history taking and physical examination was done. The gross motor function of all cases was evaluated according to Gross Motor Function Classification System- Expanded and Revised (GMECS-E and R). Magnetic resonance imaging of brain was done in all enrolled patients and reports were evaluated. MRI findings were classified as maldevelopment, cortical and subcortical gray matter lesion, periventricular white matter injury, basal ganglia lesion, normal and other findings. A total of 45 children with cerebral palsy aged between 2 to 12 years were included in this study. Mean age of the children was 4.73 (+3.17) years. Male were 31 and female were 14 in number. Functionally majority patients were in GMFCS level IV (26.7%) and level V (20%). MRI findings were abnormal in 35 (77.78%) cases. Most common abnormal MRI finding was cortical and subcortical grey matter lesions 22 (48.9%). This study revealed that cortical and subcortical gray matter lesions were significantly associated with higher level of GMFCS (IV-V) (P=0.038) and maldevelopment of brain were also significantly associated with higher level of GMFCS (P=0.01). Normal MRI findings had significant association with mild to moderate GMFCS level (I-III) (P=0.012). From this study significant relationship was found between gross motor function and MRI of brain findings in children with cerebral palsy.

Keywords: Cerebral palsy, Gross Motor Function Classification System, Magnetic resonance imaging findings

INTRODUCTION

Cerebral Palsy (CP) is one of the most common causes of chronic disability in children. The incidence of CP is about 2-2.5/ 1000 live births globally[1]. The etiology of CP is extensive, ranging from prenatal and perinatal events to postnatal insults[2]. The human brain undergoes complex organizational changes during development in and ex utero. Pathogenic events affecting the developing brain cause abnormalities or lesions, the patterns of which depend on the stage of brain development. Insult during cortical neurogenesis which occurs during 1st and 2nd trimester may cause brain lesions which are characterized by maldevelopment of the brain. During the early 3rd trimester, periventricular white matter is especially affected. Toward the end of the 3rd trimester, gray matter appears to be more vulnerable, whether it is a cortical or deep gray matter, such as basal ganglia or thalamus. In around 15% of cases of CP, clear etiology cannot be identified even after neuroimaging and metabolic investigation[3].

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Highlights

1. **MRI of brain is the preferred modality of investigation for children with cerebral palsy.**
2. **MRI findings were abnormal in majority children with cerebral palsy.**
3. **Most common abnormal MRI findings were cortical and subcortical grey matter lesions.**
4. **There is association between gross motor function and MRI findings in children with cerebral palsy.**
5. **More severe impairment of motor function was significantly associated with grey matter lesion and maldevelopment of brain.**

Subtypes of cerebral palsy are classified according to the quality and topographic pattern of motor impairment. The clinical classification that is used: (1) spastic quadriplegia (symmetric/equal and severe spasticity of all four limbs), spastic hemiplegia (spasticity in one sided upper and lower limb), and spastic diplegia (spasticity in the lower extremities is more than spasticity in the upper extremities); (2) dyskinetic (ie, athetosis, chorea, or dystonia in the absence of objective weakness or tone changes); (3) ataxic; (4) mixed (ie, both spastic and dyskinetic features are prominent)[4].

Robert Palisano introduced a new function based classification schemes focusing on function. Gross Motor Function Classification System included children upto 12 years of age in 1997. It was again expanded and revised, known as Gross Motor Function Classification System- Expanded and Revised (GMFCS-E & R) that further included an age band for youth 12 to 18 years[5].

The International Classification of Functioning (ICF) shifts the health professionals' attention from focusing on primary motor impairments to functional activities and social participation which are considered the optimal outcomes of medical services for children with CP[6]. Functional classifications are useful for setting functional goals and planning services for children with CP in health care systems[6]. According to the system, function is divided into five levels; children in Level I represent the most independent motor function and children in Level V have the least. Distinction between the levels is thought to be clinically meaningful and is based on functional abilities and limitation. This grading has been shown to be reliable across observers and invariant with increasing age. So, Gross Motor Function Classification System had a remarkably rapid uptake into clinical practice and research around the world[7].

Different studies revealed that, neuroimaging findings are abnormal in more than 80% of children, disclosing the pathogenic pattern responsible for the CP[8]. Use of MRI, as well as knowledge of its role in the understanding of pathogenesis of CP, has dramatically increased during the last 15 years. Early detection of brain abnormalities in children with cerebral palsy may help in the initiation of appropriate therapy and predict prognosis[9].

From the point of view for counseling of families, and potential implementation of prevention strategies, it would be helpful for all children with CP to have neuroimaging preferably MRI of brain as previously recommended in the American Academy of Neurology and the Child Neurology Society practice parameter[1].

In Bangladesh very limited studies have been conducted on neuroimaging in children with CP. The purpose of this study was to determine the clinical spectrum of gross motor impairment according to Gross Motor Function Classification System Extended and Revised and to observe the spectrum of MRI abnormalities and to find out the relationship between gross motor function and MRI findings in children with cerebral palsy. Therefore, Gross Motor Function Classification System may help in quick assessment of the spectrum of illness and more severe children can be picked up from primary healthcare delivery level for referral to higher centers where facilities for extensive evaluation are available. It might help in setting realistic goal for individual child for planning of early intervention and comprehensive management and more effective communication could be done with their parents.

METHODS

This cross sectional study was conducted in department of Pediatric Neurology, Institute of Paediatric Neurodisorder & Autism (IPNA) of BSMMU from October 2019 to September 2020. The objective of the study was to assess the relationship between the level of gross motor function and MRI of brain findings among the children with cerebral palsy. Children diagnosed as CP according to the current definition

aged between 2 to 12 years attending inpatient and outpatient department of department of Pediatric Neurology, IPNA, BSMMU were enrolled in this study. The children were suspected as neurometabolic diseases, neurodegenerative diseases, syndromic and who refused to do MRI were excluded from this study. Study subjects were enrolled by convenience sampling after informed written consent obtained from the parents.

Total 45 diagnosed CP children were enrolled in this study. Detailed history from parents or caregiver with special emphasis on antenatal, natal, postnatal history and physical examination was done including general examination, developmental assessment, neurological examinations and other systemic examinations. The assessment protocols were followed for all subjects. Functional classification of mobility was done according to the Gross Motor Functional Classification Extended & Revised by researcher herself. Children at GMFCS E & R level I: walk and perform all the activities of age-matched peers, albeit with limitations of speed, balance, and coordination. Children at level V needs to be transported, have extreme difficulties with trunk posture, and have little voluntary control of limb movements[10].

The MRI was done in the department of Radiology and Imaging, BSMMU. Specification of MRI machine was-field: 1.5 Tesla, brand: Siemens, model: Magnetom Avanto. MRI findings were assessed by radiologists and also cross checked by a pediatric neurologist separately who were unaware about clinical condition of that patients. MRI findings were classified into six categories: brain maldevelopment, periventricular white matter lesions, cortical and subcortical grey-matter lesions, basal ganglia lesion, other lesions, and normal findings[11]. Data were compiled and was analyzed by using SPSS Windows version 23. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. In regard to test the relationship between gross motor functions with MRI findings chi square test was applied. A "*P*" value <0.5 was considered as significant.

RESULTS

A total of 45 children aged between 2 to 12 years diagnosed as cerebral palsy were included in this study. Among them, majority (55.6%) were aged between 2-4 years. Mean age of the children was 4.73 (± 3.17) years. Male were 31 and female were 14 in number.

Almost 75% of the patients had no history of prenatal events. Other than that, 2.2% patients had maternal fever and 22% had other events. An observation was made that most of the patients (82.2%) belonged to term, 15.6% patients belonged to preterm and 2.2% patient belonged to post term. It was observed that birth weight of 30 (66.7%) patients was normal, 8 (17.8%) patients belonged to low birth weight and 7 (15.6%) had IUGR. History of perinatal asphyxia was found in 32 (71.1%) patients. Out of all the patients, 35.6% had no history of significant postnatal event, 35.6% had neonatal seizure, 20% had infection and 8.9% had neonatal hyper bilirubinemia **(Figure 1)**.

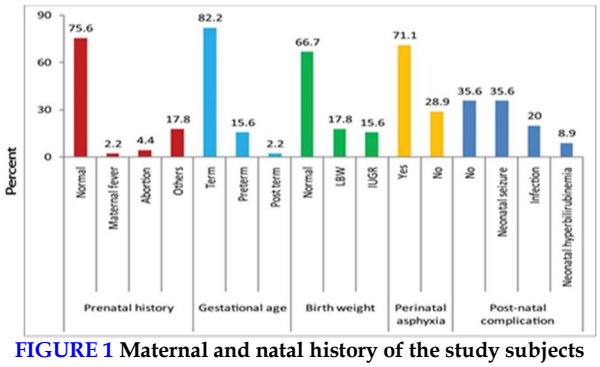


FIGURE 1 Maternal and natal history of the study subjects

Majority of patients fall into level IV (26.7%). Level I, II and III were equal (17.8%) in each and in level V there were 20% patients **(Figure 2)**.

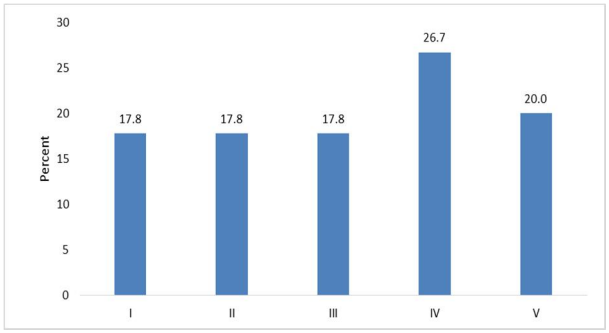


FIGURE 2 Distribution of the study patients according to gross motor function classification system level

MRI findings were abnormal in majority cases (77.78%). Normal findings were found in 10 (22.2%) patients. Most common findings were cortical and subcortical grey matter lesion found in 22 (48.9%) patients.

Maldevelopment and Periventricular white matter injury were found in 11 (24.4%) patients in each type. Basal ganglia lesions were present in 4 (8.9%) patients **(Figure 3)**.

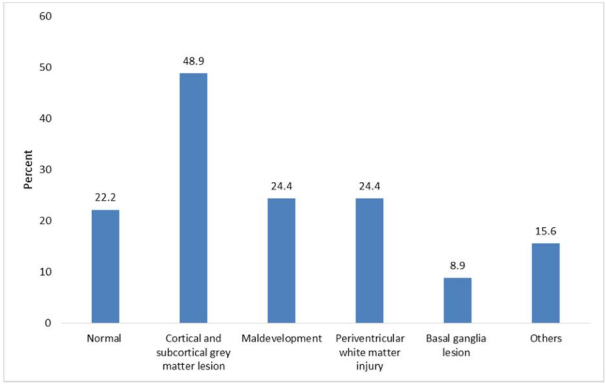


FIGURE 3 Distribution of the cerebral palsy children according to magnetic resonance imaging findings

Normal MRI findings were found more in GMFCS level I (50%). However, no cases of GMFCS V had normal MRI. The association was statistically significant (*P*=0.012). Cortical and subcortical grey matter lesions were more in level V (36.4%). However, the association was not statistically significant. Maldevelopment was found more in GMFCS level IV (54.5%). Maldevelopment were not found in level I or level II. Their association was statistically significant (*P*=0.017) **(Table 1)**.

DISCUSSION

CP is one of the most common causes of chronic disability in children. The type and severity of motor impairment are related to the site and type of lesion and also time of insult to the developing brain. Neuroimaging particularly MRI is rapidly evolving modality of investigation for understanding the pathogenesis and underlying etiology[1]. Gross motor function of children with CP can easily be assessed by the tool GMFCS-E & R. It is easy to use, valid and reliable tool and can be done by medical professionals and care giver in all levels of healthcare.

In this study, it was observed that majority of patients fall into GMFCS level IV and V **(Figure 2)**. Similar findings were found in another study[12], but different from the population study done by Towsley et al. (2011) where GMFCS 1 predominated[13]. This current study was conducted in a tertiary care hospital where severe patients were referred from different level of healthcare and that may be a cause of getting more number of severe types of CP in this series. Another cause might be parents are more likely to seek treatment for severe type of CP than milder types.

All the patients in this study were evaluated by MRI of brain. Findings were documented with respect to maldevelopment, periventricular white matter injury, cortical and subcortical gray matter lesion, basal ganglia lesion, normal finding and others. Here majority of the patients had abnormal MRI findings. Cortical and subcortical gray matter lesions were the most common type of lesion (48.9%) followed by periventricular leukomalacia, maldevelopment, and basal ganglia lesions **(Figure 3)**. These findings were consistent with a study conducted in Nepal[14] but different from a study from developed country where periventricular

TABLE 1 Relation of GMFCS* level with MRI findings (n=45)

MRI findings	GMFCS* level					*P*
	I	II	III	IV	V	
Normal	5 (50.0)	3 (30.0)	1 (10.0)	1 (10.0)	0 (0.0)	0.012
Cortical and subcortical grey matter lesion	2 (9.1)	3 (13.6)	3 (13.6)	6 (27.3)	8 (36.4)	0.077
Mal development	0 (0.0)	0 (0.0)	1 (9.1)	6 (54.5)	4 (36.4)	0.017
Periventricular white matter injury	1 (9.1)	2 (18.2)	2 (18.2)	5 (45.5)	1 (9.1)	0.491
Basal ganglia lesion	2 (50.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (25.0)	0.382
Others	0 (0.0)	2 (28.6)	2 (28.6)	2 (28.6)	1 (14.3)	0.608

*GMFCS: Gross Motor Function Classification System

Cortical and subcortical grey matter lesion (*P*=0.038) and maldevelopment (*P*=0.01) was significantly associated with severe type of GMFCS level. Normal MRI (*P*=0.012) was significantly found in mild to moderate GMFCS level **(Table 2)**.

TABLE 2 Relation of GMFCS* level with MRI findings (n=45)

MRI findings	All	GMFCS* level		*P*
		Mild/moderate (GMFCS I-III)	Severe (GMFCS IV-V)	
Normal	10 (22.2)	9 (90.0)	1 (10.0)	0.012
Cortical and subcortical grey matter lesion	22 (48.9)	8 (36.4)	14 (63.6)	0.038
Mal development	11 (24.4)	1 (9.1)	10 (90.9)	0.01
Periventricular white matter injury	11 (24.4)	5 (45.5)	6 (54.5)	0.547
Basal ganglia lesion	4 (8.9)	2 (50.0)	2 (50.0)	1.000
Others	7 (15.6)	4 (57.1)	3 (42.9)	1.000

*GMFCS: Gross Motor Function Classification System
MRI: Magnetic resonance Imaging

leukomalacia (PVL) was the most common finding [9]. MRI findings were found normal in 10 patients (22.2%) in this study. Normal MRI findings were also found in related studies[13,14].

Cortical and subcortical gray matter lesions were the commonest (48.9%) type of findings in this study. Previous studies from developed countries revealed different findings where PVL was the most common type of lesion in children with CP[15]. Among 22 patients in this group, 11 patients had mild generalized cortical atrophy, 3 patients had gross generalized cortical atrophy with temperoparietal predominance, 7 patients had multi cystic encephalomalecia, 1 patient had hemi cranial atrophy and 1 patient had focal atrophy with gliotic change. Similar findings were found by Truwit et al. (1992)[16]. Tables 1 showed majority of these patients were in higher level of GMFCS. Table 2 showed relationship between cortical and subcortical grey matter lesion and severe type of CP (GMFCS IV-V) were statistically significant (*P*=0.04). Similar findings were found by Kulak et al (2007)[17].

In this study, total 11(24.4%) patients had developmental malformation of brain. Among them 9 had corpus callosum hypoplasia, 1 had lissencenphaly and 1 had polymicrogyria. Previous studies from developed countries revealed different findings; neuronal migration disorders were the most common findings followed by corpus callosum dysgenesis[18]. Cortical malformation may have genetic etiology. So, different types of malformations may be found in different ethnic groups. Another cause of this discrepancy may be due to small sample size. Table1showed 6 (54.5%) patients having developmental malformation were in GMFCS IV and 4 (36.4%) patients were in GMFCS V level. **Table 2** showed almost all (10/11) patients with maldevelopment had severe type of CP (GMFCS IV-V). Association between functional severity and cortical maldevelopment were statistically significant (*P* = 0.01). Similar findings were found in different studies[9,19].

In this study, 9 (24.4%) patients had periventricular leukomalacia (PVL); among them 7 were term and only 2 were preterm. Similar findings were found in another study[9], but in different studies, PVL were more commonly found in preterm infants [13,17]. Here most PVL (45.5%) cases fall in GMFCS IV (Table 1). No significant association was found between PVL and GMFCS level. These findings were different from study done by Himmelman and Uvebrant (2011)[19] who found more PVL cases in milder group. Here, it was found that 6 out of 9 patients of PVL had associated corpus callosum hypoplasia which might be a cause of this severity. Other causes might be majority of these cases were term and had h/o perinatal asphyxia. But Trwit et al. (1992) found similar type of findings[16].

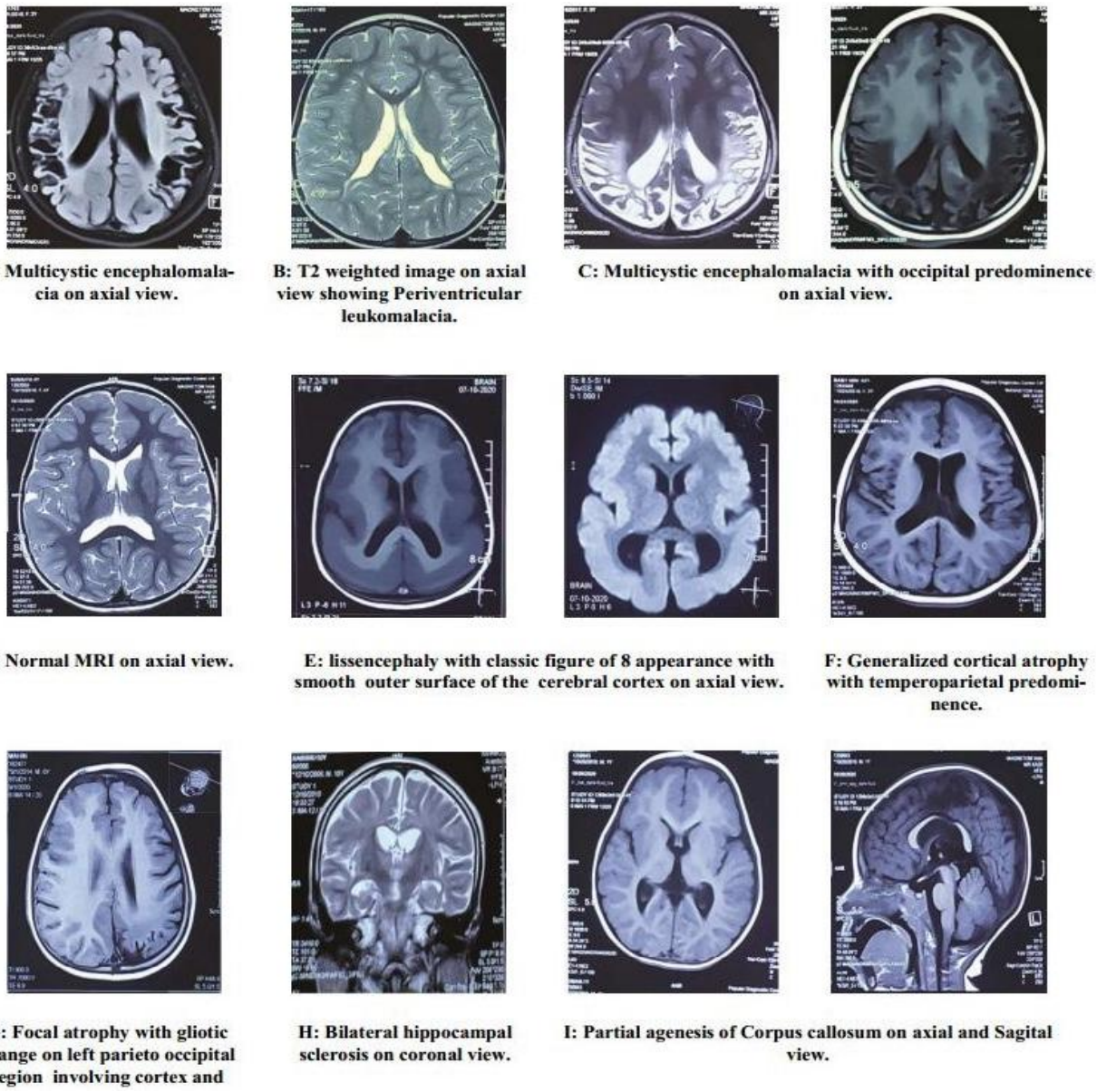
In current study, 4 (8.9%) patients had basal ganglia lesions. Among them, 2 patients had mild functional impairment (GMFCS I-III) and 2 had severe functional impairment (GMFCS IV-V). These findings were different from another study where majority patients with basal ganglia lesions fall in the severe functionally impaired group[19].

Brain MRI findings were normal in 10 (22.2%) patients. Almost all (9/10) patients of this group had mild to moderate impairment (GMFCS I-III). Similar results were found in different studies [13,20]. Table 2 showed association between mild functional severity and normal MRI findings were statistically significant (*P*=0.012). The CP children with normal MRI may have cerebral lesions or abnormalities which are too subtle to

be detected by current neuroimaging technologies. Some of these children may have indeed undetected and undiagnosed metabolic disorders. Genetic basis to their condition also should be suspected. Recent findings have implicated copy number variants and mutations in single genes in children with CP[21].

In this study, children were aged between 2 to 12 years. The mean age was 4.73 yrs (±3.17). Male: female ratio was 2.2:1 which was similar to the study done by Kundu et al. (2018)[22]. In present study, 75.6 % patients had no significant prenatal event. Unlike western figures most patients this study belonged to term gestational age. Singhi et al. (2002) also showed very similar figures like ours with 86.8% being term babies[23]. Most of the patients (71.1%) had history of Perinatal asphyxia. The high proportion of birth asphyxia associated with CP is also shown in other studies from less developed countries[15,17]. Singhi et al. (2002) commented that, although birth asphyxia in the causation of CP has been challenged, the history of birth asphyxia is found in a large number of cases[23].

In a nutshell, this study suggests that MRI is a useful



A: Multicystic encephalomalacia on axial view.

B: T2 weighted image on axial view showing Periventricular leukomalacia.

C: Multicystic encephalomalacia with occipital predominence on axial view.

D: Normal MRI on axial view.

E: lissencephaly with classic figure of 8 appearance with smooth outer surface of the cerebral cortex on axial view.

F: Generalized cortical atrophy with temperoparietal predominence.

G: Focal atrophy with gliotic change on left parieto occipital region involving cortex and

H: Bilateral hippocampal sclerosis on coronal view.

I: Partial agenesis of Corpus callosum on axial and Sagital view.

FIGURE 4 Different magnetic resonance imaging pictures of study cases

modality of investigation in revealing underlying brain pathology and also timing of insult in children with CP. Gray matter lesions were the most common abnormal MRI findings. Significant relationship was found between the level of gross motor function and MRI findings of children with cerebral palsy.

Limited studies were conducted in this field. Limitation of the study was small sample size and single centered study. Findings of this study will help further large scale multi centered studies and will aid to plan for further advances in the management of children with cerebral palsy.

Conclusion

MRI is a useful modality of investigation for children with cerebral palsy. Most of the patients had abnormal MRI findings. Gray matter lesions were the most common abnormality. Majority of patients had severe functional impairment. A significant association was found between the level of gross motor function and MRI findings of children with CP. These findings indicated that more severe motor impairment were associated with cortical and subcortical gray matter lesions and maldevelopment of brain.

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Author Contributions

- Conception and design: SA[1], SA[2], KF
- Acquisition, analysis, and interpretation of data: SA[1], RS, NN, SS, ZF, BCP, KMP, RS
- Manuscript drafting and revising it critically: SA[1], SA[2], GKK, KF
- Approval of the final version of manuscript: SA[2]
- Guarantor accuracy and integrity of the work: GKK, STA

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Conflict of Interest

Authors declare no conflict of interest.

Ethics approval

The Institutional Review Board of BSMMU approved the protocol before conducting the study. Research proposal was reviewed and approved by Institutional Review Board of BSMMU. Memo No. BSMMU/2019;11903.

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