

The burden of multiple sclerosis in China: A literature review

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Abstract

Background & Objective: Multiple sclerosis is a relatively rare disease in China as compared to other nations throughout the world. This study aimed to assess the depth and breadth of knowledge of multiple sclerosis and its consequences specifically in China via a review and synthesis of existing literature. **Methods:** We conducted a literature search and reviewed studies that either were published in MEDLINE-indexed, English-language journals, or China National Knowledge Infrastructure database-indexed, Chongqing VIP Information Co., Ltd database-indexed, or Wanfang Data database-indexed Chinese-language journals, or appeared in the grey literature including medical society websites and scientific meeting abstracts from 2005–2010. **Results:** The only study reporting epidemiological burden reported a prevalence rate of multiple sclerosis to be 1.39 per 100,000 persons. Multiple sclerosis was more prevalent among females as compared to males. Most of the studies used Poser criteria to diagnose multiple sclerosis. Corticosteroids were the mainstay used by physicians for the treatment of multiple sclerosis. Little data is available on epidemiological burden and no data is available on the economic and humanistic burden of multiple sclerosis in China.

Conclusions: Diagnostic practices and treatment of multiple sclerosis in China appear to lag behind those in Western countries. There is significant room for improvement in bettering those suffering from multiple sclerosis in China.

INTRODUCTION

Multiple sclerosis (MS) is a chronic disease that attacks the central nervous system, particularly the brain, spinal cord, and optic nerves.¹ MS is a debilitating disease with a significant deleterious effect on patients' quality of life and work productivity.² MS is a relatively rare disease in China as compared to other nations throughout the world. The World Health Organization estimates that the median prevalence of MS in the Western Pacific region, which includes China, was 5 cases per 100,000 persons between 2005 and 2007. Median incidence was found to be 0.9 per 100,000 persons. By comparison, median prevalence in Europe over the same period was 80 cases per 100,000 people and median incidence was 3.8 per 100,000 persons.³

Clinically, multiple sets of criteria for diagnosing MS exist. One early method of diagnosis, known as the Poser criteria, was introduced in 1983.⁴ The Poser criteria relied

on various combinations of symptoms, patient history, lesions of the central nervous system, and cerebrospinal fluid (CSF) abnormalities to classify MS. In 2000, McDonald *et al.*⁵ proposed new and improved diagnostic criteria that incorporate magnetic resonance imaging (MRI) and visual evoked potentials in addition to analysis of CSF. Simplifying, evidence-based revisions to the McDonald criteria were made in 2005.⁶ Chong *et al.*⁶⁻⁸ proposed modifications to the McDonald criteria for Asians with MS to increase the sensitivity and specificity of the McDonald criteria in this population, focusing mainly on differences in clinical presentations between Asian MS patients and Western MS patients.

Treatments for MS also vary. Disease-modifying therapies (DMTs) are commonly used for the treatment of MS in Western countries. DMTs have the capacity to alter the course of disease as well as treat symptoms.⁹ Common

DMTs include interferon beta (IFN β)-1a (Rebif[®]), IFN β -1b (Betaseron[®]), and IFN β -1a (Avonex[®]), glatiramer acetate (Copaxone[®]), mitoxantrone (Novantrone[®]), and natalizumab (Tysabri[®]). Corticosteroids are also used to treat MS. Corticosteroids shorten the duration of relapse but do not alter the course of the disease.¹⁰⁻¹² With the availability of DMTs, corticosteroids are now rarely used in Western countries.

The prevalence and impact of MS, methods of diagnosis, and available treatments are well characterized in Western countries where incidence and prevalence of the disease is relatively high, yet are not as well known in other countries, such as China. This study aimed to assess the depth and breadth of knowledge of MS and its consequences specifically in China via a review and synthesis of existing literature. The primary intent was to elucidate the epidemiological, economic, and humanistic burden of MS in China. The secondary aim was to classify methods of diagnosis and treatment patterns of the disease unique to China.

METHODS

In order to meet the primary and secondary aims of this study, a literature search was conducted using MEDLINE as well as China-specific databases provided by China National Knowledge Infrastructure (CNKI), Chongqing VIP Information Co., Ltd. (CQVIP), and Wanfang Data. The searches in MEDLINE were limited to English-language literature, while the searches in all databases were limited to articles on human subjects published between 1 January 2005 and 3 March 2010. Literature search term strings to best address each study aim were created and are shown in Table 1. Abstracts of each article identified in the search were manually reviewed by study investigators to assess potential inclusion in the review. In accordance with the primary and secondary study aims, articles were included if they reported epidemiology data, humanistic outcomes, economic outcomes, or diagnostic and treatment patterns of MS that were unique to China.

To augment searches performed in the databases above, “grey literature” was also

Table 1: Search strategy

Search Variable	Search Strategy
Epidemiology	“Multiple Sclerosis” and (epidemiol* or incidence or prevalence or risk factor*) and (China or Chinese)
Diagnostic patterns	“Multiple Sclerosis” and (present or presents or presentation or presenting or diagnos* or screen*) and (China or Chinese)
Treatment patterns	“Multiple Sclerosis” and (treatment* or therap* or pharmaceutical* or drug or drugs or medicine* or surger* or surgical or medication*) and (management or pattern* or use or prescribing or trend* or survey or database) and (China or Chinese)
Clinical outcomes, including natural history/progression of disease and treatment outcomes	“Multiple Sclerosis” and (progress* or prognos* or survival or mortality or “natural history”) and (China or Chinese)
Humanistic outcomes	“Multiple Sclerosis” and (“quality of life” or “quality-of-life” or “patient reported outcome” or “patient-reported outcome” or “patient reported outcomes” or “patient-reported outcomes” or satisfaction or utility or disability or “functional status” or “physical function”) and (China or Chinese)
Economic outcomes	“Multiple Sclerosis” and (cost or costs or budget* or expenditure* or resource utiliz* or economic* or pharmacoeconomic* or disab* or productiv* or (loss and work)) and (China or Chinese)

searched to identify additional useful data. This included non-indexed but authoritative published and unpublished sources, including abstracts from meetings of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), the Americas Committee on Treatment and Research in Multiple Sclerosis (ACTRIMS), and the Chinese Medical Association of Neurology and Psychiatry.

RESULTS

Identified studies

The search of primary databases yielded 744 hits. After manual review of each abstract, 41 full-text articles were identified as being potentially relevant to this analysis and were reviewed by study investigators. The supplemental search of the grey literature identified 8 additional abstracts of interest from presentations at meetings of ISPOR, ECTRIMS, ACTRIMS, and the Chinese Medical Association of Neurology and Psychiatry. Identified studies that address each primary and secondary study aim are addressed below.

EPIDEMIOLOGICAL BURDEN

Only one study, which assessed the prevalence of MS in mainland China¹³, dealt with the epidemiological burden of MS in China. The crude point prevalence of MS identified in this study was 1.39 cases per 100,000 and was based on 123 patients with a permanent residence status in Shanghai during the study period of September 2004 to August 2005.¹³ The prevalence rates were highest among patients aged 50-59 years old (2.30 per 100,000) and was higher among females as compared to males in all age groups. These prevalence estimates were made by utilizing a network of neurologists to identify the prevalent cases of MS by systematically checking the inpatient registries at all hospitals in the study area using the McDonald criteria.

Across all reviewed studies, MS was found to be more common among females as compared to males. The mean age ranged from 33 to 57 years (Table 2).

ECONOMIC BURDEN

None of the reviewed studies assessed the economic burden of MS among Chinese patients.

Humanistic burden

None of the reviewed studies assessed the humanistic burden of MS among Chinese patients.

Diagnostic patterns

The majority of the studies reviewed used Poser's criteria to diagnose MS (Table 2). One study compared the diagnosis of MS using both McDonald and Poser criteria.¹⁴ The consistency of the two criteria for MS was 78.4%, with a lower sensitivity for the diagnosis of MS for Poser criteria as compared to McDonald's criteria.

Two population-based retrospective studies reported both the mean age at diagnosis as well as the age at onset of MS.^{13,15} Results indicate a mean delay between onset of MS and diagnosis of 5 years. Among all patients (N=249), the mean age at onset was 37.4 years (males 38.3 years and females 36.7 years), while the mean age at diagnosis was 42.4 years (males 42.5 years and females 42.9 years).^{13,15}

Treatment patterns

Most of the case series studies reported use of corticosteroids for the treatment of MS. They were used either singly or in combination with other corticosteroids or immunoglobulins. Interferon, a DMT, was used in very few studies. According to the practice guideline developed by the Chinese Medical Association, corticosteroids alone or in combination with immunoglobulins are recommended during the remission period of the disease.¹⁶

DISCUSSION

The aim of this study was to review and synthesize the literature associated with MS in China. Specifically, the primary aims were to understand the burden of the disease in terms of epidemiology, economic impact, and humanistic impact. We were also interested in methods of diagnosis and treatment patterns of the disease in China. Overall, the literature review yielded limited results that failed to adequately address the study aims, particularly the primary aims.

The majority of the studies identified were case series, which limit the generalizability of the results and prevent understanding of true epidemiology of MS in China. Just one population-based study exists in the current literature that evaluates the prevalence of MS in

Table 2: Demographic characteristics and diagnostic criteria by identified studies

Study	Sample size	Female	Age at diagnosis mean (range)	Diagnostic criteria
Bi <i>et al.</i> 2009 ²⁴	34	65%	35.3 (19-60)	McDonald
Chan <i>et al.</i> 2007 ²⁵	40	80%	36.2	McDonald
Cheng <i>et al.</i> 2007 ¹³	123	64%	46.1	McDonald
Cheng <i>et al.</i> 2008 ¹⁵	249	59%	42.4	McDonald
Cheng <i>et al.</i> 2009 ²⁶	99	55%	36.4 (12-67)	McDonald
Cheng <i>et al.</i> 2009 ²⁷	Not reported	Not reported	Not reported	McDonald
Guo <i>et al.</i> 2005 ²⁸	20	55%	36.4 (14-62)	Poser
Jiang <i>et al.</i> 2009 ²⁹	170	65%	36.9 (10-69)	McDonald
Lei <i>et al.</i> 2007 ³⁰	36	72%	35.6	McDonald
Li <i>et al.</i> 2006 ³¹	15	73%	Not reported	3-point diagnosis criteria
Li <i>et al.</i> 2006 ³²	16	63%	Not reported	Not reported
Li <i>et al.</i> 2006 ³³	110	66%	34.3 (4-66)	Not reported
Li <i>et al.</i> 2007 ³⁴	78	Not reported	Not reported	McDonald
Li <i>et al.</i> 2008 ³⁵	32	100%	(20-40)	McDonald
Liu <i>et al.</i> 2006 ³⁶	60	55%	(10-65)	Poser vs. another new diagnosis criteria
Liu <i>et al.</i> 2007 ³⁷	168	70%	35 (7-58)	McDonald
Liu <i>et al.</i> 2009 ³⁸	35	57%	36.66 (5-71)	Poser
Liu <i>et al.</i> 2009 ³⁹	46	65%	33.6 (20-40)	Poser
Liu <i>et al.</i> 2009 ⁴⁰	47	Not reported	Not reported	McDonald and Poser
Long <i>et al.</i> 2008 ⁴¹	14	21%	57.7 (46-72)	Poser
Lu <i>et al.</i> 2006 ⁴²	118	41%	Not reported	Poser
Lu <i>et al.</i> 2006 ⁴³	22	55%	38.7 (15-62)	Not reported
Shan <i>et al.</i> 2007 ⁴⁴	32	69%	35.7	Poser
Shi <i>et al.</i> 2006 ⁴⁵	11	64%	(25-35)	Poser
Sui <i>et al.</i> 2005 ⁴⁶	48	42%	32	Not reported
Tian <i>et al.</i> 2008 ⁴⁷	32	50%	(4-16)	Poser
Tian <i>et al.</i> 2009 ⁴⁸	481	63%	(4-72)	Poser
Wang <i>et al.</i> 2005 ⁴⁹	40	70%	(36.45)	Poser
Wang <i>et al.</i> 2006 ⁵⁰	20	90%	38.2	Not reported
Wang <i>et al.</i> 2008 ⁵¹	110	58%	34.2 (14-60)	Poser and McDonald
Wang <i>et al.</i> 2009 ⁵²	40	60%	(20-49)	Poser
Wang <i>et al.</i> 2009 ⁵³	52	65%	34 (15-58)	Poser
Wu <i>et al.</i> 2009 ⁵⁴	37	70%	38.9 (16-60)	Poser
Xiao <i>et al.</i> 2009 ⁵⁵	46	61%	34.7 (14-69)	McDonald
Xiao <i>et al.</i> 2009 ⁵⁶	32	59%	43 (17-67)	Not reported
Xing <i>et al.</i> 2008 ⁵⁷	24	38%	31.7 (16-60)	Not reported
Xinghu <i>et al.</i> 2007 ⁵⁸	129	56%	(6-78)	Not reported
Xu <i>et al.</i> 2009 ⁵⁹	42	71%	36.54 (17-62)	McDonald
Xu <i>et al.</i> 2009 ⁶⁰	42	60%	34 (13-52)	McDonald
Xue <i>et al.</i> 2005 ⁶¹	30	57%	34.66 (12-67)	Poser
Xue <i>et al.</i> 2007 ⁶²	33	61%	33.4 (20-40)	Not reported
Yang <i>et al.</i> 2007 ⁶³	25	56%	45 (15-58)	Poser
Yang <i>et al.</i> 2008 ⁶⁴	67	42%	34.7 (4-69)	McDonald
Zhang <i>et al.</i> 2006 ⁶⁵	23	61%	42 (15-68)	Not reported
Zhang <i>et al.</i> 2009 ⁶⁶	90	58%	38.2 (6-59)	McDonald
Zhao <i>et al.</i> 2006 ⁶⁷	30	70%	(21-30)	Poser
Zhou <i>et al.</i> 2008 ⁶⁸	108	64%	36.12 (10-74)	Poser

China.¹³ This study targeted Shanghai, an urban area, and reported a prevalence of 1.39 cases per 100,000 persons. Given China's large population and disparities in health care and epidemiology reporting between urban and rural areas, it seems unlikely that one urban study accurately portrays the true prevalence of MS in China. The authors themselves acknowledge that the reported prevalence may be the lower limit of the actual prevalence in the population. Furthermore, the prevalence reported is low compared to recent estimates in neighboring Asian countries. For example, prevalence of MS in Taiwan, Hong Kong, and Japan has been estimated to be 2.96¹⁷, 4.8¹⁸, and 13.1 per 100,000 persons¹⁹, respectively. Although the World Health Organization estimates do indicate that MS is a relatively rare disease in the Western Pacific region, MS may still prove to be an underreported disease in China, and the true epidemiology burden does not appear to be well understood.

The searches conducted in this study identified no literature classifying the economic or humanistic burdens of MS in China. This is not entirely surprising considering the lack of epidemiology data available, and this uncertainty around the true impact of MS reinforces the need to better understand the burden of the disease in China.

Our findings regarding the secondary aims of this study, namely diagnostic methods and treatment of MS in China, suggest that China is less advanced than Western countries in these areas. Chinese Medical Association guidelines recommend the use of the newer McDonald criteria for the diagnosis of MS.¹⁶ The McDonald criteria lead to an earlier diagnosis of MS as compared to the older Poser criteria²⁰⁻²³, and Cheng *et al.*¹⁴ reaffirm the use of the McDonald criteria in China when they report a lower specificity of the Poser criteria when compared to the McDonald criteria in Chinese patients. Nevertheless, our literature review indicates that the Poser criteria are used in the majority of cases. The use of the less comprehensive Poser criteria for diagnosis of MS may underestimate the true prevalence of the disease and lead to under-diagnosis in China, thereby delaying the initiation of beneficial treatment. These discrepancies in diagnostic methods and their impact on treatment of patients with MS may be further exacerbated by the wealth disparities in urban and rural China. The McDonald criteria require the use of expensive MRI technology for diagnosis, while the Poser criteria does not, which may lead to lack of

adoption of the more sensitive criteria in poor rural areas, where the majority of Chinese live.

China also appears to lag behind Western countries when it comes to treating MS. Our literature review indicates that corticosteroids are the most commonly used drugs for treating MS in China. While corticosteroids alleviate symptoms of MS, they do not alter the course of the disease, as DMTs do. Aside from IFN β -1a (Rebif[®]), DMTs are not available in China, whereas they are the standard treatment of MS in Western countries. Proper access of DMTs in China may be beneficial in bringing about better outcomes in patients with MS.

The paucity of data found in this study serves to highlight the knowledge gaps that exist in comprehending the burden of MS in China. Reported prevalence appears to be quite low, and large population-based trials capable of providing estimates representative of mainland China as a whole are nonexistent. Similarly, there is no estimate of the economic or humanistic burdens of MS on Chinese society. The fact that MS is not a well-known disease in China may contribute to the fact that it appears to be an under-diagnosed and under-treated disease as well. While there are likely many societal factors that contribute to the use of the antiquated Poser criteria for diagnosis and less effective corticosteroids for treatment – notably the wealth and knowledge disparities between rural and urban Chinese regions – it is also conceivable that this is due in part to a lack of recognition of the true burden of MS.

In conclusion, this study consisted of a review of publicly available literature with the goal of classifying the burden of MS in China. Results of the literature search were limited. No country-wide epidemiological data is available, and prevalence of MS may be under-reported. No data at all is available on the economic and humanistic burden of MS in China. This lack of burden of illness data may contribute to the fact that diagnostic practices and treatment of MS in China appear to lag behind those in Western countries. There is significant room for improvement in bettering those suffering from MS in China.

DISCLOSURE

Conflict of interest: Dr. Hu is a consultant for Bayer HealthCare Pharmaceuticals. Ms. Donga and Dr. Pan are paid employees of United BioSource Corporation, which received the funding for the study and manuscript. Ms. Zhu and Dr. Wang are employed by Bayer HealthCare Pharmaceuticals.

ACKNOWLEDGEMENT

Financial support for this research was provided by Bayer HealthCare Pharmaceuticals, Montville, NJ, USA.

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