Neuro epidemiology

Multiple Sclerosis Epidemiology in East Asia, South East Asia and South Asia: A Systematic Review

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Abstract

Background: Multiple sclerosis (MS) is one of the most common chronic immune-mediated diseases of the human central nervous system and an important cause of non-traumatic neurologic disability among young population in several countries. Recent reports from East Asia, South East Asia and South Asia have proposed a low to moderate prevalence of MS in these countries. ***Methods:*** A literature review search was carried out in December 2014 in Medline, Embase, Scopus and Cochrane library to recover original population-based studies on MS epidemiology in East Asia, South East Asia and South Asia countries published between January 1, 1950 and December 30, 2014. We intended search strategies using the key words: multiple sclerosis, prevalence, incidence and epidemiology. Based on our inclusion criteria, 68 epidemiologic studies were included in this systematic review. ***Results:*** The most extensively used diagnostic criteria in the studies were McDonald's criteria. Most studies were performed in a multi-center hospital setting. The female to male ratio varied and ranged from 0.7 in India to 9.0 in China. The mean age at disease onset ranged from the lowest age of 25.3 in Iran to the highest age of 46.4 in China. MS prevalence ranged from 0.77 in 100,000 populations in Hong Kong (1999) to 85.80 in 100,000 in Iran (2013). ***Conclusions:*** Advances in MS registries around the globe allow nationwide population-based studies and will allow worldly comparisons between the prevalence and incidence in different regions that are provided to monitor estimation.

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Background

Multiple sclerosis (MS) is a chronic immune-mediated disease of the central nervous system, which usually affects young adults [1]. MS is the most important cause of non-traumatic neurologic disability among the young working-class population, resulting in an economical and significant social impact and requiring lifetime support and management [2, 3].

According to the main results from the atlas of MS in 2013, the number of patients affected with MS has increased from 2.1 million in 2008 to 2.3 million in 2013 [4].

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The prevalence and incidence of MS extensively vary among different countries and various geographical areas. Kurtzke [5] proposed to divide different areas in the world into 3 geographic regions regarding MS prevalence: (1) high >30/100,000, (2) intermediate (5–25/100,000), and (3) low risk <5/100,000.

Many epidemiological studies have been performed in Europe, north America, Canada and Australia where the prevalence of MS seems to be high, and recent studies show an increase in the disease prevalence in such regions [4, 6]. According to the globally grouped continent of 101 MS studies from the Americas, Europe, Asia, Africa and Australia/New Zealand, the worldwide median estimated incidence was 5.2 (range 0.5–20.6) per 100,000 person-years, the median estimated prevalence was 112.0 (with a range of 5.2–335) per 100,000 person-years, and the average illness period was 20.2 years (range 7.6–36.2) [7].

There are several epidemiological studies from other parts of the world conducted with different methods and results, which also demonstrate an increase in the number of patients. Countries located in Far East and South Asia were formerly considered to be located in a low prevalence zone for MS [8, 9]. Recent studies from these regions support the increase in prevalence in such regions. Here, we tried to review the epidemiological studies in Far East and South Asian countries. In this review, we tried to cover all studies conducted in such countries and estimate the latest trends and changes of prevalence and incidence rates of MS among selected countries.

Methods

Search Strategy
To determine the epidemiology of MS among countries that constitute Pan Asian Countries Treatment and Research in Multiple Sclerosis; a systematic literatures search of Medline, Embase, Scopus and Cochrane library, which allowed access to publications presented by Tehran University of Medical sciences, using the key words 'multiple sclerosis, prevalence, incidence, epidemiology' and names of countries covering the period between January 1, 1950 and December 30, 2014 was performed.

Screening and Eligibility Criteria
We utilized computer databases to find population-based studies with information and statistic on MS epidemiology with limitation to general human population studies in English language publications. Cross-sectional and cohort studies were conducted to analyze MS epidemiological features in selected articles. The title and abstract of all literatures recognized by the database were reviewed. The mentioned review of systematic literature was intended to be comprehensive; potentially eligible studies were retrieved and read in full text to confirm that they fulfilled the following

inclusion criteria in this systematic review: (1) of population-based studies with human samples among patients with MS measured by different terms of diagnosis criteria in MS among those living in Pan Asian countries; (2) containing data on the prevalence, incidence or number of MS cases in country studies; (3) MS was recognized according to global diagnostic criteria in use at the study period, the Schumacher criteria [10], Poser [11] or McDonald's criteria [12–14]; and (4) available in full text form.

We also conducted a manual hand search of reference lists of primary identified articles and relevant reviews to discover additional studies that could have been missed. The studies that did not represent the general population were excluded. Two experts reviewed the abstracts independently (if the review of abstract did not match the eligibility, the full text was reviewed). All articles that were confirmed by both reviewers for eligibility criteria were considered. Review articles, editorials and letters were excluded. The study selection flowchart was established based on PRISMA (fig. 1).

Our classification of the Pan Asian countries was based on the World Bank classification including the following 34 countries: Japan, China, Mongolia, Hong Kong, North Korea, South Korea, Taiwan, Macau, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Thailand, Viet Nam, Brunei, East Timor, Singapore, Fiji, Papua New Guinea, Samoa, Vanuatu, Tonga, Solomon Island, Bhutan, Maldives, Nepal, Sri Lanka, Bangladesh, India, Pakistan, Afghanistan and Iran [15]. Australia and New Zealand are excluded.

Pan-Asian countries were divided into 4 geographical areas such as East Asia, South East Asia, pacific, and South Asia to categorize racial or regional variations in MS across the continent [15]. We have made a comparison from collected data derived from different countries in a tabulated regional form. All abstracts were screened by 2 independent reviewers (if the abstract was not clear for eligibility to be included in the study, the whole full text review was performed) to evaluate whether articles met the including criteria completely. Articles that were considered eligible by both reviewers were retained. The study selection flow diagram was established conferring to PRISMA statement (fig. 1).

Data Extraction and Quality Assessment
Repeated publications on the same data were excluded. Based on overestimating prevalence, studies were categorized as low, undistinguishable (if data for determination risk was inadequate) or high risk. The quality scores of each study are presented in tables 1–3.

The following information was elicited into a template form by an expert reviewer: study period, study method, study region, diagnostic criteria, number of cases identified, gender ratio (female to male), onset mean age of disease, prevalence per 100,000 persons, incidence per 100,000 persons and quality score of study. Crude and consistent prevalence and incidence estimation were recorded generally and by gender, county, time length and subgroup as appropriate. Extracted information was considered by a second reviewer and accurate studies data chosen indices were selected for additional meta-analysis. The authors summarized the extracted information from each individual study in a regional table with a consistent pattern. Quality scores are presented in detail in complimentary the tables 1–3 based on Joanna Briggs critical appraisal tool [16].
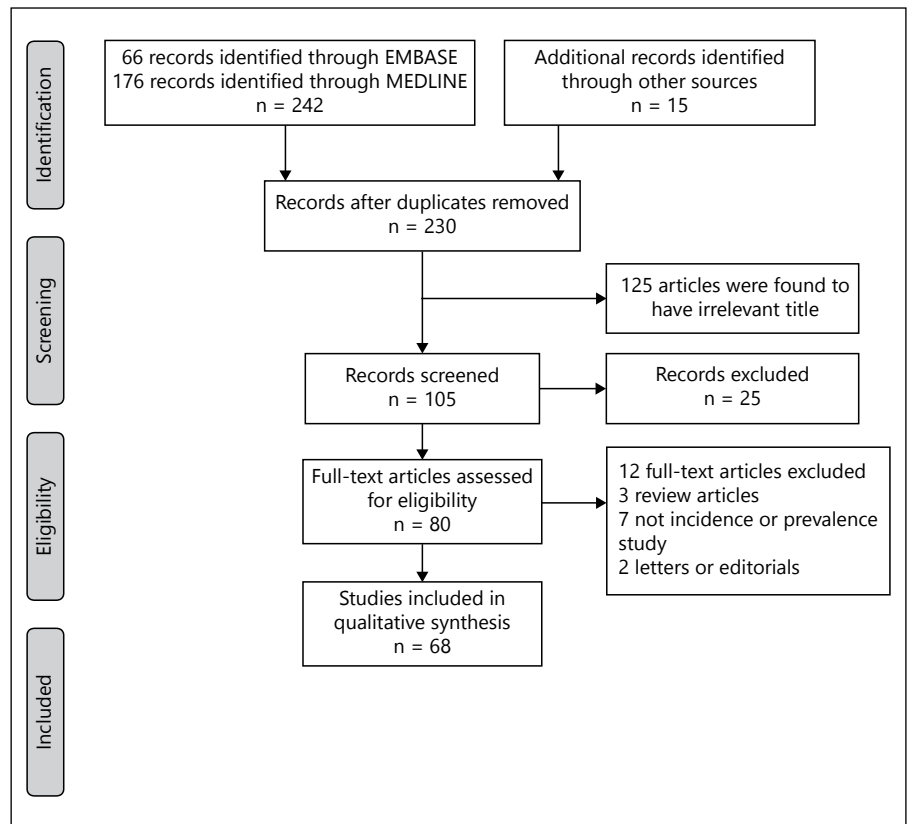
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Identification

66 records identified through EMBASE
176 records identified through MEDLINE
n = 242

Additional records identified through other sources
n = 15

Screening

Records after duplicates removed
n = 230

125 articles were found to have irrelevant title

Records screened
n = 105

Records excluded
n = 25

Eligibility

Full-text articles assessed for eligibility
n = 80

12 full-text articles excluded
3 review articles
7 not incidence or prevalence study
2 letters or editorials

Included

Studies included in qualitative synthesis
n = 68

Fig. 1. PRISMA 2009 flow diagram. Adapted from Moher et al. [98].

Results

The search approach obtained a total of 242 appropriate references among all original sources.

After excluding duplicate entries, 230 extensive literatures remained relevant to epidemiological studies of MS in Pan Asian countries. One hundred and twenty five studies had inappropriate titles, and from our screening, 25 studies were not authorized to be part of our study. In this systematic review, finally, 68 studies, excluding 12 full-text articles (number of 4 review articles, 2 editorials or letters and 6 articles which did not indicating incidence and prevalence), were included (fig. 1).

The final analysis included studies from countries such as Japan [17–29], China [30–35], Korea [36–40], Hong Kong [41–44], Taiwan [45–48] in East Asia (table 1), Malaysia [49–51] and Thailand [52–54] in South East Asia (table 2), India [55–62], Pakistan [63, 64] and Iran [65–84] in South Asia (table 3).

There was no result from Mongolia, North Korea, Macau, Cambodia, Indonesia, Lao PDR, Myanmar, Philippines, Viet Nam, Brunei, East Timor, Singapore, Fiji, Papua New Guinea, Samoa, Vanuatu, Tonga, Solomon Island, Bhutan, Maldives, Nepal, Sri Lanka, Bangladesh and Afghanistan. It was found that latest studies had higher quality in terms of content, with inclusion of the McDonald criteria. Tables 1–3 show the study duration, study method, study setting, diagnostic criteria, population size, gender (female to male ratio), mean age at disease onset, prevalence and incidence rates in selected studies.

McDonald's diagnostic criteria were the most extensively used diagnostic criteria in the studies (51.56%); in the second level, Poser criteria were used in 38.38% of studies and Schumacher criteria were used in 14.06 of studies.

The information source to obtain patient report in 36.8% of studies was used from regional MS registries, while 38.2% of information reported was based on a multi-center hospital setting and 25% of studies were based on a single-hospital setting.

Female to male sex ratio is very diverse ranging among different studies in this region, from 0.7 in India to 9.0 in China (tables 1, 3).

In general, we estimated a female to male ratio of 3.6 in this region, after including 38 studies and after consid-

Table 1. Baseline characteristic of MS in East Asia

First author	Study period	Method	Study setting	Number of cases identified	Number of cases identified	Gender ratio, F:M	Onset mean age	Prevalence in 100,000	Incidence in 100,000 incidence/100,000	Quality score
Japan										
Houzen [17]	2011	Cross-sectional study	Multicenter hospital based (Tokachi)	Poser' criteria	57	3.38:1	28.3	16.2	–	8/9
Houzen [18]	2006	Cross-sectional study	Multicenter hospital based (Tokachi)	Poser' criteria	47	3.1:1	28.4	13.1	–	9/10
Osoegawa [19]	2003	Cross-sectional study	MOH	McDonald's criteria	9,900	2.9:1	32±13	7.7	–	10/10
Tanaka [20]	1988–2002	Retrospective cohort study	Single hospital based (Tokyo)	Poser' criteria	104	2.4:1	30.7	–	–	7/8
Itoh [21]	2002	Cross-sectional study	Multicenter hospital based (Asahikawa)	Poser' criteria	37	1.8:1	29	10.2	–	7/8
Houzen [22]	2001	Cross-sectional study	Multicenter hospital based (Tokachi)	Poser' criteria	27	2.9:1	29.1±14.2	8.57	–	6/8
Kira [23]	1950–1997	Retrospective cohort study	Single hospital based (Fukuoka)	Poser' criteria	143	1.9:1	32.3	–	–	9/10
Fukazawa [24]	1986–1989	Retrospective cohort study	Multicenter hospital based (Hokkaido)	Poser' criteria	97	1.95:1	31	–	–	8/9
Kuroiwa [25]	1975–1978	Cross-sectional study	Multicenter hospital based	Schumacher criteria	65	1.7:1	–	0.8–4	–	9/10
Kuroiwa [26]	1972–1973	Cross-sectional study	MOH	Schumacher criteria	1,084	1.7:1	33±13	–	–	7/9
Shibasaki [27]	1958–1973	Case series	Single hospital based (Fukuoka)	Schumacher criteria	61	–	–	–	–	5/8
Okinaka [28]	1953–1960	Cross-sectional study	Multicenter hospital based	–	32	–	–	2–4	0.3–0.4	7/9
Okinaka [29]	1890–1955	Retrospective cohort study	Multicenter hospital based (Tokyo)	–	66	1:1	–	–	0.1	6/8
China										
Li [30]	2002–2009	Retrospective cohort study	Multicenter hospital based	McDonald's criteria	117	1.3:1	–	–	–	8/9
Liu [31]	2004–2006	Cross-sectional study	Single hospital based (Beijing)	McDonald's criteria	10	9:1	32.6	–	–	6/8
Cheng [32]	1993–2006	Retrospective cohort study	Multicenter hospital based (Suzhou)	McDonald's criteria	82	1.2:1	46.4	–	–	7/9

Table 1. (continued)

First author	Study period	Method	Study setting	Number of cases identified	Number of cases identified	Gender ratio, F:M	Onset mean age	Prevalence in 100,000	Incidence in 100,000 incidence/100,000	Quality score
Cheng [33]	2004–2005	Cross-sectional study	Multicenter hospital based (Shanghai)	McDonald's criteria	249	1.4:1	37.4	–	–	9/10
Cheng [34]	2004–2005	Cross-sectional study	Multicenter hospital based (Shanghai)	McDonald's criteria	123	1.8:1	39.8	1.39	–	10/10
Zhao [35]	1949–1977	Retrospective cohort study	Single hospital based (Beijing)	McDonald's criteria	70	1.8:1	30.6	–	–	6/8
Korea										
Kim [36]	2005–2010	Retrospective cohort study	Multicenter hospital based (Korea)	McDonald's criteria	105	2:1	30.4±9.8	–	–	9/10
Kim [37]	2000–2005	Retrospective cohort study	National Health Insurance	McDonald's criteria	782	1.26:1	38.4±13.5	3.5–3.6	–	10/10
Lee [38]	1987–2004	Retrospective cohort study	Multicenter hospital based	McDonald's criteria	62	1.48:1	35.2±13.3	–	–	8/10
Cho [39]	1991–1995	Retrospective cohort study	Single hospital based (Seoul)	Poser's criteria	35	1.3:1	34.6	–	–	5/7
Kurtzke [40]	1958–1966	Retrospective cohort study	Single hospital-based (Seoul)	Schumacher criteria	59	3.2:1	25.8	2.4	–	7/9
Hong Kong										
Chan [41]	1998–2001	Retrospective cohort study	Single hospital-based	McDonald's criteria	61	3:1	25.9	–	–	6/8
Lau [42]	1996–2006	Retrospective cohort study	Multicenter hospital based	Poser's criteria	106	3.2:1	31.8	4.8	–	9/10
Lau [43]	1999	Cross-sectional study	Multicenter hospital based	Poser' criteria	53	9.6:1	29.4	0.77	–	7/9
Yu [44]	1981–1987	Cross-sectional study	Multicenter hospital based	Poser's criteria	47	2.9:1	30	0.88	–	8/9
Taiwan										
Lai. [45]	2000–2005	Retrospective cohort study	National Health Insurance	McDonald's criteria	1,262	1:0.4	30	2.96	0.79	10/10
Chang [46]	1993–2001	Cross-sectional study	Single hospital-based (Northern Taiwan)	Poser's criteria	75	4.4:1	35.6±12.6	–	–	8/9
Tsai [47]	1985–1999	Retrospective cohort study	Bureau of National Health Insurance	Poser's criteria	43	5:1	29.93	1.9	–	6/8
Hung [48]	1954–1975	Retrospective cohort study	Multicenter hospital based	Schumacher criteria	25	3.2:1	32	0.84	–	8/9

Table 2. Baseline characteristic of MS in South East Asia

First author	Study period	Method	Study setting	Diagnostic criteria	Number of cases identified	Gender ratio, F:M	Onset mean age	Prevalence in 100,000	Incidence in 100,000 incidence/100,000	Quality score
Malaysia										
Viswanathan [49]	2008–2013	Retrospective cohort study	Single hospital based (Kuala Lumpur)	McDonald's criteria	104	5:1	28.6±9.9	–	–	8/9
Tan [50]	1968–1988	Retrospective cohort study	Single hospital based	McDonald's criteria	38	6.6:1	31	2	–	7/8
Tan [51]	1968–1986	Retrospective cohort study	Single hospital based	McDonald's criteria	30	5:1	29.7	2	–	6/8
Thailand										
Siritho [52]	1997–2004	Retrospective cohort study	Single hospital based (Bankok)	McDonald's criteria	72	6.2:1	33±12	–	–	8/9
Veijajiva [53]	1977–1993	Retrospective cohort study	Single hospital based (Bankok)	Poser' criteria	17	4:1	30.4	2	–	6/8
Jitpimolmard [54]	1967–1986	Retrospective cohort study	Multicenter hospital based (Bankok)	McDonald's criteria	50	4:1	30.4	–	–	6/8

ering that the number of cases affecting sex ratio to be larger than 70 cases. The results of female to male ratio is 3.4:1 in East Asia following, 2.1 in Japan, 1.5:1 in China, 1.6:1 in Korea, 3.2:1 in Hong Kong and 3.4:1 in Taiwan (table 1). The results of female to male ratio are 5.6 in South East Asia following, 5.1:1 in Malaysia and 6.2:1 in Thailand (table 2). The result of female to male ratio is 1.9:1 in South Asia following, 3.0:1 in Iran, 1.4:1 in Pakistan and 1.3:1 in India (table 3).

Prevalence estimation of MS was more frequent than incidence estimation of MS. The mean age at disease onset range was 21.1 in these countries, with a maximum value of 46.4 in China to a minimum of 25.3 in Iran (tables 1, 3).

In this segment, we present a brief report of MS epidemiology in selected countries by each region.

East Asia
Japan
According to our review, a large increase in prevalence was observed during the last decade from 7.7 in 2003 in the Tokachi province of Hokkaido in Northern Japan to 13.1 in 2006 and 16.2 in 2011 respectively in the same area [17, 18]. Several national surveys on MS were performed in Japan in 1972, 1982, 1989, and 2004 [19, 26, 85]; the 2004 survey was carried out by the Research Committees of Epidemiology of Intractable Diseases and Neuroimmunological Diseases. The critical information was collected in 2 phases: the first phase was about recognizing the MS patient population, and the second step was about sending self-report questionnaires to all the treated MS patients in the selected hospitals from January 1, 2003 to December 31, 2003 [19]. In Japan, the MS estimated prevalence was 7.7 in a population of 100,000 people (95% CI 7.1–8.4) [19]. Our current survey indicated the increasing female to male sex ratio of MS over 50 years from 1:1 in 1955 to 3.38:1 in 2011. The mean age at disease onset had decreased from 33 ± 13 in 1972 to 28.3 in 2011. In Japan, certain explanations for a decline in the mean age include more frequent utilization of MRI imaging as well as improved neurological care [17].

China
Cheng et al. [33] reported the MS prevalence of 1.39 per 100,000 (95% CI 1.16–1.66) in Shanghai. All studies used McDonald's criteria as diagnostic criteria among MS patients. In our reviewed studies, MS prevalence is more common among females in comparison to males [30–33, 35]. In the last 2 decades, the mean age at disease onset ranged from 46.4 in 1993 to 32.6 in 2006 [31, 32].

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Table 3. Baseline characteristic of MS in South Asia

First author	Study period	Method	Study setting	Diagnostic criteria	Number of cases identified	Gender ratio, F:M	Onset mean age	Prevalence in 100,000	Incidence in 100,000 incidence/100,000	Quality score
India										
Pandit [55]	2011–2013	Cross-sectional study	Multicenter hospital based (Mangalore)	McDonald's criteria	35	1.6:1	38.3±12.8	8.35	–	7/9
Sarma [56]	1987–1997	Retrospective cohort study (Bangalore)	National Institute of Mental Health and Neurosciences	Poser' criteria	68	2.1:1	26.3	–	–	7/9
Syal [57]	1986–1998	Prospective (to 1996) Retrospective cohort study	Multicenter hospital based	Poser' criteria	100	1.32:1	28.49±9.54	–	–	7/9
Wadia [58]	1988	Cross-sectional study	Multicenter hospital based (Bombay-Poona)	Schumacher criteria	16	0.7:1	36.53	26 Bombay 58 Poona	–	6/8
Singhal [59]	1957–1983	Retrospective cohort study	Multicenter hospital based	–	105	1.3:1	27.7	0.17–1.33	–	7/9
Chopra [60]	1968–1977	Prospective cohort study	Single hospital based (Chandigarh)	Schumacher criteria	54	1:1.7	27.8	–	–	6/9
Singhal [61]	1957–1972	Retrospective cohort study	Single hospital based (Bombay)	Schumacher criteria	74	1.5:1	27	–	–	6/9
Mathew [62]	1965–1970	Retrospective cohort study	Single hospital based	Schumacher criteria	17	1.12:1	29.6	–	–	6/9
Pakistan										
Wasay [63]	–	Retrospective cohort study	Multicenter hospital based (Karachi, Peshawar, Islamabad)	Poser' criteria	142	1.45:1	27	–	–	9/9
Wasay [64]	2009–2010	Cross-sectional study	Multicenter hospital based	–	100	1.5:1	32	–	–	8/8
Iran										
Etemadifar [65]	2013	Cross-sectional study	MOH	McDonald's criteria	42,200	3.48:1	–	54.5	5.87	9/9
Etemadifar [66]	2003–2013	Cross-sectional study	Regional MS registry (Isfahan)	McDonald's criteria	4,536	3.41:1	–	85.80 (83.3–88.4)	–	9/9
Saman-Nezhad [67]	2012	Cross-sectional study	Regional MS registry (Khuzestan)	–	448	–	30.8	43.3	–	9/9
Rezaali [68]	2011	Cross-sectional study	Regional MS registry (Qom)	Poser (to 2001) and McDonald's criteria	581	3.4	34.25±9.01	50.4	–	10/10

Table 3. (continued)

First author	Study period	Method	Study setting	Diagnostic criteria	Number of cases identified	Gender ratio, F:M	Onset mean age	Prevalence in 100,000	Incidence in 100,000 incidence/ 100,000	Quality score
Izadi [69]	2011	Cross-sectional study	MOH	–	34,605	–	–	45	–	5/7
Jajvandian [70]	2005–2011	Cross-sectional study	Regional MS registry (Khorasan)	–	105	2.38:1	27.10±8.41	12.94	–	9/9
Majdinasb [71]	2005–2011	Cross-sectional study	Regional MS registry (Khuzestan)	McDonald's criteria	1,057	3.2:1	27.6±8.2	25	–	8/9
Heydarpour [72]	1991–2011	Cross-sectional study	Regional MS registry (Tehran)	Poser' (to 2001) and McDonald's criteria	–	–	–	74.28	–	8/9
Etemadifar [73]	2003–2010	Cross-sectional study	Regional MS registry (Isfahan)	McDonald's criteria and 2005 revisions	3,522	3.37:1	28.2±9	73.37 (70.9–75.8)	9.1 (8.3–10.0)	9/9
Moghaddam [74]	2010	Cross-sectional study	Regional MS registry (Rafsanjan)	McDonald's criteria	83	4:1	–	30	–	7/9
Ghandehari [75]	2009	Cross-sectional study	Regional MS registry (Khorasan)	McDonald's criteria	71$^{\&}$ 721$^{\&\&}$ 34$^{\&\&\&}$	3.8:1$^{\&}$ 1.8:1$^{\&\&}$ 3.2:1$^{\&\&\&}$	–	8.75$^{\&}$ 12.89$^{\&\&}$ 5.34$^{\&\&\&}$	–	7/9
Hashemilar [76]	2005–2009	Cross-sectional study	Regional MS registry (Azerbayejan)	McDonald's criteria	1,000	2.7:1	32.5±8.3	27.7	–	7/9
Sharafaddinzadeh [77]	1997–2009	Cross-sectional study	Regional MS registry (Khuzestan)	McDonald's criteria	569	3.11:1	–	16.28	2.20	10/10
Elhami [78]	1989–2009	Cross-sectional study	Regional MS registry (Tehran)	Poser (to 2001) and McDonald's criteria	7,896	3.11:1	27.53±8.12	50.57 (49.46–51.68)	2.93 (2.67–3.18)	10/10
Sahraian [79]	1999–2008	Cross-sectional study	Regional MS registry (Tehran)	Poser (to 2001) and McDonald's criteria	8,146	2.6:1	27.24±8.32	51.90	–	10/10
Abedini [80]	2007	Cross-sectional study	Regional MS registry (Mazandaran)	McDonald's criteria	582	2.6:1	26.9±8.3	20.1 (18.7–22.1)	–	7/9
Etemadifar [82]	2004–2005	Cross-sectional study	Regional MS registry (Isfahan)	McDonald's criteria	1,391	3.6:1	–	35.5 (33.6–37.3)	–	10/10
Kalanie [83]	1996–2001	Cross-sectional study	Multicenter hospital based (Tehran)	Poser' criteria	265	2.5:1	27±7.4	–	–	9/10
Ebrahimi [84]	–	Cross-sectional study	Regional MS registry (Kerman)	–	932	3:1	28.35	31.75	–	9/9

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Li et al. [30] reported that amongst those with MS, the number of patients with opticospinal MS (OSMS) was higher in Northern China compared to Western countries, and limb weakness at onset was the most popular medical symptom in both OSMS and CMS patients.

Korea

The prevalence of MS in Korea was estimated to be 3.5–3.6 per 100,000 people [37]. The clinical pattern of MS in Korea is similar from that observed in other Asian countries [38].

A nationwide survey from 2000 to 2005 in Korea, utilizing several databases gathered from 38 main referral hospitals has shown an MS prevalence of 3.5–3.6 in 100,000 population [37]. Another study in Seoul, estimated the prevalence of MS to be 2.4 in 100,000 people [40]. MS is more common among women and female to male ratio is 2:1.

The mean age of onset decreased from 35.2 in 1987–2004 to 30.4 in 2005–2010 [36, 38].

According to the involved location, the most prominent detection that is of concern is the involvement of 78% of the spinal cord and 25% of the optic nerve among MS patients in Korea [36].

Hong Kong

Prevalence of MS among Hong Kong patients was estimated to be from 0.77 to 4.8 per 100,000 populations [42, 44]. Studies of MS among Chinese patients in Hong Kong indicated a worse clinical outcome of Chinese MS patients than that of Caucasian patients [42]. Epidemiological MS study in Hong Kong showed that there were 95 relapsing–remitting (RR) type, 7 progressive relapsing type and 4 primary progressive (PP) type among 106 patients [42]. Female to male sex ratio ranged from 9.6:1 in 1999 to 3:1 in 2001 [41, 42]. The mean age at onset disease decreased from 31.8 to 25.9 [41, 42].

Taiwan

The prevalence of MS increased in recent decades from 0.84 in 1975 and 1.9 in 1999 to 2.96 in 100,000 population in 2005 [45, 47, 48]. According to our review, the incidence of MS in Taiwan is 0.79 [45]. MS incidence was found to be the highest for females in the age group of 40–60 and for males in the age group of over 55 [45]. Female MS patients outnumbered males by a ratio of 2.5:1 [45].

Regarding gender, the female-to-male ratio in Taiwan is higher than it is in Western countries [86]. Among 1962 MS patients, the mean age at onset was 30 [45], and for

OSMS, the mean age at onset was 41.88. The anatomic area that was consistently affected was the spinal cord (48%), followed by the optic nerve (33%). The most common type of MS is RR in 51% of the patients, and it takes a secondary-progressive (SP) and PP course in 30 and 19% of MS patients, respectively [47].

South East Asia
Malaysia
The Malaysian populations were affected by Chinese, Indians and other native racial groups [49]. Malaysia has been considered low risk area for MS. The prevalence of MS was 2 per 100,000 populations, and the young age group remained the most frequently affected with a mean age at onset of 28.6 ± 9.9 [50]. A high female to male ratio in MS has been reported in Malaysia [50, 51]. A 6-year hospital-based study on 104 MS patients in Kuala Lumpur revealed that 89.4% of patients had the RR type, followed by 5.8% of SP and 2.9% PP course of disease [49]. Among all patients, 5% had a family history of MS. The prevalence pattern of this type of multiple MS in Malaysia is steadily changing with regard to racial distribution. The result of epidemiological study in Malaysia disclosed that the Chinese have more neuromyelitis optica and its spectrum disorders rather than MS [49].

Thailand
No population-based epidemiological study has been performed to estimate the incidence and prevalence of MS in Thailand. According to a single-based hospital study in Bangkok from 1977–1993, the prevalence of MS is 2 in 100,000 population [53]. Siritho et al. [52] reported the mean age to be 33 ± 12 during the onset of MS.

Among 72 MS patients, the female to male ratio was estimated to be 6.2:1. None of the patients had reported MS among members in their family [52].

The main body parts that got affected due to MS attacks among patients in Thailand was the optic nerve, which got affected by 51%, followed by 26% in spinal cord, 19% brainstem, 1% cerebral hemisphere and 1% optic-spinal respectively [52].

South Asia
India
There is no large epidemiological study in MS from India. Based on multicenter hospital-based statistics, the prevalence of MS increased from 1.33/100,000 to 8.35 in last 30 years [55, 59]. Female to male ratio was 1.6:1 and the mean age at onset was 38.3 [55].

Syal et al. [57] reported that RR course among 89% of MS patients followed a progressive course in 11% from the time the disease began. The OSMS was common among 71.4% of patients [59].

Pakistan

There are no population-based studies concerning prevalence or incidence for MS from Pakistan.

A multicenter hospital database from Karachi, Peshawar and Islamabad among 142 MS patients estimated that the mean age at onset was 27 years, with a female to male ratio of 1.45:1 [63].

The RR course of MS has been seen in 81%, PP in 21%, and SP in 4% of patients [63].

Iran

Based on the ministry of health report in Iran, the prevalence of MS increased from 45/100,000 in 2011 to 54.5/100,000 in 2013 [65, 69].

In capital city, Tehran, MS prevalence had increased to 74.28/100,000 in 2011 from 51.9/100,000 in 2008 [72, 79].

The annual crude incidence of MS had significantly increased from 3.77 in 2007 to 5.68/100,000 in 2013 [65]. In Iran, a higher prevalence of MS was reported from Isfahan [66].

Based on regional MS registry studies in Isfahan, the general increase in MS prevalence and incidence occurred over a decade; MS prevalence had increased from 35.5 in 2005 to 85.8 per 100,000 in 2013 and incidence had increased from 3.64 in 2006 to 9.1 in 2010 [66, 73, 81, 82].

The MS is over 3 times more common in females than in males [65]. Among MS patients, RR was reported in 84.9%. The onset mean age of disease was 27.24; positive family history of MS was recognized in 9.5% of patients in Khorasan and 12.2% of patients in Isfahan [69, 75, 76].

The most common clinical course among 87.8% of MS patients was RRMS; 6.4% had SPMS and 5.7% had PPMS. First appearance was sensory in 51.7% and visual disturbances were reported in 47.5% of patients. The lowest mean age at disease onset was 25.36 in Isfahan and the highest was 34.25 years in Qom [66, 73, 81, 82, 87].

Iran has reported variable prevalence rates of MS from different regions, the prevalence rate per 100,000 population in North Iran, Mazandaran was 20.1 [80], 27.7 in Northwest, Azerbaijan [76], 12.94 in Northeast, Khorasan [70], 16.28 in Southwest Iran, in Khuzestan [77], in central, Qom 50.4 and 31.7 in Kerman [68, 84].

Discussion

This study presents a systematic and inclusive review of 68 MS epidemiological studies in Asia. Our results are greatly restricted by the limitation of existing data, which could influence prevalence, incidence, gender ratio and the mean age at MS onset. Nationwide epidemiological studies were rare in Pan Asian countries. In addition, the different studies are bound by the variable quality of data, small number of cases identified, different diagnostic criteria and variable publication methods. Our study was restricted to only English. There are several studies in different languages, which are not possible to access because of translational difficulties.

The method for study and type of population collection were heterogeneous. Few studies estimated the incidence rate in 100,000 populations.

The key significant findings are as follows: (1) the first extensively used diagnostic criteria among these studies was McDonald's criteria. (2) The performance of a greater part of studies was in multi center hospital-based setting. (3) Generally female to male ratio was 3.6 in this region. (4) MS prevalence rate per 100,000 populations was 12.48 in this region. (5) The mean age of disease onset was 21.1.

The results of selected Asian countries were divided into 3 geographical regions (East Asia, Southeast Asia and South Asia). MS prevalence was low in the East and Southeast Asia compared to South Asia. Another study showed that MS prevalence is low in East and South Asia compared to West Asia and the Middle East [9]. Based on a study done by Kurtzke et al. [88], in 1995, the prevalence of MS was moderate (5–29/100,000) in these regions similar to Russia, Ukraine, the South Africa, the South America.

MS prevalence in East Asian countries was low and estimated to be 0.8–2 per 100,000 population [89]. MS prevalence was high in West Asia compared to East and South Asia. MS is described to be of low prevalence among the Chinese people in comparison with other Asian countries during the last decade [33].

An increase in prevalence has also been observed in other Asian countries, such as Kuwait and Jordan [90–92] but the prevalence was much lower than in European countries [93].

In the past few decades, the global prevalence and incidence patterns of MS have changed dramatically. The recent global classification of MS also indicated worldwide increase in the prevalence of MS [7].

Female to male sex ratio is high among patients in Hong Kong, Malaysia and Thailand similar to that in the

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Pourmand/Sahraian

United States [42, 50, 52, 94] when compared to the estimation of female to male ratio among countries in Europe [95].

The data point out that MS is higher in females than in males. Generally, increasing MS incidence among women in many countries can lead to higher female to male sex ratios of MS in region and this similar tendency was observed in Canada [96].

The prevalence and incidence of MS vary in different parts of Asia; however, the limited nationwide epidemiological data, weak responsiveness and limited diagnostic facilities have significantly influenced the reporting of MS in many countries in the region. Some Asian countries, including Iran and Japan, have reported an increased prevalence of MS in the last decade [17, 66].

Several studies have shown that MS is not well recognized in the Asian region. It is indicative of lack of knowledge about MS in comparison to Western countries. The national epidemiological survey information is not available, and MS prevalence may be under-estimated [8].

Analysis of MS baseline characteristic in present studies among Asian countries indicates an important task of the MS regional or national registry system for an accurate and uniform estimation of MS. The importance of these data establishment is helpful for monitoring the term and trend of MS and its characteristics in whole country populations [97].

The availability of neurologists and diagnostic tools has a strong link to MS diagnosis; consequently, the prevalence of MS may increase in this region while accessibility to these services becomes more extensive [95]. According to the Atlas of MS in 2013, the median number of neurologists per 100,000 populations is only 0.03 for low-income-group countries compared with 3.6 for high-income-group countries. The number of MRI machines that existed in 2008 has doubled in 2013 in low-income, lower-middle-income and upper-middle income countries, while still there are many differences between the number of MRI instruments in different countries.

While the number of MRI machines per 100,000 populations worldwide is 0.46 per 100,000 in 2013, the number of MRI machines in high-income, upper-middle-income countries is 1.6 and 0.4 per 100,000 populations and in lower-middle-income and low-income-countries is 0.01 per 100,000 populations.

Notably, most countries selected for our studies were belonged to the category of low income and lower middle income [4].

Disclosure Statement

Authors declare no conflict of interest.

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