



Acquired demyelinating disorders of the central nervous system in a sample of Egyptian children

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ABSTRACT

Acquired demyelinating syndrome (ADS) is a group of inflammatory immune-mediated attacks on the central nervous system's (CNS) myelin sheath, presenting as optic neuritis or transverse myelitis. The study aimed to studying ADS in children is growing, with implications for better management and outcome. This is a cross-sectional study analyzing patients with neuro-immune diseases at Al-Azhar University hospitals under 18 years old with CNS inflammatory demyelination. They undergo comprehensive medical and neurological examinations, with follow-up data collected at six-months post-onset. Diagnosis requires AQP4 antibody, clinical criteria, and additional magnetic resonance imaging (MRI) requirements. The study included 59 patients with ADS; 46 % were diagnosed with acute disseminated encephalomyelitis (ADEM), 14 % had clinically isolated syndrome (CIS), 14 % had myelin oligodendrocyte glycoprotein antibody disease (MOGAD), 20 % had multiple sclerosis (MS), and 6.8 % had neuromyelitis optica spectrum disorder (NMOSD). Most participants were urban residents. Clinical presentation showed encephalopathy in 55.9 % of participants, with ADEM having the highest prevalence (93 %). Motor symptoms were prevalent in 84.7 %, with sensory symptoms highest in the NMOSD group. Cerebellar symptoms were reported by 52 %, with ADEM having the highest rate (74 %). 20.3 % of cases had brain abnormalities on MRI scans, with no significant difference between groups. In conclusion this study provides detailed information on pediatric ADS (PADS) patients in Egypt, a developing country lacking research coverage. It investigates clinical profiles, laboratory findings, treatment, and prognosis. However, limitations include a single center experience, potential information bias, and short follow-up duration, highlighting the need for more longitudinal multicenter studies.

Introduction

Acquired demyelinating syndrome (ADS) is a set of various disorders that share the character of inflammatory demyelinated immune-mediated attacks to the central nervous system (CNS) myelin sheath [1]. It can be classified based on the disease course as either monophasic or relapsing. Monophasic ADS includes acute disseminated encephalomyelitis (ADEM) and clinically isolated syndrome (CIS) with the presentation of optic neuritis (ON) or transverse myelitis (TM), whereas the relapsing group has multiphasic disseminated encephalomyelitis (MDEM), multiple sclerosis (MS), neuromyelitis Optica spectrum disorders (NMOSD), and myelin oligodendrocyte antibody (MOG-Ab) associated disease [2,3]. It can be further classified depending on the MRI showing localization of neurological deficits to monofocal lesions like ON or TM or polyfocal lesions such as MS, ADEM, and NMOSD [2, 4]. While the greater attention of this syndrome in the literature is given

to the adults, there is an uprising interest in studying it in children [5].

With an annual incidence ranging from 0.5 to 1.66 per 100,000 children, pediatric acquired demyelinating syndromes (PADS) is considered a very rare disease [6]. Given this rarity, efforts have been made by the International Pediatric MS Study Group (IPMSSG) to facilitate collaboration in that area and propose revised PADS criteria through a consensus process [7].

Neurological impairment is the hallmark presentation of PADS, gathering under it several symptoms like sensory deficits, motor weakness, and visual disturbance [5]. Although literature lack is noticed in our setting, there are trials in other geographical areas to describe PADS and estimate its frequency [5]. Castañeda et al. conducted a retrospective cross-sectional study in the Philippines, another developing country, in which they describe the frequency of PADS subtypes, the clinical profiles of patients, including labs and MRI, response to treatment, and prognosis [5]. A nationwide survey was conducted in Japan and

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collected epidemiological and clinical features of PADS in Japanese hospitals between 2005 and 2007 [8].

Despite these diseases' similarities, they are considered distinct entities requiring proper early differential diagnosis because of the consequently different management protocols [9]. Additionally, there is underestimation of the disease burden in the developing countries, especially with the missed cases and unequipped facilities, requiring a worldwide collaboration to come up with suitable guidelines and cover this gap of knowledge [10]. Conducting this study at Al-Azhar University hospitals will enrich the literature with up-to-date information regarding PADS in Egypt.

Methods

This is an analytical cross-sectional study performed on patients who presented to the Neurology Department (outpatient and inpatient) at Al-Azhar University hospitals. The Medical Ethical Committees of the Faculty of Medicine, Al-Azhar University, and the University Council authorized this study.

Eligibility criteria

Patients must be under 18 years old and have experienced either a first-time or recurrent episode of central nervous system inflammatory demyelination, confirmed using the latest diagnostic criteria proposed by the International Pediatric Multiple Sclerosis Study Group (IPMSSG) [7]. On the other hand, children who have any of the following criteria were excluded: confirmed CNS infection (e.g., bacterial meningitis, viral encephalitis, HIV, Lyme disease, or herpes simplex encephalitis), chemotherapy or radiation-induced white matter damage, leukodystrophies (e.g., adrenoleukodystrophy, metachromatic leukodystrophy), CNS connective tissue disease (e.g., vasculitis, lupus), mitochondrial disease, brain neoplastic lesions, or combined central and peripheral demyelination.

Patient management

After providing written informed consent from participants' parents or guardians, ALL children with PADS underwent a comprehensive medical and neurological examination, including a detailed medical and neurological history, demographic and clinical information, and a full general and neurological examination. The examination included a cerebrospinal fluid examination, including CSF cellular count, cell differential, CSF glucose and protein levels, oligoclonal bands, IgG index, serum myelin oligodendrocyte glycoprotein antibodies (MOG), serum aquaporin-4 IgG, erythrocyte sedimentation rate (ESR), complete blood count (CBC), C-reactive protein (CRP), renal and liver functions, anti-neutrophil cytoplasmic antibody (ANCA), antinuclear antibody (ANA), lupus anticoagulant, double-stranded DNA, antiphospholipid antibodies, protein electrophoresis, and angiotensin-converting enzyme level if indicated. Neuroimaging was performed using magnetic resonance with gadolinium injections, and neurophysiological tests included visual evoked potentials, nerve conduction studies, and brain stem auditory potential. Follow-up data was collected six months after disease onset.

Diagnosis of the patients

Diagnosis of pediatric CIS required: 1) A monofocal or polyfocal prior CNS demyelinating disease absence. 2) Clinical CNS event with presumed inflammatory demyelinating cause. 3) No MS diagnosis based on baseline MRI features. 4) No encephalopathy.

MS diagnosis necessitated: 1) A minimum of two non-encephalopathic clinical CNS events with an inflammatory cause, separated by a minimum of 30 days, and affecting multiple CNS regions.

2) One ADEM attack preceded by a non-encephalopathic clinical

event. 3) A single acute event does not fulfill ADEM criteria, but the MRI findings fit with DIS and DIT criteria.

NMOSD was diagnosed using core criteria: 1) At least one core criterion in the presence of AQP4-antibody. 2) two core clinical criteria, and additional MRI requirements.

Pediatric ADEM required: 1) An encephalopathy unrelated to fever. 2) The first polyfocal clinical CNS event with an inflammatory demyelinating cause. 3) A brain MRI abnormality during the acute phase. 4) No new clinical and MRI findings. 5) A new event 3 months or more after the initial event, with no longer relevant timing for steroids.

MOG antibody-associated disease diagnosis required: 1) Serum positivity. 2) Clinical presentation involving optic neuritis, ADEM, transverse myelitis, or brain demyelinating syndrome. 3) Exclusion of alternative MOGAD diagnosis.

Statistical analysis

Patients were grouped according to the acquired demyelinating disorders. The Chi square test was used to compare categorical variables, while the Anova test was used to compare continuous variables. Frequency and percentages were used to describe the qualitative variables, while quantitative variables were described using mean and standard deviation.

Results

Demographic characteristics

Initially, 101 patients who had symptoms indicating demyelinating diseases were evaluated to determine if they met the criteria for inclusion. Out of these, 42 patients were eliminated. As a consequence, 59 patients had demyelination diseases (ADS). Among the patients included in the study, 27 (46 %) were diagnosed with acute disseminated encephalomyelitis (ADEM), eight (14 %) had clinically isolated syndrome (CIS), eight (14 %) had myelin oligodendrocyte glycoprotein antibody disease (MOGAD), 12 (20 %) had multiple sclerosis (MS), and four (6.8 %) had neuromyelitis optical spectrum disorder (NMOSD). There were no notable disparities in the demographic characteristics among the disorders. The age was 9.93 ± 3.66 years. The cohort consisted of 51 % males and 49 % females. Urban residency was the prevailing characteristic among all categories, with a majority of 73 %. Merely a minor fraction of individuals indicated a favorable familial history of demyelinating disorders, with a comprehensive prevalence of 3.4 %, the majority of which were observed in the MS group. 32 % of the subjects experienced an infection, and 12 % of the individuals had received a vaccination within the last four weeks as shown in [Table 1](#).

Clinical presentation

Encephalopathy was observed in 55.9 % of participants, with the ADEM group exhibiting the highest prevalence (93 %) ($p < 0.001$). Motor symptoms were prevalent, afflicting 84.7 % of participants, and there were no significant inter-group differences ($p = 0.32$). In the NMOSD group, the greatest prevalence of sensory symptoms was observed (100 %) ($p = 0.026$), and 50.8 % of all participants reported them. The overall cohort exhibited optic symptoms in 29.3 % of cases, with MOGAD having the greatest incidence at 62 %. Cerebellar symptoms were reported by 52 % of participants, with a significantly higher prevalence in the ADEM group (74 %; $p < 0.001$). Seizures were observed in 45.8 % of participants, with the ADEM group experiencing the highest rate at 70 % ($p < 0.001$). Sphincteric symptoms were reported by 67.8 % of the participants, with no dominance of any group as shown in [Table 2](#).

Table 1
Baseline characteristics.

	Overall N = 59 (100 %)	ADEM N = 27 (46 %)	CIS N = 8 (14 %)	MOGAD N = 8 (14 %)	MS N = 12 (20 %)	NMOSD N = 4 (6.8 %)	p-value
Age at presentation (Years)	9.93 (3.66)	9.37 (3.74)	9.75 (3.20)	8.38 (4.00)	11.75 (3.22)	11.75 (3.30)	0.11
Sex (Female)	29 (49 %)	11 (41 %)	5 (62 %)	4 (50 %)	7 (58 %)	2 (50 %)	0.78
Male	30 (51 %)	16 (59 %)	3 (38 %)	4 (50 %)	5 (42 %)	2 (50 %)	
Residency							0.54
Rural	16 (27 %)	8 (30 %)	2 (25 %)	1 (12 %)	5 (42 %)	0 (0 %)	
Urban	43 (73 %)	19 (70 %)	6 (75 %)	7 (88 %)	7 (58 %)	4 (100 %)	
Family history of demyelinating disease	2 (3.4 %)	0 (0 %)	0 (0 %)	0 (0 %)	2 (17 %)	0 (0 %)	0.18
Infection in the previous 4 weeks before disease onset	19 (32 %)	14 (52 %)	1 (12 %)	1 (12 %)	2 (17 %)	1 (25 %)	0.069
Vaccination in the previous 4 weeks before disease onset	7 (12 %)	7 (26 %)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)	0.095

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder.

Table 2
Clinical presentation.

	Overall, N = 59 (100 %)	ADEM N = 27 (46 %)	CIS N = 8 (14 %)	MOGAD N = 8 (14 %)	MS N = 12 (20 %)	NMOSD N = 4 (6.8 %)	p-value
Encephalopathy	33 (55.9 %)	25 (93 %)	0 (0 %)	3 (38 %)	5 (42 %)	0 (0 %)	<0.001
Motor symptoms	50 (84.7 %)	22 (81 %)	6 (75 %)	6 (75 %)	12 (100 %)	4 (100 %)	0.32
Sensory symptoms	30 (50.8 %)	8 (30 %)	5 (62 %)	5 (62 %)	8 (67 %)	4 (100 %)	0.026
Optic symptoms	17 (29.3 %)	1 / 26 (3.8 %)	2 (25 %)	5 (62 %)	7 (58 %)	2 (50 %)	<0.001
Cerebellum symptoms	30 (51.7 %)	20 (74 %)	0 (0 %)	4 / 7 (57 %)	6 (50 %)	0 (0 %)	<0.001
Spinal cord symptoms	22 (37.3 %)	4 (15 %)	4 (50 %)	5 (62 %)	5 (42 %)	4 (100 %)	0.002
Seizures	27 (45.8 %)	19 (70 %)	0 (0 %)	3 (38 %)	5 (42 %)	0 (0 %)	<0.001
Sphincter symptoms	40 (67.8 %)	18 (67 %)	4 (50 %)	5 (62 %)	9 (75 %)	4 (100 %)	0.54

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder.

Lab investigations

For the entire cohort, the CSF cell count was high in 33 (55.9 %) of the patients; cell counts between the five groups were not statistically significant ($p = 0.7891$). The CSF protein level was elevated in 31.0 (53.4 %) of the cohort, with no significant difference in CSF protein levels between the groups ($p = 0.3532$). The mean CSF glucose level was 59.2 ± 9.2 in the entire cohort. Differences in CSF glucose levels between the five groups were not statistically significant ($p = 0.7431$). The CSF OCB was high in 19 (32.2 %) in the entire cohort, with the highest percentage in the MS group (100.0 %) ($P < 0.001$). The IG G index was high in 20 (33.9 %) in the entire cohort, with the highest percentage in the MS group (83.3 %) ($P < 0.001$). Serum aquaporin 4 was positive in 4.0 (6.8 %) of the cohort. There was a significant difference in serum aquaporin 4 positivity between the groups ($p < 0.001$), with the highest percentage in the NMOSD group (100.0 %). The MOG antibody was high in 8.0 (13.6 %) in the entire cohort, with the highest percentage in the MOGAD group 8.0 (100.0 %) ($P < 0.001$), while it was not high in any of the other groups. The mean ESR was 16.7 ± 11.3 in the entire cohort. Differences in ESR between the five groups were not statistically

significant ($p = 0.9631$) as shown in Table 3.

Imaging

Brain abnormalities in the cortex were observed in 20.3 % of cases on MRI scans. However, there was no statistically significant difference between the groups, as indicated by a p-value of 0.089. Abnormalities in the deep gray matter of the brain were observed in 45.8 % of the overall sample, with the highest percentage found in the ADEM group at 70.4 % ($p = 0.002$). Abnormalities in the supratentorial white matter region of the brain were detected in 78.0 % of the entire sample, with the MS group having the greatest percentage of abnormalities at 100.0 % ($p < 0.001$). 52.5 % of the group showed abnormalities in the MRI of the infratentorial, with 77.8 % observed in individuals with ADEM, with a statistically significant p-value of 0.002. The MRI brain scan, which included intravenous contrast enhancement, revealed anomalies in 19 individuals (32.2 %) of the study population. There were no notable differences between the groups, as shown by a p-value of 0.37. Orbital involvement was observed in 8.5 % of the study population, with the highest prevalence (37.5 %) in patients with MOGAD, as indicated by

Table 3
Lab investigations according to diseases.

Diagnosis	Total (N = 59)	ADEM (N = 27)	CIS (N = 8)	MOGAD (N = 8)	MS (N = 12)	NMOSD (N = 4)	p-value
CSF cell count (High)	33 (55.9 %)	16 (59.3 %)	5 (62.5 %)	5 (62.5 %)	6 (50.0 %)	1 (25.0 %)	0.73
CSF proteins (High)	31.0 (53.4 %)	18.0 (66.7 %)	4.0 (50.0 %)	4.0 (50.0 %)	4.0 (33.3 %)	1.0 (33.3 %)	0.3532
CSF glucose Mean (SD)	59.2 (9.2)	59.1 (9.0)	57.8 (10.0)	57.2 (10.3)	62.2 (9.4)	57.5 (7.9)	0.7431
CSF OCB (High)	19 (32.2 %)	5 (18.5 %)	0 (0.0)	2 (25.0 %)	12 (100.0 %)	0 (0.0)	< 0.001
IG g index (High)	20 (33.9 %)	8 (29.6 %)	1 (12.5 %)	1 (12.5 %)	10 (83.3 %)	0 (0.0 %)	< 0.001
Serum aquaporin	4.0 (6.8 %)	0.0 (0.0 %)	0.0 (0.0 %)	0.0 (0.0 %)	0.0 (0.0 %)	4.0 (100.0 %)	< 0.001
MOG antibody	8.0 (13.6 %)	0.0 (0.0 %)	0.0 (0.0 %)	8.0 (100.0 %)	0.0 (0.0 %)	0.0 (0.0 %)	< 0.001
ESR, Mean (SD)	16.7 (11.3)	16.6 (11.4)	16.6 (10.9)	16.5 (7.1)	18.3 (15.5)	13.2 (5.4)	0.9631

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder, CSF: Cerebrospinal fluid, OCB: Oligoclonal band, IG: Immunoglobulin, ESR: Erythrocyte sedimentation rate and SD: Standard deviation.

MRI scans ($p = 0.031$). Abnormalities in the cervical spine were detected in 30.5 % of the overall group, with the highest percentage (50.0 %) seen in NMOSD, with a statistically significant p-value of 0.0201. Abnormalities in the dorsal spine MRI were observed in 20.3 % of the group, with the highest percentage (50.0 %) found in MOGAD ($p = 0.001$). Among the group, 23.7 % had aberrant visual evoked potentials (VEP), with the highest percentage (50.0 %) observed in individuals with MS, with a statistically significant p-value of 0.005. Electroencephalography (EEG) revealed abnormalities in 35.6 % of the entire group, with the largest percentage (70.4 %) observed in ADEM, which was statistically significant ($p < 0.001$) as shown in Table 4.

Treatment

In the acute stage, methylprednisolone was administered nearly to all patients at a dose of 20–30 mg/Kg, depending on patient weight and clinical severity (57 individuals, 96.6 %) of the cohort ($p = 0.0881$). Twenty patients (33.9 %) were administered IVIG during the acute stage. The differences in IVIG administration among the five groups did not show statistical significance ($p = 0.3661$). Plasmapheresis was performed during the acute phase on three individuals, accounting for 5.1 % of the overall cohort; one ADEM and two had NMOSD patients. There was a notable difference in plasmapheresis across the five groups ($p = 0.0011$). The mean ICU admission duration for the entire cohort was 2.5 ± 4.2 days. The distribution was 2.8 ± 4.2 days for ADEM, 0.6 ± 1.8 days for CIS, 1.0 ± 1.3 days for MOGAD, 8.0 ± 9.4 days for MS, and 2.5 ± 4.2 days for NMOSD, with no significant differences between groups ($p = 0.33$). Out of the complete cohort, twenty patients (33.9 %) received long-term therapy. All patients with MS and NMOSD received long-term treatment, with a statistically significant difference ($p < 0.001$) as shown in Table 5.

Follow-up and prognosis

Follow-up MRI results after six months showed that 62.7 % of cases had completely resolved lesions. Complete resolution was observed in all CIS patients (100 %) and 75 % of MOGAD patients ($p = 0.002$). New lesions appeared in 5.1 % of the cohort, predominantly in the MS group (25 %). Regression in the size and number of old lesions was seen in 32.2 % of the cohort, including 58.3 % of MS patients and 50 % of NMOSD patients. Follow-up lab investigations were positive in 5.1 % of the cohort, with no significant differences between groups ($p = 0.0521$). The mean expanded disability status scale (EDSS) score for the cohort was 0.9 ± 0.5 . Specifically, the scores were 0.2 ± 0.8 for ADEM, 0.0 ± 0.0 for CIS, 0.3 ± 0.5 for MOGAD, 2.2 ± 1.3 for MS, and 0.4 ± 0.9 for NMOSD, indicating significant differences between groups ($p < 0.001$). Mild cognitive impairment, as measured by the Symbol Digit Modalities

(SDM) test, was found in 16.9 % of the cohort, moderate impairment in 1.7 %, and no impairment in 81.4 %, with no statistically significant difference ($p = 0.85$) as shown in Table 6.

Predictors and prognosis

The logistic regression analysis revealed several significant predictors of a "good" prognosis:

Puberty Status: Prepubertal patients were 9.5 times more likely to have a good prognosis (OR = 9.50, 95 % CI: 3.39, 26.61, $p < 0.001$) compared to postpubertal patients, who had significantly reduced odds (OR = 0.057, 95 % CI: 0.014, 0.240, $p < 0.001$). MRI Lesion Load: Patients with mild MRI lesion load had 19.75 times higher odds of a good prognosis (OR = 19.75, 95 % CI: 4.27, 91.45, $p < 0.001$), while increasing lesion load decreased the likelihood of a favorable outcome by 82 % (OR = 0.185, 95 % CI: 0.06, 0.55, $p = 0.002$). Medical Intervention Timing: Early medical intervention was associated with a significantly improved prognosis (OR = 12.66, 95 % CI: 3.91, 41.03, $p < 0.001$), whereas late intervention drastically reduced the odds of a good outcome (OR = 0.04, 95 % CI: 0.0085, 0.182, $p < 0.001$).

These findings underscore the importance of puberty status, MRI lesion load, and timely medical intervention as strong predictors of prognosis, providing crucial insights for clinical decision-making.

Predictor	Odds Ratio (OR)	p-value
Puberty		
Prepuberty	9.5	< 0.001
Post-puberty	0.057	< 0.001
MRI lesion load		
Mild MRI lesion load	19.751	< .001
MRI lesion load change from mild to moderate, or from moderate to severe)	0.185	0.002
Medical treatment		
Early medical treatment	12.6667	< .001
Late medical treatment	0.0395	< .001

Discussion

The study examined the spectrum of PADS among 101 Egyptian children in the neuropediatric unit of Al-Azhar University hospitals. 59 patients with ADS were identified, with a mean age of 9.93 ± 3.66 years and a majority being educated and urban residents. Family history was almost unnoticed, except for a small MS proportion. Previous infection and vaccination were prominent in the ADEM group. The study found no gender association and no family history correlation, suggesting a

Table 4
Imaging data.

Diagnosis		ADEM 27 (45.8)	CIS 8 (13.6)	MOGAD 8 (13.6)	MS 12 (20.3)	NMOSD 4 (6.8)	Total 59 (100 %)	P-value
MRI brain (Abnormal lesion)	Cortical	9 (33.3)	0 (0.0)	0 (0.0)	3 (25.0)	0 (0.0)	12 (20.3)	0.089
	Deep gray matter	19 (70.4)	0 (0.0)	4 (50.0)	4 (33.3)	0 (0.0)	27 (45.8)	0.002
	Supratentorial white matter	26 (96.3)	1 (12.5)	6 (75.0)	12 (100.0)	1 (25.0)	46 (78.0)	<0.001
	Cerebellum and brain stem	21 (77.8)	1 (12.5)	3 (37.5)	6 (50.0)	0 (0.0)	31 (52.5)	0.002
	MRI brain with IV contrast enhancement	10 (37.0)	1 (12.5)	3 (37.5)	5 (41.7)	0 (0.0)	19 (32.2)	0.37
MRI orbit (Abnormal lesion)		1 (3.7)	1 (12.5)	3 (37.5)	0 (0.0)	0 (0.0)	5 (8.8)	0.031
MRI of cervical spine (Abnormal lesion)		9 (33.3)	1 (12.5)	2 (25.0)	2 (16.7)	4 (100.0)	18 (30.5)	0.02
MRI dorsal spine (Abnormal lesion)		1 (4.0)	4 (50.0)	2 (25.0)	1 (8.3)	4 (100.0)	12 (21.1)	<0.001
VEP		1 (4.3)	2 (25.0)	3 (37.5)	7 (58.3)	0 (0.0)	13 (23.6)	0.005
EEG	Abnormal	19 (70.4)	0 (0.0)	1 (12.5)	1 (8.3)	0 (0.0)	21 (35.6)	<0.001
	Not done	0 (0.0)	6 (75.0)	2 (25.0)	5 (41.7)	4 (100.0)	17 (28.8)	
	Normal	8 (29.6)	2 (25.0)	5 (62.5)	6 (50.0)	0 (0.0)	21 (35.6)	

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder, MRI: Magnetic resonance imaging, IV: Intravenous, VEP: Visual evoked potentials and EEG: Electroencephalography.

Table 5
Treatment data according to diseases.

	ADEM (N = 27)	CIS (N = 8)	MOGAD (N = 8)	MS (N = 12)	NMOSD (N = 4)	Total (N = 59)	p-value
Methylprednisolone in the acute stage	27 (100 %)	8 (100 %)	8 (100 %)	10 (83.3 %)	4 (100 %)	57 (96.6 %)	0.0881
IVIG in the acute stage	8 (29.6 %)	2 (25 %)	5 (62.5 %)	3 (25 %)	2 (50 %)	20 (33.9 %)	0.3661
Plasmapheresis in the acute stage	1 (3.7 %)	0 (0 %)	0 (0 %)	0 (0 %)	2 (50 %)	3 (5.1 %)	0.001
ICU admission (days), Mean (SD)	2.8 (4.2)	0.6 (1.8)	2.8 (3.0)	1.0 (1.9)	8.0 (9.4)	2.5 (4.2)	0.33
Long term therapy	1 (3.7 %)	0 (0)	3 (37.5 %)	12 (100 %)	4 (100 %)	20 (33.9 %)	< 0.001

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder, IVIG: Intravenous Immunoglobulin, ICU: Intensive care unit and SD: Standard deviation.

Table 6
Follow-up and prognosis.

	ADEM (N = 27)	CIS (N = 8)	MOGAD (N = 8)	MS (N = 12)	NMOSD (N = 4)	Total (N = 59)	P-value
Follow-up MRI							0.002
Complete resolved lesions	19 (70.4 %)	8 (100.0 %)	6 (75.0 %)	2 (16.7 %)	2 (50.0 %)	37 (62.7 %)	
Silent new lesions	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	3 (25.0 %)	0 (0.0 %)	3 (5.1 %)	
Regression in size and numbers of old lesions	8 (29.6 %)	0 (0.0 %)	2 (25.0 %)	7 (58.3 %)	2 (50.0 %)	19 (32.2 %)	
Follow-up lab investigations (Positive)	0.0 (0.0 %)	0.0 (0.0 %)	1.0 (12.5 %)	0.0 (0.0 %)	1.0 (25.0 %)	2.0 (3.4 %)	0.0521
Clinical EDSS score, Mean (SD)	0.2 (0.8)	0.0 (0.0)	0.3 (0.5)	0.5 (0.5)	2.2 (1.3)	0.4 (0.9)	< 0.001
Cognitive affection (SDM test)							0.8581
Mild	4.0 (14.8 %)	0.0 (0.0 %)	2.0 (25.0 %)	3.0 (25.0 %)	1.0 (25.0 %)	10.0 (16.9 %)	
Moderate	1.0 (3.7 %)	0.0 (0.0 %)	0.0 (0.0 %)	0.0 (0.0 %)	0.0 (0.0 %)	1.0 (1.7 %)	
No affection	22.0 (81.5 %)	8.0 (100.0 %)	6.0 (75.0 %)	9.0 (75.0 %)	3.0 (75.0 %)	48.0 (81.4 %)	

ADEM: Acute disseminated encephalomyelitis, CIS: Clinically isolated syndrome, MOGAD: Myelin oligodendrocyte glycoprotein antibody disease, MS: Multiple sclerosis and NMOSD: Neuromyelitis optica spectrum disorder, EDSS: Expanded Disability Status Scale and SDM: Symbol Digit Modalities.

similar age manifestation in Egyptian children. The study focuses on the clinical manifestations of (ADS), with neurological presentations being the most common. Motor symptoms were highly reported in all groups, with a collective proportion of 50/59 (85 %). Encephalopathy was more prevalent in the monophasic group, particularly ADEM, with a noticeable difference in prevalence. Sensory symptoms, optic symptoms and spinal cord symptoms were detected highly in the polyphasic group, with the highest reported type being NMOSD (100 %) and optic neuritis being MOGAD (62 %). Seizures were more frequent in the ADEM group. Sphincteric symptoms were also prevalent in 68 % of participants. These variable manifestations suggest the need for high clinical suspicion during assessment. Lab investigations revealed high CSF protein levels, particularly in the monophasic group (ADEM and CIS). CSF OCB was highly noticeable in MS, with a statistically significant difference in favor of the polyphasic group. IG g index was detected variably among the groups, with serum aquaporin only detected in four cases of NMOSD and MOG antibody in eight cases of MOGAD. These markers may help in subtype differentiation and diagnosis.

Imaging data is crucial in differentiating ADS subtypes, providing diagnostic insights, and aiding in targeted treatment protocols. Cortical MRI abnormalities were highly associated with ADEM (33.3 %), while MOGAD was highly reported with ADEM in deep gray matter MRI with 50 % and 70.4 %, respectively. Supratentorial MRI brain and cerebellum and brain stem MRI abnormalities were detected in all groups, specifically with ADEM (96.3 %), 77.8 %, and MS (100 %) and (50 %), respectively. MRI brain with IV contrast enhancement abnormality was noticed in all groups, limiting its applicability in disease differentiation. MRI orbit affection was reported with ADEM, CIS, MOGAD, and NMOSD, suggesting a probable pathway behind these diseases and requiring targeted treatment. Methylprednisolone is the standard treatment in the acute phase in all subtypes, while IVIG was highly reported in MOGAD and NMOSD, indicating the severity of these diseases requiring additional treatment. Plasmapheresis was only reported in ADEM and NMOSD, emphasizing the importance of emergency intervention in certain cases.

The prognosis and follow-up of ADEM and CIS are based on their acute nature, with complete resolution detected in ADEM and CIS and variability in MS, MOGAD, and NMOSD. The regression in size in nearly half of the population confirms the viability of treatment responses in

these diseases. New lesions were reported only with MS, indicating its relapsing identity and necessitating strict disease progression monitoring. Positive follow-up labs with MOGAD and NMOSD align with characteristic markers. The Expanded Disability Status Scale (EDSS) was detected highly in NMOSD, emphasizing its severity and refractoriness. Cognitive function was categorized into mild, moderate, and no impairment using the Symbol Digit Modalities (SDM) test. Most patients have no impairment, with CIS having no report of cognitive impairment, indicating a favorable prognosis. ACU admission is reported mostly with NMOSD, followed by ADEM and MOGAD, and CIS and MS.

A study conducted in the Philippines found that 77 out of 115 suspected cases of PADS were detected over ten years, with a mean age of 10.6 years and 1:1.2 female to male ratio in children <12 years of age [11]. The study also reported encephalopathy and seizures only in ADEM. Brain stem affection was mostly found in MS, visual changes in CIS, motor paralysis in MS, ADEM, and TM, sensory deficits in MS and TM, and sphincteric disturbances mostly in TM. MRI brain scans revealed 93.5 % total lesions in all types. CSF analysis indicated a frequency of cell count greater than 5/mm³ and OCB in two patients (5.9 %). Abnormal VEP was detected in MS and ADEM. EEG abnormality was reported only in ADEM. The results of this study confirmed the consistency of PADS identity across different geographical areas. However, some differences were noticed, possibly due to the difference in sample characteristics and methodology. De Mol et al. assessed PADS in Dutch patients over ten years [12]. They agreed on gender distribution, history of infection and vaccination, long ICU admission, neurological deficit, and high use of acute immunomodulatory treatment. However, they disagreed on the low presence of MOG and AQP4 antibodies, high cognitive impairment, and EDSS. Low antibody detection may be due to unavailable commercial assays and different population severity. A retrospective 15-year study conducted in India found a prevalence of CIS (27 cases) [13], followed by ADEM (16 cases) and 13 cases for each of NMOSD and MOGAD. The study also found an association of encephalopathy with ADEM, optic neuritis and MOG ABs with MOGAD, and a high-resolution percentage with immunotherapy. Gowda et al. agree with the prevalence of ADEM, high aquaporin-4 Abs with NMOSD, and good recovery of ADS with steroids [14]. Barišić et al. found no association between vaccination and inflammatory immune-mediated attacks, highlighting ADEM as a potential correlation [15]. Somma et al.

concluded mild cognitive impairment in MS and monophasic ADS, but overall cognition was similar to the corresponding age [16]. Till et al. confirmed no difference in cognition between ADS and controls [17]. Hamdy et al. described pediatric MS in Egypt, agreeing with the prevalence of motor and sensory deficits, high percentage of MRI abnormalities, high use of methylprednisolone, and long-term treatment requirements. However, cognitive impairment was higher in Hamdy et al.'s study [18].

This study on Pediatric Autoimmune Diseases (PADS) in Egyptian children possesses several strengths. The study was advantageous due to its relatively large sample size for rare disease in Egypt, which facilitated a thorough analysis. The comprehensive analysis was conducted on the population's demographics, clinical presentation, test findings, imaging, and therapy, resulting in a detailed understanding of PADS in this group. In addition, the study utilized the most up-to-date diagnostic criteria for PADS subtypes, ensuring accurate identification. Furthermore, it conducted comparisons of features among various subtypes, providing valuable insights into the variations within this group of diseases. Despite these interesting insights, the study has several limitations. The cross-sectional design's lacks the causative associations. The lack of long-term follow-up data, which limits the understanding of the disease progression and the treatment efficacy through long-term follow-ups. Additionally, the potential risk of selection bias in this study is due to the convenience sampling method. The absence of some quality-of-life scales such as the Multidimensional Fatigue Scale. All those limitations limit the generalizability of the findings through the target population.

In conclusion, this study provides detailed information regarding PADS patients in Egypt, a developing country that lacks research coverage of these rare diseases. It investigates a relatively large sample size, focusing on their clinical profiles, laboratory and radiological findings, treatment, and follow-up tracking their prognosis and comparing it with the existing literature to provide an insight into geographical variations; however, it has certain limitations. It is of a single center experience limiting the generalizability of the findings among the whole Egyptians and of a certain country suggesting information bias possibility. Additionally, the follow-up duration was short, raising the need for more longitudinal multicenter studies with a higher follow-up duration.

CRediT authorship contribution statement

Mohamed Ahmed: Writing – original draft, Validation, Investigation, Data curation, Conceptualization. **Shora Mostafa:** Writing – original draft, Formal analysis, Data curation. **Mohamed Rashad:** Writing – original draft, Methodology. **Abdel-Ghaffar Fayed:** Writing – review & editing, Visualization, Validation, Supervision, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

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