A Study of Clinical, CSF, Radiological Parameters and Outcome of Patients Presenting with Acute Transverse Myelitis

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CERTIFICATE

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INTRODUCTION

Transverse myelitis (TM) is a rare syndrome with an incidence of 1 to 8 new cases per million people per year (1) .TM is characterized by focal inflammation within the spinal cord, and clinical manifestations are due to resultant neural dysfunction of motor, sensory, and autonomic pathways within and passing through the inflamed area.There is often a clearly defined rostral border of sensory dysfunction and evidence of acute inflammation demonstrated by a spinal MRI and lumbar puncture. Autonomic symptoms consist variably of increased urinary urgency, bowel or bladder incontinence, difficulty or inability to void, incomplete evacuation or bowel constipation, and sexual dysfunction (2)

TM is the clinical manifestation of a variety of disorders, with distinct presentations and pathologies. Patients with TM should be offered immunomodulatory treatment such as steroid and plasmapheresis, though there is yet no consensus as to the most appropriate strategy. 75 to 9o% of TM patients experience monophasic disease and have no evidence of multisystemic or multiphasic disease. Most commonly, symptoms stop progressing after 2 to 3 weeks, spinal fluid and MRI abnormalities stabilize and then begin to resolve. There are several features, however, that predict recurrent disease . Patients with multifocal lesions within the spinal cord, demyelinating lesions in the brain, oligoclonal bands in the spinal fluid, mixed connective tissue disorder, or serum autoantibodies (most notably SS-A) are at a greater risk of recurrence (3). Most of the TM patients have monophasic disease, while up to 20% will have recurrent inflammatory episodes within the spinal cord (4).Some patients with TM may experience

recovery in neurologic function, regardless of whether specific therapy is instituted. Recovery, if it occurs, should begin within 6 months, and most patients show some restoration of neurologic function within 8 weeks . Recovery may be rapid during 3 to 6 months after symptom onset and may continue, albeit at a slower rate, for up to 2 years. Longitudinal case series of TM reveal that approximately one third of patients recover with little to no sequelae, one third are left with moderate degree of permanent disability, and one third have severe disabilities (1). Symptoms associated with poor outcome include back pain as an initial complaint, rapid progression to maximal symptoms within hours of onset, spinal shock, and sensory disturbance up to the cervical level (5).

REVIEW OF LITERATURE

Although several cases of "acute myelitis" were described as early as 1882, it was not until 1948 that Dr Suchett-Kaye (6), an English neurologist at St. Charles Hospital in London, first used the term acute transverse myelitis. Dr Suchett-Kaye used this term to designate a case of rapidly progressive paraparesis with a thoracic sensory level, occurring as a postinfectious complication of pneumonia. Several attempts at providing diagnostic criteria for acute transverse myelitis (TM) have been made over the past half-century, culminating in the nosology established by the International Transverse Myelitis Consortium Working Group in 2002.

Immunopathological observations confirm that TM is an immune-mediated disorder that involves cellular reactions and perhaps humoral factors that injure compartments of the spinal cord. In TM patients, it is likely that there is abnormal activation of the immune system resulting in inflammation and injury within the spinal cord. Most patients have CSF pleocytosis and blood- brain barrier breakdown within a focal area of the spinal cord, and conventional treatments are aimed at ameliorating immune activation. In 30% to 60% of the idiopathic TM cases, there is an antecedent respiratory, GI, or systemic illness (7). Molecular mimicry in TM may be associated with the development of autoantibodies in response to an antecedent infection.

Classifications of TM

Acute transverse myelopathy (which includes noninflammatory causes) and TM have often been used interchangeably throughout the published literature. One report established the following criteria for

transverse myelopathy: bilateral spinal cord dysfunction developing over a period of < 4 weeks with a well-defined upper sensory level, no antecedent illness, and exclusion of compressive etiologies (8) .Subsequently, these criteria were altered to include only those patients who developed motor, sensory, and sphincter dysfunction acutely over < 14 days, whereas patients with other neurological disease or underlying systemic diseases were excluded (9) .Other authors then defined TM as acutely developing paraparesis (no specification of a time to maximum deficit) with bilateral sensory findings and impaired sphincter function, a spinal segmental level of sensory disturbance, a stable nonprogressive course (to distinguish from progressive spastic paraparesis), and no clinical or laboratory evidence of spinal cord compression (1) . Patients were excluded if they had progressive spastic paraparesis, a patchy sensory deficit or hemicord syndrome, syphilis, severe back trauma, metastatic cancer, or encephalitis.

To further separate diseases with distinct etiologies, suggested criteria for TM were revised to include only those patients who progressed to maximum deficit within 4 weeks and to exclude other known diseases including arteriovenous malformations of the spinal cord, human T-cell lymphotropic virus-1 infection, and sarcoidosis (7) .With use of these criteria, cases of TM were classified as parainfectious, related to MS, spinal cord ischemia, or idiopathic.

Most recently (10), acute noncompressive myelopathies were classified according to an etiologic scheme: (1) those related to MS; (2) due to systemic disease (eg, SLE, antiphospholipid syndrome, Sjögren disease); (3) postinfectious; (4) delayed radiation myelopathy; (5) spinal cord infarct;

and (6) idiopathic myelopathy. The presence of MS or systemic disease was determined by standard criteria, whereas parainfectious myelopathies were diagnosed on the basis of positive IgM serology or a 4-fold or greater increase in IgG levels on 2 successive tests to a specific candidate/infectious agent. Delayed radiation myelopathy was diagnosed according to clinical history, and spinal cord infarction was diagnosed on the basis of appropriate clinical and imaging findings in the absence of other likely etiologies. Idiopathic transverse myelopathy was defined in those individuals that could not be otherwise categorized and constituted 16.5% of this series. Many systemic inflammatory disorders (eg, sarcoidosis, SLE, Behçet disease, Sjögren syndrome) may involve the nervous system and TM may be one of the possible presentations.

TMCWG criteria for TM-

The Transverse Myelitis Consortium Working Group (TMCWG) members have proposed criteria for acute Idiopathic transverse myelitis in 2002 (11).

INCLUSION CRITERIA-

1) Development of sensory, motor, or autonomic dysfunction attributable to the spinal cord.

2) Bilateral signs and/or symptoms (though not necessarily symmetric) clearly defined sensory level.

3) Exclusion of extra-axial compressive etiology by neuroimaging (MRI or myelography; CT of spine not adequate).

4) Inflammation within the spinal cord demonstrated by CSF pleocytosis or elevated IgG index or gadolinium enhancement. If none of the inflammatory criteria is met at symptom onset, repeat MRI and lumbar puncture evaluation between 2 and 7 day following symptom onset meet criteria.

5) Progression to nadir between 4 h and 21 day following the onset of symptoms (if patient awakens with symptoms, symptoms must become more pronounced from point of awakening)

EXCLUSION CRITERIA-

1) History of previous radiation to the spine within the last 10 yr

2) Clear arterial distribution clinical deficit consistent with thrombosis of the anterior spinal artery

3)Abnormal flow voids on the surface of the spinal cord c/w AVM

4)Serologic or clinical evidence of connective tissue disease sarcoidosis, Bechet's disease, Sjogren's syndrome, SLE, mixed connective tissue ds etc.)

5) CNS manifestations of syphilis, Lyme disease, HIV, HTLV-1,Mycoplasma, other viral infection (e.g. HSV- 1, HSV-2, VZV, EBV, CMV, HHV-6, enteroviruses)

6)Brain MRI abnormalities suggestive of MS

7)History of clinically apparent optic neuritis

A diagnosis of idiopathic ATM should require that all of the inclusion criteria and none of the exclusion criteria are fulfilled.

Limitations of the proposed criteria-

There were limitations to these proposed criteria that required further discussion. There may be cases that fulfill all of the proposed criteria with the exception of objective documentation of inflammation within the spinal cord. Thus, a situation in which spinal MRI shows an appropriately located high signal intensity lesion on T2-weighted sequences but no clear-cut enhancement of the abnormality following gadolinium administration could be envisioned. If the CSF were normal, then a diagnosis of ATM

would not be possible under the proposed criteria. Further, the clinical findings present in such an individual may not be consistent with a vascular myelopathy either. Nevertheless, labeling such a situation as "possible ATM" may be the best option at the moment.

Likewise, although the exclusion of cases based on the interval between symptom onset and maximal deficit is arbitrary, this criterion is felt to be valid based on the TMCWG member's clinical experience and review of the literature. Nevertheless, some vascular myelopathies will still undoubtedly fall within the current ATM criteria, whereas some patients who may have inflammatory "true" ATM may be excluded based solely on their rapid progression of symptoms. Additionally, for clinical management and research study inclusion of patients with suspected ATM, it may not be prudent to wait until the nadir is reached. Rather, treatment may be initiated with continued observation to determine if the patient ultimately meets all the criteria.

NATURAL HISTORY OF TM

TM affects individuals of all ages, with bimodal peaks between the ages of 10 and 19 years and 30 and 39 years (1,7). There is no sex or familial predisposition to TM. In 30% to 60% of the idiopathic TM cases, there is an antecedent respiratory, GI, or systemic illness (7). The term parainfectious has been used to suggest that the neurologic injury may be associated with direct microbial infection and injury as a result of the infection, direct microbial infection with immune-mediated damage against the agent, or remote infection followed by a systemic response that induces neural injury.

TM is characterized clinically by acutely or subacutely developing symptoms and signs of neurologic dysfunction in motor, sensory and autonomic nerves, and nerve tracts of the spinal cord. Weakness is described as a rapidly progressive paraparesis starting with the legs that occasionally progresses to involve the arms as well. Flaccidity maybe noted initially, with gradually appearing pyramidal signs by the second week of the illness. A sensory level can be documented in most cases.

The most common sensory level in adults is the midthoracic region, though children may have a higher frequency of cervical spinal cord involvement and a cervical sensory level (12) . Pain may occur in the back, extremities, or abdomen. Paresthesias are a common initial symptom in adults with TM but are unusual for children (13). Autonomic symptoms consist variably of increased urinary urgency, bowel or bladder incontinence, difficulty or inability to void, incomplete evacuation, or bowel constipation (14)Also common result of sensory and autonomic nervous system involvement in TM is sexual dysfunction (15) .Genital anesthesia from pudendal nerve involvement (S2-S4) results in impaired sensation in men and women. Additional male sexual problems with parasympathetic (S2-S4) and sympathetic (T10-L2) dysfunction in TM patients include erectile dysfunction, ejaculatory disorders and difficulty reaching orgasm. Corresponding female sexual problems include reduced lubrication and difficulty reaching orgasm.

REVIEWS OF WESTERN STUDIES ON TRANSVERSE MYELITIS-

The clinical presentation, blood and cerebrospinal fluid (CSF) findings as well as magnetic resonance imaging (MRI) & neurophysiological features were retrospectively analyzed in 45 unselected consecutive patients

with ATM by Harzheim et al (16). Parainfectious ATM was diagnosed in 38% of patients. The underlying infectious agent, however, was identified only in a minority of patients. In 36% of patients, the etiology remained uncertain ("idiopathic" ATM) and in 22% ATM was the first manifestation of possible multiple sclerosis (ATM-MS) according to Posner diagnostic criteria. Spinal cord MRI showed signal alterations in 96% of the patients. In ATM-MS, monosegmental involvement of the spinal cord was most frequent while spinal cord involvement of two or more segments was more common in ATM of other etiologies. Neurophysiological examinations showed evidence of peripheral nervous system (PNS) involvement in 27% of patients with ATM but not in patients with ATM-MS. Therefore, authors concluded that neurophysiological evidence of PNS involvement may provide additional discriminatory features between ATM-MS and ATM of other etiologies

De Seeze et al (10) studied 79 cases of ATM and classified the cases according to etiological group: 34 (43%) in multiple sclerosis; 13 (16.5%) in SD (systemic diseases); 11 (14%) in SCI (spinal cord infarct); five (6%) in PIM (post infectious myelopathy); and three (4%) in DRM (delayed radiation myelopathy). Myelopathies were of unknown origin in 13 (16.5%) patients. Authors evaluated clinical, spinal cord and brain MRI, CSF and evoked potentials data at admission, MRI outcome at 6 months and clinical outcome at 12 months. A statistical comparison of clinical, laboratory and outcome data was only performed between multiple sclerosis, SD and SCI patients due to the small number of cases in the other groups. A motor deficit was more frequent in SD and SCI than in multiple sclerosis where initial symptoms were predominantly sensory ($P < 0.001$). Spinal cord MRI showed lateral or posterior lesions of less than two

vertebral levels in multiple sclerosis, in contrast to SD and SCI, where lesions involved more vertebral levels and were centromedullar ($P < 0.001$). Brain MRI was most frequently abnormal in multiple sclerosis (68%), but was also abnormal in 31% of SD patients ($P < 0.05$). Oligoclonal bands in CSF were more frequent in multiple sclerosis than in SD ($P < 0.001$) and were never found in SCI. Clinical outcome at 12 months was good in 88% of multiple sclerosis cases, and poor or fair in 91% of SCI and 77% of SD.

In an another retrospective study by De Seeze et al (17) of 288 patients with ATM, 45 cases (15.6%) met the criteria for idiopathic ATM. The patients formed a relatively homogeneous group in terms of clinical and MRI data, but the prognosis was highly variable. The T2 weighted hypersignal on spinal cord MRI extended to more than two vertebral segments in all but 2 patients (95.2%). Brain MRI was performed in 38 patients and was always normal. VEPs were normal in all patients. CSF showed increased cell count and protein level in 19 cases (42.2%) and 9 cases (20%), respectively, with a mean of 24.9 cells (predominantly lymphocytes) and a mean protein level of 0.53. Oligoclonal bands were found in 8 patients (17.7%). According to the Consortium criteria, 31 patients (68.9%) had definite idiopathic ATM, and 14 patients (31.1%) had possible idiopathic ATM. In this study, author found that severe initial symptoms suggesting spinal shock were highly predictive of a poor outcome.

Reiko Miyazawa et al (18) studied reports of 50 Japanese patients (17 boys, 26 girls, 7 children of unspecified sex; mean age ± SD, 8.0 ± 3.8 years). Acute-phase and demographic features including age,

increased deep tendon reflexes, Babinski reflex, sex, preceding infection, decreased deep tendon reflexes, time course of peak neurologic impairment, treatment with prednisolone and/or high-dose methylprednisolone, and the day of illness when treatment was started were used as independent variables in a regression analysis. The dependent variable was long-term persistence of neurologic deficits. Younger patients and those without increased deep tendon reflexes or a Babinski reflex were more likely to have residual neurologic deficits such as paraplegia or tetraplegia, sensory loss and sphincter disturbance. No relationship was seen between prognosis and sex, preceding infections, decreased deep tendon reflexes, time course of peak neurologic impairment, treatment with prednisolone or high-dose methylprednisolone, or timing of treatment initiation. Age at onset and neurologic features were important for outcome prediction in ATM. Steroid therapy did not associate with better outcome.

J Bruna et al.(**19**) reviewed patients admitted and diagnosed with myelitis with two objectives: (i) to find the criteria in distinguishing between myelitis as the first episode of multiple sclerosis (MS) and idiopathic ATM; and (ii) to analyze the clinical and laboratory variables that may be used as functional prognostic markers. Out of the 45 cases Twenty-four patients fulfilled the criteria for definite ATM and 21 for possible ATM. Five patients converted to MS. Mean follow-up time was 3.5 years. There was an association between younger patients and female patients with conversion to MS. The highest Rankin score reached and increased CSF glucose levels were associated with a poor outcome. In multivariate analysis, only the admission Rankin score was associated with outcome.

Arslan Akbar Kahloon et al (20) had analyzed Twenty consecutive patients of ATM (1990-2003) fulfilling a preset criterion for demographic features, clinical presentation, laboratory investigations and neuro-imaging, to determine the presenting features and etiological classification of acute transverse myelitis (ATM) at Aga Khan University Hospital a tertiary care hospital in Pakistan. Half of the patients were males and their median age was 29 years (range 6-73 years). Fever, paraparesis, quadri-paresis and bladder dysfunction were the most common presentations. Median score on disability rating scale (DRS) was twelve. Sixty percent of the patients were classified as Idiopathic-ATM while 30% and 10% as Para infectious associated-ATM and Multiple sclerosis associated-ATM respectively.

In a joint Asian study a total of 263 patients from Hong Kong, Malaysia, Singapore, Korea, Taiwan, India and Thailand were studied by Heng Thay Chong et al (21). The mean age of onset was 31 years, and the mean duration of illness was 9.3 years. The clinical course was relapsing remitting in 79% of the patients. The mean relapse rate was0.86 attacks per annum. Forty percent of the patient had optic-spinal recurrent and 60% had Western forms of multiple sclerosis. There was a high female to male ratio of 3.8:1. Severe involvement of spinal cord is thus a universal feature of Asians with multiple sclerosis, seen in both optic-spinal recurrent and Western form of multiple sclerosis.

In one study of ATM in pediatric population (22) 10 children, with ages ranging from 8 months to 16 years, who had a diagnosis of acute transverse myelitis were studied with video urodynamics and

followed up in a tertiary paediatric neurourology clinic. The degree of recovery of bladder function was not related to the degree of motor recovery. In another pediatric study (23) Twenty-four children, aged 2 to 14 years and admitted with a diagnosis of acute transverse myelitis, were studied Sphincter dysfunction improved more slowly than did the other deficits. A full recovery was achieved by 31% of the patients; minimal sequelae were present in 25% and mild to severe sequelae in 44%. An unfavorable outcome was associated with complete paraplegia (P = .03) and/or a time to maximal deficit shorter than 24 hours (P = .005). A favorable outcome was associated with a plateau shorter than 8 days (P = .03), the presence of supraspinal symptoms (P = .01), and a time to independent walking shorter than 1 month (P = .01). The course of acute transverse myelitis in children proceeds through three stages, an initial phase, a plateau, and a recovery phase, each characterized by specific clinical features. The global outcome was found to be favorable in 56% of patients.

J. Sellner et al (24) studied 73 patients with a first-ever APTM admitted to the hospital from January 1999 to June 2005. The follow-up time ranged from 12 to 90 months .Authors concluded that patients with a first-ever APTM, a family history of MS, high EDSS at presentation, lesions on brain MRI, CSF-specific oligoclonal bands or abnormal IgG-index may indicate an increased risk for conversion to MS.

Chan KH et al (25) studied the outcome of patients after a first attack of idiopathic ATM. Idiopathic ATM patients over a 6-year period were retrospectively studied. Known causes of myelopathy were excluded. Among 32 patients studied, 20 (63%) had single ATM attack upon follow up for 39-93 months, three developed recurrent ATM related to CTD (two systemic lupus erythematosus and one anti-Ro antibody positive) and

nine (28.1%) developed recurrent neuroinflammation compatible with Idiopathic inflammatory demyelinating disease (IIDD). Among IIDD patients, three had NMO, two restricted variant of NMO, three IRTM and one classical MS.

Perumal J et al (26) studied 58 ATM patients with normal brain MRI at presentation for up to 5 years with serial neurologic and imaging studies. 17 of 58 (29%) patients developed MS of which 7 (41%) patients developed CDMS and 10 (59%) developed MS using McDonald Imaging Criteria. Mean time to CDMS by a second clinical attack was 11. 1 months compared to 19. 2 months by MRI lesions (P = 0. 03)

Pidcock FS et al (27) studied 47 patients for whom ATM occurred under the age of 18 years. Factors associated with a better functional outcome included older age at time of diagnosis, shorter time to diagnosis, lower sensory and anatomic levels of spinal injury, absence of T1 hypointensity on spinal MRI obtained during the acute period, lack of white blood cells in the CSF, and fewer affected spinal cord segments. Neither rapid progression to maximum impairment in less than 1 day nor any antecedent illness, immunization, or trauma was associated with a worse outcome.

Kim KK et al studied retrospectively , (28) 37 cases of recurrent transverse myelitus. Patients were classified as having idiopathic RTM on the basis of recurrent myelitis confirmed by clinical manifestations of myelopathy and magnetic resonance imaging findings. Idiopathic RTM occurred preponderantly in male patients and presented more often with acute transverse myelitis than did multiple sclerosis related TM (MSRTM). More than 2 relapses occurred in 6 cases (40%) of idiopathic RTM. The involved segments of spinal cord on T2-weighted images were not

significantly different in idiopathic RTM and MSRTM, with enhancing lesions mostly in the posterior columns, and the spinothalamic and spinocerebellar tracts of white matter. Additionally, almost all patients with idiopathic RTM had normal cerebrospinal fluid indexes.Thus idiopathic RTM is a disease entity distinct from MSRTM, differing in its male preponderance, absence of oligoclonal bands, frequent multiple relapses, and frequent presentation as acute transverse myelitis.

. In one study by Scott TF (29) et al , 20 consecutive patients with ATM and 16 patients with MMS were evaluated.Fifteen of 16 MMS patients and all 20 ATM patients presented with symptoms of motor dysfunction. Additionally, all patients in both groups presented with sensory complaints. MMS patients had asymmetric motor or sensory symptoms in all but one patient, whereas ATM patients exhibited symmetric weakness uniformly and symmetric sensory loss in all but one patient (statistically significant). None of the MS patients met criteria for ATM at presentation. None of the ATM patients developed MS over an average follow-up period of 4.5 years.

Al Deeb SM et al (30) analyzed the clinical, imaging, electrophysiological, laboratory findings, course and prognostic factors in 31 patients with acute transverse myelitis (20 men and 11 women; mean age, 30 years; range, 18-51 years) The myelitis was preceded by febrile illness in 25 (81%) patients. The site of the lesion was cervical in 11 (36%), upper thoracic in two (6%), lower thoracic in 16 (52%). MRI of the spinal cord was abnormal in 10 out of the 20 patients examined (50%); in the remaining 11 patients, only CT was carried out and it was normal in all of them. Somatosensory evoked potentials were abnormal in 19 (61%), while pattern-shift visual and brainstem auditory evoked potentials were normal in all

patients. CSF was abnormal in 94% of patients with pleocytosis, increased protein or both. Eighteen patients (58%) had good outcome. All patients had monophasic illness. Three variables have emerged as being associated with significant worsening of the outcome: (i) abnormal somatosensory evoked potentials; (ii) abnormal imaging and (iii) high 'deficit score' at onset. Authors concluded that acute transverse myelitis affects a complete segment of the spinal cord, is monophasic and represents a localized form of postinfectious acute encephalomyelitis.

. In one study by A. Campi, (31) et al, Spinal and cranial MR images were obtained for 30 patients with acute transverse myelopathy. The spinal cord MR findings were abnormal in 14 (46.6%) of 30 patients .In these 14 patients, the clinical levels agreed with the spinal MR findings. 5 patients had cervical cord lesions and 7 thoracic (3 of them with conus extension), 1 had involvement only of the conus medullaris, and in one case the entire spinal cord was involved

In one retrospective study of 14 cases, Scott T et al (32) found that MRI is valuable for both diagnosis and prognosis in ATM . The criteria for the diagnosis of acute transverse myelitis consisted of acute onset (over less than 3 weeks) of symmetrical motor and sensory dysfunction referable to a distinct spinal cord level, with sphincter dysfunction. Patients with abnormal MRIs of the spinal cord had significantly worse outcomes than patients with normal MRIs.

A retrospective analysis of 33 cases was conducted by Jefrey et al (7) . Cases were classified as being related to parainfectious multiple sclerosis, or spinal cord ischemia, or idiopathic. Thirty-three patients satisfied study criteria, corresponding to an incidence of 4.6 per million per year. Forty-five percent of these cases were categorized as

parainfectious, 21% as associated with multiple sclerosis, 12% as associated with spinal cord ischemia, and 21% as idiopathic. Patients with parainfectious TM suffered from spinal shock more frequently than did those with multiple sclerosis-associated TM. Patients with parainfectious TM showed evidence of spinal cord swelling, whereas patients with multiple sclerosis-associated TM had spinal cord plaques on magnetic resonance images but none showed swelling. Oligoclonal bands were absent in patients with parainfectious TM and present in three of five patients with multiple sclerosis-associated TM.

Cordonnier C et al (33) between 1994 and 2001, prospectively included 55 patients presenting with a first episode of APTM. Of the 52 APTM patients who completed the study, 30 became clinically definite MS. The predictive factors for conversion to MS were: initial sensory symptoms, latero-posterior spinal cord lesion, abnormal brain MRI and oligoclonal bands in CSF. In the MS group, the number of spinal cord lesions on MRI was the only predictive factor for a poor outcome, being statistically correlated with a higher number of relapses. On the basis of the results, author proposed that, in patients with APTM, sensory symptoms, oligoclonal bands and brain MRI are predictive factors for subsequent conversion to clinically definite MS and that within the latter patients the number of spinal cord lesions on MRI is the only predictive factor for a poor outcome.

Fifty-two patients with acute and subacute transverse myelopathy (TM) were evaluated by Ropper AH et al (34) at the Massachusetts General Hospital between 1955 and 1975 and followed for 1 to 23 years (average, 5). Twenty-four patients had paresthesias at the onset of the illness, 18 had pain, usually interscapular, 7 had leg weakness, and 3

had urine retention. An acute catastrophic onset was generally associated with back pain and led to a poor outcome in 7 and a good outcome in only 1 of 11 patients. A subacute progressive onset over several days to four weeks, generally with ascending paresthesias or leg weakness, was associated with a good outcome in 15 patients. Preceding febrile illness, treatment with corticosteroids, and the nature of CSF abnormalities had no effect on outcome. Multiple sclerosis evolved in 7 patients during the follow-up period.

REVIEWS OF INDIAN STUDIES ON TRANSVERSE MYELITIS-

J Kalita and U K Misra (35) have evaluated the role of methyl prednisolone (MPS) in the management of acute transverse myelitis (ATM).Twenty-one patients with ATM were included in a prospective hospital based study during 1992 -1997. All the patients underwent neurological examination, spinal MRI, somatosensory and motor evoked potentials of both upper and lower limbs and concentric needle EMG study. Twelve consecutive patients did not receive MPS therapy who were managed during 1992 ± 1994 and nine consecutive patients during 1995 ± 1997 received MPS therapy in a dose of 500 mg i.v. for 5 days. The clinical and neurophysiological studies were repeated 3 months later. In patients with complete paraplegia, evidence of denervation on EMG and unrecordable central motor conduction time to lower limb and tibial SEP were associated with poor outcome irrespective of MPS treatment. Global test statistics did not suggest a benfecial role of MPS therapy in the outcome of ATM.

Bansil S et al (36) have analyzed comparison between multiple sclerosis in India and the United States: a case-control study. They

carried out a case-control study to compare the disease in the two populations and used clinical, evoked potential, and MRI criteria to assess similarities and differences. Their results indicated that the rate of disease progression and frequency of involvement of the cerebral hemispheres, cerebellum, spinal cord, and brainstem were similar in the two populations. The visual system was more frequently involved in Indian patients

In another study by Kalita J (37) et al, twenty-one patients with ATM were studied and complete paraplegia, evidence of denervation on EMG and unrecordable central motor conduction time to lower limb and tibial SEP were associated with poor outcome irrespective of MPS treatment Evoked potential studies provide additional objective means for monitoring the effect of therapy in ATM.

17 parainfectious myelitis patients were studied for site, extent and severity of lesions by Pradhan S et al (38) .Three patterns were observed each having distinct clinical, electrophysiological and MRI features: 1) focal segmental myelitis-focal cord lesion with long tract signs had good prognosis; 2) ascending myelitis-continuous lesion from conus to mid-cord with upper and lower motor neuron signs (not necessarily spinal shock), dysautonomia and poor outcome; 3) disseminated myelitis-discrete lesions scattered throughout the cord with subtle signs in spinal segmental distribution, above and below the transverse level and moderate outcome. Severe autonomic dysfunction, denervation of paraspinal muscles, "dense" lesion on imaging and often (but not always) the absent somatosensory evoked potentials carried poor outcome

In another study by Kalita J et al (39)Thirty-one patients with ATM were subjected to clinical, MRI, somatosensory and motor evoked potential studies in both upper and lower limbs and concentric

needle electromyography. Authors concluded that Severity of weakness and denervation on EMG are most useful for predicting the outcome of ATM at 6 months although in early stage motor and somatosensory evoked potentials may be used instead of EMG

Seventeen patients with acute transverse myelitis were subjected to clinical evaluation, MRI scanning and concentric needle EMG by Misra UK et al (40). EMG evidence of denervation in the lower limb muscles in acute transverse myelitis suggested a poor outcome as assessed by 3-month Barthel index score .

Pandit L et al (41) have described three patients presenting with acute complete transverse myelopathy which relapsed several times at the same site. These patients, two women and one man, had two to five attacks spanning three to seven years. Oligoclonal bands were present in the CSF in one patient. Brain MRI was normal in two patients; MRI of the spinal cord was abnormal and showed cord oedema with multiple areas of hyperintense signals on T2 and proton density weighted scans and hypointense signals on T1 weighted images in areas corresponding to the clinical level, suggesting an inflammatory/demyelinating disorder. These patients may represent a relapsing demyelinating disorder restricted to the spinal cord, distinct from multiple sclerosis

Misra UK have studied (42) ten patients with ATM (age range 14-57 years; 8 men, 2 women) who were subjected to clinical, MRI and neurophysiological evaluation. The latter included median and tibial somatosensory evoked potentials (SEP), motor evoked potentials (MEP) to upper and lower limbs and concentric needle EMG in ATM. Extensive MRI changes, unrecordable MEP to lower limbs especially on lumbar stimulation

and evidence of denervation in leg muscles were found to predict a poor outcome.

Magnetic resonance imaging findings in 13 patients with acute transverse myelitis were reviewed by Murthy et al (43) . In 12 cases centrally located high intensity signal extending over few spinal segments was noted. The lesion occupied more than two thirds of the cord's cross-sectional area in 8 patients. Central dot sign was noted in 7 patients. Variable cord enlargement was seen in 5 patients. Contrast study in one patient showed peripheral enhancement.

There is not good number of studies to look for prognostic indicator of acute transverse myelitis comparing various clinical, CSF, and radiological parameters.In addition there is no clear cut known indicators for conversion of acute transverse myelitis to either multiple sclerosis and neuromyelitis optica.Indian literature about recurrent transverse myelitis is also very limited (so far only three cases have been described in Indian studies by Pandit et al (41).Although some of the electrophysiological parameters like SSEP, motor evoked potential have been described by Kalita et al (35,37,39,40) in several studies, but number of cases are few and it has been not correlated with the other clinical, CSF and various mri parameters in detail as various factors can confound the prognostic markers if sample size is very small.

AIMS AND OBJECTIVE

1) To study the clinical, radiological and CSF profile of patients presenting with acute transverse myelitis.

2) To prognosticate long term outcome of patient with acute transverse myelitis based on clinical and investigatory parameters.

3) To know clinical, CSF, and radiological parameters of recurrent myelitis .

4) To determine various indicators for conversion of ATM cases to multiple sclerosis.

MATERIAL AND METHODS

Study was conducted in Shree Chithra Thirunal Institute of medical science and technology,Trivandrum,a tertiary care referral centre in Kerala,India. Retrospective review of in hospital records from 1995 to 2007 with the diagnosis of Acute Transverse myelitis was done. Charts were studied for presence of following inclusion and exclusion criteria (Criteria for the diagnosis of transverse myelitis were modified from Jeffery et al as follows)-

Inclusion criteria-

1) Acute/ Subacute, motor and or sensory symptoms with or without sphincter dysfunction

2) Spinal segment level of sensory disturbance with a well defined upper limit.

3) Progression of symptoms to peak deficits within 3 week.

Exclusion criteria-

1)Clinical or radiological evidence of spinal cord compression .

2)Previous history of any neurological disease.

Total 78 charts were studied who were admitted in the hospital with the diagnosis of acute transverse myelitis (ATM) for the first time. If data for CSF , MRI and follow up for at least 1 year were not available ,also excluded. All patients were admitted in the acute stage in Department of neurology ,SCTIMST and discharged after appropriate management. Subsequently these patients were followed up in speciality clinic or general neurology clinic at the interval of 3 months,6 months or 1 year. We have also excluded the patients who were known case of neurological illness

which can confound the outcome. Old cases of multiple sclerosis or other demyelinating disease who have been admitted in the hospital with the diagnosis of ATM were also excluded..Thus 15 patients were excluded due to incomplete data or unable to fulfill above inclusion and exclusion criteria and total 63 case records were studied.

Following parameters were noted-

1)Clinical parameters

2)CSF study

3)Vasculitis workup

4)Workup for infective etiology

5)MRI

6)Treatment details

7)Modified Rankin Scale (MRS) at the time of admission, discharge,3 months,6 months and 1 year follow up.

Clinical parameters

1) Preceding illness-

Type of preceding illness (fever, upper or lower respiratory tract infection,urinary tract infection and other illness like diarrhea) were looked for. Duration of preceeding illness and latency period between preceding illness and neurological complaint were noted.

2) First Neurological complaint-

Weakness,Sensory complaint (Paresthesia) ,Bladder dysfunction

3)Weakness-

Type (Paraparesis /Quadriparesis),Character (Symmetrical / Asymmetrical),pattern of weakness(Ascending/Descending) and interval between Peak to nadir of weakness were noted.

4)Sensory complaint-

Presence or absence,type(positive or negative) and upper level (Cervical/thoracic/lumbar/sacral) of sensory complaint were noted.

5)Backache-

Presence or absence,type(radicular/nonradicular) and site (cervical/thoracic and lumbar) of backache were noted

6)Presence or absence of bladder,bowel,bulbar and respiratory muscle disturbances were noted.

7)History of associated systemic illness(HTN,DM,COPD ,Thyroid disease,CAD etc.) were noted.In addition development of complication due to prolonged recumbency like DVT and decubitus ulcer were also noted.

8)Neurological examination-

Neurological examination finding were noted in detail at the time of admission with special interest for GCS at the time of admission, evidence of cranial nerve involvement,evidence of spinal shock, tone, power , reflexes in all 4 limbs including plantar reflex.Type of sensory modalities involved ,upper level of sensory impairment and perianal sensory loss were also specialy looked for.

CSF Parameters-

CSF cell count, type of cells ,CSF protein ,CSF sugar with corresponding blood sugar ,CSF cultures for T.B., fungus and CSF VDRL were done in every patient ,whereas CSF for TB PCR, CSF for HSV PCR ,CSF for malignant cell ,CSF oligoclonal band and CSF IGM index were also done if clinically indicated.

Vasculitis and Infective etiology workup-

Total and differential cell count ,ESR,CRP,RA factor, ANA, Antiphospholipid antibody, anti ds DNA were done to look for any evidence of vasculitis. In addition few patients also had been evaluated with Mantoux test, antibodies for brucella and borelia.

MRI Spine and Brain-

All patient underwent MRI spine and few patients also had MRI brain. MRI spine was evaluated for-localization of levelof lesion (Cervical/thoracic/lumbar/above cervical), horizontal extent (involvement of $<2/3^{rd}$ or $>2/3^{rd}$ of the spinal cord),vertical extent (1 ,2 or more than 2 segment of the spinal cord).Evidence of cord swelling, gadolinum enhancement,pattern of cord involvement (patchy /confluent) and cord atrophy were also noted. In addition MRI brain is evaluated for nature (Plaques /Infarct /SOL / granuloma) ,location(periventricular, juxtacortical ,infratentorial and pericollasal) and no.of lesion.

Electrophysiology - Patients were also evaluated with ENMG ,VEP BAEP& ENMG .

Treatment-

Patients were treated with I.V. Methylprednisolone 20 mg/kg For 5 days .If no definite response is noted then patients were either treated with IV IG 0.4 gm/kg for 5 days or plasma exchange according to the clinical status. 5 or 7 cycles of large volume of plasma exchange was done with each cycle, 20ml/kg of plasma was taken out and exchanged with either fresh frozen plasma or human albumin. Few patients were also put on mechanical ventilator due to bulbar or respiratory muscle weakness due to extension of the lesion cranialy. Data regarding treatment offered to each patient was recorded.

Outcome-

Patients were examined repeatedly in the hospital and any sign of improvement was noted. The day in which first sign of improvement observed was noted as well as first sign of improvement (motor/sensory/bladder) was also recorded. MRS at the time of discharge as well as at 3 months ,6 months and 1year follow up were noted.

STATISTICS AND DATA ANALYSIS

This study is retrospective cohort study. For univariate analysis variables were summarized into proportion and 95 % confidence interval .For bivariate analysis all data were categorized and Chi Square test and Fisher exact test were applied to know the significance. Multivariate analysis was done using binary logistic regression analysis. Variables showing significance in bivariate analysis and those which did not show statistically significance but considered relevant and likely to influence the outcome were used as independent variables whereas good and bad outcome as per 1 year MRS were taken as dependent variables. P value less than 0.05 was considered as significant. All data analysis was done by SPSS software version 15.

RESULTS

DEMOGRAPHY-

Total 63 patients of acute transverse myelitis (ATM) were analyzed .Age range was 11 to 75 years and mean age of presentation was 37.35 years (95% CI – 33.16 to 41.54). Out of these 63 patients, 37 patients (57% ,CI-56.97 to 57.23) were male and 26 patients (42.9 % ,CI-42.77 to 43.03) were female (Table-1)

Table-1 : Sex distribution of study population

Sex	Frequency	Percent	95% CI
Male	36	57.1	56.97 to 57.23
Female	27	42.9	42.77 to 43.03
Total	63	100.0	

Mean age of presentation was 37.35 years (95% CI – 33.16 to 41.54) for females and males both. TM affected individuals of all ages ranging from 11 to 75 years , with bimodal peaks between the ages of 10 and 20 years and 30 and 39 years (figure-1)

Table-2 :Agewise distribution of cases

S.N.	Patient age group	no. of cases
1	10-20	13
2	20-30	7
3	30-40	17
4	40-50	12
5	50-60	8
6	60-70	5
7	>70	1

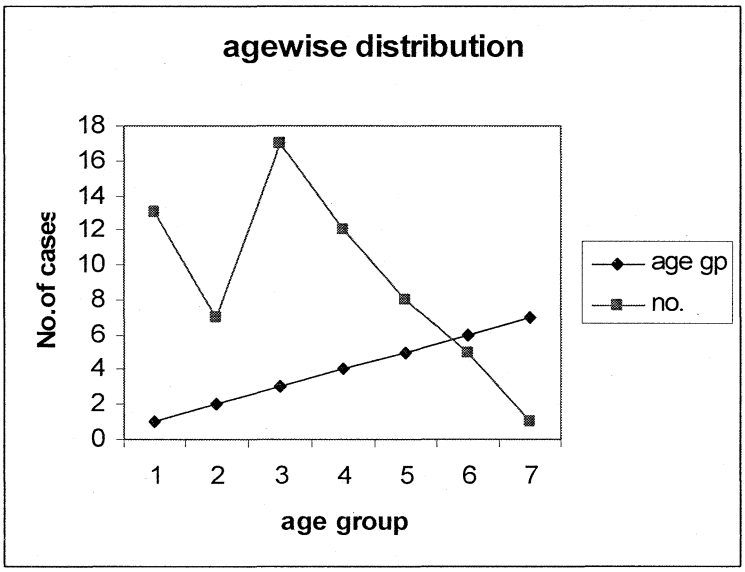

Fig-1:Bimodal peak in agewise distribution of cases

PRECEDING ILLNESS

History of preceding illness was present in 37 (57.1 % ,CI-58.58 to 58.82) patients. Preceding illness was fever without any specific cause in 22 (59.5%,CI-59.47 to 59.53) patients, respiratory tract infection in 8 (21.6%,CI-21.57 to 21.63) patients, urinary tract infection in 3 (8.1%,CI-8.07 to 8.13) patients and other illness including diarrhea in 4 patients (10.8% ,CI-10.77 to 10.83) were observed (Table-3)

Table-3: Frequency of various types of preceding illness

Type of Pr. illness	Frequency	Percentage	95% CI	
Fever	22	59.5	59.47	59.53
RTI	8	21.6	21.57	21.63
UTI	3	8.1	8.07	8.13
others	4	10.8	10.77	10.83
Total	37	100.0		

Latency period between preceding illness and neurological complaint was less than one week in 13 (35.1%,CI-35.08 to 35.12), 1-2 week in 17 (45.9%,CI-45.88 to 45.92), and was more than 2 week in 7 (18.9%,CI-18.82 to 18.92) patients (Table -4).

Table 4: Latency period between preceding illness and neurological complaint

Latency period	Frequency	Percent	95% CI	
<1 week	13	35.1	35.08	35.12
1 to 2 week	17	45.9	45.88	45.92
>2 week	7	18.9	18.88	18.92
Total	37	100.0		

HISTORY-

First neurological complaint noted was sensory disturbances in 45 (71.4%,CI-71.39 to 71.41),weakness in 9 (14.3%,CI-14.29 to 14.31) and bladder disturbances in 9 (14.3%,CI-14.29 to 14.31) patients (Table-5)

Table-5: First neurological complaint

First neurological complaint	Frequency	Percent	95% CI	
weakness	9	14.3	14.29	14.31
sensory	45	71.4	71.39	71.41
Bladder	9	14.3	14.29	14.31
Total	63	100.0		

52 patients (81.7%,CI-81.69 to 81.71) had paraparesis ,whereas 11 patients (18.3%,CI-18.29 to 18.31) had quadriparesis .Interval between onset to nadir of weakness was less than 4 hr in 2 ,4-12 hr in 10 ,12-24 hr in 13 ,24-36 hr in 9 ,36-48 hr in 9 ,48-72 hour in 13 and more than 72 hour in 7 patients (Table-6).61 patients have sensory complaints ,whereas 2 patients did not have any sensory complaints. Out of these 61patients , 12 had positive symptoms , 15 had negative

symptoms ,whereas 34 patients had both positive and negative symptoms.

Table-6:Interval between onset to nadir of weakness

Interval	Frequency	Percent	95% CI	
4-12hr	10	16.1	16.05	16.15
12-24 hr	13	21.0	20.95	21.05
24-36 hr	9	14.5	14.45	14.55
36-48 hr	9	14.5	14.45	14.55
48 -72hr	13	19.4	19.35	19.45
<4hr	2	3.2	3.15	3.25
>72 hr	7	11.3	11.25	11.35
Total	63	100.0		

Upper level of sensory complaint was cervical in 7 patients, thoracic in 44 patients, lumbar in 9 patients and sacral in 1 patients. History of backache at the time of presentation was present in 22 patients and was absent in 41 patients (Table-7) .Backache was radicular in nature in 9 patients, whereas it was nonradicular in 13 patients. Site of backache was cervical in 3 patients and lumbar in 2 patients whereas 17 patients had backache at thoracic region.

Table-7:Backache at the time of presentation

History of backache	Frequency	Valid Percent	95% CI	
absent	41	64.5	64.49	64.51
present	22	35.5	35.49	35.51
Total	63	100.0		

History of bladder disturbance was present in 56 (88.9 %,CI- 88.89 to 88.91) patients. History of bowel disturbance was present in 25 (39.7% %,CI-39.69 to 39.79) patients. History of respiratory muscles involvement

was present in 6 (4.3%,CI- 9.5 to 9.5) patients. History of bulbar dysfunction was present in 3 (4.8 %,CI- 4.795 to 4.805) patients.

History of associated systemic illness (HTN, DM, COPD ,Thyroid disease,CAD etc.) were noted in 20 (30%) patients. In addition development of complication due to prolonged recumbency like DVT and decubitus ulcer were noted in 7 (11%) patients. 3 had decubitus ulcer and 4 had DVT

Recurrent myelitis was observed in 7 patients (11.1%,CI-11.09 to 11.11)(Table-8)

Table-8:History of recurrent myelitis

History of recurrent myelitis		Frequency	percent	95% CI	
1	present	7	11.1	11.09	11.11
2	absent	56	88.9	88.89	88.91
	Total	63	100.0		

EXAMINATION-

In the upper limb tone was normal in 56 (88.9%) patients, increased in 2 (3.2%) patients and was decreased in 5 (7.9%) patients. In the lower limb tone was normal in 10 (15.9%) patients, increased in 14 (22.2%) patients and was decreased in 39 (61.9.9%) patients.

Power in the upper limb was MRC grade 0 in 3(4.8%),grade 1 in 2 (3.2%),grade 3 in 3 (4.8%) ,grade 4 in 4 (6.3 patients) and grade 5 in majority of the patient 51 (81%).

Power in the lower limb was MRC grade 0 in 28 (44.4%), grade 1 in 4 (6.3%),grade 2 in 2(3.2 %) , grade 3 in 12 (19%), grade 4 in 15 (23.8%) and grade 5 in 2 (3.2%) patients.

Deep tendon reflexes in UL were exaggerated in 1(1.6%) ,normal in 59 (93.7%) and were absent in 3 (4.8%) patients, whereas deep tendon reflexes

in LL were exaggerated in 12 (19 %) ,normal in 17 (27%) and were absent in 34 (54%) patients.

Plantars were extensor in 25 (39.7%), flexor in 3(4.8%) ,and were mute in 35 (55.6%) patients (Table-9)

Table-9: Plantar reflex at the time of admission

Plantar reflex	Frequeny	Percent
Extensor	25	39.7
Flexor	3	4.8
Mute	35	55.6
	63	100.0

Ankle clonus were present in 9 (14.3 %) patients whereas patellar clonus were present in 4 (6.3%) patients. On examination sensory impairment was found in all patient except one. 45(71.4%) patients had loss of all sensory modality including touch, pain, joint position and vibration sensory loss ,whereas 15 patients had only touch and pain loss with preserved joint position and vibration sensation. 2 Patients had isolated joint position and vibration loss only. After examination upper level of sensory loss was found to be upper cervical in 4 (6.3%,CI-6.27 to 6.33) , lower cervical in 4(6.3%,CI-6.27 to 6.33) ,upper thoracic in 23 (36.5%,CI-36.47 to 36.53), lower thoracic in 22(34.9%,CI-34.87 to 34.93), lumbar in 8(12.7%) and sacral in 1 (1.6%) patients (Table-10)

Table -10:Upper sensory level

Level	Frequency	Percent	95% CI	
Upper cer	4	6.3	6.27	6.33
Lower cer	4	6.3	6.27	6.33
Upper thor	23	36.5	36.47	36.53
Lower thor	22	34.9	34.87	34.93
Lumbar	8	12.7	12.67	12.73
Sacral	1	1.6	1.57	1.63
Total	62	100.0		

Spinal shock was present in 34 (54% ,CI-53.99 to 54.01),whereas 29 out of 63 patients did not have spinal shock..MRS at admission was 0 in 1, 2 in 4 ,3 in 8 ,14 in 16 and was 5 in 34 patients. Thus it was less or equal to 3 in 13 patients and was more than 3 in 50 patients.

CSF parameters-

CSF parameters were available in all patient except for one patient .CSF cell count were normal in 50 (80.6%,CI-80.58 to 80.62), between 5-20 in 7 (11.3%,CI-11.28-11.32) and were beyond 20 cells in 5 (8.1%,CI-8.08 to 8.12) patients. CSF showed polymorphs predominance in 5 patients and had lymphocyte predominance in 57 patients. CSF protein was normal in 34 and was high in 28 patients .CSF sugar was less than two third of blood glucose in 11 patients and was higher than two third of blood glucose in 51 patients .CSF oligoclonal band were 23 patients only and all were negative. CSF culture for fungus, bacteria and tuberculosis were not positive in any patient.

Vasculitis workup- was not positive in any patient.

MRI-

MRI spine was available in all patients.8 patient had normal MRI and 55 patients had abnormal MRI (Table -11)

Table-11

MRI	Frequency	Percent	95% CI	
normal	8	12.7	12.69	12.71
abnormal	55	87.3	87.29	87.31
Total	63	100.0		

Predominant MRI longitudinal involvement was cervical in 12 cases ,thoracic in 42 and was lumbar in 1 case (Table-12)

Table -12: MRI level

MRI level		Frequency	Valid Percent	95% CI	
1	cervical	12	21.8	21.79	21.81
2	Thoracic	42	76.4	76.39	76.41
3	lumbar	1	1.8	1.79	1.81
	Total	55	100.0		

Horizontal involvement of less than 2/3rd of cord was seen in 29/55 patients ,whereas it involved more than 2/3rd of cord in 26/55 patients Vertical involement of the lesion was restricted to only one segment in 5/55 patients ,2 segments in 10 /55patients and it involved more than 2 segments in 40/55 patients. Cord swelling was seen in 28 /55 (50.09%) patients. Gadolinum enhancement was seen in 19/55 (34.5%) patients. In one patient contrast was not given .Cord atrophy was seen in only 5 /55 (9.1%) patients. Brain involvement was seen in 12 patient.Cord involvement pattern was patchy in 13 patients and was confluent in 42 patients .

ELECTROPHYSIOLOGY-

ENMG,VEP & BAEP was done only if clinically indicated and hence it was done in 24 patients and found abnormality (prolonged P 100 latency) in only 4 patients i.e.6.3% patient with CI between 6.28 to 6.32. ENMG was done only if clinically indicated and hence it was done in 17/63 patients and found abnormality in only 6 patients .BAEP was done in 5 patients and was found to be normal in all.

Treatment-

Total 52 (82.5%) patients were treated with intravenous methyl prednisolone ,if patient's symptoms remained refractory to the steroid treatment then it was followed by plasma exchange in 3 (4.8%) patients and IV

Immunoglobin in 3(4.8%) patients ,whereas in 2(3.2%) patients there was no response with IV Ig hence he was further treated by plasma exchange.Out of the total 63 patients ,3(4.8%) patients improved by themselves without any specific treatment. 3 /63 patients required ventilatory support during hospital stay due to respiratory muscle weakness, for 2 week in 2 patients and for 1 week in 1 patient.

Time lag between onset of illness and treatment was less than 24 hr in 4(6.3%) patients, 48 hr in 14 patients,2-7 days in 29 patients, 1-2 week in 13 patients and more than 2 week in 3 patients (Table -13)

Table 13: Time lag between onset of illness and treatment

Time lag	Frequency	Percent	95% CI	
<24 hr	4	6.3	6.28	6.32
48 hr	14	22.2	22.18	22.22
2-7 days	29	46.0	45.98	46.02
1-2 week	13	20.6	20.58	20.62
> 2 week	3	4.8	4.78	4.82
Total	63	100.0		

First sign of improvement observed in the hospital stay was within less than 2 days in 4 patients,4 days in 15 patients, between 1-2 week in 24 patients, more than 2 week in 6 patients and no improvement was observed in 14 patients (Table-14)

Table 14: interval between admission and first sign of improvement

interval	Frequency	Percent	95%CI	
<2 days	4	6.3	6.27	6.33
4 days	15	23.8	23.77	23.83
1-2 week	24	38.1	38.07	38.13
No imp	14	22.2	22.17	22.23
> 2 week	6	9.5	9.47	9.53
Total	63	100.0		

First sign of improvement observed was motor in 13 patients, sensory in 39 patients, bladder in 1 patients and was mixed in 10 patients (Table 15).

Table 15: First sign of improvement

First sign	Frequency	Percent	95% CI	
motor	13	20.6	20.57	20.63
sensory	39	61.9	61.87	61.93
bladder	1	1.6	1.57	1.63
mixed	10	15.9	15.87	15.93
Total	63	100.0		

OUTCOME

MRS at discharge was 6 in 2 patients,5 in 29 patients, 4 in 13 patients ,3 in 7 patients,2 in 7 patients and 1 in 5patients.

Table 16: MRS at discharge

MRS discharge	Frequency	Percent	95% CI	
1	5	7.9	7.87	7.93
2	7	11.1	11.07	11.13
3	7	11.1	11.07	11.13
4	13	20.6	20.57	20.63
5	29	46.0	45.97	46.03
6	2	3.2	3.17	3.23
Total	63	100.0		

MRS at 3 month was 6 in 3 patients,5 in 6 patients, 4 in 20 patients ,3 in 10 patients, 2 in 9 patients,1 in 12 patients and 0 in 3 patients.

Table 17: MRS at 3 month

MRS 3 month	Frequency	Percent	95% CI	
0	3	4.8	4.76	4.84
1	12	19.0	18.96	19.04
2	9	14.3	14.26	14.34
3	10	15.9	15.86	15.94
4	20	31.7	31.66	31.74
5	6	9.5	9.46	9.54
6	3	4.8	4.76	4.84
Total	63	100.0		

MRS at 6 month was 6 in 3 patients,5 in 6 patients, 4 in 15 patients ,3 in 10 patients, 2 in 9 patients, 1 in 13 patients and 0 in 7 patients

Table 18.1: MRS at 6 month-

MRS 6 month	Frequency	Percent	95% CI	
0	7	11.1	11.06	11.14
1	13	20.6	20.56	20.64
2	9	14.3	14.26	14.34
3	10	20.6	20.56	20.64
4	15	19.0	18.96	19.04
5	6	9.5	9.46	9.54
6	3	4.8	4.76	4.84
Total	63	100.0		

MRS at 1 year was 6 in 3 patients,5 in 6 patients, 4 in 12 patients ,3 in 13 patients, 2 in 9 patients, 1 in 13 patients and 0 in 7 patients

Table 18.2: MRS at 1 year

MRS 1 year	Frequency	Percent	95% CI	
0	7	11.1	11.06	11.14
1	13	20.6	20.56	20.64
2	9	14.3	14.26	14.34
3	13	20.6	20.56	20.64
4	12	19.0	18.96	19.04
5	6	9.5	9.46	9.54
6	3	4.8	4.76	4.84
Total	63	100.0		

GROUPS –

According to MRS at one year patients were divided into good prognosis (MRS$\leq$ 3) and poor prognosis (MRS>3) group.21 were in poor outcome group whereas 42 patients were found to be in good outcome group after 1 year.

Table 18.3: 2 groups according to 1 yr MRS

Outcome	Frequency	Percent	95% CI	
Poor Outcome	21	33.3	33.18	33.42
Good Outcome	42	66.7	66.58	66.82
Total	63	100.0		

BIVARIATE ANALYSIS-

Various clinical ,CSF and MRI parameters were compared between poor outcome and good outcome group.P values were calculated by Chi square test or Fisher exact test.

Table-19: Results of bivariate analysis-

Variables		**OUTCOME**		**Total**	**P value**
		Poor (n=21)	**Good (n=21)**		
Preceding illness	**yes**	10	27	37	0.279
	no	11	15	26	
First neurological complaint	**weakness**	4	5	9	0.273
	sensory	16	19	45	
	bladder	1	8	9	
Weakness type	**yes**	16	33	49	0.49
	no	5	6	11	
Onset	**More than 48 hours**	**10**	**10**	**20**	0.055 *
	lessthan 48 hours	**11**	**32**	**43**	
Backache	No	10	30	40	**0.155**
	yes	10	12	22	

Bladder	yes	20	36	56	0.408
	no	1	6	7	
Respiratory	**yes**	5	1	6	0.0133 *
	no	16	41	57	
Bulbar	yes	3	0	3	0.033 *
	no	18	42	60	
Systemic illness	**no**	15	28	43	0.88
	yes	7	13	20	
Recurrent meylitis	**yes**	3	4	7	0.68
	no	18	38	56	
Plantar	**extensor**	4	21	25	0.017 *
	nonextenso	17	21	38	
Ankle clonus	**yes**	2	7	9	0.7
	No	19	35	54	
Sensory level	**cervical**	3	5	8	0.866
	others	18	36	54	
Spinal shock	yes	16	18	34	0.012 *
	no	5	24	29	
CSF Cell count	**normal**	16	34	50	0.113
	high	4	8	12	
CSF protein	**normal**	9	25	34	0.28
	high	11	17	28	
Csf sugar	yes	7	4	11	0.028 *
	no	13	38	51	
Mri abnormality	**no**	0	8	8	0.043 *
	yes	21	34	55	
Mri level	**cervical**	5	7	12	0.77
	others	16	27	43	
Mri horizontal extent	**Less than**	6	23	29	0.004 *
	More than	15	11	26	

Mri vertical	<2	2	13	15	0.02 *
	>2	19	21	40	
Cord swelling	no	5	22	27	0.003 *
	yes	16	12	28	
cord atrophy	**yes**	19	31	50	1.00
	no	2	3	5	
Mri pattern	yes	3	10	13	0.329
	no	18	24	42	
Treatment lag	**< 48 hr**	4	14	18	0.453
	>48 hr	17	28	45	
Improvement day	**Less than 2 week**	7	36	43	0.000025 *
	More than 2 week	14	6	20	
Mrs at discharge	**poor**	10	27	37	0.002*
	good	11	15	26	
MRS at admission	**Less or equal to3**	0	13	13	0.004 *
	Less or equal to3	21	29	50	

Bivariate analysis showed significant association (*) with outcome in following parameters-interval between onset to nadir of weakness in less than 48 hrs(p=0.055),respiratory muscle weakness (p=0.0133), bulbar muscle weakness (p=0.033), spinal shock (p=0.012), low CSF sugar (p=0.028),cord swelling in MRI (p=0.003), vertical involvement more than 2 segment (p=0.02) ,horizontal involvement of more than 2/3 rd of cord (p= 0.004),high MRS at admission ,high MRS at discharge and no sign of improvement within 2 week (p=0.000025) were associated with poor prognosis ,whereas extensor plantar response(p=0.017) was associated with good prognosis.

Binary Logistic Regression-

Dependant variable were outcome at one year (based on MRS score).Independent variables taken were statistically significant variables in bivariate analysis and variables thought to be biologically significant .

Cox & Snell $R^2 = 0.505$. which indicates good strength of the model.

On multivariate analysis significant variables found were-

1) Backache
2) Cord swelling in MRI
3) First sign of improvement within 2 weeks
4) MRS at admission

Table 20-Results of binary logistic regression analysis

Variables		Sig. Exp(B)		95.0% C.I.for EXP(B)	
		Lower	Upper	Lower	Upper
	Backache	.059	.000	.000	1.954
	mri swelling	.048	.000	.000	.859
	Imp. day	.002	.043	.006	.302
	Mrs ad. status	<0.05	.000	.000	.
	Constant	.738	.		

Table 21-Predictors of long term outcome in acute transverse myelitis

Confirmed	1)Backache 2)MRS at admission 3)Cord swelling 4)First sign of improvement within 2 weeks
Probable	1)interval between onset to nadir of weakness in less than 48 hrs(p=0.055), 2)respiratory muscle weakness (p=0.0133), 3)bulbar muscle weakness (p=0.033), 4)spinal shock (p=0.012), 5)low CSF sugar (p=0.028),

	6)normal mri (p=0.043) 7)vertical involvement more than 2 segment (p=0.02) 8)horizontal involvement of more than 2/3 rd of cord (p= 0.004) 9)no sign of improvement within 2 week (p=0.000025) 10)extensor plantar response(p=0.017) 11)mrs at discharge (p=.0.002)
Evidence inconclusive	Age,Sex,Preceding illness,latency period between preceding illness and neurological complaint ,type of weakness,backache,bladder involvement,associated systemic illness,recurrent myelitis,ankle clonus,upper level of sensory involvement,Csf cell count,CSF protein Cord involvement pattern,

RECURRENT TRANSVERSE MYELITIS -

Out of 63 patients, 7 (11%) had recurrent transverse myelitis. Out of these 7 patients,2 developed neuromyelitis optica in 2 yr and 4 year after the first episode.3 patients presented with asymmetrical weakness, 3 had symmetrical weakness, whereas 1 had only sensory complaint with upper level at T6 in the first episode. 2 patients had spinal shock in the first episode.All patients had paraparesis in the first episode and only one had quadriparesis in the first episode.5 had recurrent episode at the same segment whereas 2 had varying segments involvement with each episode.

All had normal CSF parameters except for mild CSF protein elevation in one patient. CSF for oligoclonal band was normal in all patient. Spinal angiography done in 4 patients were normal. Detail vasculitis workup was negative in all patient.One patient had normal MRI in the first

episode (presented with sensory complaint alone).One had cervical cord involvement,whereas 5 had thoracic involvement in first episode.Horizontal extension of the lesion was less than 2/3rd in 4 and was >2/3rd in 2 patients. Vertical extension of the lesion was more than 2 cord segment in 5 and was two segment in one patient.3 had cord swelling and 3 did not have cord swelling.2 had patchy involvement of cord ,whereas 4 had confluent involvement of the cord in the first episode. None of these MRI parameters were found to be significant indicator for recurrence of the lesion (Table 22).

Table 22:Comparison of various mri parameters between recurrent and nonrecurrent TM patient

variables		recurrence	No recurrence	total	P value
mri	mri-n	1	7	8	p =1.00
	Mri-abnormal	6	49	55	
Mri level	cervical	1	11	12	p= 0.884
	thoracic	5	38	43	
Horizontal extent	<2/3 rd	4	25	29	p =0.672
	>2/3 rd	2	24	26	
Vertical exyent	<2 segt	1	15	16	p = 1
	>2 seg	5	43	49	
Cord swellin	absent	3	24	27	p = 1
	Present t	3	25	28	
Pattern	patchy	2	11	13	p =0.554
	confluent	4	38	42	

Multiple sclerosis-

3 patients (4.66%) developed multiple sclerosis in follow up fulfilling Revised Mcdonald criteria for dissemination in space and time thus fitting into diagnosis of RRMS .In addition one patient had dissemination in space without dissemination in time ,thus fulfilling the criteria for probable MS.

DISCUSSION

Studies comparing clinical, laboratory and radiological profiles of the ATM patients are scarce, especially from the developing countries. Thus, this study was conducted to review the characteristics of presentation and etiological classification of acute transverse myelitis at Shree Chithra Thirunal institute of medical science and technology Trivandrum, Kerala a tertiary care center in southern India.

Total 63 patients fulfilled the criteria for acute transverse myelitis (ATM) as proposed by Jaffrey et al (7) . Out of these 63 patients,37 (57.1% ,CI- 56.97 to 57.23) were male and 26 patients (42.9 % ,CI-42.77 to 43.03) were female, thus There was no sex predisposition to TM found in our study, same as those of other studies (1,7). Mean age of presentation was 37.35 years (95% CI – 33.16 to 41.54) for females and males both.. TM affected individuals of all ages ranging from 11 to 75 years , with bimodal peaks between the ages of 10 and 20 years and 30 and 39 years same as found in previous other studies (1,7).Age and sex were not found to have any significance with long term outcome.

History of preceding antecedent illness was present in 37 (57%) patients with most common being fever without any specific cause in 22, respiratory tract infection in 8, urinary tract infection in 3 and other illness including diarrhea in 4 patients. In other studies the frequency of preceding antecedent illness was found to be 30-60% (7) . Latency period between preceding illness and neurological complaint was 1-2 week in 45% cases , less than one week in 35% and was more than 2 week in 19% cases. Jafery et al found the mean interval from infection to onset of neurological symptoms was 9+_ 6 days with preceding respiratory tract

infection in 73% ,gastroenteritis in 13% and generalized flu like symptoms in 13% cases. History of preceding antecedent illness was not found to have any significance with long term outcome in our study.

The most common first neurological complaint noted was sensory complaint in 71.4%,whereas weakness and bladder disturbances were the first complaint in 14.3% each in our study. Jafery et al found 43% patient presented with paraesthesia ,43% with pain and 14% with weakness. In our study 61 patients had sensory complaints. Out of these 61 patients , 12 had positive symptoms , 15 had negative symptoms ,whereas 34 patients had both positive and negative symptoms. Upper level of sensory complaint was cervical in 7 patients, thoracic in 44 patients, lumbar in 9 patients and sacral in 1 patients.

52 patients (81.7%) had paraparesis ,whereas 11 patients (18.3%) had quadriparesis at the peak of their deficit, difference was not significant ,when analysed for outcome.Time interval between onset to nadir of weakness was less than 48 hour in 20 patients and was more than 48 hour in 43 patients. Patients with rapid onset were found to have poor outcome by bivariate analysis ,however multivariate analysis did not show any significance .In a study by Defresne et al (23) of Twenty-four children, aged 2 to 14 years with a diagnosis of acute transverse myelitis an unfavorable outcome was associated with complete paraplegia ($P = .03$) and/or a time to maximal deficit shorter than 24 hours ($P = .005$) .

History of new onset backache at the time of weakness was present in 22 patients. Backache was radicular in 9 patients, whereas it was nonradicular in 13 patients. History of backache was found to be associated with poor outcome in multivariate analysis. In one of the very old studies (34) authors studied 52 patients with acute and subacute transverse

myelopathy , 18 had backache usually interscapular. An acute catastrophic onset was generally associated with back pain and led to a poor outcome in 7 and a good outcome in only 1 of 11 patients. Thus backache was found to be poor prognostic study in one of the earlier study same as our study.

Respiratory and bulbar dysfunction was present in 6 and 3 patient each at the time of peak deficit , which was found to have significant association with long term poor outcome in bivariate analysis ,however in multivariate analysis it was not significant. 2 patients with respiratory and bulbar involvement and 1 patient with respiratory involvement alone were expired in the acute stage, whereas rest 3 with respiratory and 1 with bulbar muscle involvement for whom PLEX /IV ig and ventilatory support was given had long term better outcome. Respiratory and bulbar involvement in TM can occur due to cranial extension of lesion resulting into involvement of cervical cord and medulla in acute period ,but if patient survives in acute stage , then it does not have significant correlation with long term outcome.

Upper level of sensory examination after examination was found to be cervical in 8 patients. There was no significant correlation between upper level of sensory examination and long term outcome as compared to previous study (27) in which lower sensory and anatomic levels were associated with good outcome ,but that study included persons with age less than 18 year only whereas our study population included pediatric and adult patient together .In our study Spinal shock was present in 34 whereas 29 out of 63 patients did not have spinal shock, which was found to have significant association with long term poor outcome in bivariate analysis ,however in multivariate analysis it was not significant . In a retrospective study (17) of 288 patients with ATM spinal shock was found

to be highly predictive of a poor outcome whereas Reiko Miyazawa et al (18) studied reports of 50 Japanese patients of ATM and no relationship was seen between prognosis and sex, preceding infections, decreased deep tendon reflexes, time course of peak neurologic impairment, treatment with prednisolone or high-dose methylprednisolone, or timing of treatment initiation.

MRS at admission was less than or equal to 3 in 13 patients and was more than 3 in 50 patients which was found to be significant prognostic indicator for long term outcome by univariate as well as by multivariate analysis. J Bruna et al.(19) studied 45 cases of ATM and The highest Rankin score reached and increased CSF glucose levels were associated with a poor outcome whereas in multivariate analysis, only the admission Rankin score was associated with outcome. Same finding was also noted in study by al deep SM et al (30) in which high 'deficit score' at onset was associated with poor outcome.

CSF parameters were available in all patient except for one patient in whom it was traumatic. CSF cell count were normal in 50 (80.6%), and was abnormal in 12 patients with cell count ranging from 10 to 100 cells. Majority of them (57 patients) had lymphocyte predominance. CSF protein was normal in 34 and was high in 28 patients. CSF sugar was less than two third of blood glucose in 11 patients and was higher than two third of blood glucose in 51 patients. CSF oligoclonal band were available in 23 patients only and all were negative.The only significant CSF parameter found to have significant association with long term poor outcome in bivariate analysis was low CSF sugar ,however in multivariate analysis it was not found to be significant .In one of the study (19) of ATM by J Bruna et al increased CSF glucose levels was found to be associated with a

poor outcome .CSF cultures and PCR for infective etiology was negative in all patients.

MRI spine was available in all patients.8 patients had normal MRI and 55 patients had abnormal MRI . (31) Campi et al have also found the spinal cord MR findings abnormalities only in 14 (46.6%) of 30 patients of ATM and 53% had normal MRI. In our study predominant MRI longitudinal involvement was cervical in 12 cases ,thoracic in 42 and was lumbar in 1 case . Horizontal involvement of less than $2/3^{rd}$ of cord was seen in 29/55 patients ,whereas it involved more than $2/3^{rd}$ of cord in 26/55 patients. Vertical involement of the lesion was restricted to only one segment in 5/55 patients ,2 segments in 10 /55patients and it involved more than 2 segments in 40/55 patients. Cord swelling was seen in 28 /55 (50.09%) patients. Gadolinum enhancement was seen in 19/54 (34.5%) patients.(In one patient contrast was not given). Cord atrophy was seen in only 5 /55 (9.1%) patients. Cord involvement pattern was patchy in 13 patients and was confluent in 42 patients.Cord edema, horizontal involvement of more than $2/3^{rd}$ of cord and vertical involement of more than 2 cord segment had significant association with long term poor outcome in bivariate analysis.

It is well known fact that patients with normal MRI had good prognosis (27) . Absence of T1 hypointensity on spinal MRI obtained during the acute period was associated with good outcome (32). After retrospective study (30) of 14 cases, al deep SM et al had concluded abnormal MRIs of the spinal cord had significantly worse outcomes than patients with normal MRIs . In earlier studies various MRI parameters have not been compared for relative significance as prognostic marker for outcome. In our study various imaging parameters were analyzed by

multivariate analysis and cord swelling was the only parameter found to have significant association with poor outcome.

Very few Indian studies have analyzed mri finding in TM and their prognostic significance .In one study by Murthy et al (43) Magnetic resonance imaging findings in 13 patients with acute transverse myelitis were reviewed. In 12 cases centrally located high intensity signal extending over few spinal segments was noted. The lesion occupied more than two thirds of the cord's cross-sectional area in 8 patient, however correlation of MRI parameter with outcome was not studied. In another study , Kalita and Mishra (42) studied patients with ATM and concluded EMG in ATM, extensive MRI changes, unrecordable MEP to lower limbs especially on lumbar stimulation and evidence of denervation in leg muscles seem to predict a poor outcome however they had very small study group(only 10 patient were included) and comparison between various mri parameters were not done . In another study by Pradhan et al (38) severe autonomic dysfunction, denervation of paraspinal muscles, "dense" lesion on imaging and often (but not always) the absent somatosensory evoked potentials were found to have poor outcome.

Total 52 (82.5%) patients were treated with intravenous methyl prednisolone ,if patient's symptoms remained refractory to the steroid treatment then it was followed by plasma exchange in 3 (4.8%) patients and IV Immunoglobin in 3(4.8%) patients ,whereas in 2(3.2%) patients there was no response with IV Ig hence they were further treated by plasma exchange.Out of the total 63 patients ,3(4.8%) patients improved by themselves without any specific treatment. 3 /63 patients required ventilatory support during hospital stay due to respiratory muscle weakness, for 2 week in 2 patients and for 1 week in 1 patient .In our study majority of

patient (82.5%) were treated with IV methylprednisolone, thus efficacy and potency of IV MP is not being studied in our study .However in one of the study done in India by Kalita and Mishra (37) 21 patients with ATM were studied and complete paraplegia, evidence of denervation on EMG and unrecordable central motor conduction time to lower limb and tibial SEP were associated with poor outcome irrespective of MPS treatment. Global test statistics did not suggest a benfecial role of MPS therapy in the outcome of ATM in that study .

First sign of improvement observed was sensory in majority (39 patients), motor in 13 patients whereas 10 patients had improvement in motor and sensory signs together and only one patient had improvement in the bladder disturbance as the first sign of improvement. This indicates in our study group ATM sensory complaints were the first feature to improve and bladder complaints remained for longer time and last to improve. In one of the study (22) of ATM in pediatrics population 10 children, with ages ranging from 8 months to 16 years were evaluated and author found that the degree of recovery of bladder function was not related to the degree of motor recovery.

Majority of the patients showed some signs of improvement within 2 week. If patient did not show sign of improvement within 2 weeks ,then long term prognosis was found to be bad by univariate and multivariate analysis. Thus interval between ictus and first sign of improvement was found to be significant prognostic factor for long term prognosis in our study.

RECURRENT TRANSVERSE MYELITIS-

Out of 63 patients, 7 (11%) had recurrent transverse myelitis. Out of these 7 patients,2 developed neuromyelitis optica in 2 yr and 4 year after the first episode.Thus 3.17% patient of TM and 28.57% of recurrent TM developed NMO in follow up , however NMO antibodies level were not done. 3 patients presented with asymmetrical weakness, 3 had symmetrical weakness, whereas 1 had only sensory complaint with upper level at T6 in the first episode. 2 patients had spinal shock in the first episode.All patients had paraparesis in the first episode and only one had quadriparesis in the first episode.5 had recurrent episode at the same segment whereas 2 had varying segments involvement with each episode.

All had normal CSF parameters except for mild CSF protein elevation in one patient. CSF for oligoclonal band was normal in all patient. Spinal angiography done in 4 patients were normal. Detail vasculitis workup was negative in all patient.One patient had normal MRI in the first episode (presented with sensory complaint alone).One had cervical cord involvement,whereas 5 had thoracic involvement in first episode.Horizontal extension of the lesion less than $2/3^{rd}$ in 4 and was $>2/3^{rd}$ in 2 patients. Vertical extension of the lesion was more than 2 cord segment in 5 and was two segment in one patient.3 had cord swelling and 3 did not have cord swelling.2 had patchy involvement of cord ,whereas 4 had confluent involvement of the cord in the first episode. In bivariate analysis none of these MRI parameters were found to be significant indicator for recurrence of the lesion.

In one of the Indian case series (41) three patients with acute complete transverse myelopathy were described which relapsed several

times at the same site. These patients, two women and one man, had two to five attacks spanning three to seven years. Oligoclonal bands were present in the CSF in one patient. Brain MRI was normal in two patients; MRI of the spinal cord was abnormal and showed cord oedema with multiple areas of hyperintense signals on T2 and proton density weighted scans and hypointense signals on T1 weighted images in areas corresponding to the clinical level, suggesting an inflammatory/ demyelinating disorder. These patients may represent a relapsing demyelinating disorder restricted to the spinal cord, distinct from multiple sclerosis.

In another retrospective analysis (28) of 37 cases in which 15 cases of idiopathic RTM and 22 cases of multiple sclerosis related transverse myelitis (MSRTM) were reviewed and concluded that idiopathic RTM is a disease entity distinct from MSRTM, differing in its male preponderance, absence of oligoclonal bands, frequent multiple relapses, and frequent presentation as acute transverse myelitis.

3 patients had 2 episodes, 3 had 3 episodes whereas one patient had total 4 episodes.Time interval between relapses varied from one month to 10 year.One patient had 2 relapses ,whenever steroid is being tapered i.e. one month after first episode and 8 year after first episode. MRI brain was normal in all patient and CSF for oligoclonal band were negative, and these patient were not fulfilling criteria for MS.ENMG study and VEP were also normal in these patients . In one study of recurrent myelitis (25) among 32 patients studied, 20 (63%) had single ATM attack upon follow up for 39-93 months, three developed recurrent ATM related to CTD and nine (28.1%) developed recurrent neuroinflammation compatible with IIDD. Among IIDD patients, three had NMO, two restricted variant of NMO, three IRTM and one had classical MS.

In our study Out of these 7 patients of RTM ,2 developed neuromyelitis optica and 5 had idiopathic RTM. Our idiopathic RTM group patients also had similar clinical and imaging profile as described by Chan et al (25) and most probably have relapsing demyelinating disorder compatible with IIDD, which is described in Asian population suggesting difference in presentation of demyelinating disease between Asian and Western population .

Multiple sclerosis-

3 patients (4.9 %) developed multiple sclerosis in follow up fulfilling Revised Mcdonald criteria for dissemination in space and time thus fitting into diagnosis of RRMS .In addition one patient had dissemination in space without dissemination in time ,thus fulfilling the criteria for probable MS. Out of these 4 patients 3 were male and 1 was female, age ranged between 27 to 42 year. J Bruna et al .studied 45 cases of ATM and 5 patients (11%) converted to MS. Mean follow-up time was 3.5 years. There was an association between younger patients and female patients with conversion to MS.

In one study 58 ATM patients with normal brain MRI at presentation were studied (26) for up to 5 years ,17 of 58 (29%) patients developed MS of which 7 (41%) patients developed Clinicaly definite MS (CDMS) and 10 (59%) developed MS using McDonald Imaging Criteria. In another study (29) none of the 20 ATM patients developed MS over an average follow-up period of 4.5 years.

In our study all patients of RRMS had presentation with acute onset parapresis with spinal shock and MRI suggestive of horizontal involvement of more than $2/3^{rd}$ cord area and vertical extension of lesion

to more than 3 cord segment. One patient (R.B.) had long sement cord involvement extending from C5 to L1 cord segment. VEP showed prolonged P100 latency in only 1 patient, whereas ENMG and CSF for oligoclonal band were normal in all patients. None of our 4 patient of MS had family history of MS.

During first episode of TM all 4 had normal MRI brain. They had new clinical episode and developed new MRI lesion idicating dissemination in space and time in 1 to 3 year follow up. In a retrospective analysis of 45 patients, Michael Harzheim et al (16) found 22% cases of ATM was the first manifestation of possible multiple sclerosis (ATM-MS) and monosegmental involvement of the spinal cord was most frequent while spinal cord involvement of two or more segments was more common in ATM of other etiologies.

De Seeze et al (10) studied 79 cases of ATM and found multiple sclerosis in 34 (43%) cases , initial symptoms were predominantly sensory ($P < 0.001$) and spinal cord MRI showed lateral or posterior lesions of less than two vertebral levels in multiple sclerosis. Thus in western studies frequency of ATM-MS was 20-40% as compare to 6.34% in our study. Another difference was absence of CSF oligoclonal band and long sement cord involvement in our ATM-MS patient. In one study by J Sellner et al (24) 73 patients with a first-ever APTM were evaluated and authors concluded that a family history of MS, high EDSS at presentation, lesions on brain MRI, CSF-specific oligoclonal bands or abnormal IgG-index may indicate an increased risk for conversion to MS.

Bansil S (36) carried out a case-control study to compare MS in the India and the United States and used clinical, evoked potential, and MRI criteria to assess similarities and differences. Their results

indicated that the rate of disease progression and frequency of involvement of the cerebral hemispheres, cerebellum, spinal cord, and brainstem were similar in the two populations. In the joint Asian study (21) a total of 263 patients of MS from various Asian countries were studied and found 40% percent of the patient had optic-spinal recurrent and 60% had Western forms of multiple sclerosis. Severe involvement of spinal cord is thus a universal feature of Asians with multiple sclerosis, seen in both optic-spinal recurrent and Western form of multiple sclerosis .In another recent study from Pakistan (20) 20 consecutive patients of ATM were studied and only 2 patient (10%) had conversion into MS. Thus opticospinal variant of MS is found to be more common in this part of the world however Asian/Indian study data for cases of ATM as the first manifestation of multiple sclerosis (ATM-MS) is not available. In our study ATM as the first manifestation of MS only in 4 patient (6.34%) and 7 patients (11%) had recurrent TM and 2 patient (3.1%) developed Neuromyelitis optica .None of the ATM-MS patients had monosegmental involvement.

CONCLUSION

Retrospective analysis of 63 patients of acute transverse myelitis in this study revealed history of backache at the time of presentation, MRS at the time of admission, cord swelling in MRI and time interval between ictus and first sign of improvement are the confirmed significant prognostic indicators for long term outcome.

Other parameters found to be of probable significant prognostic indicators for long term outcome are interval between onset to nadir of weakness in less than 48 hrs, respiratory muscle weakness ,bulbar muscle weakness ,spinal shock, low CSF sugar ,normal MRI ,vertical involvement more than 2 segment, horizontal involvement of more than 2/3 rd of cord ,no sign of improvement within 2 week, extensor plantar and MRS at discharge.

7/63 patients (11.11%) developed recurrent transverse myelitis ,out of which 2 patients (28.57%) developed neuromyelitis optica and 5 (71.43%) had idiopathic recurrent transverse myelitis (R-TM) . These R-TM patients had normal spinal angiography and vsculitic workup and were steroid responsive with 2 to 4 episodes of recurrent TM. Thus R-TM is the demyelinating disease which does not fit into any of the previously well described demyelinating diseases like ADEM, MS or neuromyelitis optica .

Only 4/63 patients (6.35%) developed MS in the follow up. Clinical, MRI and CSF parameters of these patients were different from those described in the western literature.

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