Original Research Article

Clinical profile of 50 adults with demyelinating diseases of central nervous system - A prospective observational study

T. Murali Venkateswara Rao[1*], U. Ganga Prasad[2]

[1]Associate professor, [2]Assistant Professor
Department of General Medicine, NRIGH, Chinakakani, Andhra Pradesh, India
[*]Corresponding author email: **muralivenkateswararao.t@gmail.com**

International Archives of Integrated Medicine, Vol. 3, Issue 11, November, 2016.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 31-10-2016 **Accepted on:** 11-11-2016
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: T. Murali Venkateswara Rao, U. Ganga Prasad. Clinical profile of 50 adults with demyelinating diseases of central nervous system - A prospective observational study. IAIM, 2016; 3(11): 143-150.

Abstract

Introduction: Demyelinating disorders of CNS are characterized by inflammation and selective destruction of central nervous system (CNS) myelin. In spite advancements in diagnostic techniques, studies on Indian adult population on the subject are very scarce. The current study is aimed to document clinicopathological profile of primary and secondary demyelinating disease of CNS in adult patients, presenting to a tertiary care teaching hospital.

Materials and methods: The current study was prospective observational study of 50 patients presenting to a tertiary care teaching hospital with various symptoms suggestive of demyelinating CNS disorders and were clinically confirmed.

Results: A total of 50 participants were recruited into the study. Highest proportion of subjects was below 20-year age group. The proportion of females (58%) was higher than that of males (42%). Paraplegia was the most common clinical presentation in study population, which was seen in 13 (26%) participants.. The most common level of spine involved was dorsal spine in 17 (34%) subjects and equal number of subjects had cervico dorsal spine involvement. Demyelinating Transverse myelitis was the most common type of demyelinating disorder seen in study population, which was diagnosed in 42% of the study subjects. Multiple sclerosis was present in 24% of the subjects and 22% of the subjects had ADEM. Secondary demyelination was present in 4 (8%) of the subjects and only 2 (4%) of the subjects had DEVICS. Among the causes of secondary demyelination HIV was the most common cause, present in 4% of cases. Herpes zoster and chicken pox were present in 1 (2%) of cases each in study population.

Conclusions: Demyelinating disorders of the central nervous system are common among younger age

group females. Primary demyelinating diseases are more common than secondary demyelinating diseases. Clinically isolated demyelination syndrome patients need regular follow up with MRI imaging in due course. Patients with more than three segmental involvement in spinal cord and those with more than three peri-callosal, peri- ventricular and posterior fossa lesions in MRI images has poor clinical recovery after treatment. MRI brain and spine provides more prognostic information than clinical assessment.

Key words

Demyelinating diseases, Central nervous system, Clinical profile.

Introduction

Demyelinating disorders of CNS are characterized by inflammation and selective destruction of central nervous system (CNS) myelin [1]. The peripheral nervous system (PNS) is spared and most patients have no evidence of an associated systemic illness. Inflammatory demyelinating diseases of the central nervous system occur throughout the world and are the foremost cause of the non-traumatic neurological disability in young adults [2-7]. Multiple sclerosis is the most common of these disorders. However Multiple Sclerosis represents only one member of a family of CNS idiopathic inflammatory demyelinating diseases which also include acute transverse myelitis, Acute disseminated encephalomyelitis, (ADEM) and Neuromyelitis optica (Devics disease) [3, 8-11]. Although these disorders are all similarly characterized by focal CNS demyelination they vary in their clinical course, prognosis, regional distribution, pathology and pathogenesis [11].

Advances in the imaging modalities like various latest developments in magnetic resonance imaging (MRI) and spectroscopy have aided not only accurate clinical diagnosis of this spectrum of diseases, but also accurate prognostication [11, 12]. Recent progress has occurred in understanding the cause, the genetic components, and the pathologic process and therapeutic options available for these diseases [1, 4, 7, 13, 14]. In spite of these advancements, studies on Indian adult population on the subject are very scarce. The current study is aimed to fill this knowledge gap, which can help in clinicians in better understand these spectrum disorders and provide better diagnostic and treatment services.

Aim

- To study the clinicopathological profile of primary and secondary demyelinating disease of CNS in adult patients, presenting to a tertiary care teaching hospital.

Materials and methods

Study design: The study was a prospective observational study.

Study setting: The study was conducted in NRI Medical College and General Hospital, which is tertiary care teaching hospital.

Study period: The study was conducted over the period of 18 months from April 2012 to September 2013.

Study population: The study population involves fifty suspected cases of demyelinating disease of central nervous system. The patients were selected from general medical ward and neuro medical ward.

Inclusion criteria

- Subjects aged above 13 years
- Both genders
- Presenting with symptoms suggestive of long tract involvement (like pyramidal tract, MLF, posterior column, cerebellar pathways) with or without optic nerve and bladder involvement.

Exclusion criteria

- Patients who were critically ill
- Subjects with no evidence for Long Tract Involvement

Ethical issues

The study was approved by institutional human ethics committee. Informed written consent was obtained from all the participants. Confidentiality of personal information was maintained throughout the study.

Source of data

All the eligible subjects satisfying inclusion criteria and were willing to participate in the study were subjected to

- Detailed history taking including history of recent respiratory tract infection, vaccination, fever, viral exanthema, radiation and drug intake.
- Detailed neurological examination.
- Ophthalmological examination.
- Routine blood and urine investigation.
- ELISA for HIV
- Antigen for Hepatitis B.
- VDRL – ELISA for Syphilis.
- Vasculitis Profile: ANA , DS-DNA, P-ANCA, C-ANCA, Antiphospholipid Antibody
- CSF Analysis (pleocytosis, biochemistry, oligoclonal band)
- MRI Brain and spine.

All the patients were treated with 1g IV methyl prednisolone for 5 days. Then put on oral prednisolone tapering dose and Azathioprine 2 mg/kg /d. All the patients were reassessed after 6 weeks. In cases of multiple sclerosis, the neurological deficit assessed with the help of KURTZKE -EDSS score and correlate the disability score with MRI findings.

Statistical analysis

Statistical analysis was done by IBM SPSS version 21. Descriptive analysis of clinical, imaging, CSF analysis and treatment response related parameters was done. Mean and standard deviation was used to summarize quantitative parameters and frequency and proportion was used to summarize categorical paramters.

Results

A total of 50 participants were recruited into the study. Highest proportion of subjects was below 20-year age group. The proportion of subjects who were aged 21 to 25, 26 – 30 were 125 and 14% respectively. None of the study subjects were above 60 years of age group in the study. The proportion of females (58%) was higher than that of males (42%) as per **Table - 1**.

Table - 1: Age and gender distribution of study participants (N=50).

Parameter	Number	Percentage
Age group (Years)		
20 and below	12	24.0%
21-25	6	12.0%
26-30	7	14.0%
31-35	5	10.0%
36-40	3	6.0%
41-45	5	10.0%
46-50	2	4.0%
51-55	5	10.0%
56-60	5	10.0%
61 and above	0	0.0%
Gender		
Males	21	42.0%
Females	29	58.0%

Paraplegia was the most common clinical presentation in study population, which was seen in 13 (26%) participants. It was followed by paraperisis, seen in 22%, bladder disturbances seen in 20% and quadriperesis seen in 16% of participants. Only sensory involvement was seen in 6% of the subjects. Quadriplegia, Monoperesis, hemi paresis, B/L INO and motor deficit with optic nerve involvement were seen in 4% of the subjects each. Only 1(2%) person had ataxia (**Table - 2**).

The most common level of spine involved was dorsal spine in 17 (34%) subjects and equal number of subjects had cervico dorsal spine involvement. Cortical and sub cortical structures were involved in 15 (30%) subjects. Brain stem, cervical cord, cerebellum with peduncle and

lumbo sacral spine were involved in 8(16%), 7 (14%), 4 (8%) and 2 (4%) subjects respectively (**Figure - 1**).

Table - 2: Clinical presentation in study population (N=50).

Clinical presentation	Cases	Proportion
Paraplegia	13	26.0%
Paraperesis	11	22.0%
Bladder involvement	10	20.0%
Quadriperesis	8	16.0%
Sensory involvement	3	6.0%
Quadriplegia	2	4.0%
Monoperesis	2	4.0%
Hemiparesis	2	4.0%
B/L INO	2	4.0%
Motor with optic nerve Involvement	2	4.0%
Ataxia and sensory	1	2.0%

Demyelinating Transverse myelitis was the most common type of demyelinating disorder seen in study population, which was diagnosed in 42% of the study subjects. Multiple sclerosis was present in 24% of the subjects and 22% of the subjects had ADEM. Secondary demyelination was present in 4 (8%) of the subjects and only 2 (4%) of the subjects had DEVICS (**Table – 3**).

Table - 3: Frequency of demyelinating disorders.

Diagnosis	Cases	%
Demyelinating Transverse myelitis	21	42
Multiple sclerosis	12	24
ADEM	11	22
Secondary Demyelination	4	8
DEVICS	2	4

Elevated CSF protein was the most common CSF finding, present in 98% of the study population. Lymphocytic pleocytosis was present in 90% of the subjects, Oligocloncal banding was present in 54% of the subjects (**Table - 4**).

Among the causes of secondary demyelination HIV was the most common cause, present in 4% of cases. Herpes zoster and chicken pox were present in 1 (2%) of cases each in study population (**Table - 5**).

Table - 4: CSF findings in study population (N=50).

CSF findings	Cases	Proportion
Lymphocytic pleocytosis	45	90%
Elevated CSF proteins	49	98%
Oligoclonal banding	27	54%

Table - 5: Aetiology of secondary demyelination (N=50).

Secondary Demyelination	Cases	Frequency
HIV	2	4.0%
Herpes zoster	1	2.0%
Chicken pox	1	2.0%

All the patients of this study were treated with pulse steroid regimen, Inj. Methyl Prednislone 1G Daily for 5 days. Majority (54%) of the study population showed good response to steroids. Moderate steroid response was seen in 14 (28%) of patients and remaining 9 (18%) of patients had minimal steroid response (**Table – 6**).

Table - 6: Analysis of treatment response in study population (N=50).

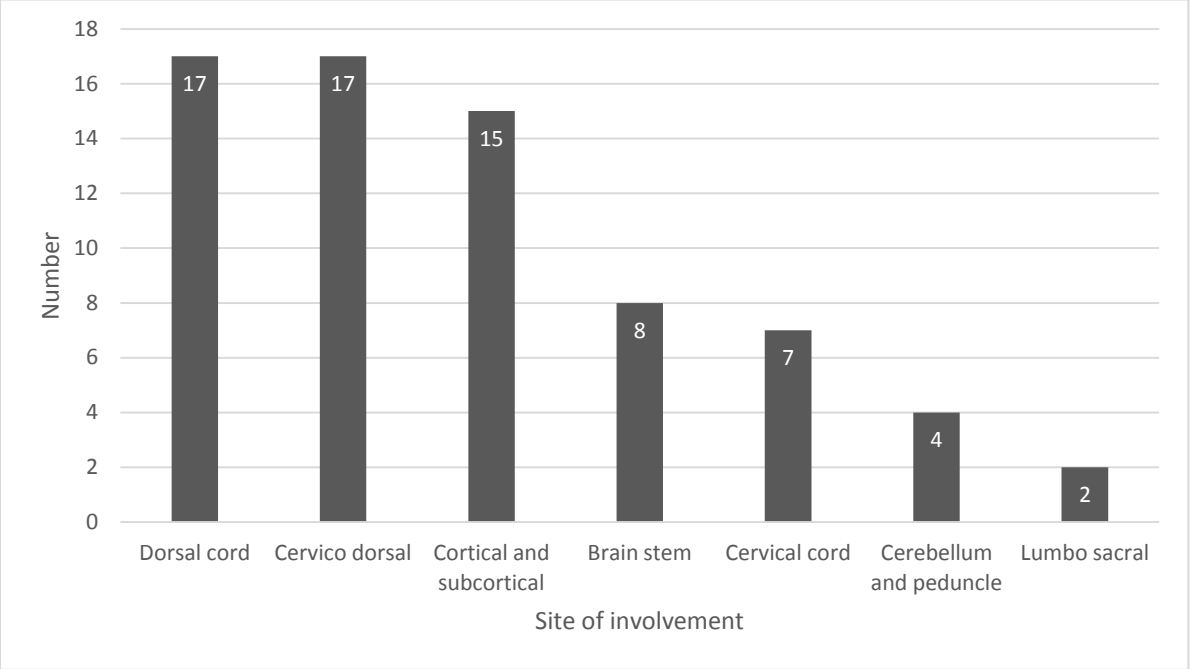
Response to steroids	Cases	Percentage
Good response	27	54%
Moderate	14	28%
Minimal	9	18%

Discussion

Studies documenting the clinic pathological profile are scarce from India. Even though advent of new diagnostic techniques has made etiological confirmation of these diseases, possible in many settings, the availability of these advanced techniques is in limited to only few tertiary centres in resource poor settings like India. Hence studies on clinical and etiological profile studies can help in clinicians to have high

index of suspicion and refer these patients to appropriate care. In the current study, the age distribution in demyelinating disorders of the central nervous system showed that younger age groups were more affected, as 50% of the patients belong to less than 30 years of age. Females were more affected (58%), than males (42%) in the current study. The study findings are in agreement with studies by Pohl D. [11], Koudriavtseva T., et al. [15], and Zhou Z., et al. [16] etc., which have highlighted the predilection of young people to the demyelinating disorders.

Figure - 1: Site of involvement of spinal cord in study population (N=50).



In the current study, the clinical presentation varied from motor weakness in the form of paraplegia, Paraperesis, quadriplegia, quadriperesis, Monoperesis, or rarely hemiplegia, two patients presented with optic atrophy and paraplegia. Two patients presented with bilateral INO with past history of similar illness. Paraplegia or paraperisis was the most common clinical presentation, as documented by many previous studies by Barnett M. H., et al. [1], Eckstein C., et al. [3]. Sensory involvement in the form of paraesthesia, brain stem involvement in form of bilateral INO, optic nerve involvement with optic atrophy, cerebellar ataxia, and bladder involvement. Optic nerve involvement reported in a study by Argyriou A. A. and N. Makris [17] and DeLuca G. C., et al. [18].

In this study, 90% of the patients showed lymphocytic pleocytosis in CSF analysis.49 patients of this study showed elevated CSF proteins. The measure of oligoclonal band in CSF is to assess the intrathecal production of Ig G. About 75% of multiple sclerosis patients usually show positive oligoclonal band in CSF studies but in this study, only 54% of patients showed positive oligoclonal band in CSF. Many studies in the past by Haines J. D., et al. [19], Shi Q., et al. [20], Stilund M., et al. [21] and Burman J. and A. Svenningsson [22] etc. have documented similar findings of increased CSF protein, lymphocytosis and oligo clonal bands in CSF as important features in diagnosis of demyelinating disorders of CNS. These studies have also documented the role of various other inflammatory markers like Interleukins, CSF glycoproteins and lactate etc in diagnosis of demyelinating diseases.

In MRI Imaging studies, the regional distribution of the various sites of involvement of demyelination is as follows. The most common

level of spine involved was dorsal spine in 17 (34%) subjects and equal number of subjects had cervico dorsal spine involvement. Cortical and sub cortical structures were involved in 15 (30%) subjects. Brain stem, cervical cord, cerebellum with peduncle and lumbo sacral spine were involved in 8 (16%), 7 (14%), 4 (8%) and 2 (4%) subjects respectively. MRI findings of the current study are in confirmation with studies published by Rovira Canellas A. [23], Gass A., et al. [24], Pohl D [11] and Harada M. [25] etc., which have documented high utility of MRI in these disorders, even though there were minor variations across the studies in most common site of involvement. Vasculitis profile was done only in 4 patients randomly among which one patient is positive for ANA and one patient is positive for P-ANCA.

In this study, Demyelinating Transverse myelitis was the most common type of demyelinating disorder seen in study population, which was diagnosed in 42% of the study subjects. These patients had 70-80% chance of developing multiple sclerosis later as the MRI images of these cases showed more than three T2 weighted lesions in spinal cord. Hence these patients need further regular follow up with MRI imaging studies. Studies by Canellas A. R., et al. [9], Eckstein C., et al. have documented similar findings.

Multiple sclerosis was present in 24% of the subjects and 22% of the subjects had ADEM. In many of the previously published studies by Pohl D. [11], Zhou Z., et al. [16] multiple sclerosis was the most common demyelinating disorder, in contrary to the current study. Secondary demyelination was present in 4 (8%) of the subjects and only 2 (4%) of the subjects had DEVICS Four patients were diagnosed to have Secondary Demyelination, among which two cases were HIV ELISA positive, one case occurred following Herpes Zoster, one case occurred following chicken pox. Viral etiology has been proved to one of the major causes of demyelinating disorders as documented in studies by Weiner L. P., et al. [26], Wender M. [27], Irkec C. [28] and Halsey N. A., et al.[29] etc.

The disability score in MS is calculated with KURTZKE'S Expanded Disability Status Score (EDSS) Scoring system. One patient had EDSS score of 2.0 Six patients had EDSS score between 3- 3.5 Two patients had EDSS score between 4-4.5 Three patients had EDSS score of 6.0 Patients with periventricular T2 weighted lesions and posterior fossa lesions in MRI had more disability with EDSS score of 6.0. So the MRI imaging studies provide more prognostic information than clinical assessment.

All the patients were treated with 1 g IV methyl prednisolone for 5 days. Then put on oral prednisolone tapering dose and Azathioprine 2 mg/kg/d. All the patients were reassessed after 6 weeks. 54% of the patients showed good response. 28% of the patients showed moderate response and 18% of the patients showed minimal response. The response to steroid therapy was good in 75% of MS patients, 50% of the idiopathic demyelinating transverse myelitis patients and in 46% of the ADEM cases.

All the patients were followed up for six weeks after steroid therapy. The recovery form neurological impairment was good in 75% of MS patients, 50% of the idiopathic demyelinating transverse myelitis patients and in 46% of the ADEM cases. In Devics disease there was only minimal improvement in visual function. This is because of their late presentation to the hospital. Patients who had more than three segmental involvement in spinal cord and those with more than three peri callosal, peri ventricular and posterior fossa lesions in MRI images showed poor clinical recovery.

Conclusions

Demyelinating disorders of the central nervous system are common among younger age group females. Primary demyelinating diseases are more common than secondary demyelinating diseases. Clinically isolated demyelination

syndrome patients need regular follow up with MRI imaging in due course. Patients with more than three segmental involvement in spinal cord and those with more than three peri-callosal, peri- ventricular and posterior fossa lesions in MRI images has poor clinical recovery after treatment. MRI brain and spine provides more prognostic information than clinical assessment.

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