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Clinical, Laboratory and Neuroimaging of Acquired Demyelinating Syndrome of the Children Admitted in a Tertiary Care Hospital in Bangladesh

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Abstract:

Background: Acquired demyelinating syndrome (ADS) are autoimmune inflammatory disorder affecting the white matter of brain, optic nerve and spinal cord, and it has long been unrecognized. Early diagnosis and proper management slow the disease progression and reduce mortality and morbidity.

Objective: To find out the clinical, laboratory and neuroimaging patterns of ADS in children in Bangladesh.

Materials and Methods: A cross-sectional study was conducted from July 2020 to January 2021 in the Department of Pediatric Neurology, National Institute of Neuroscience and Hospital, including 37 children <18 years who had acute neurological deficits and MRI evidence of demyelination. After enrollment detailed history, physical examination, CSF study, oligoclonal bands (OCBs), and anti-NMO antibody was done and managed accordingly. Statistical analysis was done using SPSS version 22.

Result: The mean age was 8.79 ± 2.94 years, males were predominant. Most of the patients (24) had limb weakness (78.6%), headache (46.9%), altered consciousness (42.4%) and visual disturbance (39.4%). Monophasic ADEM (43%) followed by NMOSD (24%), TM (21%), ON (6%) and MS (6%) were common ADS. Common findings of brain imaging were bilateral (42.4%), multifocal (57.57%), juxtacortical (36.4%) and periventricular (24.2%) demyelinating lesions.

Conclusion: This study concluded that pediatric ADS had diverse clinical and radiological presentations, which were difficult to recognize for substantial clinical overlap.

Key Word: Children, Acquired demyelinating disease, ADEM, NMOSD, ON

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Introduction:

Acquired demyelinating diseases (ADS) are a heterogeneous group of autoimmune inflammatory disorders affecting the white matter of the central nervous system including optic nerve and spinal cord. Acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS), Neuromyelitis Optica (NMO), Transverse Myelitis (TM), optic neuritis (ON), and clinically isolated syndromes are commonly presented ADS.[1 2] The reported incidence of ADS is 0.5–1.66 per 100,000 children.[3 4 5] The incidence of ADS in children in Bangladesh is unknown. The cause of primary demyelinating disorders is unknown, but T cell-mediated autoimmune targeting of myelin basic protein is suspected.[1] The concept of primary demyelination implies the destruction of the myelin sheath and oligodendrocytes with relative preservation of other nervous system components.

Clinical features of ADS include acute or chronic onset motor weakness, sensory impairment, visual loss, and bowel or bladder symptoms which may be focal or multifocal neurological deficiency. Bilateral or unilateral painful vision loss, reduced visual fields and color perception are the hallmarks of ON. Demyelination of the spinal cord is termed as transverse myelitis mostly

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presented with motor, sensory, and bowel and bladder symptoms may be the initial presentation of NMO/MS. Rapidly developing encephalopathy combined with multifocal neurologic deficit are the classic features of ADEM. On the other hand, MS presented as relapsing-remitting without encephalopathy. Clinically isolated syndrome (CIS) represents a monophasic disorder or is the forerunner of the recurrent demyelination that characterizes MS remains an ongoing challenge. Along with clinical course; neuroimaging, neuroinflammatory marker in the CSF is the integral part of diagnosis of demyelinating disorder.[6]

Recent studies have heightened awareness that these disorders are prevalent not only in adults but also in children. It is essential to understand the spectrum of phenotypes, laboratory findings, and imaging features of ADS. Early diagnosis and appropriate management can significantly slow disease progression and reduce both mortality and morbidity. However, detailed data on ADS in children in Bangladesh is lacking. To the best of my knowledge, this is the first study of ADS in Bangladesh. This study was undertaken to define the clinical profile, laboratory and imaging characteristics of demyelinating diseases in children in Bangladesh, facilitating early recognition and effective management.

Methodology:

This cross-sectional study was conducted from July 2020 to January 2021 in Department of Pediatric Neurology, National Institute of Neuroscience and Hospital. Children aged 1-18 years with sudden onset neurological deficit compatible to ADS such as motor weakness, sensory disturbances, visual impairments, ataxia and bowel and bladder involvement with radiological evidence of demyelination in brain, spinal cord or orbit were included in this study. After enrollment patients were clinically evaluated thoroughly and informed written consent was taken from parents. Data were collected by predesigned structured questionnaire. A detailed history was taken and clinical examination was done. History related to age at onset, preceding illness, course of the disease, clinical presentation, time from symptom onset to diagnosis, and developmental history was taken. Thorough general and neurological evaluation was done. Higher psychic function, visual assessment, motor, sensory and cerebellar function were evaluated at baseline. If any patient presented with visual impairment, then further ophthalmological evaluation was done by neuro ophthalmologist in National Institute of Ophthalmology. After admission magnetic resonance imaging (MRI) of brain, spine with contrast and MRI of Orbit in both axial and coronal view, fat suppression with contrast was done accordingly and features of demyelination were recorded. For a thorough evaluation, cerebrospinal fluid (CSF) analysis, including routine tests for cell counts, protein levels, and sugar content, along with testing for oligoclonal bands (OCBs) were done in all patients. Anti-NMO antibodies were sent for only 15 patients due to financial constraint. Clinical pattern of demyelinating disease was recorded. Based on clinical, laboratory and imaging findings, ADS was classified into Acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS), neuro myelitis optica (NMO), transverse myelitis (TM), optic neuritis (ON) and clinically isolated syndromes (CIS). ADS with a single episode are considered monophasic, while those with more than one episode are termed multiphasic course. All cases treated by standard protocol.

Statistical Analysis was performed with SPSS software, versions 22.0. Categorical or discrete data was summarized in frequency counts and percentages. This study was approved by ethical committee of national institute of neurosciences and hospital.

Result:

Among the study cases mean age were 8.79 ± 2.94 years, male were predominant. Most of them had monophasic course 28 (84.8%) and average 23.69 ± 36.92 days was required to establish diagnosis, 18 (54.5%) had preceding illness. Limb weakness with pyramidal sign was prominent clinical feature (78.6%) followed by headache (46.9%), altered consciousness (42.4%), visual disturbance (39.4%), 6 (18.2%) had seizure, optic nerve was involved in 5 (15.2%) cases. Common demyelinating disorders among the study cases were monophasic ADEM (43%) followed by NMOSD (24%), TM (21%), ON (6%), and (6%) MS. Bilateral (42.4%), multifocal (57.57%), juxtacortical (36.4%) and periventricular (24.2%) demyelinating lesions were common brain imaging finding among the study cases. Majority of the cases had long extend TM 7/15 (46.66%) on MRI spine and 8.33% had optic nerve enhancement. Mean Cell count in CSF study was 7 (2-30), protein was 27.90 ± 11.38mg/dl, OCB found 2 (18.1%) and anti NMO Ab was positive 6/11 (40%) cases.

Table-I

Socio-demographic profile among the study cases (n=37)

Variable	Frequency (%)
Age (Years) mean ± SD	8.79 ± 2.94
Sex (M:F)	1.2: 1
Preceding illness	18 (54.5%)
Course of the disease	
Monophasic	28 (84.8%)
Multiphasic	5 (15.2%)
Age of onset (Years) mean ± SD	8.56 ± 3.19
Time from symptom onset to diagnosis (days)	23.69 ± 36.92

Table-II

Clinical characteristics among the study cases (n=37)

Variable	Frequency
Limb weakness	26 (78.6%)
Headache	15 (46.9%)
Altered consciousness	14 (42.4%)
Visual disturbance	13 (39.4%)
Seizure	6 (18.2%)
Involuntary movement	4 (12.1%)
Bowel bladder involvement	4 (12.1%)
Impaired higher psychic function	14 (42.4%)
Cranial nerve involvementOptic nerve	5 (15.2%)
Oculomotor nerve palsy	2 (6.1%)
Trochlear nerve palsy	1 (3%)
Abducent nerve palsy	1 (3%)
Pyramidal sign	26 (78.6%)
Quadriplegia	18 (54.4%)
Paraplegia	8 (24.2%)
Sensory impairment	8 (24.2%)
Cerebellar sign	
Ataxia	3 (9.1%)
nystagmus	2 (6.1)
Involuntary involvementTremor	3 (9.1%)

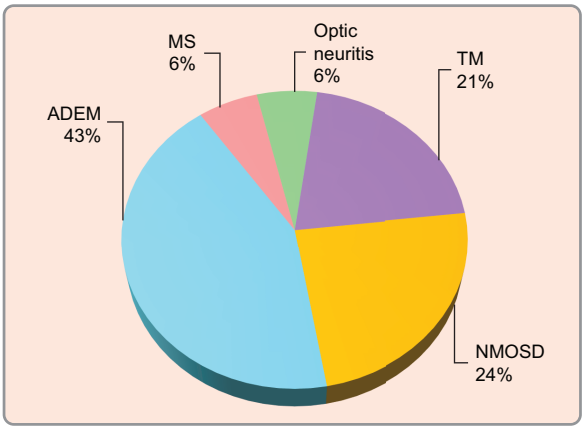

Figure 1: *Pattern of demyelinating disorder among the study cases n=37*

Table-III

Laboratory findings among the study cases (n=37)

Variable	Frequency
Anti NMO Ab (15)	6 (40%)
CSF study	
Cell (leukocyte count)/cmm	7 (2-30)
Protein(mg/dl)	27.90 ± 11.38
Oligoclonal band (11)	2 (18.1%)

Table-IV

Neuroimaging findings among the study cases (n=37)

Neuroimaging	Frequency (%)
MRI of brain (37)	
Abnormality	21(54.5%)
Lesions	
Multifocal	19 (57.5%)
Bilateral	14 (42.4%)
Unilateral	7 (21.2%)
Uni focal	4 (12.1%)
White matter changes/lesions	
Juxta cortical	12 (36.4%)
Periventricular white matter	8 (24.2%)
Deep white matter	3 (9.1%)
Callosal white matter	2 (6.1%)
Thalamic lesion	3 (9.1%)
Basal ganglion hyper-intensity	2 (6.1%)
MRI of spine (15)	
LETM	7 (46.66%)
Short segment TM	5 (33.33%)
MRI of orbit (12)	
Optic nerve enhancement	1 (8.33%)

Discussion:

Acquired Demyelinating Syndrome (ADS) of the central nervous system in children spans a wide spectrum. These conditions may be mono-phasic and self-limiting or multi-phasic. Clinical, radiological, CSF and other investigations to differentiate different demyelinating disorders, thus helping to plan treatment with the aim of improving outcomes without much residual disability. In this study among 37 study cases mean age was 8.79 ± 2.94 years. Julia O'Mahony et al[7] observed in their study, that the mean age of presentation was 10.4 (5.8–13.6) years, which was similar to the present study. Another study[8] differed from this, they found age of onset was 15.07 ± 2.72 (4–18) because they enrolled patients who had been diagnosed at the age d"18 and who were, at the time of the study, over the age of 18. The current study found male predominance. Some studies also indicate a slight male predominance[9] which was consistent with the present study. One study found females were predominant before 12 years 1.1:1[10] The female/male ratio in another cohort was 1.7:1.[11] This finding slightly differs from the present study due to different enrollment criteria. This study showed most of the cases had a monophasic course. A similar finding was noticed in Julia O'Mahony's study, 79.2% had a monophasic course. In this study, an average of 23.69 ± 36.92 days was required to establish diagnosis. This may be due to a lack of awareness among both parents and clinicians regarding demyelinating disorder. One study[12] has found a wide spectrum in the time from reporting of first symptoms to the seeking of medical care since symptoms may occasionally be attributed to other reasons or the family's perception to see if symptoms resolve spontaneously. Symptoms may occur during or shortly after an infectious illness and may be difficult to distinguish from that infectious disease process. In the current study limb weakness (78.6%) due to quadriplegia (54.4%) was a prominent clinical feature followed by headache (46.9%), altered consciousness (42.4%), visual disturbance (39.4%), seizure (18.2%) and cerebellar sign (9.1%) which differed with other study[13] where patients experienced their first events with a myriad of neurologic symptoms including ON (19.4%), brainstem dysfunction (18.5%), sensory impairment (11.3%), ATM (10.5%), and motor dysfunction (10.5%). Another study[10] found ataxia was the most commonly documented localized neurologic deficit, present in 30 (43.5%) of 69 children. TM was diagnosed in 102 children based on clinical localization, 62 (60.8%) of whom had mono-focal TM, Poly focal deficits without encephalopathy occurred in 52 (18.4%) children. In this study, the common demyelinating disorder among the study cases was ADEM (43%) followed by NMOSD (24%) and TM (21%), ON (6%). Julia O'Mahony et al[7] found that Sixty-nine (24.4%) of 283 patients met the diagnostic criteria for ADEM at presentation, 11 of whom experienced concurrent TM and 4 of whom experienced concurrent ON. Inaloo et al[10] had different findings from the present study as the most prevalent disease was MS at 36.5%, followed by ADEM 26.1%, ON 17%, TM 15.9% and Devic disease 4.5% which is due to the different referral system. In that study, some of the cases were referred from adult neurologists and ophthalmologists. In this study, bilateral, multifocal, juxtacortical and periventricular demyelinating lesions were common imaging findings among the study cases. The majority of the cases had longitudinally extended TM on MRI spine which differed from an Iranian study. [13] They found 48.9% deep white matter involvement and 32.9% had spinal cord lesions. They also found 6.8% optic nerve, 2.3% basal ganglia, and thalamus 6.8% involvement which was consistent with the present study.

Limitations: This study does have some limitations. The sample size was relatively small because of the rarity of ADS cases, and the follow-up period was brief, which restricted our understanding of long-term outcomes.

Conclusion: This study reveals a diverse range of clinical, laboratory, and radiological presentations among children with acquired demyelinating syndromes (ADS). Acute disseminated encephalomyelitis (ADEM) was identified as the most prevalent form of ADS, typically exhibiting a monophasic course. A large-scale, multi-center study with a significant sample size is necessary to make informed recommendations regarding acute demyelinating syndromes in children.

Conflict of interest: None

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