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Research Article

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Acute Disseminated Encephalomyelitis (ADEM): Short Term Motor Outcome of Hospital Admitted Patients

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Abstract

Introduction: Among the neuroinflammatory disorder of CNS, Acute Disseminated Encephalomyelitis (ADEM) is a multifocal, sub-acute or acute onset disease that has got current interest of neurologists for its better outcome. Very few studies have been carried out on ADEM particularly in adults of our country. So we performed the study to describe short term motor outcome of hospital admitted ADEM patients.

Objective: To assess the motor outcome of hospital admitted ADEM patients at 06 weeks of steroid.

Methods: A prospective, observational study was conducted over 18 (eighteen) months period from May 2014 to November 2015 on 50 (fifty) patients of ADEM of all age group at neurology department of Chittagong Medical College Hospital (CMCH), Chittagong, Bangladesh.

Results: The core of our results shows that most subjects (56%) were of 40-60 years whereas 12% were of <20 Years. 62% was middle class group and male gender (52%) predominated in the study. Infection has got an important association in that study and 52% patients gave preceding history of viral infection within 04 weeks of ADEM symptoms. During assessment of short term motor outcome we found 74% patients improved with a mortality rate of 24% and 02% was dropped out cases. Highly significant ($p<0.001$) improvement of disability status measured in modified Rankin Scale (mRS) seen in most patients. Among 37 follow up cases 30 (**81.1**%) patients had initial unfavorable mRS (Score 4-5). After treatment at 06 weeks mRS Score improved into favorable (Score 0-3) in 31 (**83.8**%) patients. Regarding motor variables highly significant improvement also found in GCS, best motor response, muscle power (MRC grade) in upper and lower limbs, deep tendon reflexes, and plantar response. Range of initial GCS was 4-15 which improved into 9-15 after treatment at 06 weeks in 37 improved study subjects. 34% patients got motor or motor parts of mixed cranial nerve palsy. Improvement was significant ($p<0.05$) for cranial nerve palsy, motor seizure but non-significant ($p>0.05$) for motor aphasia. CSF reactivity was seen in 66% of 44 CSF studied ADEM cases where the mean of raised protein was 76.11mg/dl with a range of 42-135mg/dl.

Conclusion: In our study short term motor outcome was good in 74% of patients which is highly significant.

Keywords: ADEM; Acute Disseminated Encephalomyelitis; mRS; Modified Rankin Scale; GCS; Glasgow Coma Scale

List of abbreviations: ADEM: Acute Disseminated Encephalomyelitis; AHL: Acute Hemorrhagic Leukoencephalitis; CNS: Central Nervous System; CSF: Cerebrospinal Fluid; CT: Computed Tomography; DTR: Deep Tendon Reflex; DW: Diffusion Weighted; GCS: Glasgow Coma Scale; ICSOL: Intracranial Space Occupying Lesion; ICU: Intensive Care Unit; IVIg: Intravenous Immunoglobulin; MBP: Myelin Basic Protein; MRC: Medical Research Council; MRI: Magnetic Resonance Imaging; MS: Multiple Sclerosis; OCB: Oligoclonal Band; PNS: Peripheral Nervous System; PE: Plasma Exchange; SPSS: Statistical Package for Social Science

Introduction

Demyelinating diseases are immune mediated and Acute Disseminated Encephalomyelitis (ADEM) is a disease predominantly

affecting white matter of CNS which is almost always monophasic [1]. ADEM is characterized clinically by rapid development of focal or multifocal neurological dysfunction and pathologically by perivascular inflammation, edema and demyelination within CNS [2]. The most precise clinical and pathological observations regarding ADEM are derived from case studies in which there has been a close link between the specific viral infection or vaccination and the syndrome arising after acute measles infection or rabies vaccine (tissue culture) administration can be considered the prototype of the illness [3,4].

In post infectious ADEM the neurologic syndrome generally begins late in the course of viral illness [4]. But in severe cases onset may be abrupt with rapid (hours to days) progression [2]. Initial features include encephalopathy, seizures, and focal & multifocal signs reflecting cerebral (e.g., hemi paresis), brainstem (e.g., C.N palsies) and spinal cord involvement (e.g., bladder involvement). Other reported finding includes- movement disorder & ataxia [2,4]. Frequent neurologic symptoms and signs described in various combinations include unilateral or bilateral pyramidal signs, acute hemiplegia, ataxia, cranial nerve palsies, visual loss due to optic neuritis, seizures, spinal cord involvement, impairment of speech (slow, slurred, or aphasia), and hemiparesthesia, with invariable involvement of mental status, ranging from lethargy to coma.

High index of suspicion is required to diagnose ADEM cases because many features are shared by diseases, like- stroke, multiple sclerosis, ICSOL etc. Usually preceding history of viral infection or vaccination, subacute onset but progressive course, multifocal CNS or sometimes PNS involvement are clinical clues to suspect ADEM cases. MRI of Brain sometimes with spinal cord is the cornerstone of investigation to diagnose ADEM. Multifocal demyelinating lesions involving predominantly white matter or subcortical areas of brain with or without contrast enhancement are usual MRI findings of ADEM [5]. Besides this, raised protein in CSF usually with lymphocytic pleocytosis seen in many ADEM patients.ADEM causes significant morbidity for which most patients require hospitalization. Recovery can begin within days. Spontaneous natural recovery can occur but it is very slow that of why corticosteroid is given to hasten recovery. Resolution is occasionally noted within a few days but more often evolves over the course of weeks or months. Complete recovery occurs in most cases (50%) of ADEM. Mortality various from 10-30% depending on severity of cases, disease burden, management facilities, comorbid conditions etc [4].

Most of previous ADEM studies had elaborated outcome in children but not in adults. The results of these studies in terms of clinical feature and natural evolution were clearly different from those of paediatric series [6-9]. Our research in Chittagong Medical College was undertaken to assess the short term (6 weeks) motor outcome of hospital admitted ADEM cases.

Pathophysiology

Acute disseminated encephalomyelitis (ADEM) is an immune mediated inflammatory disorder of central nervous system (CNS) which is commonly preceded by an infection, and predominantly affects white matter of the brain and spinal cord [10]. ADEM is characteristically a monophasic illness that is commonly associated with an antigenic challenge (febrile illness or vaccination) which is believed to function as a trigger to the inflammatory response underlying the disease [11]. ADEM was first described by Lucas in 1790 (Figure 1).

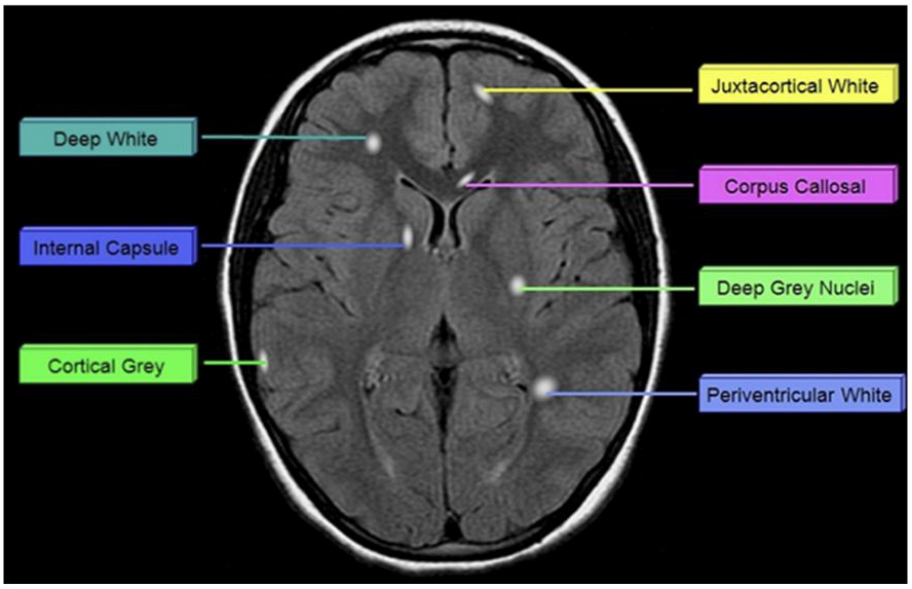

Figure 1: Potential location of lesions in patients with acquired demyelination

International MS Study Group monophasic ADEM criteria [5]

- No history of prior demyelinating event
- First clinical event with presumed inflammatory or demyelinating cause

- Acute or subacute onset
- Affects multifocal areas of central nervous system
- Must be polysymptomatic
- Must include encephalopathy (i.e, behavioral change or altered level of consciousness
- Neuroimaging shows focal/multifocal lesion (s) predominantly affecting white matter
- No neuroimaging evidence of previous destructive white matter changes
- Event should be followed by clinical or radiologic improvements (although may be residual deficits)
- No other etiology can explain the event
- New or fluctuating symptoms, signs, or magnetic resonance imaging findings occurring within 3 months are considered part of the acute event

The precise mechanism implicated in ADEM is not well known, but there is a general consensus that ADEM is an immune mediated disorder resulting from an autoimmune reaction to myelin [12]. There are two basic mechanisms proposed to cause ADEM.

Molecular mimicry theory: This theory relies on the idea that myelin antigens (like myelin basic protein, MBP) could share a structural similarity with antigen determinants on the infecting pathogen. Antiviral antibodies produced by infected host mediated immune response thought to cross react with myelin antigens that share a similar structure, inadvertedly producing an autoimmune response. Myelin proteins have shown resemblance to several viral sequences, and cross reactivity to immune cells has been demonstrated. T cells to human herpesvirus-6 (HHV-6), influenza virus have been shown to cross react with MBP antigen [13,14]. Enhanced MBP reactive T-cell response have been demonstrated in patients with post infectious ADEM and enhanced anti- MBP antibodies have been shown in patients with post vaccinal ADEM following vaccination with simple rabies vaccine [15,16]. Recently ADEM has also been shown to be associated following H1N1 09 influenza vaccination [17].

Inflammatory cascade theory: Tissue of nervous system is thought to be damaged secondary to viral infection resulting in leakage of myelin based antigen into systemic circulation through an impaired blood brain barrier. These antigens promote a T-cell response which in turn causes secondary damage to nervous system tissue through an inflammatory response.

Magnetic Resonance Imaging (MRI) of Brain and Spinal Cord

It is the most important paraclinical tool available to aid in the diagnosis of ADEM and to distinguish the clinical presentation from other inflammatory or noninflammatory neurological diseases. Typical MRI findings described in ADEM are widespread, bilateral, asymmetric patchy areas of homogenous or slightly inhomogenous increased signal intensity on T2 weighted imaging within the white matter, deep gray nuclei, and spinal cord. Within the white matter juxtracortical and deep areas are involved more frequently than is periventricular white matter which is an important feature in contrast to patients with Multiple Sclerosis (MS) [5,18]. In addition lesions involving corpus callosum which are considered typical in MS are rarely seen in ADEM. Infratentorial lesions are common including the brainstem and cerebellar white matter. With respect to lesion size and morphology variation is seen ranging from small round lesions to large amorphous irregular lesions. Lesions typically appear simultaneously with clinical presentation. However delayed appearance of MRI abnormalities upto 01 month after clinical symptom onset has been described [5]. So a normal MR image within first few days after symptom onset suggestive of ADEM doesn't exclude the diagnosis [5].Contrast enhancement in lesions of ADEM is variable and has been reported in 30% to 100% of patients with ADEM in nonspecific pattern (nodular, diffuse, gyral, complete or incomplete ring) (Figure 2).

Proposed commonalities in ADEM MR imaging appearance
- Bilateral asymmetric/symmetric involvement (rarely unilateral)
- White matter>gray matter, but usually both affected
- Deep/juxtacortical white matter>periventricular white matter
- Both supratentorial and infratentorial lesions (less commonly either/or)
- Small>medium>large, but often all sizes are present in same patient
- Variable contrast enhancement

Spinal cord involvement in ADEM has been described in 11% to 28% cases. Typical spinal cord lesion is large and swollen, showing variable enhancement and predominantly affects the thoracic region [10]. Complete resolution of MRI abnormalities after treatment has been described in 37% to 75% of patients with ADEM and partial resolution in 25% to 53% of patients. It is suggested that reassessing the patient with at least two additional MRI after first normal MRI over a period of 05 yrs from initial attack, is the appropriate way to confirm the absence of ongoing accrual of lesions.

A review of MRI is specifically targeted for the following:
1) Absence of diffuse bilateral lesion pattern, 2) Presence of two or more periventricular lesions, as these criteria allowed distinction of patients with MS in the first attack from patients with monophasic ADEM, with a sensitivity of 81% and a specificity of 95%.

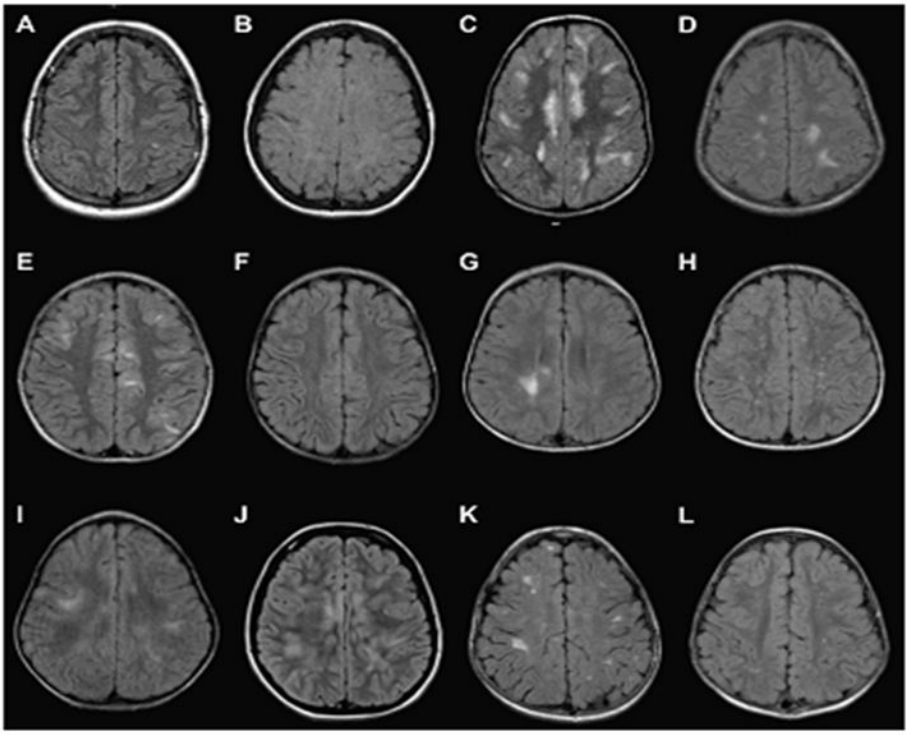

Figure 2: Axial FLAIR images of brain showing multiple hyperintense (demyelinating) lesions of ADEM involving different areas of cerebral hemispheres

Computed Tomography (CT) of the Brain

Few studies comment on CT findings in ADEM. Most studies indicate that CT is unrevealing when completed early in the disease and that the imaging modality is insensitive for smaller demyelinating lesions. The most common reported abnormalities are discrete, hypodense areas within cerebral white matter and juxtracortical areas.

Other advanced MR imaging modalities:

MR Spectroscopy (MRS)

Within acute phase an elevation of lipids and reduction of myoinositol/creatine ratio has been reported, with no change in N-acetylaspartate (NAA) or choline values. As disease progresses there is reduction of NAA and increase in choline (with corresponding reduction in NAA/creatine and NAA/ choline ratio) in regions corresponding to areas of high signal intensity onT2 weighted imaging [19,20]. This findings suggest a transitional neuronal loss and is in contrast to the situation in MS, whereby there is prompt choline elevation caused by increased level of myelin breakdown products, glycerophosphocholine and phosphocholine [21].

Diffusion Weighted (DW) Imaging

DW changes are variable and highly dependent on the stage of the disease. If DW image is completed within first 07days of clinical onset a pattern of restricted diffusion may sometimes be seen which subsequently changes to a pattern of increased diffusion thereafter.

Materials & Method

A prospective, observational study was conducted in neurology department of Chittagong Medical College Hospital (CMCH) for 18 (Eighteen) months from May 2014 to November 2015, patients who were clinically and radiologically diagnosed as ADEM. Inclusion criteria were all ADEM patients admitted in Chittagong medical college hospital, and exclusion criteria were ADEM patients with previous history of stroke, ADEM patients who received steroid before our initial assessment and patient unwill to participate in the study.

Procedure of the Study

After history taking, thorough clinical examination & consistent MRI findings, study population was selected fulfilling the inclusion and exclusion criteria. All patients or their 1st degree relatives were informed about our study and written witnessed consent was taken from them. Common routine & relevant investigations were done for those hospital admitted ADEM patents. MRI of brain with or without whole spine survey were done by GE 1.5 Tesla 16 channel (HDXT) MRI machine considering clinical pattern of involvement and were reported by qualified radiologist. For lumbar puncture and CSF study consent was taken from conscious

and mentally sound patients or from guardian of others. 44 patients gave consent and 06 denied. 02ml of CSF was collected in left lateral position with aseptic precaution and CSF was studied only for cytology, biochemistry and bacteriology. The CSF study results were added in supporting investigational parameters of ADEM. All of our study population were managed with currently recommended, easily available, cost effective treatment i.e. IV methylprednisolone (10 to 30 mg/kg/day, maximum 1 g/day) for 05 (five) days followed by gradually tapering of oral prednisolone (1mg/kg/day) for total 06 (six) weeks. IV methylprednisolone was started immediately after diagnosis of ADEM was confirmed with fulfillment of ADEM diagnostic criteria.

For short term motor outcome disability status was measured using mRS (modified Rankin Scale), other motor components by using motor outcome variable chart that included-Glasgow coma scale (GCS), motor aphasia, cranial nerve palsy, motor system examination findings, number of motor seizure, etc., These components of motor variables were assessed initially during enrolment of cases in our study. After acute management for few days to weeks most patients were to discharge from hospital and asked to come for follow up in neurology department at 06 weeks after completion of oral steroid course. Contact number of all study cases or of their close caregivers were noted. At 06 weeks we found 37 patients were alive, 12 died of and 01 dropped out. Among 37 patients most were improved and came in neurology department. During follow up initially assessed neurological parameters i.e. mRS, motor variables were reassessed by the researcher himself with direct supervision of assistant professor of neurology department of CMCH.

After obtaining written informed permission from ethical committee of CMCH, all data were collected and were processed by computer based statistical analysis using windows computer software devise with SPSS- 20. The numerical values of our study were expressed in mean, median, standard deviation and comparison was done by t-test, whereas those of categorical values were expressed in number, percentage and comparison was done by chi square (χ^2) test. Statistical significance was set at $p<0.05$ & confidence interval at 95% level.

Results and Observation

Table 1 indicates improved outcome at 06 weeks is highly significant ($p<0.001$) in middle class group but it is not significant ($p>0.05$) in male gender and >40 years population.

Socio-demographic Variables		Outcome		Total (n=50)	χ2 Test Significance
		Improved (n=37)	Death & Others (n=13)		
		n (%)	n (%)	n (%)	
Age Group	<40 Years	13 (35.1)	1 (7.7)	14 (28.0)	$\chi2=3.594$ $P=0.058^{NS}$
	≥40 Years	24 (64.9)	12 (92.3)	36 (72.0)	
Sex	Male	20 (54.1)	6 (46.2)	26 (52.0)	$\chi2=0.241$ $P=0.624^{NS}$
	Female	17 (45.9)	7 (53.8)	24 (48.0)	
Socio-economic Condition	Middle Class	27 (73.0)	4 (30.8)	31 (62.0)	$\chi2=7.273$ $P=0.007^{HS}$
	Lower Class	10 (27.0)	9 (69.2)	19 (38.0)	

*NS = Not Significant (P>0.05); HS = Highly Significant (P<0.001)

Table 1: Association between socio-demographic variables and outcome among the study subjects

Table 2 shows highly significant ($p<0.001$) improvement of mRS at 06 weeks and 83.8% patients has got favorable mRS at 6 weeks.

	modified Rankin Scale					
	N	MEAN	± SD	MEDIAN	RANGE	SIGN.*
Initial	37	4.30	0.78	4.00	3–5	t=12.552
After Treatment at 6 Weeks	37	1.89	1.35	2.00	0–4	$P<0.001^{HS}$

*Paired samples t-test. HS = Highly Significant (P<0.001)

Among Improved Subjects (n=37)	modified Rankin Scale	
	Favorable mRS (0-3)	Unfavorable mRS (4-5)
	n (%)	n (%)
Initial	7 (18.9)	30 (81.1)
After Treatment at 6 Weeks	31 (83.8)	6 (16.2)

Table 2: *Distribution of modified *Rankin Scale (mRS)* for assessment of motor outcome among the improved study subjects (with t-test significance)

Table 3 shows highly significant improvement in GCS (initial range 4-15 improved into 9-15 at 06 weeks).

	Glasgow Coma Scale (GCS)					
	N	MEAN	±SD	MEDIAN	RANGE	SIGN.*
Initial	37	10.41	3.23	11	4–15	t=7.408
After Treatment at 6 Weeks	37	14.32	1.47	15	9–15	P<0.001^{HS}

* Paired samples t-test. HS = Highly Significant (P<0.001)

Table 3: *Distribution of *Glasgow Coma Scale* (GCS) for assessment of motor outcome among the improved study subjects (with t-test significance)

Highly significant improvement of Best motor response component of GCS is seen Table 4 (initial range 2-6 improved into 4-6 at 6 weeks).

	Best Motor Response					
	N	MEAN	±SD	MEDIAN	RANGE	SIGN.*
Initial	37	4.35	1.34	4	2–6	t=6.799
After Treatment at 6 Weeks	37	5.76	0.55	6	4–6	P<0.001^{HS}

*Paired samples t-test. HS = Highly Significant (P<0.001)

Table 4: Distribution of *Best motor response of GCS* for assessment of motor outcome among the improved study subjects (with t-test significance)

Table 5 shows highly significant improvement of Muscle Power in Upper & Lower limbs.

	Muscle Power (Upper Limb)					
	N	MEAN	± SD	MEDIAN	RANGE	SIGN.*
Initial	37	2.81	0.94	3	1-5	t=12.421
After Treatment at 6 Weeks	37	4.43	0.80	5	2-5	P<0.001^{HS}

* Paired samples t-test. HS = Highly Significant (P<0.001)

	Muscle Power (Lower Limb)					
	N	MEAN	± SD	MEDIAN	RANGE	SIGN.*
Initial	37	2.73	0.90	3	1-5	t = 11.453
After Treatment	37	4.35	0.89	5	2-5	P<0.001^{HS}

Table 5: Distribution of *Muscle Power* in affected limbs for assessment of motor outcome among the improved study subjects (with **t**-test significance)

Deep Tendon Reflex in Upper Limb (After Treatment at 6 Weeks)	Deep Tendon Reflex in Upper Limb (Initial)			Total (n=37)	χ2 Test Significance
	Brisk (n=22)	Normal (n=13)	Reduced (n=2)		
	n (%)	n (%)	n (%)	n (%)	
Brisk (n=13)	13 (59.1)	0 (0.0)	0 (0.0)	13 (35.1)	χ2=49.919 P<0.001^{HS}
Normal (n=22)	9 (40.9)	13 (100.0)	0 (0.0)	22 (59.5)	
Reduced (n=2)	0 (0.0)	0 (0.0)	2 (100.0)	2 (5.4)	

*HS = Highly Significant (P<0.001)

Deep Tendon Reflex in Lower Limb (After Treatment at 6 Weeks)	Deep Tendon Reflex in Lower Limb (Initial)			Total (n=37)	χ2 Test Significance
	Brisk (n=22)	Normal (n=12)	Reduced (n=3)		
	n (%)	n (%)	n (%)	n (%)	
Brisk (n=13)	13 (59.1)	0 (0.0)	0 (0.0)	13 (35.1)	χ2=49.494 P<0.001^{HS}
Normal (n=21)	9 (40.9)	12 (100.0)	0 (0.0)	21 (56.8)	
Reduced (n=3)	0 (0.0)	0 (0.0)	3 (100.0)	3 (8.1)	

*HS=Highly Significant (P<0.001) Improvement of deep tendon reflexes in all four limbs is highly significant as shown in Table 6.

Table 6: Association between *Deep Tendon Reflexes* in affected limbs at initial phase and after treatment at 06 weeks among the study subjects (with χ2test significance)

Table 7 shows highly significant change of plantar reflex at 06 weeks.

Plantar Reflex (After Treatment at 6 Weeks)	Plantar Reflex (Initial)		Total (n=37)	χ2 Test Significance
	Extensor (n=28)	Flexor (n=9)		
	n (%)	n (%)	n (%)	
Extensor (n=15)	15 (53.6)	0 (0.0)	15 (40.5)	χ2=8.109 P=0.004^{HS}
Flexor (n=22)	13 (46.4)	9 (100.0)	22 (59.5)	

*HS = Highly Significant (P<0.01)

Table 7: Changes of *Plantar Reflexes* at initial phase and after treatment at 06 weeks among the study subjects (with χ2 test significance)

32% of study population got cranial nerve palsy and mostly it was right facial nerve (upper motor neuron lesion) and among improved 37 patients, 05 (**13.5%**) patients had residual cranial nerve palsy at 06 weeks as shown in Table 8.

Cranial Nerve Involvement	*At Initial Phase*	*After Treatment at Six Weeks*
	n (%)	*n (%)*
VII (Right)	8 (16.0)	3 (8.1)
VII (Left)	7 (14.0)	2 (5.4)
VII (Right), IX, X, XI	1 (2.0)	0 (0.0)
Nil	34 (68.0)	32 (86.5)
Total	**50**	**37**

Table 8: *Distribution of motor or motor part of mixed *Cranial Nerve involvement* at initial phase and after treatment at 06 weeks among the study subjects

Table 9 shows significant improvement of Cranial Nerve palsy at 6 weeks.

Cranial Nerve Palsy (After Treatment at 6 Weeks)	Cranial Nerve Palsy (Initial)		Total (n=37)	χ2 Test Significance
	Present (n=16)	Absent (n=21)		
	n (%)	n (%)	n (%)	
Present (n=5)	5 (31.3)	0 (0.0)	5 (13.5)	χ2=5.150 P=0.023^{S}
Absent (n=32)	11 (68.7)	21 (100.0)	32 (86.5)	

*S = Significant (P<0.05)

Table 9: Association between motor or motor part of mixed *Cranial Nerve palsy* at initial phase and after treatment at 06 weeks among improved study subjects (With χ2 test significance)

Table 10 shows significant improvement of motor seizure.

	No. of Motor Seizures					
	N	MEAN	± SD	MEDIAN	RANGE	SIGN.*
Initial	37	2.14	5.09	**0**	0–20	t = 2.549 P = 0.015^{S}
After Treatment	37	0.00	0.00	0	–	

S = Significant (P<0.05)

Table 10: Distribution of *motor seizures* for assessment of motor outcome among the improved study subjects (with t-test significance)* Paired samples t-test

Regarding motor aphasia Table 11 denotes non-significant (P>0.05) change after 06 weeks.

Motor Aphasia (After Treatment at 6 Weeks)	Motor Aphasia (Initial)		Total (n=37)	χ2 Test Significance
	Present (n=9)	Absent (n=28)		
	n (%)	n (%)	n (%)	
Present (n=1)	1 (11.1)	0 (0.0)	1 (2.7)	χ2=3.198 P=0.074^{NS}
Absent (n=36)	8 (88.9)	28 (100.0)	36 (97.3)	

*NS = Not Significant (P > 0.05)

Table 11: Association between *motor aphasia* at initial phase and after treatment at 06 weeks among improved study subjects (with χ2test significance)

Conclusion

In Chittagong Medical College Hospital from May 2014 to November 2015 we included 50 patients in our observational, prospective study. Among 50 patients, 37 patients were eligible for follow up. 12 (24%) died of and 01 (2%) dropped out. During follow up (i.e., second assessment after six weeks) initially assessed parameters were reassessed in neurology ward of CMCH. The profile of Socio demography of the study reflects that most study subjects (56%) were of 40-60 years age group. Table 1 demonstrates association between selected socio-demographic variables and outcomes among the study subjects. Here we found highly significant ($p<0.001$) association of improved outcome in middle class group.

Table 2 shows that among 37 improved patients initial favorable mRS score (0-3) found in 07 (18.9%) patients, whereas 30 patients (**81.1%**) had unfavorable mRS (4-5). After treatment with 06 weeks steroid course these figures significantly improved into favorable mRS in **83.8%** patients and unfavorable mRS in 16.2%. We also observed unfavorable mRS in 11 and favorable mRS in 01 patient initially who later died of during 6 weeks follow up period. Previous study results showed good outcome in 50-75% patients and favorable mRS in 80-90% cases [1,3,5,8-10]. In our study improvement was 74% and favorable mRS was in **83.8%** patients which are closed to previous study results done in abroad.

To date very few studies were focused particularly on motor outcome variables of nervous system examination for ADEM patients. Though previous studies in different countries and in different age group showed overall favorable prognosis of motor outcome, we analyzed here systematically considering individual components of motor outcome variables, like- Best motor response of GCS, motor or motor part of mixed cranial nerves, muscle power in MRC grade, deep tendon reflexes, plantar response, motor seizure and overall functional status in modified Rankin scale (mRS). As motor components are affected predominantly in ADEM patients and chief cause of morbidity and mortality our study results could provide a better and elaborative understanding of individual motor variables in ADEM patients.

Table 3 shows range of GCS among 37 improved patients. Initial range of GCS was 4-15 which had improved into 9-15. $p<0.001$ indicates highly significant improvement of GCS score at 06 weeks. Table 4 shows range of best motor response among improved (37) patients. Initial range of 2-6 had improved into 4-6 at 06 weeks. Here $p<0.001$ reflects highly significant improvement of best motor response of GCS. Table 5 describes initial range of muscle power among improved 37 patients in upper & lower limbs were 1-5 which improved into 2-5 after 06 weeks. This highly significant improvement of muscle power in MRC grade could aided in fast recovery of motor disability and favorable mRS at 06 weeks.

Table 6 & 7 describe highly significant changes of DTR and plantar reflexes. Improvement of these clinical signs may serve powerful indicator of improvement of upper motor neuronal lesion in affected parts of the body and ultimately overall short term motor outcome of ADEM patients.

Among 50 patients Table 8 shows in 32% cases motor or motor parts of mixed cranial nerve were involved, which is in accordance with recently published study [10]. The commonest affected one was facial nerve (upper motor neuron lesion).Table 9 denotes improvement of cranial nerve palsy among 37 followed up patients. Here we found significant improvement ($p<0.05$). Among 16 cranial nerve affected patients 11 (68.75%) improved at 06 weeks. Table 10 indicates significant improvement of motor seizure whereas Table 11 reflects that in ADEM patients motor aphasia was not improved significantly ($p>0.05$) at 06 weeks. Considering all of these variables (numerical and categorical) it can be said that outcome particularly motor outcome was very good in our study which is very close to previous study results [1,3,8].

So motor outcome of our ADEM patients at 06 weeks of steroid determined by mRS and motor outcome variable chart was very good though it differs in some aspects of different regions of the body. Finally, we can say, short term motor outcome was good in 74% of patients which is highly significant.

Limitations

1. Pediatric age group of ADEM patients were not extensively searched out.
2. Most study populations were not provided with 06 weeks hospital stay care management.
3. Sample of our study was only 50 (Fifty) which might not reflect real situation.
4. OCB in CSF was not evaluated as it was very costly and not easily available investigation.

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