

CLINICAL SPECTRUM OF MULTIPLE SCLEROSIS AT A TERTIARY CARE HOSPITAL IN PAKISTAN

Hoori Shahwar¹, Syed Wasim Akhter², Shaukat Ali³

ABSTRACT

Objective: To assess the clinical presentation of multiple sclerosis.

Methodology: This hospital based observational study was carried out from November 2004 to June 2005 at the Department of Neurology Jinnah Post Graduate Medical Center Karachi. Patients of multiple sclerosis (MS) diagnosed on Poser's criteria were observed on the basis of age at the onset, gender, family history, symptoms and signs, clinical course, magnetic resonance imaging, visual evoked potentials, cerebrospinal fluid and oligoclonal bands.

Results: Out of 20 patients there were 13 females with M:F ratio of 1:2. Mean age at presentation was 25.8 years. Family history was negative. Clinical presentation included pyramidal weakness (75%), visual defect (70%), sphincter disturbances (60%), sensory impairment (35%), cerebellar signs (30%) and paroxysmal spasm (25%). The clinical course of multiple sclerosis included Relapsing and Remitting RRMS (55%), Secondary Progressive SPMS (20%), Primary Progressive PPMS (15%) and Progressive Relapsing PRMS (10%). Optico-spinal type was seen in 55%. Magnetic resonance imaging of brain was positive in 75% and of cervico-dorsal in 100%. Visual evoked potential was abnormal in 85% and oligoclonal bands were present in 5%.

Conclusions: Multiple Sclerosis (MS) is not uncommon in Pakistan. The study revealed that young females were affected more compared with men with a ratio of 2:1 and mean age of onset was 25.8 years. Clinical type is in agreement with Asian variety of disease with high occurrence of optico-spinal presentation and low yield of oligoclonal band.

KEY WORDS: Multiple Sclerosis, Optico-Spinal MS, Oligoclonal Bands.

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1. Hoori Shahwar,
Department of Neurology,
Jinnah Post graduate Medical Center Karachi.
2. Syed Wasim Akhter,
Department of Neurology,
Baqai Medical University Karachi.
3. Shaukat Ali,
Department of Neurology,
Jinnah Postgraduate Medical Center Karachi.
Baqai Medical University Karachi,
Karachi - Pakistan.

Correspondence:

Dr. Hoori Shahwar,
Department of Neurology,
Jinnah Postgraduate Medical Center,
Karachi, Pakistan
E-Mail: drhoori@gmail.com

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INTRODUCTION

Multiple Sclerosis (MS) is an acute immune-mediated inflammatory disease that causes focal demyelination of the central nervous system (brain and spinal cord); it also causes axonal loss. There is evidence for limited remyelination of indeterminate significance.^{1,2} The disease is characterized by dissemination in space and time i.e. the lesions involve separate parts of the central nervous system and occurs at different times. It usually begins in early adult life and pursues a variable course, causing significant morbidity.² The variation in prevalence according to geographical location and modification of clinical picture by ethnic factors are all well known features of the disease.³ MS is more prevalent in Caucasians and has been extensively studied and reported from

the West.⁴ There have been a few studies reported from Asia, particularly from south Asia.⁵⁻⁷ Optic nerve and spinal cord involvement, with predominant visual impairment in the beginning of the course are more common in the Asian variety.⁸ The aim of present study was to assess the clinical pattern and course of MS at a tertiary care center in Pakistan.

METHODOLOGY

The study was conducted at Jinnah post-graduate medical centre, Karachi, one of the largest tertiary care hospitals in Pakistan. A total of twenty patients with MS fulfilling Poser's criteria⁹ were studied from November 2004 till June 2005. The parameters for clinical presentation included: age at the onset, gender, family history, pyramidal weakness, visual defect, sphincter disturbances, sensory impairment, cerebellar signs and paroxysmal spasm. The clinical course included: Relapsing remitting, secondary progressive, primary progressive and progressive relapsing MS. Topography of MS comprises of: spinal only, optico-spinal, optico-cranial, optico-spino-cranial, optico-spino-cerebellar, spino-cerebellar and cerebellar-only. Opticospinal MS, which is one of the presentations of MS, was considered when bilateral visual impairment and transverse myelitis developed concomitantly or within several weeks of each other, with or without subsequent improvement.^{8,10} Patients were also classified into the following categories based on Poser's criteria as:

Clinically definite, lab supported definite, clinically probable, lab supported probable MS. Investigations including blood tests, MRI studies, VEP test and CSF analysis were carried out in all patients to substantiate the diagnosis of MS and to exclude other diseases, particularly connective tissue disorders. Blood tests comprised of complete blood counts, ESR, biochemistry and, where required, antinuclear antibodies, double strength DNA and rheumatoid factor. CSF analysis was done for oligoclonal bands. VEP was performed for the evidence of central demyelination. MRI was performed to show multiple white matter lesions in the brain or intramedullary plaques in the spinal cord.

RESULTS

The total number of patients studied was twenty. The females were 13 with male to female ratio of 1:2. The mean age of presentation was 25.8 years; in males it was 27.8 years and in females 25 years. According to Poser's criteria out of 20 cases 13(65%) were CDMS, while 7(35%) were CPMS.

As far as the clinical course of MS is concerned, out of 20 patients eleven (55%) followed the RRMS, four (20%) had SPMS, three (15%) were in PPMS and only two (10%) were in PRMS. The most common presentation of MS with motor weakness and pyramidal tract involvement was noted in 75%, followed by visual impairment in 70%, sphincter disturbance in 60%, sensory disturbances 35%, cerebellar involvement in 30% and paroxysmal spasm in 25% of the cases. (Table-I)

Table-I: Distribution by symptoms

<i>Clinical features</i>	<i>Male (n=7)</i>	<i>Female (n=13)</i>	<i>Total (n=20)</i>	<i>%</i>
Abdominal reflexes	5	12	17	85
Motor weakness	4	11	15	75
Pyramidal tract	4	11	15	75
Visual disturbances	3	11	14	70
Sphincter disturbance	4	8	12	60
Sensory disturbances	3	4	7	35
Cerebellar	3	3	6	30
Fatigue ability	1	4	5	25
Cranial nerve	1	1	2	10
Uhthoffs phenomena	1	—	1	5

Table-II: Conclusive findings on investigations

<i>INV</i>	<i>Male (n=7)</i>	<i>Female (n=13)</i>	<i>Total (n=20)</i>	<i>% Conclusive</i>
VEP	5	12	17	85
MRI (Brain)	7	13	20	
Abnorma	2	13	15	75
MRI (Spinal)	4	8	12	
Abnormal	4	8	12	100
OCB	1	—	1	5

As regards topography 55% of our patients have optico-spinal form, in which 20% were fulfilling the criteria of pure optic spinal MS, or Neuromyelitis optica, and 35% have had optico-spinal MS, with positive brain MRI., as well as 15% was optico-spino-cerebellar, and only 10% had cerebellar only. (Table-II) CSF examination was normal in 19/20 patients thus it was positive for oligoclonal band in 5% only. VEP was performed in all cases and it was abnormal and keeping with a demyelinating disorder in 17(85%) of the cases.

All 20 cases underwent brain MRI in which 15(75%) had the findings compatible with MS. We have done cervico-dorsal MRI in 12 cases, which showed demyelination in all cases. Brain and spinal both MRI was done in 12 cases, in which four cases (20%) had normal scan of Brain with plaques in spinal MRI involving more than three segments of vertebra. (Table-III).

DISCUSSION

Multiple Sclerosis is less common in tropical countries. Three neuroepidemiological studies from different parts of south Asia did not document any case of multiple sclerosis.¹¹ Iran and Srilanka are considered to be area of low prevalence of MS,^{5,7} Although several reports are available from India.^{12,13,14} As per our knowledge so far there is no in depth study available from Pakistan regarding prevalence of MS or its clinical spectrum.¹⁵

In our study, the mean age of presentation was 25.8 years. In males it was 27.8 years while in female it was 25 years which is similar as reported by Singhal and Wadia¹⁴ and Bhatia

et al,¹⁶ which was also 26 years. Instead of that in one of Brazilian series¹⁷ the mean age of presentation was higher as compared to our study, in which the mean age of presentation was 32 years. This might be related to a longer interval of time between onset of disease and clinical diagnosis. The youngest case reported in the present study was 17 years and oldest was 40 years old.^{14,15,18,19}

The female to male ratio was 2:1 in our study as well as in five studies from different parts of Asia which showed male preponderance (range 1.25-2) and one study has shown female predominance. Kurtzke et al have, however, shown female predominance (female: male-1.8: 1) among US veterans.²⁰ In Brazilian series, there is also predominance of female.^{17, 21}

In our study the relapsing-remitting form (RR) (65%) is the most common form, followed by secondary progressive form (35%) which is same as reported by Singhal and Wadia,¹⁴ and Bhatia et al.,¹⁶ compared to that in Brazilian series in which RRMS is 91%, followed by PPMS is 8% and only 1% is SPMS.^{17, 22} An increased frequency of visual involvement is a common feature in Asian variety.²³⁻²⁵ In our study pyramidal involvement is the most common presentation (75%) followed by optic involvement (70%), sensory disturbances in 35% and cerebellar involvement (30%) of the cases. This feature correlates well with the earlier observation from south Asia²³ and Japan.²⁵

OSMS is a unique demyelinating disease characterized by recurrent optic neuritis and myelitis, and rare or minor involvement of the brain^{24,26} relatively higher female/male ratio, a

Table-III: Topography of Multiple Sclerosis

Topography	MRI Brain 20(7Mand13F)75%	MRI Spine 12(4Mand8F)60%	Male (n=7)	Female (n=13)	Total (n=20)	%
Pure-optico-spinal	-VE	+VE	3	1	4	20
Optico-spinal	+VE	+VE	—	7	7	35
Optico-spino-cerebellar	+VE	—	1	2	3	15
Cerebellar only	+VE	—	—	2	2	10
Optico-spino-cerebral	+VE	—	1	1	2	10
Optico-spino-cranial	+VE	—	—	1	1	5
Spinal only	-VE	+VE	1	—	1	5

Table-IV: Comparison between Asian and Western MS

Mean	Age in years	M:F	Clinical Course (%)	OSMS (%)	Clinical features (%)
Southern Brazil (Dr.Walter etal, 2001) (200 cases)	32	1:8.1	RRMS 91 PPMS 8 SPMS 1	3.5	Cerebellar - 63 Sensory - 53 Motor - 49.5 ON-39.5
West Bangal (Gangopadhay G, etal, 1999) (45 cases)	31.8	1:15	RRMS 48 RPMS 33 SPMS 17	22.2	Motor - 82.2 Sensory - 75.5 ON - 71.1
South Asia (Syal P.etal, 1999) (100 cases)	28.49	1:1.32	RPMS 89 SPMS 11	7	Motor - 87 Sensory 65 ON - 57 Cerebellar - 44
Europe, finland. (M-L Sumelahti,1979-93) (1060 cases)	35	2:1	RRMS 78 PPMS 28		Cerebellar - 82 Motor - 18 Sensory - 39 ON - 11
Present Study (20 cases)	25.8	1:2	RRMS 55 SPMS 20 PPMS 15	55	Motor - 75 ON - 70 Sensory - 35.5 Cerebellar - 30

lower frequency of CSFOB.²⁷ In our study there were four (20%) of cases which have pure OSMS with normal brain MRI with male predominance as male: female ratio was 3:1, oligoclonal band were negative in all four cases spinal cord lesions extending over three vertebral segments on spinal cord MRI, with gadolinium enhancement. However 10 cases (8.5%) of pure OSMS were reported in Japanese series^{28,29} of 118 cases of multiple sclerosis, with definite female preponderance and negative CSFOB.

Many investigators in Western countries have reported that relapsing OSMS is a type or variant of multiple sclerosis,^{30,31} and that OSMS phenotype may occur in classical multiple sclerosis in which demyelinating lesions are disseminated throughout the CNS. In our study 7(35%) of optico-spinal cases had recurrent optic neuritis and transverse myelitis with positive brain MRI.

Papaiz-Alvarenga et al²⁷ who had the series with the largest proportion of African Brazilian (31.8%) patients reported 5.6% with OSMS clinical form, Leite et al,³² had 15.6%, whereas Lana - Peixoto,²¹ with 24% of African Brazil-

ian patients, reported, a prevalence of 12% with OSMS and suggested that his patients presented a clinical form more alike the Asian MS patients.

Major difference in Caucasians and South Asian series has been the incidence of cerebellar involvement, which was found in over 80% in the former and³³ 30-58% in the later.²⁴ This is corroborated in our study also in which only 30% of patients had cerebellar involvement.

MRI has now become one of the key investigations in the diagnosis of multiple sclerosis. It is reported to be positive in a varying percentage of cases in different studies, the figures ranging from 50% to 95%.^{34,35}

In our study, the Brain MRI showed lesions consistent with MS in 75% of cases, as well as the spinal MRI has shown 100% accuracy. The true accuracy of MR imaging remains difficult to determine but the overall yield is reported to be 80%.^{35,36} The high sensitivity of MRI is offset by its lack of specificity, though certain characteristics may strongly favor MS, none of them are diagnostic by themselves.

CSFOB represent abnormal synthesis of gamma globulins in the Cerebral Spinal Fluid

and therefore strongly implicate an immunopathological process.^{37,38} It has been found that in Caucasians the CSFOB are found in a higher number of cases (90%) and tend to remain stable during the course of disease whereas in Asian studies³⁹ its incidence has been found to be ranging between 33 to 45%.^{40,41} In our study positivity of oligoclonal band is only 5%. Evoked potentials are useful to identify clinically silent lesions in the visual pathways the incidence of abnormalities on VEPs in various studies^{42,43} range from 75-97%. In our study abnormalities in VEP's were also found in 85% of patients.

During comparison with other studies the prevalence of MS in Brazil^{27,32} is estimated at the mean age of 32 and its occurrence in females is eight fold to males, substantially lower than in Western countries. However, the proportion of patients with RRMS in this population is reported to be higher than in Western populations.

In our Study we found that MS in Asian countries has several patterns that distinguish MS in Pakistan from MS in Western countries.³³ Occurrence of disease in female patients is quite high as compared to male the ratio in West is 1:15 whereas in Pakistan it is 1:2 as shown in Table-IV. Moreover the number of cases of RRMS were observed quite low as compared to other areas. Only 55% patients were reported to have RRMS as compared to 91% in Brazil and 89% in South Asia. Clinical features of MS in our study indicate that occurrence of cerebral cases was lower as compared to other regions.

CONCLUSIONS

We can conclude that MS is not uncommon in Pakistan. The mean age at onset was slightly lower compared to the other series, and there was a greater preponderance of women, as has been seen the world over. The clinical pattern is more similar to the Asian series than the western series. The incidence of OSMS was found to be higher than that reported in Japanese, South Asian and Brazilian series. The CSFOB are less seen than other Asian and western studies.

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