



## A HOSPITAL-BASED PROSPECTIVE STUDY FROM CENTRAL INDIA ON NEUROLOGICAL PROFILE OF PATIENTS WITH CLINICALLY ISOLATED SYNDROME.

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### ABSTRACT

**Background:** The first clinical episode of symptoms and signs suggestive of an inflammatory demyelinating illness of the central nervous system (CNS) is known as clinically isolated syndrome (CIS). It can be mono or multifocal, affecting different areas of the CNS.

**Aims & objectives:** The goal of this study was to assess the patient profile of patients with clinically isolated syndrome (CIS).

**Materials and Methods:** Over the course of a year, the study was done at the Department of Neurology at a tertiary healthcare centre in Central India. On the basis of inclusion and exclusion criteria, a total of 98 cases were included in the study. The study procedure was described to all patients, and their agreement was obtained. The demographic, clinical, and radiological findings were all documented and examined.

**Results:** Females (n=70) outnumbered males (n=28) in the CIS population. The average age of the patients was 25.08. Optic neuritis (n=76) was the most common CIS symptom, followed by myelitis (n=12), brainstem/cerebellar (n=4), and multifocal (n=6). The majority of CIS patients (n=78/98) had MRI lesions. In the optic neuritis group (n=56/78), MRI lesions were found in 74% of cases, with 100% in the myelitis, brainstem/cerebellar, and multifocal subgroups. The majority of the optic neuritis patients (n=76/98) exhibited unilateral, painful vision loss with colour desaturation, afferent papillary defect, optic disc edoema, and all had demyelinating type VEP abnormalities.

**Conclusion:** The phrase "clinically isolated syndrome" (CIS) refers to a first clinical episode with symptoms that are suggestive of multiple sclerosis (MS). According to the findings of this study, CIS is more common in women, with a preference for young adults, and optic neuritis is the most common clinical presentation, followed by myelitis, brainstem/cerebellar, and multifocal groups. The most essential non-invasive tool for diagnosing and prognosticating CIS patients is magnetic resonance imaging (MRI).

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

### INTRODUCTION

Optic neuritis, transverse myelitis, internuclear ophthalmoplegia, trigeminal neuralgia, and other brainstem, long-tract motor, and/or sensory symptoms are all included in the phrase Clinically Isolated Syndrome<sup>1,2</sup>. Clinical onset of Multiple Sclerosis, isolated demyelination syndrome,

first demyelinating event, first presentation of Multiple Sclerosis, first attack of Multiple Sclerosis, and focal isolated idiopathic inflammatory demyelinating illnesses are some of the other terms used to describe CIS<sup>2</sup>. It is usually used on adults between the ages of 20 and 45 who have experienced acute or subacute symptoms that peak within one to three weeks. The attack should persist at least

24 hours and be free of fever or infection, as well as clinical signs of encephalopathy. CIS is frequently monophasic in time and monofocal in space, with indications indicating a lesion in the optic pathway, spinal cord, brainstem, cerebellum, or, in rare cases, the cerebral hemisphere<sup>3</sup>. Some patients with CIS, however, exhibit clinical signs of spread in space (multifocal) impacting two or more sites. Because CIS can be monophasic, some patients may not develop new symptoms or brain MRI lesions that are typical of MS<sup>4</sup>. Understanding MS prognostic variables following a CIS may thus aid in identifying patients who are more likely to develop clinically confirmed MS and have continuous disease activity<sup>5</sup>. Baseline MRI findings have been proven to have the highest predictive value in determining the chance of CIS conversion to MS. The goal of our research is to look at the demographic, clinical, and radiological aspects that influence prognosis in CIS patients.

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## **MATERIALS AND METHODS**

**Study settings:** Over the course of a year, the study was done at the Department of Neurology at a tertiary healthcare centre in Central India. The Institutional Research Committee and the Institutional Human Ethics Committee both gave its clearance. It was done in the form of a prospective study.

**Inclusion criteria:** Within three months of their initial presentation, patients with their first clinical episode suggestive of CIS (Clinically Isolated Syndromes) were enrolled in the study. The study comprised patients aged 20 to 45 years old who presented with symptoms suggestive with CIS within three months of their initial presentation, which occurred without fever, infection, or encephalopathy and progressed for two to three weeks.

**Exclusion criteria:** Patients with increasing symptoms at the time of onset, those who did

not meet the CIS diagnosis, and those with symptoms or signs suggestive of other inflammatory illnesses (e.g., acute disseminated encephalomyelitis (ADEM), neuromyelitis optical (NMO), or vasculitis) were excluded.

**Procedure:** On the basis of inclusion and exclusion criteria, a total of 98 patients were included in the study. The study process was explained to all of the patients, and informed consent was acquired. The patient's demographic information (age and gender) was taken down. They underwent an MRI scan to determine the number of lesions. For the estimate of lesions, a standard MRI approach was used. Data from demographics, clinical trials, and MRI scans were evaluated and compared.

**Statistical analysis:** The information was presented in the form of a number, a percentage (%), and a mean. For the analysis, the Statistical Package for Social Sciences (SPSS 20.0) version was utilised.

## **RESULTS**

Females (n=70) outnumbered males (n=28) in the gender comparison of CIS patients (Table-1). Males had an average age of 28.46, while females had an average age of 23.24. In comparison to males, females showed a younger age propensity for CIS incidence. The average age of the participants in the study is 25.08. The majority of the patients had optic neuritis (n=76), 12 had myelitis, 6 had multifocal, and only 4 had brain stem/cerebellar issues in their clinical presentation (Table-2). The majority of CIS patients (n=78/98) had MRI lesions. MRI lesions were found in 74% of the optic neuritis patients (n=56/78), with 100% in the myelitis, brainstem/cerebellar, and multifocal categories.

In MRI, 38 patients had 1-3 lesions, 34 had 4-8 lesions, and 20 patients had no abnormalities. Six of the individuals had more than nine lesions. The majority of the optic neuritis patients (n=76/98) had unilateral (56), painful vision loss (52), colour desaturation

(32), afferent pupillary defect (60), optic disc edoema (44), and all had demyelinating type VEP abnormality (76). MRI lesions were discovered in 74 percent of patients with optic neuritis (56/78). 0 lesions were discovered in

20 of the 76 patients (26.31 percent), 1-3 lesions in 36 of the 76 patients (47.36 percent), 4-8 lesions in 18 of the 76 patients (23.68 percent), and  $\geq 9$  lesions in 2/76 (2.63 percent).

**Table 1: Distribution of patients based on the gender**

Gender	Number (n=98)	Percentage (%)
Male	28	29%
Female	70	71 %

**Table 2: Distribution of patients based on clinical presentation**

Clinical presentation	Number (n=98)	Percentage (%)
Optic neuritis	76	78 %
Myelitis	12	12 %
Brain stem/ Cerebellar	4	4 %
Multifocal	6	6 %
Clinical presentation	Number (n=98)	Percentage (%)

## DISCUSSION

A total of 98 patients with Clinically Isolated Syndromes were observed for two years in our study. Females made up 70 percent of the group, while males made up 28 percent. The ratio of females to men is 2.5:1, which is consistent with other Indian research by Chopra J et al. In a prior research conducted in Bengal by G. Gangopadhyay, S. K. Das, P. Sarda, and others, the female to male ratio was 2.5:1. In the study by Orton SM, Herrera BM, Yee IM, et al., the female:male ratio was also 2:1. Richards RG, Sampson FC, Beard SM, Tappenden P, Richards RG, Sampson FC, Beard SM, Tappenden P, Richards RG, Sampson FC, Beard SM, Beard SM, Beard SM, Beard SM, Beard SM, Beard Females are 23.48 years old on average, while males are 28.92 years old<sup>6-8</sup>. The average age of both males and girls was 25.04 years, which is consistent with earlier Indian studies. In our study of 98 individuals with Clinically Isolated Syndromes, 76 (77.55%) had Optic neuritis, 12 (12.24%) had Myelitis, 6 (6.12%) had Multifocal clinical presentations, and 4 had Brainstem/Cerebellar clinical presentations. As a result, ophthalmic neuritis was the most common clinical manifestation of Clinically Isolated Syndrome. Our findings are consistent with those of other Indian

studies<sup>9,10</sup>. There was a significant frequency of optic and spinal cord involvement in early MS literature from diverse parts of India. In 1985, Jain and Maheshwari released data on 354 MS cases from nine Indian centres. The initial presentation of optic neuritis (OPN) was reported in 22.2-58 percent of individuals seen at five of these locations. Recent research have revealed a frequency of 23.6 percent in the north west by P. Syal and 53.3 percent in the east of the country by G. Gangopadhyay, S. K. Das, P. Sarda et al, which is much higher than western data. Optic neuritis was the first symptom in 23.6 percent of patients in a study by P. Syal et al, and 44 percent of patients in south Indian studies by G. R. K. Sarma and D. K. Nagaraj. Our research found that 77.5 percent of patients had optic neuritis as their first symptom, which is similar to the 53.33 percent found in a study conducted at our institute by G. Gangopadhyay et al. However, our findings contrast from those of western studies in terms of CIS presentation: Miller et al found that 21% of patients had ON, 46% had spinal cord syndromes, 10% had brainstem-cerebellar syndromes, and 23% had multifocal abnormalities<sup>11</sup>. While 30.9 percent of patients in a Kuwaiti research by R. Alroughani et al exhibited spinal cord

symptoms at the time of beginning. Involvements of the brainstem/cerebellum and optic pathways were detected in 17.5 percent and 23.7 percent of patients, respectively, while 7.2 percent of patients had multifocal involvements. So, unlike western research, which shows that spinal cord involvement is more common, our findings support Indian studies, which show that optic neuritis is the most common CIS presentation<sup>12-14</sup>. The profile of 76 individuals with optic neuritis, the majority of whom had unilateral eye involvement, ocular pain, RAPD, colour desaturation, and optic disc edoema, matched data from earlier studies - Beck RW, Trobe JD, Moke PS, et al. In our study, 12 out of 98 (12.24 percent) patients had myelitis as the second most common manifestation of Clinically Isolated Syndrome. This is in compared to the findings of other Indian studies. According to P. Syal, the next most prevalent initial manifestation among Indian patients was acute onset of motor weakness<sup>15,16</sup>.

## CONCLUSION

A CIS is defined as a first clinical and neurological event in the central nervous system induced by inflammatory demyelination that lasts less than 24 hours and is caused by inflammation/ demyelination in one (monofocal) or multiple (multifocal) sites in the CNS. A CIS, on the other hand, does not always indicate that the patient has or will develop MS. A CIS, on the other hand, implies a risk of MS developing months or even years later. According to the findings of this study, CIS has a female preponderance compared to males, with a predisposition for young people. Optic neuritis (ON) is the most common CIS manifestation, followed by myelitis/spinal cord and brainstem/cerebellar subtypes. The most essential non-invasive tool for diagnosing and prognosticating CIS patients is magnetic resonance imaging (MRI).

## REFERENCES

1. Scalfari A, Neuhaus A, Degenhardt A et.al.,. The natural history of MS: a

geographically based study 10: relapse and long-term disability. *Brain* 2010;133:1914-29.

2. Confavreux C, Vukusic S. Natural history of MS: a unifying concept. *Brain* 2006;129:606-16.
3. Orton SM, Herrera BM, Yee IM et.al.,. Sex ratio of multiple sclerosis in Canada: a longitudinal study. *Lancet Neurol* 2006;5(11):932-36.
4. Goodin DS, Frohman EM, Garmany GP, et.al.,. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002;58(2):169-178.
5. 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* 2002;6(10):1-73.
6. Bhatia M, Behari M, Ahuja GK. Multiple sclerosis in India: AIIMS experience. *J Assoc Physicians India* 1996;44:765-67.
7. Brex PA, Ciccarelli O, O'Riordan OJI, Sailer M, Thompson AJ, Miller DH. A longitudinal study of abnormalities on MRI and disability from multiple sclerosis. *The New England Journal of Medicine* 2002;346(3):158-64.
8. Leibowitz U, Antonovsky A, Medalie JM, Smith HA, Halpern L, Alter M. Epidemiological study of multiple sclerosis in Israel. II. Multiple sclerosis and level of sanitation. *Journal of Neurology Neurosurgery and Psychiatry* 1966;29(1):60-8.
9. Wadia NH, Trikannad VS, Krishnaswamy PR. HLA antigens in multiple sclerosis amongst Indians. *Journal of Neurology Neurosurgery and Psychiatry* 1981;44(9):849-51.
10. Kelly MA, Jacobs KH, Penny MA et.al. An investigation of HLA-encoded genetic susceptibility to multiple

- sclerosis in subjects of Asian Indian and Afro-Caribbean ethnic origin. *Tissue Antigens* 1995;45(3):197-202.
11. Kankonkar S, Jeyanti G, Singhal BS, Shankarkumar U. Evidence for novel DRB1G15 allele association among clinically definite multiple sclerosis patients from Mumbai, India. *Human Immunology* 2003;64(4):478-82.
  12. Singhal BS, Wadia NH. Profile of multiple sclerosis in the Bombay region: on the basis of critical clinical appraisal. *Journal of the Neurological Sciences* 1975;26(2):259-70.
  13. Jacobs L, Beck R, Simon J *et al.*,. Intramuscular interferon beta-1a therapy initiated during the first demyelinating event in multiple sclerosis. *N Engl J Med* 2000;343:898-904.
  14. Frohman EM, Goodin DS, Calabresi PA *et al.*,. The utility of MRI in suspected MS: report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. *Neurology* 2003;61(5):602-11.
  15. Alroughani R, Al Hashel J, Lamdhade S, Ahmed SF. Predictors of Conversion to Multiple Sclerosis in Patients with Clinical Isolated Syndrome Using the 2010 Revised McDonald Criteria. *International Scholarly Research Network ISRN Neurology* 2012. (Article ID 792192, 6 pages doi:10.5402/2012/792192).
  16. Singhal BS. Multiple sclerosis and related demyelinating disorders in Indian context. *Neurol India* 1987;35:1-12.