

Multiple sclerosis: a retrospective review of 30 cases from Singapore

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Abstract

A retrospective review of 30 patients with definite, probable and possible multiple sclerosis (MS) seen at a tertiary hospital over a 5-year period was performed. There was high female-male sex ratio of 9:1 with an average age of onset of 36.3 years. The commonest pattern of disease was relapsing-remitting MS (73%) with an average relapse rate of 1.21 per year; followed by primary-progressive MS (23%) and progressive-relapsing MS (3%). The commonest presenting problem was myelopathy (43%). Over an average follow-up period of 7 years, 80% developed spinal cord involvement at some stage; 43% optic nerve, 32% brainstem/cranial nerve, 23% cerebellar and 21% cortex/subcortical involvement. Brainstem, visual and somatosensory evoked responses detected subclinical lesions in 32% of cases. Magnetic resonance imaging of central nervous system showed demyelinating lesions in 93% of which two-thirds were asymptomatic. The cerebrospinal fluid oligoclonal band was detected in 1 of 9 patients tested. Urinary tract infections (20%) and depression (13%) were the commonest complications. After an average disease-duration of 7 years, 1 patient has died and only 7 are functionally independent. MS in Singapore is characterised by predominant optico-spinal involvement with poor functional outcome.

Key words: Multiple Sclerosis, Singapore

INTRODUCTION

Multiple Sclerosis (MS) is not a common disease in Singapore and other parts of Asia. Nevertheless, it is a disease of considerable morbidity; and perhaps more importantly affects young people at their prime. As the disease is common in the West the epidemiological and clinical data of MS is well documented. Prevalence in the UK is estimated to be 50-80/100000, in some parts like the Shetland and Orkney Islands up to 300/100000.

Unfortunately there are few population-based prevalence studies in Asia. In 1968 Kutzke¹ estimated the prevalence of MS in South Korea to be 2/100000. The Japanese found the prevalence of MS to vary from 0.7 to 3.8 / 100000 with little if any variation with latitude.² Zhao et al³ estimated that MS accounts for 1.1-1.4% of total neurological admissions in various hospitals in China, compared to 6-10% in the West. In Hong Kong the prevalence was reported to be 0.88/100000.⁴

In Southeast Asia there are also no formal epidemiological data on MS. Tan et al had found the prevalence of MS in Malaysia to about 2/100000.⁵ Vejjajiva reported his estimate of Thailand's prevalence of MS to be also about 2/100000.⁶ The earliest reported case of MS in

Singapore was in 1970 by Gwee and Toh.⁷ Subsequently an ethnic Chinese was confirmed by autopsy to have MS in 1985.⁸

Perhaps more interesting than the difference in prevalence of MS between the East and the West is the difference in clinical picture. This was alluded to as early as 1958 by Okinaka et al when they described the clinical characteristics of MS in Japan.⁹ Kuroiwa et al¹⁰ reported a large study comparing 488 Oriental cases of MS from 6 Asian countries with 177 Hungarian cases. Comparison of the clinical picture revealed similar natural history such as sex ratio, age of onset and clinical course. However there was a greater incidence of visual loss and visual disability in the Oriental cases. In addition recurrent transverse myelopathy was more common. Zhao et al's study of 256 cases of MS from different parts of China also showed similar results.³ The experience reported from South India by Gouri-Devi et al¹¹ was not different. The basis of this difference may be genetic. Kelly et al found that the haplotype DRB1*1501, DQA1*0102, DQB1*0602 significantly associated with Caucasian population with MS were not found to predispose to MS in Shanghai Chinese.¹²

Kira et al believe that the Oriental form of MS may indeed be a different disease

altogether.¹³ They studied 34 patients with disseminated central nervous system involvement (Western-type MS) and compared them with 23 patients with selective optic nerve and spinal cord involvement ('Asian-type MS'). The Western-type MS patients had more brain lesions on MRI (47% Vs 17%) and were associated with the DR-2 associated DRB1*1501 and DRB5*0101 alleles (41.2% vs 0%). To understand characteristics of patients with MS in Singapore, we conduct a retrospective review of all patients diagnosed to have this disease in a single tertiary hospital, over a 5 year period.

MATERIALS AND METHODS

Tan Tock Hospital is an urban general hospital with a tertiary Neurology department in Singapore. Medical records of all patients with a possible diagnosis of MS were retrieved. The clinical features and investigatory findings were reviewed. Poser's criteria¹⁴ was used as the basis of diagnosis, and Lublin's classification based on standardization recommended in the international survey was used for defining the clinical course.¹⁵

RESULTS

Clinical characteristics

A total of 30 cases were studied. 23 (77%) were

Chinese, 2 (7%) were Malay, 1 (3%) was Indian, 3 (10%) were Caucasians and 1 (3%) was of mixed-descent. There were 27 females and only 3 males. The female-male sex ratio was 9:1. The mean age at the onset of disease was 36.3 with a range of 17-56 years. A family history of MS was present in only 1 patient and only the three Caucasians had spent a significant period of time in the temperate region.

Using Poser's criteria¹⁴ the majority (73.3%) can be classified as Clinically Definite MS, 16.6% as Clinically Probable MS and the rest (3 cases) had enough evidence to support a diagnosis of Possible MS. There were no cases of Laboratory Supported MS because of the low yield of cerebrospinal fluid oligoclonal bands.

Most of the patients (22) had a Relapsing-Remitting form of MS (RRMS); 7 had Chronic Progressive MS and 1 patient had Progressive-Remitting MS (Figure 1). For patients with RRMS the average number of relapses was 5.95 and the average relapse-rate was 1.21 per year.

The most common site of involvement at first presentation was spinal cord (43%) followed by brainstem and cranial nerves (20%), optic nerve (16.6%), cortex and subcortical structures (16.6%) and cerebellum (3.3%). Subsequently 80% of patients had involvement of the spinal cord at some point in their illness, 43% optic nerve involvement, 32% brainstem-dysfunction/cranial neuropathies, 23% cerebellar affliction

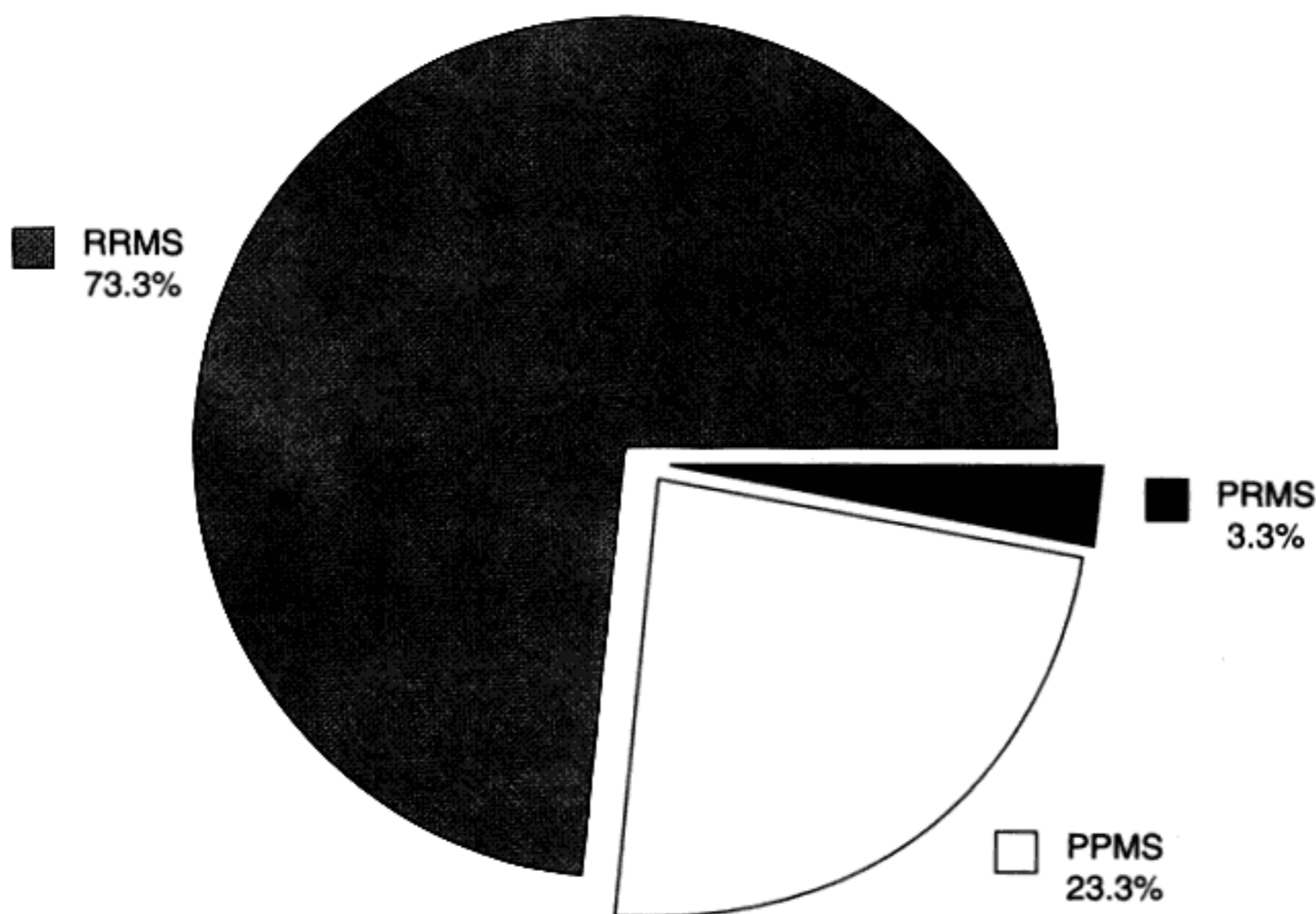


FIG. 1: Clinical subtypes of multiple sclerosis
RRMS: Relapsing-remitting multiple sclerosis, PRMS: Progressive-remitting multiple sclerosis,
PPMS: Primary-progressive multiple sclerosis

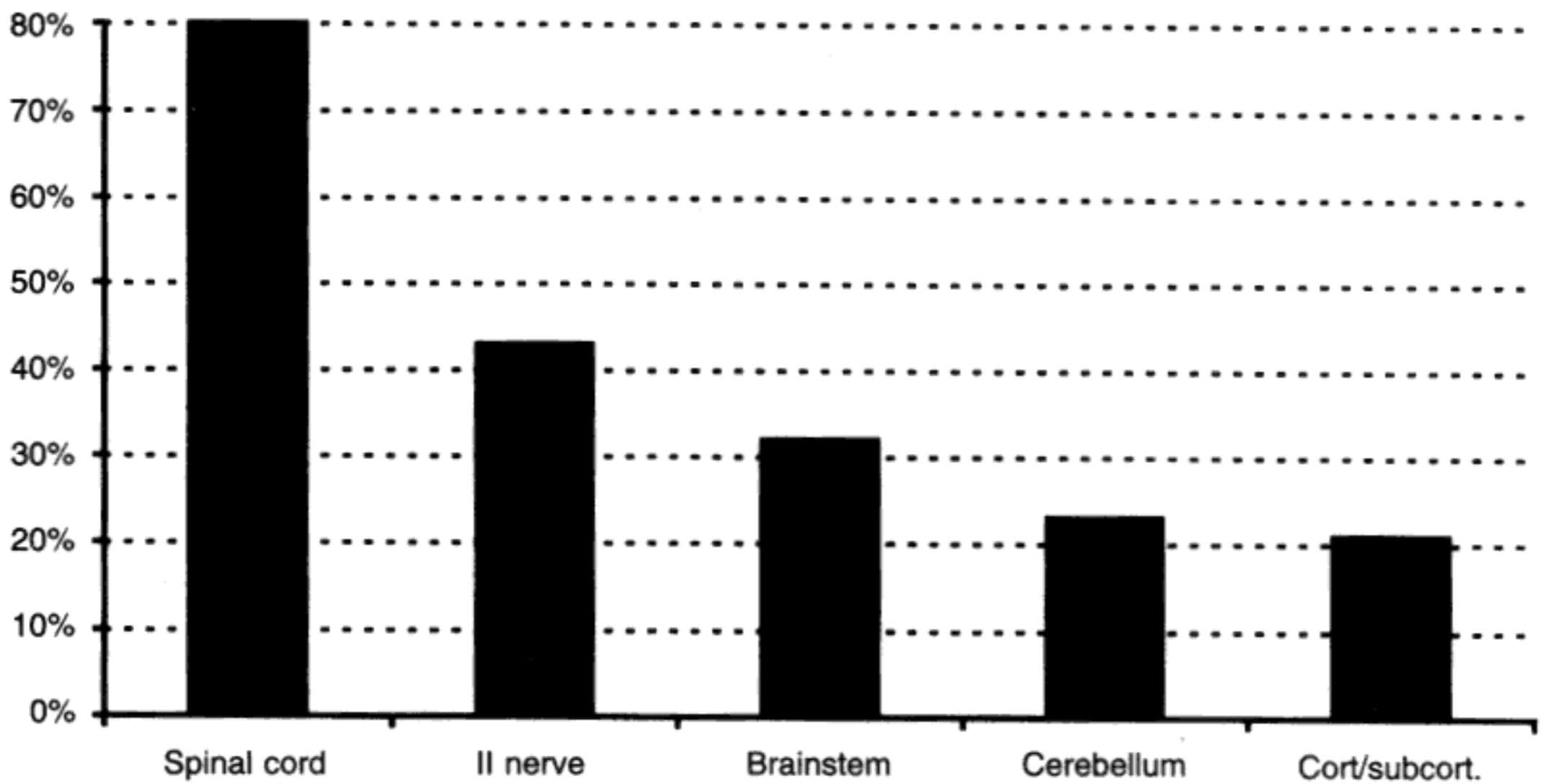


FIG. 2: Sites of involvement
Cort: cortical
Subcort: subcortical

and 21% cortical/subcortical disease (Figure 2).

Investigations

Brainstem, visual and somatosensory evoked potentials were abnormal in 86% of patients; 32% in clinically asymptomatic areas. MRI showed abnormalities consistent with MS in 25 of the 27 cases (93%) for which MRI was done. In 16 cases (59%), there was evidence of disease activities in clinically uninvolved parts of central nervous system. There was a remarkably low positivity rate in test for detecting CSF oligoclonal bands, with only one positive out of 9 patients tested. Zonal electrophoresis was used to detect the oligoclonal bands for majority of patients in this study. During the past one-and-half years agarose isoelectric focusing followed by immunoperoxidase staining was used in the hospital. The latter technique is recognized to have a higher sensitivity of 84%.¹⁶ It was also the technique used in the only patient who was tested positive. Six patients however had raised CSF IgG on immune electrophoresis.

Treatment

Almost all patients with RRMS received either intramuscular ACTH or intravenous methylprednisolone for acute relapses, the latter being favored in the last few years. Interval treatment was given for only three patients; Azathioprine for two and beta-interferon for one. The most commonly used symptomatic treatment was baclofen for spasticity

carbamazepine for paroxysmal symptoms and antidepressants. However the cornerstone of treatment of the majority of patients was intensive rehabilitation. Twelve patients received in-hospital rehabilitation at a specialized rehabilitation centre, the majority for periods exceeding four weeks. The clinical outcome was favorable in these patients, many regaining their previous function to a significant degree.

Complications

The most common complications were bladder dysfunction (usually a combination of detrussor muscle instability and sphincter dysynergia with retention of urine in 30% of patients), urinary tract infections (20%) and depression (13%).

Prognosis

Information on the present status was available for 22 patients with an average disease-duration of 8 years. One patient has passed away from urinary tract infection and septicaemia. Of the remaining 21 patients, only 32% are functionally normal, 48% need aids and or assistance to ambulate, 10% are wheel-chair bound and 10% are bed-ridden (Figure 3).

DISCUSSION

Till to-date, there is no population surveys to estimate the prevalence of MS in Singapore. Based on personal communication with the neurologists working in the various public and

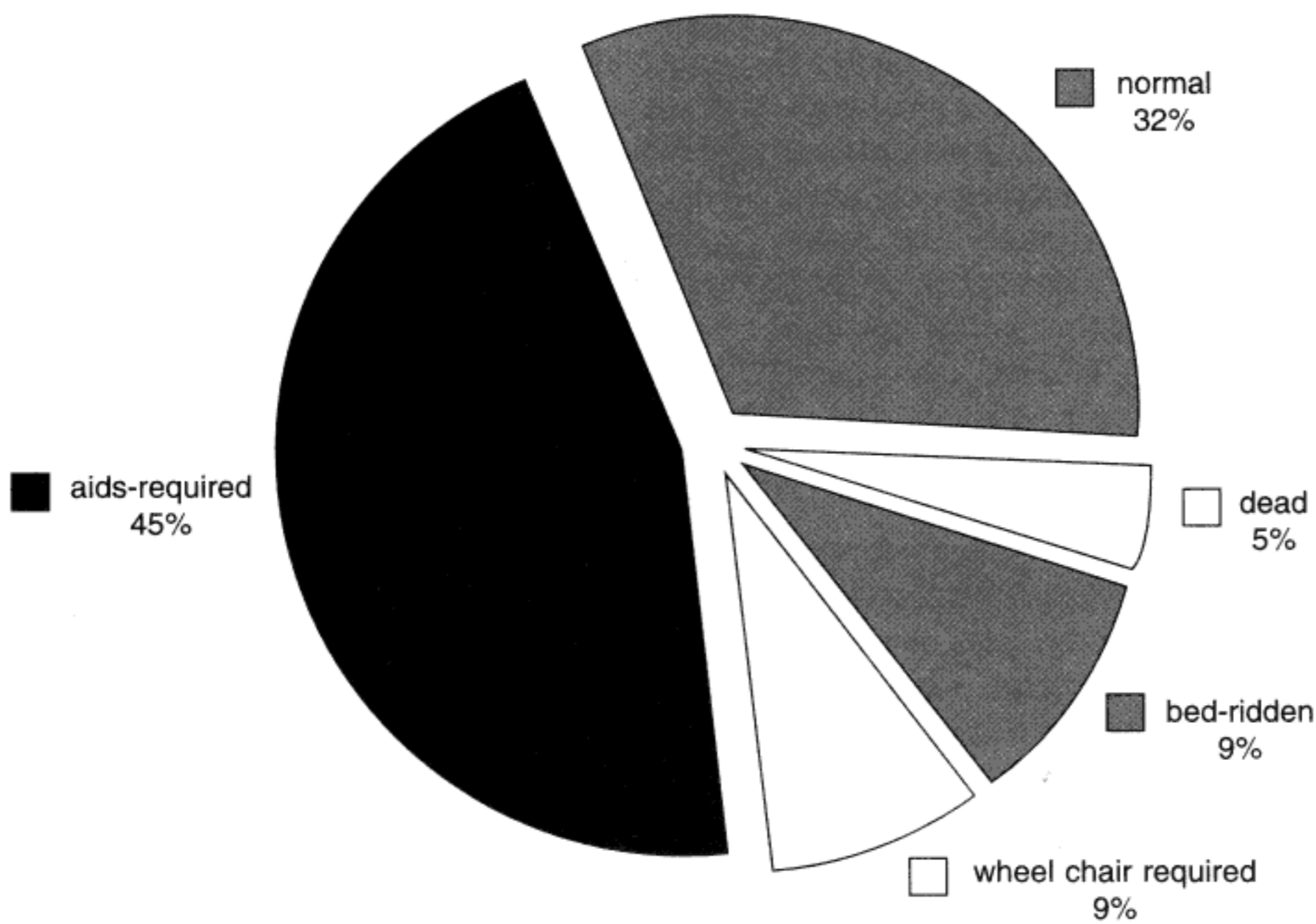


FIG. 3: Present functional status

private hospitals, there were about 80 cases of MS in the Republic with 3.5 million population with the prevalence of about 2/100000 population. The prevalence of MS in Singapore is thus likely to fall in the low frequency area which is less than 5/100,000 population. MS has been said to occur more commonly in females. In our study, the female-male sex ratio of 9:1 appears disproportionately high. There has been previous reports from other parts of Asia also showing high female-male ratio. Hung reported a female-male ratio of 4.5:1 for his patients from Taiwan¹⁷ and Tan reported a ratio of 6.6:1 for Malaysia.¹⁸ The rare occurrence of similar family history has also been noted by other authors in Asia.^{11,18,19} The average age of onset and the relapse-rate are similar to experiences elsewhere.

As expected from the data from other studies in the East, our patients, the majority of whom are Chinese, have predominant involvement of the spinal cord (80%) and optic nerve (43%). However, myelopathy as an initial presentation is not only common in the so-called Asian form of MS but is also seen commonly in the West. Various studies based on patients in the West have reported spinal cord involvement at presentation of 42-76%,²⁰ which is close to our figure of 43%. However, recurrent acute transverse myelitis has been noted to be more common among the Asian patients.^{10,18,19} Classical Devic's Disease²¹ where the optic

neuropathy and myelopathy occur simultaneously or within a short period of each other (6 weeks) was not seen in any of our patients. This was also observed by Tan in his review of 30 patients with MS in Malaysia.²²

Although the clinical manifestations are mainly optico-spinal, evoked potentials and MRI show typical disease in other parts of the central nervous system. Tan et al studying a similar group of patients in neighbouring Malaysia found that the positivity for visual, brainstem and somatosensory evoked potentials in asymptomatic MS patients was 32%, 27% and 31% respectively.⁵ This is comparable to our overall asymptomatic-site positivity of 32%. The low yield of oligoclonal bands in our study could reflect another peculiar characteristic or may be due to technical reasons already alluded to. This needs further study.

The frequent involvement of the spinal cord and optic nerve in our patients result in considerable morbidity even at the early stages of the disease. Only 32% of our patients were able to walk and function without aids or assistance after average disease duration of seven years. In the Malaysian series by Tan²², 16 out of 30 patients were wheel chair or bed-ridden over an average follow-up of 7.6 years.

The recurrent myelopathy not unexpectedly causes urological complications frequently. One third of patients needed permanent indwelling catheter or clean intermittent catheterisation

(CIC) for prolonged periods. With impaired vision and reduced hand function CIC is not an easy task, forcing the clinicians to the use of indwelling catheters. This probably explains the high incidence of urinary tract infections. The impaired mobility and the urological difficulties are important predisposing factors to severe reactive depression. The relatively low incidence of depression in this study may be due to under-recognition or under-reporting.

In conclusion, the prevalence of MS in Singapore probably falls in the low frequency area in the world distribution of MS. It seems to occur much more commonly in females. There is usually no family history. MRI and evoked potentials are useful tools in demonstrating asymptomatic lesions. Relapsing-remitting form of MS is the most common type. It often presents initially as myelopathy and subsequently affects the spinal cord and optic nerves most. This results in considerable morbidity relatively early in the course of the disease. Morbidity is related to poor mobility, bladder dysfunction, recurrent urosepsis and depression. Prolonged specialized in-hospital rehabilitation may have a favorable influence on functional outcome.

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