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Disability profile and the factors affecting functional outcome in Malaysian motor neurone disease population

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Abstract

Background & Objective: The accurate knowledge on the individual spectrum of disabilities and the course of the disease is important for timely medical and rehabilitation management of patients with motor neurone disease in terms of clinical prediction and clinical decision making. The objectives of this study are to identify the disability profile, functional outcome, fatigue and the correlation between fatigue and domains of functional decline in Malaysian motor neurone disease population. *Methods:* Thirty motor neurone disease patients undergoing rehabilitation programme in University Malaya Medical Centre completed a questionnaire to report the symptoms and problems affecting their daily life, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale depicting their function level and Fatigue Severity Scale to determine their fatigability status. Revised Amyotrophic Lateral Sclerosis Functional Rating Scale was repeated after 6 months to measure the functional decline. *Results:* The mean age was 60 years with men more affected than women (3:1). The main symptoms reported were weakness (93%) and weight loss (83%). Majority of them had difficulties in performing domestic chores (77%) and engaging in social life (73%). No statistically significant factors were found to be associated with functional decline among the Malaysian motor neurone disease patients. Decline in respiratory function was shown to be statistically significant among the fatigued motor neurone disease patients (p=0.032).
Conclusion: This study is a stepping stone to future researches pertaining to rehabilitation in motor neuron disease which helps to tackle this population's multifaceted disabilities ensuring a meaningful quality of life. A paradigm shift is needed to provide pulmonary rehabilitation to these population especially the ones with fatigue to dampen the progressive deterioration of respiratory function enhancing their quality of life.

Keywords: Disability profile; motor neurone disease; functional outcome; rehabilitation; fatigability

INTRODUCTION

Motor neurone disease (MND) is a neuro-degenerative condition that affects primarily the motor neurons in the brain and spinal cord. The incidence of MND is predominant among the Caucasian population ranging from 1.5 to 3.3 cases per 100,000 per year whereas among Asians, the incidence and mortality rates of MND are regarded to be lower although there have been relatively few studies.[1]

MND is a progressive fatal disease with wide variety of disabilities and functional impairments. Most people die within 2–3 years of developing symptoms, but 25% are alive at 5 years and 5–10% at 10 years.[2]

A set of relevant International Classification of Functioning, Disability and Health category (ICF) has yet to be identified in MND and would be particularly useful in both clinical and research settings given the rare incidence of MND and its diverse nature of symptoms. The heterogenicity of MND poses a challenge to the multidisciplinary neuro-palliative rehabilitation management.[3] The timing of appropriate interventions be it medical or rehabilitative is important and requires accurate knowledge of the individual course of disease however there is a lack of studies on common

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disabilities and prognostic factors of functional decline in MND patients.

Fatigue in MND is one of most common reported symptoms but it is understudied and overlooked by clinicians.[4] It is essential to understand and be aware of how fatigability affects the functional outcome in MND patients in order to pave way for an effective rehabilitation management among these patients.

The objectives of this study are to identify the disability profile, functional outcome, fatigue and the correlation between fatigue and domains of functional decline in the Malaysian MND population.

METHODS

Participants and setting

MND patients undergoing neuro-palliative and rehabilitation programme in University Malaya Medical Centre (UMMC) were recruited to participate in this study. UMMC is one of the largest medical health care centers in Kuala Lumpur, the capital of Malaysia. It houses major tertiary neurology, rehabilitation and palliative centers in Malaysia and its referral base, although primarily from Kuala Lumpur and its surrounding area, also includes other parts of the country.

MND patients are first attended by physicians at the neurology department for a thorough clinical and laboratory assessment to confirm the diagnosis of MND. The patients are then referred to the rehabilitation unit and/or palliative unit based on the patients' needs. The MND patients that are referred to the rehabilitation department are seen in an outpatient clinical setting for a proper assessment and to be referred to physiotherapy, occupational therapy and/or speech therapy if deemed necessary for regular therapies as outpatient. Long term multidisciplinary care is given to these patients through a regular combined outpatient clinic conducted by the neurologist, rehabilitation physician and palliative physician.

The selective criteria for this study included patients with confirmed diagnosis of MND by a neurologist, ability to participate in rehabilitation program which includes physiotherapy/ occupational therapy and/or speech therapy sessions and age of 18 years and above. Exclusion criteria included those with severe cognitive impairment, substantial medical, neurological or psychiatric disorder, bed bound and those on assisted breathing. This study was approved by the UMM Medical Ethics Committee.

30 patients fulfilling the inclusion and exclusion criteria were consecutively enrolled between January 2017 till April 2018, to participate in this prospective cross-sectional study. Informed consent was obtained from every patient recruited in this study.

Demographic and clinical characteristics

A pre-designed structured face to face interview was carried out to obtain demographic details and clinical characteristics of participants. Care giver or decision maker was involved if there were communication barrier to the patient due to speech impairment or communication difficulties following MND. In certain cases, further sociodemographic and clinical details were obtained from the patient's medical record in UMMC's database.

Disability profile

Each participant completed a bilingual (English and Malay) open-ended self-report questionnaire to identify their disability profile. This questionnaire was based on the one used to assess the disability profile in Australian MND population.[5] Participants were asked, 'What are the main problems you face in your everyday life? If possible, can you list and prioritize up to 10 issues that you feel are the most pressing problems you face in everyday life?'. No additional questions, prompts, suggestions of expected specific problems or checklists were given to gain firsthand information about problems due to MND. From the participant responses, listed problems were categorized thematically based on the ICF domains namely impairments in body structure or function, activity limitations and participation restrictions. Issues unrelated to disability have not been included in this study as they are not the primary focus.

Functional outcome

Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) was used to measure the functional outcome at initial contact and after 6 months either face to face or via phone. The ALSFRS-R measures global function and activities of daily living in 4 major domains: bulbar (speech, salivation, swallowing), fine motor (handwriting, cutting food and handling utensils, dressing and hygiene), gross motor (turning in bed and adjusting bed clothes, walking, climbing stairs), respiration (dyspnea, orthopnea

and respiratory insufficiency). This is a 48-point measure of disability in MND with excellent validity and reliability[6], and can be administered over the phone.[7] It is determined by scoring 0–4 for each of the 12 domains and higher scores indicate better outcomes.

Fatigability

Fatigability among participants was assessed using Fatigue Severity Scale (FSS) at initial contact. This self-report 9-item scale measures the severity of fatigue and its effect on a person's activities and lifestyle in patients with a variety of disorders. The items are scored on a 7-point scale with 1 = strongly disagree and 7= strongly agree. The minimum score is 9 and the maximum score possible is 63. The FSS scores are directly proportional to fatigue severity. The cut-off point of FSS was set at 40 based on a previous study in which MND participants scoring 40 and above were classified to have clinically significant fatigue.[8]

Statistical analysis

Data of this study was gathered and analyzed using SPSS version 23. Descriptive statistics were used to represent the disability profile. Factors associated with functional status decline were analyzed using Mann Whitney U test, Kruskal Wallis test and independent t-test.

RESULTS

Demographic and clinical characteristics data

Table 1 represents the demographic and clinical features of the 30 participants recruited in this study. The mean age was 59.73 years with men more affected than women (3:1). Majority of the participants were of Chinese ethnicity (63.3%) and slightly more than half of those that participated had at least 1 comorbidity (53.4%). In regards to the clinical features of MND, 15 of them which accounts for half of the patients recruited had lower limb onset while the rest had either upper limb or bulbar onset of MND. The ratio of riluzole users versus non-users was 2:1.

Disability profile

Figure 1, 2 and 3 depict the impairments, activity limitations and participation restrictions faced by the MND patients recruited respectively.

The top 3 issues that were reported among the MND patients recruited were weakness, weight loss and fatigue. Almost all of them (93.3%) reported weakness be it upper limbs, lower limbs or both whereas 25 patients (83.3%) had complained of weight loss since being diagnosed with MND. The least common impairment that was reported among these patients was disturbances of bowel functions namely constipation.

In regards to activity limitation among the MND participants, issues reported were categorized into limitations of 4 main activities namely self-care, mobility, communication and domestic chores. Majority of them, 23 patients (76.7%) reported of having issues in performing domestic chores be it cleaning, cooking or laundering.

Restriction of community participation among the MND patients were mainly along the aspects of driving, employment and social life. Social life in this context represents any activity that help participants to develop or maintain interpersonal relationships with people within their immediate surroundings or general public. Social life engagement was found to be the most common challenge faced by the participants (73.3%).

Functional outcome

3 of the participants passed away during the course of the study. Therefore, only 27 out of 30 MND patients were able to complete the functional reassessment after 6 months. Table 2 picturizes the functional decline of participants in the course of 6 months.

The association between demographic and clinical characteristics of MND patients and their functional degradation over the span of 6 months which is represented by the ALSFRS-R decline value is as shown in Table 3.

Based on the analysis, none of the factors analyzed were statistically significant ($p<0.05$) in affecting functional decline among the MND patients. Although there were numerical differences in terms of functional decline between genders in which the female MND population had a larger functional decline in comparison to their male counterparts, it was not robust enough to be statistically significant.

Fatigability

Table 4 depicts the effect of fatigability on various functional domains among MND patients. There was no statistically significant relationship between fatigue and general functional deterioration in MND population. However, further analysis of the different functional domains within the ALSFRS-R demonstrated that fatigue

Table 1: Demographics and clinical characteristics of MND participants

Variable	Average/frequency (n=30)
Age [mean±SD (range)]	59.73±11.74 (35-88)
≤54	10 (33.3)
55-64	7 (23.3)
≥65	13 (43.3)
Gender (*n*; %)	
Male	22 (73.3)
Female	8 (26.7)
Ethnicity	
Malay	7 (23.3)
Chinese	19 (63.3)
Indian	4 (13.3)
Comorbidities (*n*; %)	
None	14 (46.7)
1	8 (26.7)
≥2	8 (26.7)
Site of Onset (*n*; %)	
Bulbar	6 (20.0)
Upper limb	9 (30.0)
Lower limb	15 (50.0)
Age of symptom onset [mean ± SD (range)]	55.73±13.60 (21-82)
≤54	12 (40.0)
55-64	11 (36.7)
≥65	7 (23.3)
Duration between symptom onset to diagnosis (in months) [(mean ± SD (range)]	16.10±19.57 (1-108)
≤12 months	17 (56.7)
>12 months	13 (43.3)
Usage of Riluzole (*n*; %)	
Yes	10 (33.3)
No	20 (66.7)

was significantly associated with worsening respiratory domain (p=0.032).

DISCUSSION

The mean participant age, gender predominance, ethnic distribution, site of onset (bulbar vs limb), mean age of onset and time since symptom onset to diagnosis were consistent to those reported by previous studies locally and internationally.[1,5,9] Riluzole is an FDA approved drug used in MND. It is a neuroprotective drug that blocks glutamatergic neurotransmission in central nervous system preventing glutamate excitotoxicity which may contribute to neuronal death in MND. Riluzole consumption among Malaysian MND population were significantly less compared to MND populations from other parts of the world.[10,11] This is likely attributed to riluzole's high affordability and its limited benefit whereby it is proven that riluzole prolongs median survival by only two to three months if taken for at least 18 months.[12]

This is the first study in Malaysia that describes the disability profile of patients with MND. Although the impairments in MND are very wide and heterogenous, certain impairments such as weakness, spasm/cramps and emotional disturbances are commonly

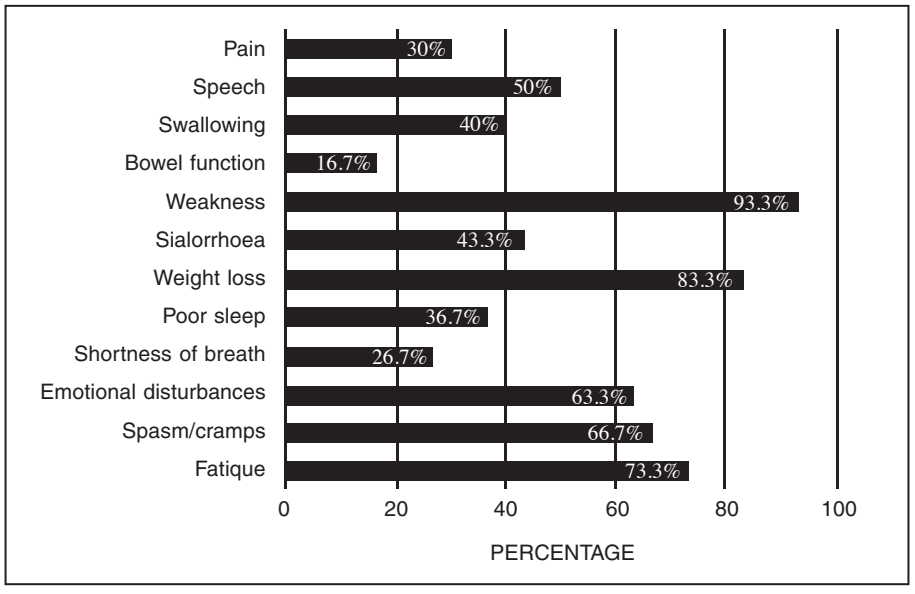

Figure 1. Impairments (body structure and function) of MND participants

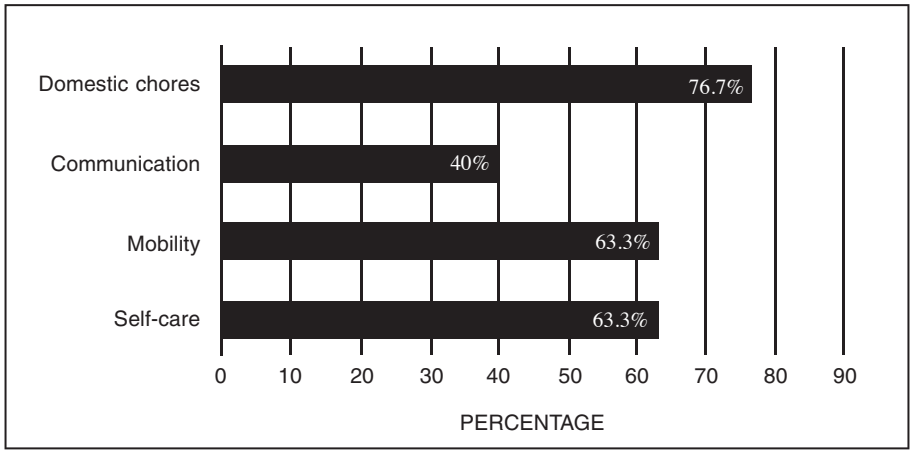

Figure 2. Activity limitations of MND participants

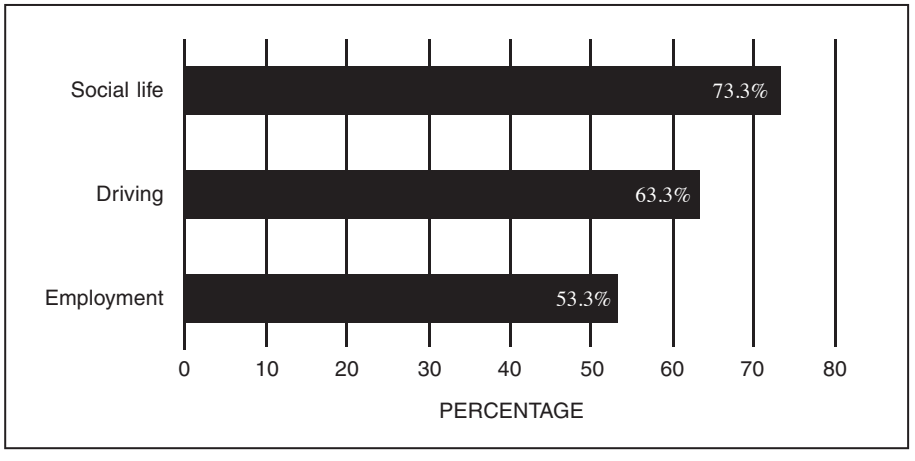

Figure 3. Participation restriction of MND participants

Table 2: Functional outcome of MND participants at baseline and at 6 months

	ALSFRS-R at Baseline	ALSFRS-R at 6 months	Decline in ALSFRS-R
N	30	27	27
Mean	35.50	28.81	6.85
Median	36.50	32.00	5.00
Standard deviation	6.32	9.36	4.54
Minimum	22	10	2
Maximum	45	42	17

Table 3: Association of demographic factors and clinical characteristics to decline in ALSFRS-R score in 6 months

Variable	Decline in ALSFRS-R score in 6 months (n=27)		
	Mean	SD	*p* value
Gender[1]			
Male	5.70	3.29	0.179
Female	10.14	6.15	
Ethnicity[2]			
Malay	6.14	2.97	
Chinese	6.83	4.73	0.984
Indian	9.50	9.19	
Age[2]			
54 and less	6.60	2.76	
55-64	6.00	5.59	0.548
65 and above	7.55	5.48	
Comorbidities[2]			
None	6.85	4.04	
1	6.71	4.23	0.722
≥2	7.00	6.22	
Site of onset[2]			
Bulbar	6.80	4.60	
Upper limb	7.33	5.32	0.997
Lower limb	6.54	4.29	
Age of symptom onset[2]			
54 and less	6.25	2.63	
55-64	6.44	5.81	0.447
65 and above	8.67	5.72	
Duration between symptom onset to diagnosis[1]			
≤12 months	6.75	4.80	0.716
>12 months	7.00	4.36	
Riluzole usage[1]			
Yes	6.88	5.67	0.658
No	6.84	4.15	

[1] *Mann-Whitney U test*
[2] *Kruskal Wallis test*

Table 4: Effect of fatigability on functional domains

Functional domains	FSS score	n	ALSFRS-R score decline in 6 months		
			Mean	Std. Deviation	*p* value
Overall function [1]	Less than 40	12	4.75	2.22	0.053
	40 and above	15	8.53	5.25	
Bulbar [1]	Less than 40	12	1.83	2.79	0.867
	40 and above	15	1.73	2.12	
Fine motor [2]	Less than 40	12	1.75	1.60	0.063
	40 and above	15	3.07	1.91	
Gross motor [1]	Less than 40	12	1.58	1.88	0.277
	40 and above	15	1.93	1.34	
Respiratory [1]	Less than 40	12	0.33	1.16	0.032
	40 and above	15	2.20	3.12	

[1] *Mann-Whitney U test*

[2] *Independent t-test*

well recognized throughout the spectrum of disease severity in MND. Weight loss which previously an underestimated symptom, was one of the top reported problem among the MND population studied. Factors that are inherent in MND contributing to weight loss includes loss of appetite, dysphagia, dyspnoea, emotional disturbances and progressive muscular atrophy. Weight loss reflects nutritional status decline and it is considered to be a negative predictor of survival in MND patients.[13] Unfortunately, it is often undertreated in clinical practice. Moving forward, it is vital to perform routine nutritional status assessment for all patients and render nutritional therapy if necessary.

The studied population had more issues in terms of performing domestic chores as compared mobility and self-care in contrast to a previous similar study in Australia.[5] Over the years, the availability of many ambulatory and adaptive aids/equipment has certainly assisted patients in the aspects of mobility and personal care. Domestic chores performance in these patients can be enhanced by adapting one's environment or adding major installations. Social life among MND patients was largely affected by social embarrassment, limited mobility, speech and communication difficulties. Social isolation can lead to emotional disturbances and depression. The latter features require further attention to allow patients to have a more meaningful quality of life.

We failed to identify significant demographic and clinical characteristics that are associated with functional decline in our MND patients in line with previous established evidence.[14] The progression rate and the course of disease in MND is very diverse and heterogenous making it difficult to identify the factors affecting functional status among MND patients.

Fatigue in MND is mainly attributed to physical causes due to motor neuron degeneration. In addition, associated conditions occurring in MND such as depression, sleep problems, respiratory insufficiency and weight loss also may increase fatigue. It has been reported that there is no association between fatigue and general functional outcome among MND population[15] and this study is no exception to it. However, further exploration exposed that fatigue significantly affects respiratory function mainly due to diminishing strength and endurance of respiratory muscles in these patients. Fatigue is prevalent in MND and has a significant impact on quality of life, thus it is important to overcome this impairment. In terms of rehabilitation, patients should be advised to pace their daily activities and exercises be it aerobic or strengthening exercises to prevent fatigue from setting in. Focus should be shifted on providing routine pulmonary rehabilitation to MND patients especially the ones with fatigue to dampen the progressive deterioration of respiratory function.

The limitations in this study include single centred survey with a small sample size limited by time, rarity and high mortality rates that comes with MND. Furthermore, the functional assessment was only done twice within 6 months which is too short a time to gauge one's

functional course. In future, further studies recruiting larger sample size through multicentre approach with frequent functional assessment throughout a course of prolonged duration are required to establish the factors affecting the status of functional decline among MND patients to facilitate rehabilitation management. Future studies should also investigate the impact of rehabilitation programs on disease progression.

In conclusion, this study is a door to future researches revolving around rehabilitation in MND. Framework of ICF as championed by the World Health Organization should be explored in larger MND population ideally through regional collaboration enabling the establishment of ICF core sets specifically for MND to provide the best multidisciplinary care to this population. Focus should be shifted to render routine nutritional assessment and care if needed to all MND patients and also to provide pulmonary rehabilitation to these patients especially the ones with fatigue to dampen the progressive deterioration of respiratory function. Implementing these measures will lead to an enhanced quality of life amongst this population.

DISCLOSURE

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