



# Evaluation of demographic, clinical and paraclinical characteristics of children with acute disseminated encephalomyelitis

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**Keywords:** Acute disseminated encephalomyelitis, Children, Viral infection

## Abstract

**Introduction:** Acute disseminated encephalomyelitis (ADEM) is an immunologically mediated inflammatory demyelinating disorder that commonly occurs following a viral infection or vaccination.

**Objectives:** This study aimed to evaluate the demographic, clinical and paraclinical characteristics of children with ADEM.

**Patients and Methods:** In a retrospective study, all children who had a definite diagnosis of ADEM were included in the study. Demographic information (including age and gender), epidemiological features (season of onset, history of previous vaccination and previous infection), clinical signs of ADEM, paraclinical features and also clinical outcomes were extracted from patients' records and entered into a researcher-made checklist. All data were collected, classified and entered into SPSS version 21 for statistical analysis.

**Results:** A total of 27 patients with ADEM were studied out of which, 16 (59.3%) were male and 11 (40.7%) were female. The mean age of patients was  $5.21 \pm 4.37$  years, the youngest of which was three months and the oldest patient had 13 years old. The highest incidence (33.3%) was observed in autumn and 66.7% of patients had a history of recent infection. Electroencephalographic (EEG) findings were abnormal in 55.6% of patients. The most common clinical finding of abnormal EEG was motor disorders (51.8%). Among those who conducted MRI, 71.4% of them had cortical lesions in the brain. In the majority of cases (51.9%), the treatment achieved with intravenous immunoglobulin (IVIG) alone and complete recovery.

**Conclusion:** The ADEM in this region has relatively similar epidemiological features to those studied worldwide and the favorable treatment of our cases has led to a satisfactory percentage of complete clinical recovery.

**Keywords:** Acute disseminated encephalomyelitis, Children, Viral infection

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## Introduction

Acute disseminated encephalomyelitis (ADEM) is an immunologically mediated inflammatory demyelinating disorder that commonly occurs following a viral infection or vaccination. The clinical symptoms include a range of mild neurological disorders to rapid and fulminant outcomes (1). Symptoms of ADEM often include various neurological and systemic symptoms. Neurological disorders are usually multifocal and often involve changes in mental status and/or altered levels of consciousness (2). Often before encephalopathy, lethargy, headache and vomiting occur. The onset of neurological symptoms is sudden and is characterized by focal motor symptoms, altered levels of consciousness or both (3). Peripheral nerve disorders have also been reported in some cases (4). ADEM can occur at any age, however most cases have reported an average age of between 5 and 8

## Key point

Acute disseminated encephalomyelitis is accompanied by abnormal electroencephalographic findings. The most common clinical finding of abnormal EEG was motor disorders and almost most of them have cortical lesions in the brain.

years with mild male gender preference. The reported incidence in the pediatric population is between 0.07 and 0.4 per 100 000 per year. Many patients experience a temporary fever before ADEM occurs (5). Magnetic resonance imaging (MRI) shows a significant increase in signal in white matter. The corpus callosum and regions around the ventricle are usually involved. The cerebrospinal fluid (CSF) is often normal. Rare malformations include mild lymphocytic pleocytosis and



increased protein concentration (3).

High-dose intravenous methylprednisolone therapy is helpful in approximately 50% of cases (3). ADEM may reveal as a single lesion, however, 10%–29% of children with early-onset of ADEM will have additional attacks of myelin elimination (6). The prognosis and response to treatment vary in this disease. Childhood ADEM often has favorable outcomes and complete clinical recovery is expected in these conditions, while serious complications in childhood ADEM are rare (2,7). However, a significant recurrence rate of about 2% to 29% has been reported for this disease (8,9). ADEM is also the first manifestation of multiple sclerosis (MS), which may occur in 0% to 57% of cases (7,9).

Some studies on the characteristics of this disease in the region and especially in our country are not comprehensive and therefore accurate information on the status of this disease in order to manage health planning is important. In one study, the most common early manifestations were ataxia (60%), altered consciousness (60%), fever and vomiting (46%). CSF abnormalities were found in 70% of patients. MRI revealed brain lesions in 93% of subcortical white matter, 80% of the cerebral cortex, 59% in the white matter around the ventricle and 47% in the cerebral cortex and deep gray matter (10). On the other hand, Pohl et al conducted a study on 28 patients under the age of 16 with ADEM in Germany. They found that 65% of patients had CSF pleocytosis with a mean of CSF white blood cell count of 28/ $\mu$ L and a protein of 40 mg/dL. Additionally, MRI lesions were reported in 86% of cases. They estimated the incidence of ADEM in children under the age of 16 in Germany to be 0.07 per 100 000 of population per year (11).

### Objectives

The present study was designed to evaluate the demographic, clinical and paraclinical characteristics of ADEM among patients referred to a hospital in Urmia during 2010-2016.

### Patients and Methods

#### Study design and participants

This retrospective study was performed on children with ADEM who referred to Shahid Motahari hospital of Urmia from 2010 to 2016 through a convenience sampling method. All children who had a definitive diagnosis of ADEM were included in the study. Accordingly, all patient records were extracted from the hospital archive and reviewed by a senior medical student (intern). Incomplete, unable to be read records and uncertain cases were excluded. Demographic information (including age and gender), epidemiological features (season of onset, history of previous vaccination and previous infection), clinical signs of ADEM, paraclinical features (including findings obtained from electroencephalography, MRI, CSF fluid analysis, peripheral blood test, erythrocyte sedimentation

rate (ESR) and C-reactive protein (CRP) and clinical outcomes (recovery with neurologic complications, complete recovery and mortality) were extracted from patient records and if needed, by contact with patients and entered into a researcher-made checklist.

### Ethical issues

Human rights were respected in accordance with the Helsinki Declaration 1975, as revised in 1983. The informed consent was taken from the patients. The study was approved by ethics committee of Urmia University of Medical Science (Ethical cod# IR.UMSU.REC.1396.175). This study was extracted from the medical thesis of Tohid Nasiri at this university (Thesis #96-09-32-2933).

### Statistical analysis

All data were collected and entered into SPSS version 21. Descriptive data were presented in frequency (percentage), mean  $\pm$  standard deviation, table and frequency graph.

### Results

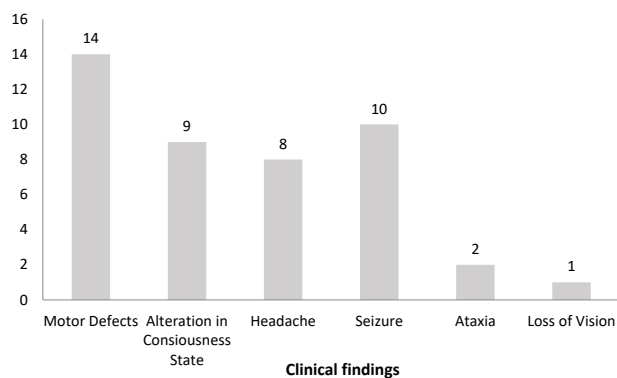
In this study, a total of 27 patients with ADEM were studied. Of them, 16 (59.3%) were male and 11 (40.7%) were female. The mean age of all patients was  $5.21 \pm 4.37$  years, the youngest of which had three months old and the oldest of them was 13 years old. Four patients (14.8%) were infected in spring, six patients (22.2%) in summer, 9 patients (33.3%) in autumn and 8 patients (29.6%) in winter. Among them, 18 patients (66.7%) reported a history of recent infection (up to a month ago) and 9 patients (33.3%) did not report. Four patients (14.8%) had a history of recent vaccination (up to a month ago) and 23 patients (85.2%) did not mention such a history. Only 9 cases (33.3%) had electroencephalography in the patients' records, of which the results of four patients (44.4%) were normal and the results of five patients (55.6%) were abnormal. In terms of CSF fluid lymphocyte level, the mean lymphocyte level was  $10.13 \pm 25$  %, since the lowest being zero and the highest being 98%. Thus, 12 (80%) of the CSF cases showed normal lymphocyte count (below 5%) and 3 (20%) showed abnormal lymphocyte count (above 5%) (Table 1).

Clinical findings also showed motor disorder in 14 cases (51.8%), altered consciousness in 9 cases (33.3%), headache in 8 cases (29.6%), seizures in 10 cases (37%), ataxia in 2 cases (7.4%) and visual loss in one case (3.7%) (Figure 1). In terms of polymorphonuclear counts in CSF fluid, the mean polymorphonuclear count was  $5.13 \pm 13.45$  ( $\times 1000/\text{mm}^3$ ) with the lowest being zero and the highest being  $45$  ( $\times 1000/\text{mm}^3$ ). Moreover, in 13 cases (86.7%) the polymorphonuclear count in CSF fluid was normal (zero) and in two cases (13.3%) was abnormal (greater than zero) (both of which were due to being highly bloody as shown in Table 2).

CSF protein levels were normal (less than 40 mg/dL) in nine cases (60%) and abnormal in six cases (40%) and

**Table 1.** Frequency distribution of patients by season

Variable		Absolute frequency	Relative frequency
Season	Spring	4	14.8%
	Summer	6	22.2%
	Autumn	9	33.3%
	Winter	8	29.6%
Recent infection history	Yes	18	66.7%
	Female	9	33.3%
Recent vaccination history	Yes	4	14.8%
	No	23	85.2%
Electroencephalogram	Normal	4	44.4%
	Abnormal	5	55.6%
Lesion site in MRI	Brain cortex	10	71.4%
	Midbrain	1	7.1%
	The areas around the ventricle	1	7.1%
	Brain stem	1	7.1%
	Basal ganglia	1	7.1%

**Figure 1.** Frequency distribution based on clinical findings.

in terms of glucose levels in CSF fluid, all 15 CSF fluid samples (100%) had normal glucose levels.

The mean ESR level in all patients was  $32.66 \pm 26$  mm/h, the lowest being 3 mm/h and the highest of which being 108 mm/h. Therefore, ESR levels were normal (less than 30 mm/h) in five cases (18.5%) and abnormal (more than 30 mm/h) in 22 (81.5%) patients. The mean CRP level was  $12.15 \pm 20.61$  mg/L in all patients, the lowest of which was zero and the highest was 70 mg/L. Thus, CRP levels in 19 patients (70.4%) were normal (below 10mg/L) and in 8 patients (29.6%) were abnormal (above 10 mg/L). In terms of leukocytosis level, the mean leukocytosis level was  $5671.59 \pm 3824.11/\mu\text{L}$ . The lowest amount of it was 1500/ $\mu\text{L}$  and the highest amount was 16643/ $\mu\text{L}$ . Therapeutic modality in 14 patients (51.9%) was intravenous immunoglobulin (IVIG) alone, in 8 patients (29.6%) pulse cortisone alone and in 5 patients (18.5%) was both IVIG and pulse cortisone in combination (Table 2).

**Table 2.** Frequency distribution for polymorphonuclear counts of CSF liquid

Variable		Absolute Frequency	Relative frequency
Lymphocyte counts CSF	Normal	12	80%
	Abnormal	3	20%
PMN counts in CSF	Normal	13	86.7%
	Abnormal	2	13.3%
Protein concentration in CSF	Normal	9	60%
	Abnormal	6	40%
CSF liquid glucose	Normal	15	100%
	Abnormal	0	0
Level (mm/hr) ESR	Normal	5	18.5%
	Abnormal	22	81.5%
Level (mg/L) CRP	Normal	19	70.4%
	Abnormal	8	29.6%
Therapeutic modality	IVIG	14	52.9%
	Pulse cortisone	8	29.6%
	Both	5	18.5%

## Discussion

Encephalomyelitis following infection is a common childhood central nervous system disorder that is responsible for 10 to 15% of all acute encephalitis in the United States (9). ADEM is an immunologically mediated inflammatory demyelinating disorder that commonly occurs following a viral infection or vaccination. The underlying pathology affects the white matter of the central nervous system. The clinical symptoms of this disease are wide, ranging from mild neurological dysfunction to rapid and fulminant outcomes. The prognosis and response to treatment vary. Childhood ADEM often has favorable outcomes and complete clinical recovery is expected (14). However, studies on the characteristics of this disease in the region and especially in Iran are not comprehensive and therefore accurate information on the status of this disease to manage health planning is important. Therefore, our study was designed to evaluate the demographic, clinical and paraclinical characteristics of ADEM among patients referred to Motahari hospital of Urmia between 2010 -2016.

As a result of this study, a total of 27 patients with a diagnosis of ADEM were referred to our center in this period. The mean age of all patients was  $5.21 \pm 4.37$  years. The majority of patients were male (59.3%). The prevalence of the disease was mostly in autumn (33.3%) and 66.7% of patients had a history of a recent respiratory tract infection. Electroencephalographic (EEG) findings were abnormal in 55.6% of those who conducted the electroencephalogram. The most common clinical findings were motor disorders with 51.8% prevalence. Among the patient who conducted MRI, 71.4% had cortical lesions. In the majority of cases (51.9%) only IVIG treatment was applied with complete recovery in 92.6%.

In the study by Murthy et al (13), the authors studied 18

children with ADEM in New York, similar to the present study, 72% of patients had recent upper respiratory tract disease. In the present study, however 66.7% of patients had a history of recent infection. In a study by Samile and Hassan et al (10), 46.4% of patients had a history of upper respiratory tract disease while similar to our study; a low percentage (13.6%) had a recent vaccination history. Therefore, it can be concluded that recent infection in children can be considered as one of the causes in association with or before ADEM.

We also found gender predominance was favored by the males, whereas in similar studies, including the study by McDonald et al (17), Murthy et al (13), Chakravarty (18) and Ozawa et al (19) there was no gender prevalence. Although the prominence was not very significant in our study, it points out to a different distribution of the disease across the region.

The study by Lin et al (15) showed, among the 42 ADEM patients, the most common symptoms included muscle weakness and loss of speech and bulbar symptoms. In the study by Visudtibhan et al (14), the authors examined 16 patients with ADEM, which 31.3% of the patients had pleocytosis and 31.3% showed increased protein in CSF fluid. We found elevated protein levels of CSF fluid in 55.6% of the patients while pleocytosis was observed in 13.3% of them. Similarly in the study of Lin et al (15) CSF abnormalities including pleocytosis and total protein increase were reported in 66.7% of children. Accordingly, in the study of Torisu et al (16), pleocytosis and increased protein in CSF fluid were reported in 81% and 35% of the patients with ADEM, respectively. The cause of the differences in reported prevalence can be explained by differences in studied populations and consequently racial differences between studied populations, differences in laboratory kits along different time periods of study.

The study by Anlar et al (8), examined the outcomes and prognosis of ADEM in children. They found among 46 patients with this disease who were followed for one year, 71% had a complete recovery. In similar studies also, the complete recovery interval ranged from 57 to 81% (2,20-22). However, our results showed the overall recovery rate was 92.6%.

This percentage primarily reflects the good performance of the studied center in the treatment of patients with ADEM, however compared to the higher percentage than the global average, it can be attributed to the lower sample size, lower follow-up time and different criteria in studies to define complete recovery of the disease.

## Conclusion

It can be concluded that ADEM in this region has relatively similar epidemiological features to those in the world studied and the favorable performance of the region's treatment system has resulted in a satisfactory percentage of complete clinical outcomes in these patients. Therefore, it is recommended that current treatment in the future be

maintained in the region and such studies be carried out in different regions of the country by examining higher sample sizes and also cohort studies should be conducted to follow longer-term complications.

## Limitations of the study

Totally, 27 patients with ADEM were studied. The major limitation of this study is small sample size due to the rarity of the disease.

## Authors' contribution

AG and EA were the main investigators, collected the data and wrote the first draft. TN and HM designed the study, and also read and corrected the draft. All authors read and signed the final manuscript.

## Conflicts of interest

The authors declare that they have no conflicting interest.

## Ethical considerations

Ethical issues (including plagiarism, double publication) have been completely considered by the authors.

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