

A retrospective study on the clinico-demographic profile of multiple sclerosis patients in various tertiary care hospitals in Mangalore city of South India

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ABSTRACT

Objectives. To study the risk factors, clinical presentations, course of the disease, investigations and management practices in MS.

Materials and methods. Records of 23 patients diagnosed with MS using the McDonald diagnostic criteria were analysed.

Outcomes. The mean age at diagnosis was 34.6±17.1 years. 17 (73.9%) patients were females. Early and late onset MS were present among 2 (8.7%) and 4 (17.4%) patients respectively. The most common symptom at diagnosis was paraesthesia [9 (39.1%)]. Motor symptoms and sensory symptoms at the time of diagnosis were present among 9(39.1%) patients each.

20 (87%) patients had motor system involvement, 9 (39.1%) had sensory system involvement, 12 (52.2%) had cranial nerve involvement, 4 (17.4%) had sphincter dysfunction and 2 (8.7%) had cerebellar involvement. Relapsing and remitting MS (RRMS) were present among 18 (78.3%) patients. Oligoclonal bands were present among 17 (73.9%) patients. Vitamin D levels in the blood were found deficient among 4 (80%) out of 5 patients with available reports of the same. Juxtacortical region was the most common [9 (39.1%)] site of involvement. Steroids were used for management among majority [12 (52.2%)] of the patients. Non-pharmacological methods for management constituted only physiotherapy which was advised among 13 (56.5%) patients. Improvement in treatment outcome were seen among 19 (82.6%) patients.

Conclusions. Almost three fourth of the patients were females. RRMS was the most common course of the disease. Juxtacortical region was the most common site involved. Steroids were most commonly used for management. More non-pharmacological methods need to be introduced for MS management.

Keywords: multiple sclerosis, risk factors, clinical features, investigations, management, hospital based study

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory disease associated with demyelination and degeneration of the nervous system. It leads to both cognitive and physical disability among the affected. In the Western world, it has been reported to be the

most common cause of non-traumatic neurological disability among young adults [1].

The total MS patients in India in 2016 was estimated to be 204,460 (uncertainty Interval 182,397 to 231,531) [2]. In 2013, the crude prevalence of MS in the current setting, namely Mangalore city, was 8.3 per 100,000 population [3].

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Article history:

Received: 8 July 2021
Accepted: 22 August 2021

Its occurrences and distributions are heterogeneous due to the differences in the genes and the environmental conditions at various settings [4]. Heterogeneity is also seen in the course of the disease and its response to treatment [5].

The current approach in MS management aims to prevent neurodegeneration by starting treatment early during the inflammatory stages of the disease [5]. Considering the various immunopathological subtypes of MS, clinical profiling of the patients help in undertaking appropriate management practices [6]. The detailed profiling exercise need to be complemented by assessment of biomarkers and various diagnostic modalities which help in the decision making process for providing individualized therapeutic care [7]. This study was therefore done to study the risk factors, clinical presentations, course of the disease, investigations and management practices in MS, among patients attending various tertiary care hospitals in Mangalore city of south India.

MATERIALS AND METHODS

This study was conducted at one government and three private tertiary care hospitals, affiliated to two private medical colleges during the months March, April and May 2019. It was a retrospective record based cross sectional study. The ethics approval was first obtained from Kasturba Medical College Institutional Ethics Committee on 20th March 2019. The approval number was IEC KMC MLR 03-19/82. It was then obtained from Father Muller Medical College Institutional Ethics Committee dated 14th May 2019. The approval number was FMMCIEC/CCM/129/2019.

Records of all confirmed patients with MS over the past 10 years (starting from 2009), at these hospitals, were analysed and the information were recorded in a proforma. Patients were diagnosed using the McDonald diagnostic criteria for MS. The proforma was content validated by a neurologist. Data regarding socio demographic details, age at diagnosis, clinical symptoms and signs, course of the disease, co-morbidities, risk factors like genetic defects, family history of MS, investigation findings, treatment and its outcomes were recorded by the investigators.

Data entry and analysis were done using IBM SPSS for Windows version 25.0, Armonk, New York. Fisher's Exact test was used to test association. p value <0.05 was used as the criterion for significance.

RESULTS

23 patients with multiple sclerosis were included in this study.

The mean age of the patients was 36.6 ± 16.8 years and it ranged from 20 years to 74 years. Majority were females [17 (73.9%)] and were from urban areas [20 (87%)] (Table 1). The mean age at diagnosis was 34.6 ± 17.1 years. It ranged from 18 years to 73 years. The mean age at diagnosis among males was 45.7 ± 19.5 years and among females was 31.3 ± 15.8 years ($t = 1.318$, $P = 0.214$). The proportion of patients with early onset or juvenile MS (≤ 18 years) were 2 (8.7%). Both these patients were females ($P = 1$). Late onset of disease (≥ 50 years) were seen among 4(17.4%) patients. Among them, males and females were 2 patients each ($P = 0.2705$).

There was no patient with positive history of genetic diseases or any other autoimmune diseases or with any family history of MS. Five (21.7%) patients were vegetarians.

TABLE 1. Socio-demographic distribution of patients with multiple sclerosis

Socio-demographic variables	Number	Percentage
Age distribution (years)		
20	2	8.7
21-30	10	43.5
31-40	4	17.4
41-50	3	13.1
51-60	1	4.3
61-70	1	4.3
>70	2	8.7
Gender		
Males	6	26.1
Females	17	73.9
Marital status		
Married	14	60.9
Unmarried	9	39.1
Occupation (n = 4)		
Labourers	2	50.0
Student	1	25.0
Teacher	1	25.0
Place of residence		
Urban	20	87.0
Rural	3	13.0
Total	23	100.0

Out of the 23 patients, 14 (60.9%) did not suffer from any co-morbidities. Twelve (52.2%) among the MS patients were monosymptomatic and 11 (47.8%) were polysymptomatic at the time of diagnosis. The most common symptoms at diagnosis were paraesthesia [9 (39.1%)] followed by vision impairment [7 (30.4%)]. Motor symptoms and sensory symptoms at the time of diagnosis were present among 9(39.1%) patients each (Table 2).

TABLE 2. Distribution of clinical features among patients with multiple sclerosis (n = 23)

Characteristics	Number	Percentage
Symptoms at diagnosis*		
Paraesthesia	9	39.1
Vision impairment	7	30.4
Difficulty in walking	5	21.7
Bowel/bladder dysfunction	4	17.4
Severe fatigue	4	17.4
Eye pain	2	8.7
Reduced cutaneous sensations	2	8.7
Vertigo	2	8.7
Headache	2	8.7
Movement disorders	2	8.7
Others [†]	5	21.7
Signs at diagnosis*		
Decreased muscle power	13	56.5
Diminished visual acuity	7	30.4
Extensor plantar reflex	5	21.7
Absent tendon reflex	4	17.4
Exaggerated tendon reflex	3	13.0
Quadriplegia	2	8.7
Hypertonia	2	8.7
Ataxia	2	8.7
Others [†]	2	8.7
Course of the disease		
Primary progressive	2	8.7
Clinically isolated syndrome	2	8.7
Relapsing and remitting	18	78.3
Chronic progressive	1	4.3
Co-morbidities*		
Thyroid disorders	4	17.4
Hypertension	2	8.7
Psychosis	2	8.7
Migraine/Tension headache	2	8.7
Ischaemic heart disease	1	4.3

*Multiple responses

[†]Difficulty in speech 1, Breathing difficulty 1, Behavioural changes 1, Back pain 1, Restriction of movement of knee joint 1

[†]Paraplegia 1, Hypotonia 1

One among the patients with early onset MS and 3 among the patients with late onset MS had motor symptoms at the time of presentation (P = 1). None among the patients with early onset MS and 1 among the patients with late onset MS had sensory symptoms at the time of presentation (P = 1). Out of the total 23 patients, 20 (87%) had motor system involvement, 9 (39.1%) had sensory system involvement, 12 (52.2%) had cranial nerve involvement, 2 (8.7%) had cerebellar involvement and 4 (17.4%) had sphincter dysfunction. At the time of diagnosis, both the patients with early onset MS presented with visual impairment, while 1 each of them presented with movement disorders and difficulty in walking.

At the time of diagnosis, symptoms like vision impairment, vertigo and paraesthesia were present

in 1 patient each and signs like bowel/bladder dysfunction and difficulty in speech were present among 1 out of the 4 patients with late onset MS.

Relapsing and remitting MS (RRMS) were present among 18 (78.3%) patients. RRMS was seen among both the patients with early onset MS. It was also present among 3 out of 4 patients with late onset MS. One of the patient with late onset MS had clinically isolated syndrome (CIS). Neuromyelitis optica spectrum disorder (NMOSD) or Devic's disease was present in one patient.

Vitamin D levels in the blood were found deficient among 4(80%) out of 5 MS patients with available reports of the same. Oligoclonal bands (OCBs) in the cerebro spinal fluid (CSF) were found in 17(73.9%) patients Juxtacortical region was the most common site of involvement among majority [9(39.1%)] of the patients as identified in the MRI scan (Table 3).

TABLE 3. Laboratory and investigatory findings among patients with multiple sclerosis (n = 23)

Laboratory parameters	Number	Percentage
Vitamin D levels (n = 5)		
Deficient (<20 ng/ml)	4	80.0
Normal	1	20.0
ESR levels (n = 12)		
Normal	10	83.3
Raised	2	16.7
Blood urea levels (n = 14)		
Normal	8	57.1
Raised	6	42.9
Blood creatinine levels (n = 14)		
Reduced	1	7.1
Normal	12	85.8
Raised	1	7.1
MRI findings [#]	23	100.0
CSF examination findings [†]	23	100.0
Collagen profile [‡]	6	26.1
Funduscopy [§]	5	21.7
Electrophysiological studies of the nerves	5	21.7
CT scan findings ^{**}	2	8.7

[#]Lesions in: Juxtacortical region 9, Periventricular region 8, Cervical spine 5, Pyramidal tract 4, Cerebellum 3, Pons 3, Parietal lobe 3, Optic nerve 3, Optico brainstem cerebello spinal region 3, Brainstem 3, Thoracic spine 3, Calloso-septal interface 2, Corpus callosum 2, Frontal lobe 2, Juxtacallosal region 1, Insular region 1, Temporal lobe 1, Occipital lobe 1, Gangliocapsular region 1, External capsule 1, Midbrain 1, Dorsolumbar spine 1, Opticospinal region 1, Spinothalamic region 1, Acute transverse myelitis 1

[†] Oligoclonal bands 17, Raised protein levels 11, Increase in T - Lymphocytes 11, Adenosine deaminase present 3, Raised gamma globulins 2, Raised IgG antibodies 1, Raised beta-1 Globulins 1, Increase in neutophils 1, Normal CSF report 1

[‡] Normal 3, ANA raised 2, ANA borderline 1

[§] Optic atrophy 3, Macular edema 2

^{||} Normal 2, Prolonged latency 2, Mild prolonged latency 1

^{**}Bulging of the cervical spinal cord and indenting anterior subarachnoid space 1, Demyelination of spinal nerves 1

Steroids like methylprednisolone and prednisolone were prescribed among 12 (52.2%) patients. Immunosuppressant like azathioprine was prescribed among 10 (43.5%) patients. Disease modifying drugs (DMDs) such as beta interferons and Teriflunomide were prescribed among 9 (39.1%) patients (Table 4). All the patients on DMDs had RRMS. Non-pharmacological method constituted only physiotherapy and it was advised among 13 (56.5%) patients. Improvement in treatment outcome were seen among 19 (82.6%) patients. One out of the 2 patients with early onset MS ($P = 0.3241$) and 2 out of the 4 patients with late onset MS ($P = 0.1246$) showed improvement with treatment.

TABLE 4. Management practices among patients with multiple sclerosis (n = 23)

Management*	Number	Percentage
Azathioprine	10	43.5
Methylprednisolone	9	39.1
Beta Interferons	8	34.8
Prednisolone	3	13.0
Vitamin D3	3	13.0
B complex vitamins	2	8.7
Myoinositol	2	8.7
Antioxidants	2	8.7
Others [#]	8	34.8
Physiotherapy	13	56.5
Treatment outcome		
Improved with treatment	19	82.6
Did not improve	4	17.4

*Multiple responses

[#]Mycophenolate Mofetil 1, Teriflunomide 1, Baclofen 1, Gabapentin 1, Thiamine 1, Calcitriol 1, Multivitamins 1, Calcium 1

DISCUSSION

The mean age at diagnosis of MS in this study was 34.6 years. In studies done in Egypt [8], Chandigarh, India [9], Brazil [10] and New Delhi, India [11], the mean age at onset was 25.6, 28.5, 32.2 and 33.3 years respectively. The delayed age at diagnosis in this study as a consequence of delayed age at onset could be due to the influence of varying genetic and environmental factors in the setting on the disease aetiology. Previous Indian studies reported, mean age at onset among males as 31.8 years [12] and 33.5 years [13] and among females as 29.1 years [12] and 26.4 years [13]. Similar observation was made in the present study where the mean age at diagnosis was earlier among females. In this study, 8.7% of the total patients had early onset of MS. Early onset have been reported among 3 to 5% MS patients [14]. Both the patients with early onset MS in this study and 77.5% in an Italian study were females [15]. The late age at onset of MS were reported among 17.4% patients in this study. This was more than the proportion of 6.3% reported in the Egyptian study [8]. Half

of the patients with history of late onset MS in the present study, and 36.9% in a Canadian study were males [16].

In this study 73.9% and 60% to 90.7% of MS patients in previous studies were females [10,12,15,17-21]. Like most other autoimmune disease, MS is also seen more commonly among females [22]. In a study done in Kashmir, India [20], most patients (90.2%) were from rural areas which was in contrast to our findings where most patients were from urban areas. In another study done by Malli et al in Mangalore, urban living was a significant risk factor for MS [23]. These observations again support the role of local environmental factors in MS aetiology.

As many as 80% patients with known status of vitamin D in the present study, had deficient levels in the blood. A study done in Mangalore, by Pandit et al reported that vitamin D levels were significantly lower among MS patients [24]. In the present study, 21.7% patients were vegetarians. Malli et al. reported that vegetarian diet was a significant risk factor for MS [23]. There was no report of family history of MS among any of the patients in this study. However 4.6% of MS patients in a Sudanese study [21] and 13.8% in an Italian study [15] had positive history of the same.

Majority of the patients in this study and 81.1% patients in the Egyptian study were monosymptomatic at the time of diagnosis.[8] The most common symptoms at the time of diagnosis in this study were sensory paraesthesia followed by vision impairment and difficulty in walking. In the study done in Calcutta, India, visual impairment (33%) followed by weakness of the limbs (31%) and paraesthesia (20%) were the most common initial symptoms in MS [12]. Another study done in Kashmir, India reported, visual involvement (40%) followed by weakness of the limbs (35%) and sphincter involvement (20%) as the most common presenting symptoms [13]. Reduced visual acuity were reported among 27.6% MS patients in the Sudanese study compared to 30.4% reported in this study [21]. Optic nerve involvement were reported among 57% patients in the study done in Chandigarh, India [9] and among 3 (13%) patients in this study. Visual involvement is a common feature in the Asian variety of MS [25]. Motor symptoms at the time of diagnosis were reported by 39.1% patients in this study and by 35.3% [21], 50% [26] and 62.3% [19] patients in studies done elsewhere. Sensory symptoms at the time of diagnosis were also reported by 39.1% patients in this study which was more than the proportion of 10% reported in the study done in Kashmir, India [13]. In this study, NMOSD was present in one patient. Its prevalence in south Indian population was found to be 2.7 per 100,000 population [3]. In this

study, psychosis was present among 8.7% patients. Psychiatric problems such as depression (22.2%), anxiety (21%) and aggressive behaviour (13.7%) were also reported in a Canadian study [18]. In a study done in Bangalore, India, 51.6% of MS patients suffered from depression [27]. Severe fatigue was reported by 17.4% patients in this study. In the study done in Bangalore, India, depression was associated with fatigue among MS patients [27]. This emphasizes the need for screening various psychiatric disorders while managing patients with MS. In the Asian variety of MS, spinal cord and optic nerve involvement were seen commonly [25]. In a study done in Calcutta, India, lesions in the posterior column and spinothalamic regions were present in 55% and 51% patients respectively [12]. The study done in Kashmir, India reported, pyramidal tract (70%) followed by spinothalamic and posterior column (50%) and cerebellar (25%) region as the most common site of lesion in MS [13]. Another study done in Chandigarh, India reported pyramidal tract involvement among 87% patients [9]. In the present study, lesions were more common in the juxtacortical region.

Majority of patients (78.3%) in this study had RRMS. In about 85% patients, MS is known to begin as an acute clinical episode or CIS that evolves into a RRMS course. After a gap of about 15 years, it progresses into a secondary progressive MS (SPMS) course that leads to chronic disability. The other 15% patients start with the primary progressive MS (PPMS) course of the disease [28]. Previous studies reported CIS among 4.5% [8], 13.3% [29], 52.7% [15], PPMS among 0% to 48.9% [8-13,20,29,30], RRMS among 33.3% to 89% [8-11,13,15,19-21,29,30] and chronic progressive course among 16.3% to 37.1% [8,10-13,15,20,21,29,30] patients. The present study observed RRMS among 100% patients with early onset MS and 75% patients with late onset MS. The Italian study reported RRMS among 84.5% and 79.5% patients with early and late onset MS respectively [15].

Presence of OCBs in the CSF were found in close to three-fourth of the patients. It is reported to be present in over 95% patients with MS [31]. It indicates an immuno-pathological process involving an abnormal synthesis of gamma globulins in the CSF. Its presence in CSF but absence in the serum reflects a local B-cell response accompanying inflammation in the central nervous system. Its presence with the carriage of HLA-DRB1*15 hastens disease progression [32]. Raised protein level was another common finding in CSF among patients in this study, substantiating the inflammatory role of this disease [33]. Increase in adenosine deaminase levels were seen in few patients. Therefore it needs to be included among the differential diagnosis of disorders with

ADA elevation in the CSF [34]. Collagen profile showed raised anti-nuclear antibody titre in 33.3% of patients in this study. This is reported to increase in the early stages of MS and it later normalizes within a year [35].

The most common drug used for management in this study was steroids probably because good number of patients in this study had relapses with disabilities. In the Sudanese study, methylprednisolone and prednisolone were given among 65% and 7% MS patients respectively [21]. Steroids are preferred drugs used for managing disabling relapses such as motor system disabilities, optic neuritis and acute ataxia [36]. Steroids inhibit proinflammatory cytokines and apoptosis of T cells thereby, benefit patients with autoimmune conditions like MS [37]. Immunosuppressant drug, azathioprine was prescribed for 43.5% patients in this study and among 34.7% patients in the Egyptian study [8]. DMDs were given among 39.1% patients in this study and among 19.3% [8], 37% [16], 55.4% [11], 72% [10] patients in other studies. In this study 50% patients, and in the Canadian study [16] 41.2% patients with RRMS, were managed with DMDs. Use of DMDs in the management of RRMS benefits patients by reducing both frequency and severity of relapses and helps minimize the risk of disability and nerve atrophy among them [38]. Half of the RRMS patients in this study were not treated with DMDs probably due to its high cost. Non-pharmacological methods for management constituted only physiotherapy, advised among 56.5% patients. Other non-pharmacological methods like yoga therapy were not part of MS management. Yoga has been found to be beneficial in the management of neurogenic bladder [39].

Although non improvement with treatment were reported among 17.4% patients, no casualties were observed in this study. On the contrary, the Egyptian study reported 2(0.6%) deaths among the MS patients [8].

A limitation of the study was that there were missing information in few case records.

CONCLUSIONS

The age at diagnosis among patients was found to be delayed at this setting. Almost three fourth of MS patients were females. Juxtacortical region was the most common site of involvement. RRMS was the most common course of the disease. The proportion of progressive cases were minimal. Steroids were the most common drug used for MS management. Non-pharmacological methods were minimally used for MS management in the setting. Even though there was no casualty, disabling symptoms like visual impairment, muscle weakness, paralysis,

bowel and bladder impairment, and psychiatric morbidities were present among patients. These disabling morbidities might have caused impairment in the quality of life of MS patients in this setting. Hence MS need to be diagnosed early, particularly among high risk groups, like the female population and managed. In order to recognize its varied clinical presentation and course of the disease, a comprehensive clinical assessment among patients along with use of more non-pharmacological interventions is required in patient care at this setting.

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