

ORIGINAL RESEARCH

Clinical Characteristics of Multiple Sclerosis Patients Complicated by Disabilities and Analysis of Risk Factors Related to Disease Progression

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ABSTRACT

Objective • To analyze the clinical characteristics of multiple sclerosis (MS) patients complicated by disabilities in China, and to discuss the related factors of disease progression.

Methods • Ninety-three MS patients presented to our hospital between March 2017 and December 2019 were selected as the research participants to conduct a retrospective analysis. Demographic information, onset time, onset age, clinical symptoms, MS types, and Expanded Disability Status Scale (EDSS) score were collected from all patients, and preliminary observation was made on MS cases in China. Subsequently, patients were grouped according to their sex, onset age and MS types to observe the differences in clinical characteristics of MS under different conditions. Finally, Logistic analysis was conducted to analyze the related factors affecting disease progression in MS patients.

Results • MS was likely to occur in all age groups, among which the 30-40 age group had a slightly higher predilection.

Women were more predisposed to MS, with motor symptoms as the major clinical presentations. The number of patients with sensory symptoms and the frequency of episodes in the past year were higher in female patients than in male patients ($P < .05$). Clinical isolated syndrome (CIS) patients had lower baseline ESDD than relapsing remitting MS (RRMS) patients ($P < .05$). According to Logistic regression analysis, baseline ESDD score and the frequency of episodes in the past year were independent risk factors affecting MS progression ($P < .05$).

Conclusions • The clinical characteristics of MS in the Chinese population are basically similar to those in foreign countries, but RRMS accounts for a relatively low proportion. The ESDD score and the frequency of episodes in the past year are independent risk factors for MS progression. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Multiple sclerosis (MS) is the most common demyelinating disease of the central nervous system. In the acute active phase, there are multiple inflammatory demyelinating plaques in the central white matter, while the old lesions form calcified plaques due to glial fiber hyperplasia. The disease is characterized by multiple lesions, remission and recurrence, and is more likely to occur in the optic nerve, spinal cord and brain stem, with a high predilection for the young and middle-aged and a higher incidence in females than in males.¹ According to statistics, the incidence of MS varies greatly among regions, with an incidence of approximately 100-200/100 000 in northern Europe and the northern United States, but less than 1/100 000 in countries near the equator.² However, with the variation tendency of the global epidemic, the incidence of MS is increasing year by year.³ MS is diffuse with complex clinical symptoms, which can manifest as neuritis, limb paralysis, nystagmus, and other conditions.⁴ At present, the specific etiology of MS has not been fully defined, and it is clinically believed that genetic

factors, environmental factors, virus infections, and autoimmune reactions may all lead to MS.⁵ At present, researchers in Japan, South Korea, the United States and other countries have carried out comprehensive reports on the epidemiological and clinical characteristics of MS,⁶⁻⁸ but there is still a lack of reliable reference for the clinical features of MS patients in China. As we all know, the incidence of MS has obvious regional differences, so early identification and accurate diagnosis are of great significance to ensure the prognosis and safety of MS patients.⁹ Over the past three decades, the time from onset to diagnosis of MS patients has been significantly shortened, possibly due to the continuous revision and improvement of diagnostic criteria and the popularization of magnetic resonance imaging.¹⁰ But there are still a certain number of patients whose diagnosis is delayed for various reasons. Statistics indicate that about 40% of new MS cases take more than 2 years from the onset to a definite diagnosis.¹¹

Consequently, this study summarized the clinical characteristics and diagnosis of MS patients in China based on the results of the MS patient survey project, so as to provide a reliable reference and guidance for future MS diagnosis and management.

SUBJECTS AND METHODS

Research population

Ninety-three MS patients presented to our hospital between March 2017 and December 2019 were selected as the research participants to conduct a retrospective analysis. Demographic information, medical history, and medical treatment of all patients were completed by neurologists of our hospital. This project strictly followed the Declaration of Helsinki, with informed consent obtained from all participants.

Criteria for patient enrollment and exclusion

Adults patients (aged ≥ 18 years) meeting the diagnostic criteria for MS¹² and complicated with disabilities were included. Cases were excluded according to the following criteria: (1) other central nervous system diseases; (2) motor dysfunction caused by other diseases such as cerebral infarction and cerebral hemorrhage; (3) disability or neurological impairment due to congenital diseases, trauma and other reasons; (4) serious immunodeficiency diseases such as HIV, or use of hormonal or immunosuppressive therapy within one month before admission; (5) incomplete clinical data.

MS classification

Referring to MS diagnostic criteria,¹³ MS was divided into clinical isolated syndrome (CIS), relapsing remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS). The severity of neurological functional impairment was assessed using the Kurtzke Expanded Disability Status Scale (EDSS),¹³ with higher scores indicating more serious neurological deficits. Further, patients were grouped according to the baseline EDSS and the last EDSS

Table 1. Clinical characteristics of MS

Projects	n	Percentage (%)
Age	38.09 \pm 10.93	-
Sex	Male	54
	Female	78
Type of MS	CIS	26
	RRMS	64
	SPMS	2
	PPMS	1
Number of episodes in a year	2.01 \pm 1.08	-
Clinical symptoms	Vision symptoms	34
	Motor symptoms	60
	Sensory symptoms	46
	Brainstem symptoms	20
	Cerebellar symptoms	36
	Sphincter dysfunction	22
baseline EDSS score	0-3.0	54
	3.5-6.5	36
	7.0-10	3

Abbreviations: MS, multiple sclerosis; CIS, clinical isolated syndrome; RRMS, relapsing remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Kurtzke Expanded Disability Status Scale.

change, and those with progressive MS (PMS) and those without were considered as PMS group and non-PMS group, respectively. PMS was determined as an increase of ≥ 1.0 points when the baseline EDSS was ≤ 5.5 points, and an increase of ≥ 0.5 points when the baseline EDSS was above 5.5.

Data acquisition

Demographic information, onset time, onset age, clinical symptoms, MS type, and EDSS score were collected from all patients.

Statistical analysis

The data were statistically analyzed by SPSS26.0 software, and a significance level of $P < .05$ ($\alpha=0.05$) was used in all analyses. Gender, history of smoking and drinking, and other categorical data were recorded by [n(%)] and compared by the chi-square test. Age, EDSS, and other continuous variables were recorded with ($\bar{x} \pm s$) and compared with the independent sample t test. Related factors were identified using the Logistic regression analysis.

RESULTS

Clinical characteristics of MS

Based on the clinical data of all patients, MS was likely to occur in all age groups, with a slightly higher prevalence in the 30-40 age bracket. Most of the patients were women, and the clinical symptoms were primarily motor, sensory, and cerebellar symptoms. The baseline EDSS score was mostly 0-3.0, and RRMS accounted for the highest proportion. Table 1

Differences in clinical features of MS between men and women

Patients were first grouped based on their sex, and it was found that male patients ($n=35$) and female patients ($n=58$) had no statistical difference in age, onset time and MS type ($P > .05$). In terms of clinical symptoms, more female patients suffered from sensory symptoms compared with male patients ($P < .05$). In addition, the frequency of episodes in the past year was higher in females than in males ($P < .05$). Table 2.

Table 2. Differences in clinical features of MS between men and women

Projects	Male patients (n=35)	Female patients (n=58)	t or χ^2	P value
Age	37.66±9.36	38.34±11.85	0.293	.771
Type of MS			0.742	.863
CIS	10(28.57)	16(27.59)		
RRMS	24(68.57)	40(68.97)		
SPMS	1(2.86)	1(1.72)		
PPMS	0(0.00)	1(1.72)		
Number of episodes in a year	1.51±1.09	2.31±0.96	3.477	<.001
Clinical symptoms				
Vision symptoms	13(37.14)	21(36.21)	0.008	.928
Motor symptoms	20(57.14)	40(68.97)	1.333	.248
Sensory symptoms	12(34.29)	34(58.62)	5.171	.023
Brainstem symptoms	8(22.86)	12(20.69)	0.061	.805
Cerebellar symptoms	12(34.29)	24(41.38)	0.463	.496
Sphincter dysfunction	8(22.86)	14(24.14)	0.020	.888
baseline ESDD score			1.279	.528
0-3.0	23(65.71)	31(53.45)		
3.5-6.5	11(31.43)	25(43.10)		
7.0-10	1(2.86)	2(3.45)		

Abbreviations: MS, multiple sclerosis; CIS, clinical isolated syndrome; RRMS, relapsing remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Kurtzke Expanded Disability Status Scale.

Differences in clinical characteristics of different MS types

Subsequently, we divided the patients into CIS group (n=26) and RRMS group (n=64) according to their MS types. Due to the small number of patients with SPMS and PPMS, they were not included in the analysis. The results showed no notable differences in sex, age, onset age and attack frequency between CIS and RRMS groups ($P > .05$). As far as clinical symptoms are concerned, CIS patients mostly showed sensory symptoms, while RRMS patients tended to present motor symptoms ($P < .05$). Besides, CIS patients had lower baseline ESDD than RRMS patients ($P < .05$). Table 3.

Univariate analysis of MS progression

According to the difference between baseline ESDD and the last ESDD, patients were grouped into either the PMS group (n=14) or the non-PMS group (n=79). No significant inter-group differences were observed in clinical symptoms, and gender composition ($P > .05$). But patients in the PMS group were older, with higher baseline EDSS and frequency of episodes in the past year than the non-PMS group ($P < .05$), indicating that the above indicators may be potential risk factors affecting MS progression. Table 4.

Multivariate analysis of MS progression

The above single factor indicators with differences were assigned and input into SPSS as covariates, and PMS was used as an independent variable, for multiple Logistic regression analysis. The output results revealed that age was not an independent factor affecting MS progression ($P > .05$), while baseline ESDD and the frequency of episodes within one year were independent risk factors ($P < .05$). See Table. 5 and 6 for details.

DISCUSSION

By observing the clinical characteristics of Chinese MS patients, we found that the percentage of RRMS in Chinese MS patients is very low, which is very significantly different from that reported abroad.^{14,15} These results can provide great help for future clinical diagnosis and treatment of MS.

Table 3. Differences in clinical characteristics of different MS types

Projects	CIS group (n=26)	RRMS group (n=64)	t or χ^2	P value
Age	39.08±10.25	37.70±11.40	0.233	.595
Sex			0.007	.932
Male	10(38.46)	24(37.50)		
Female	16(61.54)	40(62.50)		
Number of episodes in a year	2.12±0.82	1.94±1.15	0.716	.476
Clinical symptoms				
Vision symptoms	9(34.62)	25(39.06)	0.156	.693
Motor symptoms	2(7.69)	58(90.63)	57.220	<.001
Sensory symptoms	25(96.15)	21(32.81)	29.690	<.001
Brainstem symptoms	6(23.08)	14(21.88)	0.015	.901
Cerebellar symptoms	10(38.46)	26(40.63)	0.036	.849
Sphincter dysfunction	4(15.38)	18(28.13)	1.625	.202
baseline ESDD score			8.319	.016
0-3.0	21(80.77)	33(51.56)		
3.5-6.5	4(38.46)	32(50.00)		
7.0-10	1(3.85)	2(3.13)		

Abbreviations: MS, multiple sclerosis; CIS, clinical isolated syndrome; RRMS, relapsing remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Kurtzke Expanded Disability Status Scale.

Table 4. Univariate analysis of MS progression

Projects	non-PMS group (n=79)	PMS group (n=14)	t or χ^2	P value
Age	35.14±8.48	54.71±7.98	8.031	<.001
Sex			0.577	.447
Male	31(39.24)	4(28.58)		
Female	48(60.76)	9(71.43)		
Type of MS			0.936	.817
CIS	21(26.58)	5(35.71)		
RRMS	55(69.62)	9(64.29)		
SPMS	2(2.53)	0(0.0)		
PPMS	1(1.27)	0(0.0)		
Number of episodes in a year	1.87±0.98	2.79±1.31	3.046	.003
Clinical symptoms				
Vision symptoms	27(34.18)	7(50.00)	1.284	.257
Motor symptoms	52(65.82)	8(57.14)	0.391	.532
Sensory symptoms	36(45.57)	10(71.43)	3.181	.075
Brainstem symptoms	15(18.99)	5(35.71)	1.971	.160
Cerebellar symptoms	29(36.71)	7(50.00)	0.886	.347
Sphincter dysfunction	16(20.25)	6(42.86)	3.365	.067
baseline ESDD score			22.180	<.001
0-3.0	51(64.56)	3(21.43)		
3.5-6.5	28(35.44)	8(57.14)		
7.0-10	0(0.0)	3(21.43)		

Abbreviations: MS, multiple sclerosis; CIS, clinical isolated syndrome; RRMS, relapsing remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Kurtzke Expanded Disability Status Scale.

Table 5. Assignment Table

Projects	Assignment
Age	No assignment is required for the measurement information
Number of episodes in a year	No assignment is required for the measurement information
baseline ESDD score	The assignment of 0-3.0 is 0, 3.5-6.5 is 1, and 7.0-10 is 2
MS progression	The assignment of non-PMS is 0, PMS is 1

Abbreviations: MS, multiple sclerosis; PMS, progressive multiple sclerosis; EDSS, Kurtzke Expanded Disability Status Scale.

Table 6. Multivariate analysis of MS progression

Projects	β	S.E.	χ^2	P value	OR (95%CI)
Age	0.626	1.116	3.262	.079	2.622(1.842-8.633)
Number of episodes in a year	-0.942	1.874	7.162	<.001	3.419(2.841-6.063)
baseline ESDD score	1.126	0.871	14.162	<.001	4.164(3.064-7.633)

Abbreviations: MS, multiple sclerosis; EDSS, Kurtzke Expanded Disability Status Scale; β , regression coefficient; S.E., standard error; OR, odds ratio.

In this study, MS patients were found to be mainly 30-50 years old and mostly female, which is similar to the statistical results of western countries.^{16,17} Among the specific types of MS, RRMS accounted for the highest proportion in this study, which is relatively low compared with previous studies (for example, RRMS is reported to account for more than 80% in the study of Solaro et al et al.).¹⁸ This may be due to the differences in the characteristics of MS in China and abroad, or the contingency caused by the small number of cases included in this study. On the other hand, the most common clinical symptoms of MS

patients in this study were motor, sensory, and cerebellar symptoms, which are roughly the same as those reported in western and Asian countries.¹⁹ The EDSS score is an important method to evaluate the degree of disability in MS patients. Asian patients are shown to have a higher disability degree than patients in western countries, with the EDSS score of RRMS patients in western countries mostly under 4.²⁰ In this study, the majority of patients had an EDSS score of 0-3.0, with a higher score for PMS. This suggested the importance of early diagnosis and intervention for MS patients, so as to slow down or prevent the accumulation of physical disabilities related to frequent relapses or progressive disease.

Subsequently, no significant difference was identified in the clinical characteristics of MS patients of different genders. However, female MS patients were found to suffer more from sensory symptoms and a higher frequency of episodes in the past year than male patients, suggesting that we need to pay more attention to female MS patients. Research has linked the higher incidence of MS in females to endocrine hormones and immune system.²¹ Due to the particularity of physiological structure, the endocrine function of women fluctuates greatly with an obviously worse stability than men,²² which directly leads to a higher risk of MS. Among different MS types, CIS patients showed lower baseline ESDD scores than RRMS patients, which is also in line with the pathological manifestations of MS. As we all know, CIS refers to the first episode of MS and does not all necessarily progress to MS, which may explain the lower ESDD score in CIS patients.²³

In the analysis of MS progression, we finally found that baseline ESDD and the frequency of episodes in the past year were independent risk factors for MS progression. The relationship between ESDD and MS has been repeatedly confirmed in many studies,^{24,25} so it won't be covered here. MS, as a disease prone to recurrent attacks, is mainly caused by repeated damage to patients' neurological function, which gradually involves multiple parts of the body.²⁶ Therefore, effectively controlling the onset of MS may also become the key to preventing MS from progressing in the future. The experimental results of this study will undoubtedly provide a new research direction for future MS diagnosis and treatment.

However, given that it is a single-center retrospective study, the results of this study are influenced by multiple factors. First of all, due to geographical factors, this study may be more in line with the characteristics of local patients in this area. Second, the small sample size of this study makes it necessary to validate our research results in a large-scale cohort study. Third, the study spanned a large period of time. Although we tried to record the clinical data and follow-up data objectively and accurately, there may inevitably be some bias. Finally, due to various reasons such as lack of follow-up awareness in some patients, or referrals to hospitals in developed areas, our research lacked dynamic observation of the whole course of disease in all patients and failed to analyze the efficacy of different treatment schemes. Later, a more comprehensive analysis will be conducted to address all of the above limitations to provide a more reliable reference.

CONCLUSION

Conclusively, the clinical features of MS in the Chinese population are basically similar to those in foreign countries, such as age of onset, sex, and symptom cluster composition and proportion. However, RRMS accounts for a relatively low proportion of MS in China, showing obvious regional characteristics. At the same time, ESDD and the frequency of episodes in the past year were identified as independent risk factors for MS progression, which can be used to formulate future prevention and treatment strategies for MS, thus providing patients with a more reliable prognostic guarantee.

CONSENT TO PUBLISH

All authors gave final approval of the version to be published.

CONFLICTS OF INTEREST

The authors report no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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