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Registry of inflammatory demyelinating diseases of the central nervous system in the Asia-Pacific region

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Abstract

Background and Objective: Comparable data are sparse for inflammatory demyelinating diseases of the central nervous system (CNS) in the Asia-Pacific region, and we aimed to establish a registry of patients with such diseases in the region. *Methods*: A network of neurologists in the Asia-Pacific Region was established to register patients with the targeted diseases. A standardized register form and relevant instructions in English, translated into the local language when needed, were prepared before the study start and used for data collection. *Results*: Eight study centres from different countries/areas participated in the study. In total, 857 patients with a validated diagnosis of different inflammatory demyelinating diseases of the CNS were registered, 591 females and 266 males with a female-to-male ratio 2.2. The mean age at onset for all patients was 35.9 (SD: 12.9) years, significantly younger (p = 0.010) for females (35.1 years, SD: 12.6 years) than for males (37.6 years, SD: 13.4 years).
Conclusion: Patients with different inflammatory demyelinating diseases of the CNS were in the first time registered in a multi-centre study from eight countries/areas in the Asia-Pacific region. A platform and basis has been established for further study in the field.

INTRODUCTION

Inflammatory demyelinating diseases comprise a heterogeneous group of disorders that affect the nervous system, central or peripheral.[1] Demyelination is the pathological process in which myelin sheaths are destroyed or lost from around axons.[2] Inflammatory demyelinating diseases of the central nervous system (CNS) include multiple sclerosis (MS), neuromyelitis optica (NMO), clinically isolated syndrome (CIS), acute demyelinating encephalomyelitis, and others. It has been observed that there are differences in inflammatory demyelinating diseases between different populations, regarding prevalence, clinical presentations, and even pathogenesis. In order to disclose if such differences exist in the Asia-Pacific region, comparable data are needed from different populations in the region.

It was suggested in 2005 at the Third MS Forum Pan-Asian Conference "MS Across Continents: Advances in the Knowledge of MS in Asia", in Sydney, Australia, that a registry of different inflammatory demyelinating diseases of the CNS should be conducted in the Asia-Pacific region, so that comparable data and results could be obtained by using the same methodology. Then, a group of experts was set up for preparation of the registry and an agreement was reached in 2006 by a group of researchers from MS Forum Pan-Asian Committee to conduct the register.

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We intended to register patients with different inflammatory demyelinating diseases of the CNS from the participating centres in the Asia-Pacific region, identify the full spectrum of presentations for demyelinating diseases, compare potential differences between patients from Australia and patients from the other centres in Asia, and provide a platform and basis for further studies in the field.

METHODS

This is a multi-center survey and a hospital-based investigation. All patients attending at local hospitals with a validated diagnosis of demyelinating disease by neurologists from the participating centres during the study period would be included in the registry. All participating hospitals are general hospitals serving to the local general population.

We had reviewed and discussed a number of register forms used previously in different surveys in the other continents or countries, and finally prepared a register form and relevant instructions for our registry before the study starting. We discussed in detail the contents together with leaders from all participating centres and a steering group of experts had been established responsible for any questions and relevant issues during the study period. The standardized registry form and relevant instructions were made in English and would be translated into local languages by each centre when needed. The study period was set for one-year investigation ended on 31 December 2008.

Our registry included patients with different demyelinating diseases of the CNS, either relatively frequent diseases, including MS, NMO, or rare diseases such as acute disseminated encephalomyelitis (ADEM) were included. However, demyelinating diseases of the peripheral nervous system, such as Guillain-Barré syndrome, were not included.

We collected information of the patients including demographic backgrounds, such as name, gender, date of birth, address; clinical presentations, including initial symptoms; and results of laboratory examinations, from MRI and various viral antibody tests. Ethical approval for the study was obtained by each participant institution from local ethical committee.

All completed register forms were sent to the centre in Shanghai for central data-treatment. Data from all register forms were entered into two datasets with the same structure by different people separately, and then the two datasets were cross-checked for discrepancies to avoid typing mistakes. Comparisons of results were made between patients from Australia and the patients from the other centres in Asia.

Statistical Package for the Social Sciences (SPSS) for Windows was used for statistical analysis. Statistical significance for differences between proportions was assessed using $\chi 2$ and Fisher's exact tests, when appropriate. Student's t-test or an analysis of variance (ANOVA) test was used for continuous data and comparison of the duration between categories.

RESULTS

There were 857 patients in our registry, 266 males and 591 females. They were from 8 countries/areas; 378 patients from Australia, 213 from mainland China, 104 from India, and the other 162 patients from the other 5 countries/regions (Table 1). The female-to-male ratio of all registered patients was 2.2.

The mean age at onset was 35.9 (SD: 12.9) years for all 857 patients, significantly younger ($p = 0.010$) for females (35.1 years, SD: 12.6 years) than for males (37.6 years, SD: 13.4 years). The age at onset for most of the patients, more than three fourths, was within the age group of 20-49 years, and the distribution was similar for males and females in general (Table 2); while most cases (73%) were in the age group of 30-59 years for the current age at the end of 2008 (Figure 1), almost 10 years older than the age at onset. The mean current age was 45.9 (SD: 13.9) years for all patients, and no significant difference ($p = 0.202$) was found between males (46.8 years, SD: 13.4) and females (45.5 years, SD: 14.1).

Numbers of different diagnoses of demyelinating disease in our registry are presented in Table 3. There were 663 (77.4%) patients with MS, 79 (9.2%) patients with CIS, 47 (5.5%) patients with NMO, 37 (4.3%) patients with ADEM, and 31 (3.6%) patients with the other various diagnoses, like recurrent transverse myelitis, possible MS, and others.

There were 378 patients from Australia and 479 patients from the other areas in Asia, and comparisons were made for a number of characteristics between the two groups of patients. The female-to-male ratio was found to be significantly higher ($p = 0.001$) for patients from Australia (3.1) than that (1.75) for patients from Asia.

The mean age at onset was similar ($p = 0.907$)

Table 1: Registered patients with demyelinating diseases of CNS in Asia-Pacific Region

Country/region	Females	Males	Total (%)	F/M ratio
Australia	286	92	378 (44)	3.1
Mainland China	113	100	213 (25)	1.1
India	69	35	104 (12)	2.0
Korea	43	21	64 (7)	2.0
Malaysia	53	9	62 (7)	5.9
Vietnam	15	4	19 (2)	3.8
Taiwan China	10	1	11 (1)	10.0
Indonesia	2	4	6 (1)	0.5
Total	**591**	**266**	**857 (100)**	**2.2**

for patients from Australia (35.9 years, SD: 12.3 years) and patients from Asia (35.8 years, SD: 13.4 years); while the mean current age was significantly older ($p < 0.001$) for patients from Australia (49.3 years, SD: 13.0 years) than patients from Asia (43.2 years, SD: 14.0 years). The mean disease duration was significantly longer ($p < 0.001$) for patients from Australia (13.4 years, SD: 9.9 years) than patients from Asia (7.4 years, SD: 7.0 years).

Distributions of clinically involved sites in the CNS at the initial attack and over the entire course of the disease for all patients by gender were presented in Table 4. As indicated, the site in the CNS was determined according to the clinical symptoms or signs. For all patients, 30% had symptoms or signs at onset indicating the lesions in the cerebrum, 35% in the spinal cord, and 24% in the optic nerves. The distribution of the sites was similar for males and females. Because there could be more than one site involved for one patient, the sum would be more than 100%.

For all patients, the most frequent site of clinical lesions in the CNS over the entire course was the spinal cord (46%), followed by the cerebrum (38%), and the optic nerves (32%). For the differences between males and females, there were more female patients with the sites of the spinal cord and the cerebrum than male patients, while fewer female patients with the sites of the brainstem and the cerebellum than male patients.

Comparisons of the clinically involved sites in the CNS at the initial attack and over the entire

Table 2: Age at onset for all patients by gender

Age group (years)	Females		Males		Total	
	No.	%	No.	%	No.	%
0-9	8	1.4	4	1.5	12	1.4
10-19	52	8.8	21	7.9	73	8.5
20-29	163	27.6	54	20.3	217	25.3
30-39	173	29.3	67	25.2	240	28.0
40-49	130	22.0	69	25.9	199	23.2
50-59	44	7.4	41	15.4	85	9.9
60-69	12	2.0	9	3.4	21	2.5
70+	9	1.5	1	0.4	10	1.2
Total	**591**	**100**	**266**	**100**	**857**	**100**

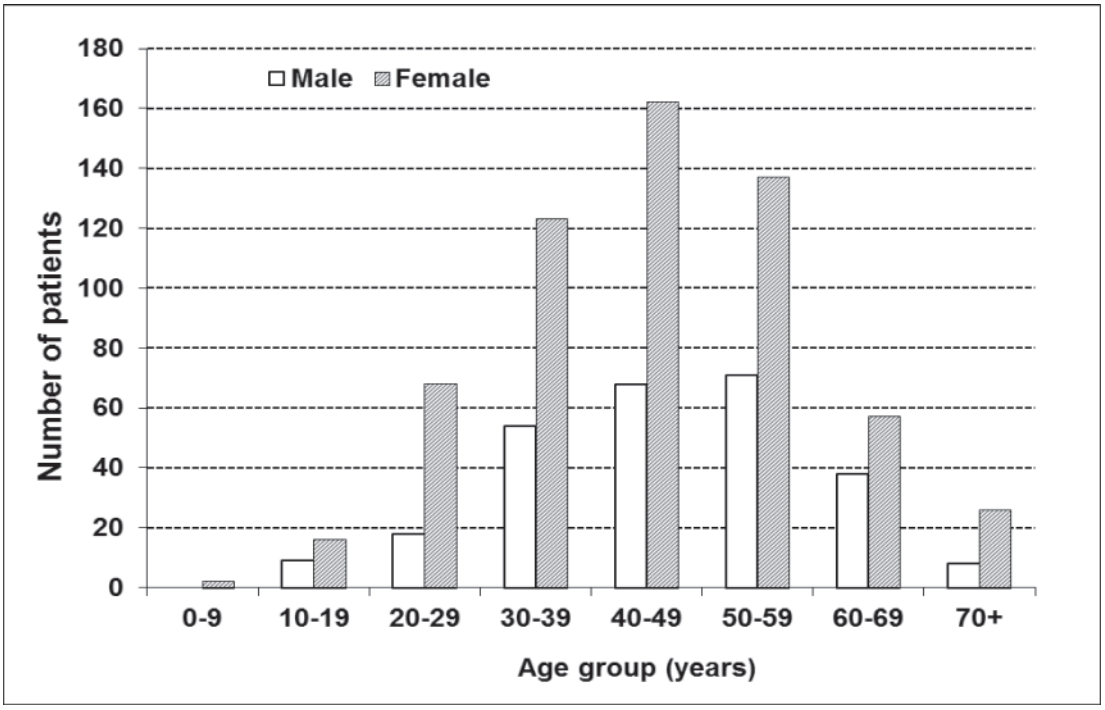

Figure 1: Distribution of current age for all patients

course of the disease between patients from Australia and patients from Asia were presented in Table 5 and statistically significant differences of the sites were found for all sites. Patients from Australia had significantly more lesions in the cerebrum, while significantly fewer lesions in the other parts of the CNS, than patients from Asia; either at the initial attack or over the entire course.

DISCUSSION

It has been observed that distribution of inflammatory demyelinating diseases may be different between various populations. For example, prevalence rates of MS can vary from more than 200 cases per 100,000 inhabitants in southeast Scotland[3] and northern Ireland[4] to less than 1 in 100,000 in a number of Asian countries.[5,6] Characteristics of clinical presentations in patients with MS can be also heterogeneous from different populations.[7-11] Researchers have been trying to disclose the underline cause of the differences for many decades and no definite conclusion can be reached up to now. The present study intended to make some contributions in this regard.

Differences of study results can be due to the differences of study methods, particularly if the

Table 3: Registered diagnoses of demyelinating diseases of CNS in Asia-Pacific Region

Diagnosis	Females	Males	Total (%)	F/M ratio
Multiple sclerosis	467	196	663 (77.4)	2.4
Clinically isolated syndrome	47	32	79 (9.2)	1.5
Neuromyelitis optica	36	11	47 (5.5)	3.3
Acute disseminated encephalomyelitis	23	14	37 (4.3)	1.6
Others	18	13	31 (3.6)	1.4
Total	**591**	**266**	**857 (100)**	**2.2**

Table 4: Clinically involved sites in the CNS at the initial attack and over the entire course of all patients by gender

Site in CNS	At the initial attack						Over the entire course					
	Male (n=266)		Female (n=591)		Total (n=857)		Male (n=266)		Female (n=591)		Total (n=875)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Cerebrum	82	30.8	173	29.2	255	29.8	104	39.1	300	50.8	404	46.2
Spinal cord	94	35.3	204	34.5	298	34.8	90	33.8	246	41.6	336	38.4
Optic nerve	53	19.9	152	25.7	204	23.8	82	30.8	194	32.8	276	31.5
Brainstem	38	14.2	62	10.5	100	11.7	70	26.3	101	17.1	171	19.5
Cerebellum	20	7.5	31	5.2	51	5.9	43	16.2	67	11.3	110	12.6

studies are conducted in different countries or populations. For the current study, we aimed to keep the same methodology of the investigation for all participating centres, in order to warrant the comparability of study results. Therefore, the different distributions of the age at onset, lesion sites in the CNS, female-to-male ratio of patients might really exist between populations. The differences between the patients from Australia and the patients from the other centres in Asia may imply different genetic backgrounds or mechanisms for inflammatory demyelinating disease between the populations, which need to be further investigated in the future.

In our registry, patients with MS account for more than three fourths of all, which may indicate the importance of MS in the demyelinating diseases of the CNS, although Asia is usually recognized as a region with relatively low prevalence of MS.

The mean current age was almost 10 years older than the mean age at onset, which might indicate the disease duration in general. The mean age at onset was similar for patients from Australia and patients from Asia, while the significantly older current age for patients from Australia could be explained by their significantly longer disease duration than patients from Asia.

In our study, all diagnoses were made by neurologists. Although we did not restrict which diagnostic criteria should be used for a specific disease, the most recent revised diagnostic criteria were generally adopted. For example, the McDonald diagnostic criteria of MS[12,13] were used for most of the MS patients (89% of those with the information of diagnostic criteria used), and the Poser Diagnostic Criteria for MS[14] were followed only for a small part of the MS patients. For NMO, the revised diagnostic criteria by Wingerchuk *et al*[15] were used for most of the NMO patients.

The limitation of the present study is a hospital-based and cross-sectional investigation, which may imply selection bias. For example,

Table 5: Comparison of clinically involved sites in the CNS at the initial attack and over the entire course between patients from Australia and patients from Asia

	At the initial attack					Over the entire course				
	Patients from Australia (n=378)		Patients from Asia (n=479)		p value	Patients from Australia (n=378)		Patients from Asia (n=479)		p value
Site in CNS	No.	%	No.	%		No.	%	No.	%	
Spinal cord	167	44.2	88	18.4	<0.001	122	32.2	282	58.9	<0.001
Cerebrum	98	25.9	200	41.8	<0.001	201	53.2	135	28.2	<0.001
Optic nerve	74	19.6	131	27.3	0.008	66	17.5	210	43.8	<0.001
Brainstem	30	7.9	70	14.6	0.003	34	9.0	110	23.0	<0.001
Cerebellum	13	3.4	38	7.9	0.006	34	9.0	137	28.6	<0.001

the unusual high female-to-male ratio (10.0) of the patients from Taiwan could be the result of a selection bias or due to chance. In addition, the large proportion of patients with MS in our registry may in part result from the fact that most researchers in our study group are very interested in the field of MS research. However, it is the first multi-centre study on the topic with researchers from a number of countries in the Asia-Pacific region, and it could be the first step for further cooperation in the field with the same study method to get comparable results. In particular, population-based and longitudinal follow-up investigations are very much needed and would produce more reliable data and a more complete picture for the targeted diseases in the region.

In the future, we would like to make population-based investigation, so that comparison of prevalence of the target diseases could be possible.

In conclusion, patients with different inflammatory demyelinating diseases of the CNS were in the first time registered in a multi-centre study from eight countries/areas in the Asia-Pacific region. Characteristics of the patients were described and differences were analyzed between the patients from Australia and the patients from the other centres in Asia. MS was found to be the most commonly encountered demyelinating disease in this registry, even in Asian patients. A platform and basis has been established for further study in the field.

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DISCLOSURE

Conflict of interest: None.

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