Outcomes of patients with multiple sclerosis at a neurorehabilitation unit in Saudi Arabia

Abdulaziz M. Al Mosallam, MBBS, SBPMR, *Ahmad Z. Qureshi,* MBBS, FCPS (PMR), *Abdussalam A. Alshehri,* MBBS, SBEM, *Fayez M. Alshehri,* MBBS, *Sami Ullah,* MBBS, FCPS (PMR).

ABSTRACT

الأهداف: لتقييم تأثير إعادة التأهيل من فريق متعدد التخصصات على المرضى الذين يعانون من مرض التصلب العصبي المتعدد في المرضى السعوديين.

الطريقة: تم تضمين المرضى الذين يعانون من التصلب المتعدد الذين خضعوا لإعادة تأهيل المرضى الداخليين في مدينة الملك فهد الطبية بين عامي 2009م و2015م. تم إجراء تحليل للبيانات بأثر رجعي. تم اختبار الاختلافات في معيار الاستقلال الوظيفي ومدة الإقامة بين مختلف المجموعات على أساس العمر ونوع الجنس ونوع المرض بطبيعة الحال باستخدام اختبار T مستقل. تم استخدام ارتباط بيرسون للتحقيق في الارتباط بين معيار الاستقلال الوظيفي، و مدة الإقامة والمتغيرات الأخرى. أجريت هذه الدراسة بين شهر يونيو وحتى سبتمبر لعام 2016م.

النتائج: تم التعرف على ما مجموعه 24 مريضا. وكان متوسط العمر حوالي 36 عاما. في حين كان متوسط عمر ظهور المرض 31 سنة. تراوحت مدة المرض بين 1 و 20 سنة بمتوسط 7 سنوات. وكان النوع الأكثر شيوعاً من مرض التصلب العصبي المتعدد نوع إعادة التراجع (45.8%). وأظهرت درجة فيم عند التنويم والخروج منه متوسط 77.5 و 97.25 على التوالي. وتراوحت درجة الكسب FIM بين 2 و 51 بمتوسط 18.58. فيما تراوحت الكفاءة فيم من 0.09 إلى 0.95. كان هناك ارتباط كبير بين هاتين الفئتين العمريتين مع كفاءة FIM p=0.043.

الخاتمة: إعادة تأهيل المرضى الداخليين هو تدخل مهم في المرضى الذين يعانون من التصلب المتعدد المزمن ويحسن الاستقلال الوظيفي.

Objectives: To assess the impact of inpatient multidisciplinary rehabilitation on a Saudi Arabian population of patients with multiple sclerosis (MS).

Methods: We retrospectively analyzed the data of patients with MS who underwent inpatient rehabilitation between 2009 and 2015 at King Fahad Medical City (KFMC). Differences in Functional Independence Measure (FIM) scores (used in rehabilitation settings to assess the functional independence of patients) and length of stay (LOS) were measured between patients of different ages, sexes, and types of MS and analyzed using the independent t-test. The Pearson correlation coefficient was used to investigate the correlation between FIM, LOS, and other variables.

Results: In total, 24 patients were identified, with an average age of 36 years. The average age at disease onset was 31 years. Disease duration ranged from 1-20 years, with a mean of 7 years. The most common type of MS was relapsing-remitting (45.8%). The mean FIM score at admission was 77.5 and at discharge 97.25. Functional independence measure gain ranged from 2-51, with a mean of 18.58. Functional independence measure efficiency (FIM gain divided by LOS) ranged between 0.09-0.95. The length of stay ranged between 21-95 days, with a mean of 37.79 days. There was a significant association between age and FIM efficiency (p=0.043).

Conclusions: Inpatient rehabilitation is an important intervention that improves the functional independence of patients with chronic MS.

Multiple sclerosis (MS) is a chronic inflammatory demyelinating autoimmune disease with a female preponderance and an estimated prevalence of 30-190 cases per 100,000 people in Europe.[1] Because of its early onset, progressive course, and long survival time, MS can lead to long-term disability with a significant negative impact on personal and social life.[2,3] Among neurologic diseases, it is the third most common cause of disability, with 50% of patients requiring a walking aid and 10% requiring a wheelchair within 15 years of onset; within 25 years of onset, more than 90% of patients experience significant functional impairments.[4,5] Life expectancy in patients with MS is reduced by about 5-10 years compared with age-matched individuals without MS.[6] Around 2 million people worldwide are affected by MS.[7] In young adults, this disabling neurodegenerative disease of the central nervous system is considered the leading cause of non-traumatic disability.[8] In the Middle East, the risk of MS has recently been reported to be moderate to high.[9] The Kurtzke classification places the Middle East in a low-risk zone for MS; however, a moderate-to-high prevalence in areas within the region (31-55 cases per 100,000 individuals), especially among women, has recently been reported.[10,11] Thus, MS represents a considerable burden to Middle Eastern countries. In the Kingdom of Saudi Arabia, the prevalence of MS is poorly documented. Reviews of epidemiologic studies have suggested that it is underdiagnosed and that its prevalence is increasing.[10,11] A few studies have reported an increase in the prevalence of MS in the Kingdom of Saudi Arabia to 40/100,000 in 2008 from 25/100,000 in 1998.[9,12] Likewise, there are no data on the effects of inpatient rehabilitation in the Arabian Peninsula. In the literature, common treatment strategies are based on a combination of pharmacotherapy and rehabilitation. In daily practice, multidisciplinary rehabilitation (MDR) is often recommended to patients with MS. However, the evidence regarding the outcomes of MDR is contradictory. Some trials have reported improvements in impairment and in the mental component of a health-related quality of life measure, but others have shown that MDR improves the experience of people with MS in terms of activity and participation without changing the level of impairment.[13,14-16] The overall evidence on the efficacy of MDR is limited by variation in the clinical presentation of MS and problems associated with study methodology.[13] In this study, we assessed the impact of short-term inpatient MDR in a Saudi-Arabian population of patients with MS to identify the clinical predictors of effective rehabilitation treatment. At KFMC, both inpatient and outpatient services are included in the neurorehabilitation program. King Fahad Medical City treats patients from all regions of the country, including those internally transferred from the National Neuroscience Institute within KFMC. The integrated neurorehabilitation program was deemed to meet the standards of the Commission on Accreditation of Rehabilitation Facilities.[17]

Methods. This study was conducted at the specialized neurorehabilitation unit of the Rehabilitation Hospital at KFMC after obtaining institutional review board approval. All patients with MS who were admitted to the neurorehabilitation and underwent intensive MDR between 2009 and 2015 were included in the study. Patients with an acute relapse or a prior admission for rehabilitation in the preceding 3 months were excluded. Demographic measures including age, sex, duration of disease, date of onset, and type of MS were recorded. Functional Independence Measure (FIM) scores were used to evaluate the functional status at admission (FIMa) and functional status at discharge (FIMd).[18,19] Functional independence measure gain was calculated as the FIMd minus the FIMa. Functional independence measure efficiency was calculated as the FIM gain divided by the length of stay (LOS). The length of stay was measured in days. Data were collected retrospectively using the electronic chart reviewer at the hospital.

Statistical analysis. The demographic and clinical characteristics of the study's participants were reported as means (standard deviation [SD]) for continuous variables and counts (percentages) for categoric variables. Differences in FIM scores and LOS between age, sex, and MS type groups were tested using the independent t-test. The Pearson correlation coefficient was used to investigate the correlation between FIM, LOS, and other clinical variables. All statistical analyses were performed using the Statistical Package for the Social Science (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA); a 2-tailed *p*-value of 0.05 was considered statistically significant.

Results. In total, 24 patients with complete data were identified. There were 7 (29.2%) men and 17 (70.8%) women. Their ages ranged between 16-64 years, with a mean of 35.75±10.99 years (**Table 1**). There

was no significant difference in FIM efficiency between the male and female patients (*p*=0.18).

The age at disease onset ranged between 15-47 years, with a mean of 30.75±10.89 years. The correlation between FIM efficiency and age at disease onset was not significant (correlation coefficient= –0.059, *p*=0.78).

Disease duration ranged between 1-20 years, with a mean of 7 years (SD=5.14 days). There was a poor correlation between disease duration and FIM efficiency (correlation coefficient= –0.002, *p*=0.99).

Overall, 11 patients (45.8%) had relapsing-remitting MS. The remaining 13 patients (54.1%) had progressive relapsing MS: 5 patients (20.8%) had primary progressive MS; 3 patients (12.5%) had secondary progressive MS; 3 patients (12.5%) had primary relapsing MS; and the type of MS was unknown in 2 patients (8.3%). Functional independence measure efficiency was not significantly correlated with MS type (*p*=0.51).

The mean FIM scores at admission was 77.5±16.92 and at discharge was 97.25±17.31). The FIM gain ranged between 2-51, with a mean of 18.58±12.06. Overall, the mean FIM efficiency was 0.5±0.27, and ranged between 0.09-0.95 (**Table 1**).

The LOS ranged between 21-95 days, with a mean of 37.79±11.08 days. There was no significant correlation between LOS and FIM efficiency (correlation coefficient= 0.021, *p*=0.99).

Discussion. Strategies for the treatment of MS vary worldwide, so it is important to determine the outcomes of MS rehabilitation in specific populations. Data regarding the functional outcomes of rehabilitation in Saudi Arabian patients with MS is lacking. This may be attributable to a lack of reporting, the unavailability of comprehensive rehabilitation services, or poor awareness of rehabilitation among health-care providers and patients with MS in the country.

Table 1 - Characteristics of the patients enrolled.

No.	Sex	Age (years)	Age at onset of illness (years)	MS type	Duration of illness (years)	LOS (days)	FIMa	FIMd	FIM gain	FIM efficiency
1	M	27	21	RRMS	6	95	83	90	7	0.11
2	M	31	29	RRMS	3	42	80	105	25	0.59
3	M	36	31	PRMS	4	42	77	104	27	0.6
4	F	35	15	SPMS	20	42	86	110	24	0.57
5	F	64	47	PRMS	17	42	67	82	15	0.3
6	F	45	42	RRMS	3	35	87	120	33	0.9
7	F	43	30	PPMS	13	35	54	66	12	0.3
8	F	16	15	RRMS	1	21	117	121	4	0.1
9	M	41	30	PPMS	11	68	47	98	51	0.7
10	M	28	16	RRMS	12	35	70	73	3	0.88
11	M	40	33	SPMS	7	38	73	98	25	0.6
12	F	56	40	RRMS	16	34	84	101	17	0.5
13	F	23	19	PPMS	4	23	88	108	20	0.8
14	F	41	35	SPMS	6	44	66	84	18	0.4
15	F	24	23	Unknown	1	21	70	72	2	0.09
16	F	47	44	Unknown	3	47	54	62	8	0.17
17	F	27	22	RRMS	5	37	81	97	16	0.43
18	F	25	19	PPMS	6	28	82	91	9	0.2
19	F	27	18	PPMS	9	28	96	127	31	0.9
20	F	33	31	RRMS	2	40	57	95	38	0.95
21	F	51	44	PRMS	7	30	98	111	13	0.43
22	F	38	35	RRMS	3	47	82	106	24	0.58
23	F	45	39	RRMS	6	41	103	114	11	0.2
24	M	35	32	RRMS	3	28	58	102	17	0.6
Mean (SD)	-	35,75 (10.99)	30,75 (10.89)	-	7 (5.14)	37,79 (11.08)	77,55 (16.92)	97,25 (17.31)	18,58 (12.06)	0.5 (0.27)

MS - multiple sclerosis, LOS - length of stay, FIMa - FIM score at admission, FIMd - FIM score at discharge, FIM - Functional Independence Measure, RRMS - relapsing-remitting MS, PRMS - primary relapsing MS, PPMS - Primary progressive MS, SPMS - secondary progressive MS, SD - standard deviation

This research highlights the correlations between demographic features, types of disease, and functional outcomes in patients with MS undergoing inpatient rehabilitation. In our study, age was the single most significant variable and was found to have a strong association with FIM efficiency. The average age of patients was around 31 years, and 4 patients had early onset MS, i.e. disease onset before 18 years of age. None of the patients in our study had late-onset MS, i.e. disease onset after 50 years of age. This is consistent with previous studies, which have reported that the onset of MS usually begins in early adulthood, typically between the ages of 20 and 40 years.[20] Multiple Sclerosis mainly affects young adults; hence, there is a need to consider rehabilitation options in the early stages of the disease, because it is a chronic disabling condition.

In the Gulf region, the female:male ratio of patients with MS varies from 0.87 in Oman to 4.3 in Saudi Arabia.[21,22] However, in our study, the female:male ratio was 2.42 because our study population consisted of 17 women and 7 men. This emphasizes the need for greater resources to treat female patients, who have special requirements in our country for cultural, religious, and personal reasons. Saudi Arabian women prefer female therapists in situations where physical contact is required during treatment. Female patients also are not placed in rooms shared with male patients, and they are expected to be treated by female nurses. There are separate units and therapy areas for women in hospital settings. If there is a shortage of space, female and male patients are usually treated at different times. Their psychosocial issues are preferably addressed by female therapists or team members. The high prevalence of MS in women requires the modification of rehabilitation programs to meet the needs of female patients. Thus, the demand for female rehabilitation clinicians and health-care providers in the region remains very high.

Funcional independence measure is a reliable and valid tool to assess the functional independence of patients with MS.[23] In patients with MS, the clinometric of FIM for the impact of disability is well established.[24] Internationally, FIM has been validated for the documentation of everyday self-sufficiency and levels of neuromotor disability.[25] Functional independence measure explores functional areas of personal care, sphincter control, mobility, locomotion, cognitive capacity, and interpersonal relationships, assigning to each a graduated score on a 7-level scale. The average FIM score at discharge of our patients was 97.25, which is fairly low compared with the FIM of 116.3 reported in a study conducted in the Czech Republic involving 35 patients.[26] This discrepancy may be due to disease chronicity, because the mean duration of disease in our patients was 7 years. However, our results are comparable to Medicare data from the United States (US) on patients with MS who underwent inpatient rehabilitation.[27] The FIM gain of 18.58 points in our study is also comparable with US Medicare data reported in 2012, which showed a FIM gain of 21.3 points. Similarly, the FIM score at discharge was 82 points in the Medicare patients, whereas it was 97.25 points in our patients. The comparatively high FIM scores in our patients may be due to the fact that our patients had a fairly long LOS, i.e. 38 days, during inpatient rehabilitation, whereas the Medicare patients had an inpatient rehabilitation stay of 15 days. In contrast, in a British study involving 41 patients who underwent rehabilitation, the patients stayed 10 days longer than in our study.[28] Given the variation in LOS reported globally, FIM efficiency was included as an outcome measure in our study to reflect the FIM gain adjusted to the LOS; however, we were unable to find any international comparisons for the FIM efficiency of MS patients. Even in our study, sex, type of MS, disease duration, age of onset, and LOS showed no significant association with FIM efficiency. Considering the small number of patients included in our study (n= 24), our results are poorly comparable with the Medicare data, which was collected from 4,669 patients; however, our analyses may serve as a benchmark for future studies.[29]

Rehabilitation plays a vital role in improving the physical and psychologic abilities of patients with MS. Rehabilitation focuses on reducing symptoms and limitations at the level of activity and participation. These interventions, which improve the quality of life of patients with MS, also emphasize personal and environmental factors.[29] Favorable outcomes of inpatient rehabilitation in patients with MS have been confirmed by some studies.[28,30] There are also studies that state that short-term improvements in clinical and functional outcome measures can be achieved with intensive inpatient rehabilitation programs.[31]

However, the unique aspect of our study was that most of the patients had chronic MS and still showed considerable functional gains. The mean duration of disease was 7 years, and most of our patients had relapsing-remitting MS.

In conclusion, inpatient rehabilitation is an important intervention that improves functional independence in patients with chronic MS. Data regarding the use of FIM efficiency as an outcome measure for patients with MS is scarce. Functional independence measure efficiency can be used to demonstrate functional gains in relation to LOS; however, further studies on a larger

scale are necessary both nationally and internationally to confirm these findings.

References

1. Rosati G. The prevalence of multiple sclerosis in the world: an update. *Neurol Sci* 2001; 22: 117-139.
2. Pfleger CC, Flachs EM, Koch-Henriksen N. Social consequences of multiple sclerosis (1): early pension and temporary unemployment--a historical prospective cohort study. *Mult Scler* 2010; 16: 121-126.
3. Pfleger CC, Flachs EM, Koch-Henriksen N. Social consequences of multiple sclerosis. Part 2. Divorce and separation: a historical prospective cohort study. *Mult Scler* 2010; 16: 878-882.
4. Frohman EM, Racke M, van Den Noort S. To treat, or not to treat: the therapeutic dilemma of idiopathic monosymptomatic demyelinating syndromes. *Arch Neurol* 2000; 57: 930-932.
5. Weinshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, et al. The natural history of multiple sclerosis: a geographically based study. 2. Predictive value of the early clinical course. *Brain* 1989; 112: 1419-1428.
6. Ryan M, Piascik P. Providing pharmaceutical care to the multiple sclerosis patient. *J Am Pharm Assoc (Wash)* 2002; 42: 753-766.
7. Dutta R, Trapp BD. Pathogenesis of axonal and neuronal damage in multiple sclerosis. *Neurology* 2007; 68: S22-31.
8. Heydarpour P, Khoshkish S, Abtahi S, Moradi-Lakeh M, Sahraian MA. Multiple sclerosis epidemiology in middle East and North Africa: a systematic review and meta-analysis. *Neuroepidemiology* 2015; 44: 232–244.
9. Bohlega S, Inshasi J, Al Tahan AR, Madani AB, Qahtani H, Rieckmann P. Multiple sclerosis in the Arabian Gulf countries: a consensus statement. *J Neurol* 2013; 260: 2959-2963.
10. Multiple Sclerosis International Federation. Atlas of MS 2013. 2013 [Accessed June 3, 2017]. Available from: http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf.
11. Maghzi AH, Ghazavi H, Ahsan M, Etemadifar M, Mousavi S, Khorvash F, et al. Increasing female preponderance of multiple sclerosis in Isfahan, Iran: a population-based study. *Mult Scler* 2010; 16: 359-361.
12. Daif AK, Al-Rajeh S, Awada A, Al Bunyan M, Ogunniyi A, AbdulJabar M, et al. Pattern of presentation of multiple sclerosis in Saudi Arabia: analysis based on clinical and paraclinical features. *Eur Neurol* 1998; 39: 182-186.
13. Solari A, Filippini G, Gasco P, Colla L, Salmaggi A, La Mantia L, et al. Physical rehabilitation has a positive effect on disability in multiple sclerosis patients. *Neurology* 1999; 52: 57-62.
14. Khan F, Turner-Stokes L, Ng L, Kilpatrick T. Multidisciplinary rehabilitation for adults with multiple sclerosis. *Cochrane Database Syst Rev* 2007; 2: CD006036.
15. Freeman JA, Langdon DW, Hobart JC, Thompson AJ. The impact of inpatient rehabilitation on progressive multiple sclerosis. *Ann Neurol* 1997; 42: 236-244.
16. Freeman JA, Langdon DW, Hobart JC, Thompson AJ. Inpatient rehabilitation in multiple sclerosis: do the benefits carry over into the community? *Neurology* 1999; 52: 50-56.
17. CARF International. Comprehensive Integrated Inpatient Rehabilitation Programs. 2017 [Accessed November 4, 2017]. Available from: http://www.carf.org/Programs/ProgramDescriptions/MED-Inpatient-Rehab-Hospital/.
18. Dodds TA, Martin DP, Stolov WC, Deyo RA. A validation of the functional independence measurement and its performance among rehabilitation inpatients. *Arch Phys Med Rehabil* 1993; 74: 531-536.
19. Hobart JC, Lamping DL, Freeman JA, Langdon DW, McLellan DL, Greenwood RJ, et al. Evidence-based measurement: which disability scale for neurologic rehabilitation? *Neurology* 2001; 57: 639-644.
20. Tullman MJ. Overview of the epidemiology, diagnosis, and disease progression associated with multiple sclerosis. *Am J Manag Care* 2013; 19: S15-20.
21. Tharakan JJ, Chand RP, Jacob PC. Multiple sclerosis in Oman. *Neurosciences (Riyadh)* 2005; 10: 223-225.
22. Yaqub BA, Daif AK. Multiple sclerosis in Saudi Arabia. *Neurology* 1988; 38: 621-623.
23. Brosseau L, Wolfson C. The inter-rater reliability and construct validity of the Functional Independence Measure for multiple sclerosis subjects. *Clin Rehabil* 1994; 8: 107-115.
24. Granger CV, Cotter AC, Hamilton BB, Fiedler RC, Hens MM. Functional assessment scales: a study of persons with multiple sclerosis. *Arch Phys Med Rehabil* 1990; 71: 870-875.
25. Data Management Service of the Uniform Data System for Medical Rehabilitation and the Center for Functional Assessment Research. Guide for use of the uniform data set for medical rehabilitation including the functional independence measure (version 3.1). Buffalo (USA): State University of New York; 1990.
26. Konečný L, Pospíšil P, Dufek M, Drlíková L, Anbais FH, Erajhi AA, et al. Functional impairment in multiple sclerosis. *Scripta Medica (Brno)* 2007; 80: 225-232.
27. Morley MA, Coots LA, Forgues AL, Gage BJ. Inpatient rehabilitation utilization for Medicare beneficiaries with multiple sclerosis. *Arch Phys Med Rehabil* 2012; 93: 1377-1383.
28. Gaber TA. Oo WW, Gautam V, Smith L. Outcomes of inpatient rehabilitation of patients with multiple sclerosis. *NeuroRehabilitation* 2012; 30: 97-100.
29. Kesselring J, Beer S. Symptomatic therapy and neurorehabilitation in multiple sclerosis. *Lancet Neurol* 2005; 4: 643-652.
30. Salhofer-Polanyi S, Windt J, Sumper H, Grill H, Essmeister M, Diermayr G, et al. Benefits of inpatient multidisciplinary rehabilitation in multiple sclerosis. *NeuroRehabilitation* 2013; 33: 285-292.
31. Liberatore G, Clarelli F, Nuara A, Ungaro D, Gatti R, Rovaris M, et al. Predictors of effectiveness of multidisciplinary rehabilitation treatment on motor dysfunction in multiple sclerosis. *Mult Scler* 2014; 20: 862-870.