Original Research Article

Study of profile of patients with clinically isolated syndrome: A hospital based prospective study

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Abstract

Background: Clinically isolated syndrome (CIS) describes the first clinical episode of symptoms and signs suggestive of an inflammatory demyelinating disorder of the central nervous system (CNS) It can by mono or multifocal affecting the various parts of the CNS. The present study aimed to evaluate profile of patients with CIS. **Materials and Methods:** The study was conducted in the Department of Neurology, Bangur Institute of Neuroscinces, Kolkata during the period of Jan 2013 to Dec 2014. A total of 49 cases were included in the study on the basis of inclusion and exclusion criteria. All patients were explained study procedure and consent was obtained. Demographic, clinical and radiological observations were recorded and analyzed. **Results:** Majority of CIS patients were Females (n=35) compared to males (n=14). Mean age of patients was 25.04 years. Maximum patients of CIS had optic neuritis ((n=38), followed by myelitis (n=6), brainstem/cerebellar (n=2) and multifocal (n=3) presentation. Majority of CIS patients had MRI lesions (n=39/49).Within the optic neuritis group (n=28/39)73.68% had MRI lesions, 100% each in myelitis, brainstem/cerebellar and multifocal subgroups. Within the optic neuritis(n=38/49) which formed the major subgroup presentation, majority had unilateral, painful vision loss with color desaturation, afferent papillary defect, optic disc edema and all showed demyelinating type VEP abnormality. **Conclusion:** Clinically isolated syndrome (CIS) is a term that describes a first clinical episode with features suggestive of multiple sclerosis (MS). The present study results conclude that CIS has got female prepondarence, with predeliction for young adults and that optic neuritis forms most common clinical presentation, followed by myelitis, brainstem/cerebellar and multifocal groups. MRI forms the single most important non-invasive tool for diagnosis and prognostication of CIS patients.

Keywords: Brain stem, Clinically Isolated Syndrome, MRI, optic neuritis, Multiple sclerosis, inflammation.

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INTRODUCTION

The term Clinically Isolated Syndrome is used to describe and define a group of disorders that represent a CNS demyelinating attack including optic neuritis, transverse myelitis, internuclear ophthalmoplegia, trigeminal neuralgia, and other brainstem, long-tract motor, and/or sensory symptoms. Other description of CIS include: clinical onset of Multiple Sclerosis, isolated demyelination syndrome, first demyelinating episode, first presentation of multiple sclerosis, first attack of Multiple Sclerosis, and focal isolated idiopathic inflammatory demyelinating disorders. It is typically applied to adults aged 20-45 years who developed acute or Subacute presentation of symptoms reaching a peak within one to three weeks. The

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attack should last for at least 24 hours and occur in the absence of fever or infection, with no clinical features of encephalopathy. CIS is isolated in time (i.e., monophasic), and it is usually isolated in space (i.e., monofocal) with signs indicating a lesion in the optic pathway, spinal cord, brainstem, cerebellum, or rarely the cerebral hemisphere. However, some patients with a CIS have clinical evidence of dissemination in space (i.e., multifocal) affecting two or more locations9. Since CIS could be monophasic, some of the patients may not subsequently develop new symptoms or brain MRI lesions consistent with MS. Therefore, understanding the prognostic factors for MS after a CIS may help identifying patients who are at higher risk for developing clinically definite MS and have ongoing disease activity. It has been shown that baseline MRI findings have the most predictive Value in evaluating the risk of CIS conversion to MS. The aim of our study is to assess the demographic, clinical and radiological prognostic factors in CIS patients.

MATERIALS AND METHODS

Study settings: The study was conducted in the Department of Neurology, Bangur Institute of Neuroscinces, Kolkata in the period of Jan 2013 to Dec 2014. Ethical approval was obtained from Institutional Research Committee and Institutional Human Ethics Committee. It was conducted as prospective study.

Inclusion criteria

Patients with their first clinical event suggestive of CIS-Clinically Isolated Syndromes were included in the study within 3 months of their initial presentation. Those patient's aged between 20-45 years, within 3 months of initial presentation, suggestive of CIS, occurring in the absence of fever or infection or encephalopathy, progressive for 2- 3 weeks were included in the study.

CLINICAL CRITERIA MRI CRITERIA

1. Optic neuritis 1. 1 GD enhancing lesion
2. Myelitis 2. >= 9 T2 lesions of which
3. Internuclear ophthalmoplegia a. 1 infratentorial lesion.
4. Brainstem/cerebellar symptoms/signs b. 1 Juxtacortical lesion.
5. Dysarthria c. 3 Periventricular lesions.
6. Sensory symptoms.

Exclusion criteria

Patients with progressive symptoms at onset, those who did not satisfy the CIS definition, or those who had symptoms or signs suggestive of other inflammatory disorders (e.g., acute disseminated encephalomyelitis (ADEM), neuromyelitis optical (NMO), or vasculitis were excluded.

- Not showed CIS symptoms progression
- CIS due to infection
- CIS due to secondary inflammatory disorders
- CIS due to vascular disorders
- Patients with other co-morbid conditions like diabetes, hypertension, head injury, trauma and vitamin-D deficiency.

Procedure

A total of 49 patients were included in the study on the basis of inclusion and exclusion criteria. All the patients were explained study procedure and inform consent was obtained. The patient's demographic data (age, gender) was noted. They were subjected to MRI to evaluate the number of lesions. Standard MRI procedure was followed for the estimation of lesions. Demographic, clinical and MRI data was analyzed and compared.

Statistical analysis: The data was expressed in number, percentage (%) and mean. Statistical Package for Social Sciences (SPSS 20.0) version used for analysis.

RESULTS

The gender comparison of CIS patients showed maximum number of females (n=35) than males (n=14) (Table-1). 28.92 were the mean age of males and 23.48 is mean age of females. Females had younger age predilection for CIS occurrence than compared to males. The mean age of study population is 25.04 years. In the clinical presentation most of the patients showed optic neuritis (n=38), 6 showed myelitis and 3 multifocal and Only 2 patients had brain stem/cerebellar problems (Table-2). Majority of CIS patients had MRI lesions(n=39/49.Within the optic neuritis group(n=28/39)73.68% had MRI lesions, 100% each in myelitis, brainstem/cerebellar and multifocal subgroups). 19 patients showed 1-3 lesions, 17 showed 4-8 lesions and 10 patients did not show any lesions in MRI. 3 patients showed more than 9 lesions. Within the optic neuritis(n=38/49) which formed the major subgroup presentation, majority had unilateral(28), painful vision loss(26), with color desaturation (16), afferent pupillary defect (30), optic disc edema(22) and all showed demyelinating type VEP abnormality(38). MRI lesions were found in 73.68% (28/39) of patients with optic neuritis. 0 lesions found in 10/38(26.31%), 1-3 lesions in 18/38 (47.36%), 4-8 lesions in 9 /38(23.68%) patients and >=9 lesions in 1/38(2.63%) patients.

Table 1: Distribution of patients based on the gender

Gender	Number (n=49)	Percentage (%)
Male	14	28.57
Female	35	71.42

Table 2: Distribution of patients based on clinical presentation

Clinical presentation	Number (n=49)	Percentage (%)
Optic neuritis	38	77.55
Myelitis	6	12.26
Brain stem/Cerebellar	2	4.08
Multifocal	3	6.12

DISCUSSION

In our study 49 patients presenting with Clinically Isolated Syndromes were followed up for 2 years. Females formed the majority with 35 and males were 14. The Female: Male ratio being 2.5: 1 which is in agreement with other Indian studies by Chopra JS, Radhakrishnan K, Sawhney BB *et al*: Multiple sclerosis in North-west India, 1980335, and Bhatia M, Behari M, Ahuja GK: Multiple sclerosis in India, 1996 337. The female to male ratio was 2.5:1, in a previously done study from eastern India from our own institute by G. Gangopadhyay, S. K. Das, P. Sarda *et al*., "Clinical profile of multiple sclerosis in Bengal," *Neurology India,* 1999120. As also the female: male ratio being 2:1, in the study by Orton SM , Herrera BM, Yee IM , *et al*. Sex ratio of multiple sclerosis in Canada, *Lancet Neurol.* 2006165, Richards RG, Sampson FC, Beard SM, Tappenden P. A review of the natural history and epidemiology of multiple sclerosis: implications for resource allocation and health economic models. *Health Technol Assess.* 2002167. Average age among females - 23.48 Years and among males - 28.92 years. Overall average age including females and males was 25.04 years, which is comparable to previous Indian studies - Chopra JS, Radhakrishnan K, Sawhney BB *et al*: Multiple sclerosis in Northwest India, 1980335, Singhal BS: Multiple sclerosis and related demyelinating disorders in Indian context, 19 8 7336, Bhatia M, Behari M, Ahuja GK: Multiple sclerosis in India, 1996337 In our study of 49 patients with Clinically Isolated Syndromes - 38 (77.55%) patients were of the Optic neuritis, 6 (12.24%) were of Myelitis, 3 were of Multifocal (6.12%) and 2 were of Brainstem/Cerebellar clinical presentations. So Optic neuritis as a clinical presentation formed the major subtype of Clinically Isolated Syndrome. Our study results are similar to other Indian studies data. Early literature on MS from different parts of India suggested that there was high prevalence of optic and spinal cord involvement. In 1985 Jain and Maheshwari, Multiple sclerosis: Indian experience in the last thirty years," *Neuroepidemiology,* 77 1985, 115 published data on 354 cases of MS from 9 different centers in India. Optic neuritis (OPN] as the initial presentation was seen in 22.2-58 % of cases seen at 5 of these centers. Recent studies have shown a frequency of 23.6% from the north west by . P. Syal, S. Prabhakar, A. Thussu, S. Sehgal, and N. Khandelwal, "Clinical profile of multiple sclerosis in North-West India, 1999118,44% from the south of the country - . G. R. K. Sarma and D. K. Nagaraj, "Multiple sclerosis in South India, 2005119, and 53.3% from the east of the country- G. Gangopadhyay, S. K. Das, P. Sarda *et al*., "Clinical profile of multliple sclerosis in Bengal," *Neurology India,* 1999120. which is significantly high as compared to western data. The study by P. Syal *et al*, showed optic neuritis as initial presentation in 23.6% and from south Indian studies it was 44%, G. R. K. Sarma and D. K. Nagaraj. Our study result, Optic neuritis as initial presentation in 77.5% is comparable to the result obtained in a study from our institute by G. Gangopadhyay, S. K. Das, P. Sarda *et al*, which was 53.33%. But our study results differ from the western study data in terms of CIS presentation- Miller *et al* reported that 21% presented with ON, 46% with spinal cord syndromes, 10% with brainstem-cerebellar syndromes, and 23% with multifocal abnormalities. In a Kuwaitian study by R. Alroughani *et al*, while 30.9% of patients had spinal cord symptoms at onset. Brainstem/cerebellar and optic pathway involvements were seen in 17.5% and 23.7% of patients, respectively and 7.2% of patients presented with multifocal involvements. So in terms of CIS presentation, unlike western data where spinal cord involvement is more common, our study results support Indian studies with Optic neuritis as the most common CIS presentation. The profile of 38 patients with Optic neuritis- majority had unilateral eye involvement associated with ocular pain, RAPD, color desaturation and optic disc edema matches various other study data - Beck RW, Trobe JD, Moke PS, *et al*. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the optic neuritis treatment trial. *Arch Ophthalmol.* 78 2003229-230. Frohman EM *et al* and Abou Zeid N, Bhatti MT- Acute inflammatory demyelinating optic neuritis: evidence-based visual and neurological considerations, 2008231 Myelitis formed second major presentation of Clinically Isolated Syndrome in our study, 6 out of 49(12.24%} patients. This is in comparison with other Indian studies data. Acute onset of motor weakness was the next common initial presentation seen in 27-31% of Indian patients as evidenced by P. Syal, and the one previous study from our institute by G. Gangopadhyay, S. K. Das, P. Sarda *et al.*

CONCLUSION

A CIS is defined as a first clinical and neurological event event due to inflammatory demyelination of the central nervous system, suggestive of MS lasting ≥ 24 hours and is caused by inflammation/ demyelination in 1 (monofocal) or more (multifocal) sites in the CNS. However, the occurrence of a CIS does not necessarily mean the patient has or will develop MS. Rather, a CIS indicates a risk for subsequent development of MS months or even years later. The present study results conclude that CIS has got female prepondarence compared to males, with predeliction for young adults. The most Common CIS presentation is optic neuritis (ON), followed by myelitis/spinal cord and brainstem/cerebellar subgroups. MRI forms the single most important non-invasive tool for diagnosis and prognostication of CIS patients

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