

Effect of Strength and Balance Training on Fatigue in Patients with Multiple Sclerosis



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1.ABSTRACT

Background: Fatigue is one of the most prominent and disabling symptoms of multiple sclerosis (MS). It occurs in 75-95% of MS patients. The nurse must be aware of both pharmacological and non-pharmacological management of Multiple Sclerosis related fatigue (MSRF). Strength and Balance training (SBT) is one of exercises which have proven to be promising nonpharmacological interventions for MS patients who have fatigue complaint. Therefore, the aim of the study, was to evaluate the effect of strength and balance training on fatigue in patients with multiple sclerosis. Methodology, Quasi-experimental study with a purposive sample of totally 90 MS patients from both gender who were admitted to neurology department at Mansoura University Hospital was enrolled in this study. Patients were assigned equally to control and intervention group. Data were collected using three tools: Structured Interview Questionnaire, Modified Fatigue Impact Scale and Strength and Balance Training Observational Checklist. Results, there was a significant decrease in fatigue among the study group who practiced strength and balance training compared to control group according to the Modified Fatigue Impact Scale (p -value ≤ 0.05). Conclusion, the study concluded that the strength and balance training have a significant effect in reducing fatigue among MS patients.

Key words: Fatigue, Multiple Sclerosis, Patients, Strength and Balance Trainin

2.Introduction:

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS). The prevalence rate of MS has increased in recent years, with approximately 2.2 million people worldwide suffering from MS. (Moghaddam et al., 2021). Over the last few decades, there has been a definite upward trend in MS prevalence in the Middle East, which is consistent with the global trend. Between 2008 and 2013, the Multiple Sclerosis International Federation Atlas found a 10% increase in global MS prevalence, from 30 to 33 per 100,000 people (Yamout, Assaad, Tamim, Mrabet & Gouider, 2020). The prevalence of MS in Egypt has been found to be 14.1 / 100,000 (El-Tallawy et al., 2016). People with multiple sclerosis (PWMS) experience different symptoms. Fatigue is the most reported symptom in people with multiple sclerosis (PWMS). It occurs in 75-95% of MS patients. Thus, it reduces the ability of individuals to perform the activities of daily life (Al Abbad, 2020). The nurse plays an important role in managing fatigue symptom. Basic management for multiple sclerosis-related fatigue (MSRF) can be broadly classified as a pharmacological or non-pharmacological intervention (Kratz, Atalla, Whibley, Myles, Thurston & Fritz, 2020). Studies examining the effectiveness of pharmacological

interventions have shown only minor effects, while nonpharmacological interventions such as exercises have shown promising results (Miller & Soundy, 2017). One of these exercises is strength and balance training (SBT) which reduces fatigue by improving muscle strength and endurance in MS patients (Tramonti, Di Martino, Foglia & Chisari, 2020).

The study aim: the aim of the study was to evaluate the effect of strength and balance training on fatigue in patients with multiple sclerosis.

Research Hypotheses:

Patients who perform strength and balance training will experience less fatigue and complaint than who don't perform strength and balance training.

3. Methodology:

3.1 Research Design: Quasi experimental research design was utilized in this study.

3.2 Setting: This study conducted at inpatient neurological department and outpatient clinic at Mansoura University Hospital

3.3 Participants: A purposive sample of 90 adult patients with multiple sclerosis divided into two matched groups (45 each): control group who received routine hospital care and study group who

received routine hospital care in addition to strength and balance training

3.3.1 sample size

sample size calculated through clin calc.com sample size calculator software, at 5% α error (95.0% significance) and 20.0% β error (80.0% power of the study), assuming the Average score of modified fatigue impact scale (MFIS) at baseline is (35.6 ± 17.2) and after 3 month training is (28.8 ± 15.5) (Novotna., et al., 2019). The calculated sample size was 90; 45 in control group and 45 in study group.

The study participants met the following criteria:

Inclusion criteria:

- Patients' age was between 20 and 60 years old, both sexes and whose expanded disability status scale (EDSS) ≥ 2 .

Exclusion criteria:

- Patient with severe disability according to expanded disability status scale.

3.4 Tools: Three tools were used to collect the data and achieve the aim of the study as follows:

3.4.1 Tool I: Structured Interview Questionnaire

This tool was developed by the researcher based on literature review Al-Abdullah& Siddiqui, (2018); Guillamo, et al, (2018) and it consists of two parts:

Part I: Demographic characteristics including: age, gender, marital status, educational level and occupation.

Part II: Medical assessment sheet, include body mass index (BMI), expanded disability status scale (EDSS), present & history of comorbid diseases (diabetes mellitus, hypertension, cardiac diseases and osteomalacia).

3.4.2 Tool II: Modified Fatigue Impact Scale (MFIS)

This scale was adopted from Fisk, Ritvo and Archibald, (1994) and translated into Arabic by the researcher. It's a multidimensional scale designed to assess the perceived impact of fatigue related to different aspects of daily life. It consists of 21 standardized questions, where each item has five levels of response. The scale assessed perceived impact of fatigue on physical, cognitive and psychosocial function.

Scoring system of modified fatigue impact scale:

Total Modified fatigue impact scale Score: The total MFIS score will range from 0 to 84. It computed by adding scores on the physical, cognitive, and psychosocial subscales. A higher

score means fatigue is more significantly affecting patient life.

3.4.3 Tool III: Strength and Balance Training Observational Checklist

This tool was developed by the researcher based on literature review (Seguin, Epping, Buchner, Bloch, & Nelson, 2002; Sands, Wurth & Hewit, 2012). It was used to observe the practicing of strength and balance training among patients with multiple sclerosis. It consists of 20 exercises of strength and balance. Each exercise has 2 Responses either done or not done to assess abilities and competency of the study participants to carry out all exercises.

Scoring system of Strength and Balance Training Observational Checklist

The modified FAS consisted of all patients from the FAS for whom sufficient

exercise compliance was established, i.e. who had completed 70% of the scheduled exercise sessions during mo

The competency to the exercise practice is established when the participant had completed $\geq 75\%$ of the scheduled strength and balance exercises (Mäurer et al., 2018).

3.4.4 Ethical consideration

- Oral and written consent was obtained from the patients after illustration the aim of the study, the researcher emphasized to the patients that they have the right to withdraw from the study at any time.
- Patient was informed that refusal to participate in the study wouldn't influence their care.
- Anonymity, privacy, safety and confidentiality were absolutely assured throughout the study.

3.5 Data collection:

Data collection extended over a period of six months started from the beginning of November 2020 to the end of April 2021. The study was carried out through the following three phases:

Phase I: Preparatory phase

- A written approval to conduct the study from Research Ethics Committee of Faculty of Nursing and the responsible authority of Mansoura University hospital for the collection of data. Then the researcher prepared the tools based on the recent literature review and it were tested for validity & reliability, and then essential modifications were done accordingly. A pilot study was carried out before starting data collection on 10% (9 patients) of available patients before starting the data collection and

they were excluded from the total studied sample.

- The researcher met the multiple sclerosis patients who have fatigue and meet the inclusion criteria. Then the researcher divided them into 2 equal groups: control and study group. The researcher assessed the demographic and medical data of control and the study group using tool I (part 1&2) & also assessed fatigue using tool II.
- A simple colored booklet was developed for patients and reviewed by a panel of 5 experts of medical surgical nursing also in this phase.

Phase II: Implementation phase

Strength and balance exercises (SBT) was conducted at a neurology clinic. This training consisted of 20 exercises which practiced by participants in the study group through the period of 12 weeks. **According to American College of Sport medicine**, strength and balance training must be continued for 12 weeks to build strength and reduce fatigue (Callesen, Cattaneo, Brincks& Dalgas, 2018). These exercises included:-warming, squat, wall push up, toe stand, finger marching, biceps curl, overhead press, side leg raise, knee extension, back leg raise, hamstring curl, knee marching, walking the line, single limb stance with arm, pelvic tilt, floor back extension, resistance band stretch, and cool down (chest, arm, hamstring and calf).

Exercises were divided into training sessions, considering exercising the upper and lower extremities in each session. Each training session started by 5-minute warm-up (walking), 30-45 minutes of SBT and terminated by 5 minutes of cool-down.

Phase III: Evaluation phase

- Every participant in the study group was assessed for fatigue by using tool II (MFIS) after 48 hours from the last session of strength and balance training (post-test) and the result compared to pre -test.
- Also, the participants in the control group were assessed for fatigue by using tool II (MFIS) after 12 weeks of the study and the result compared to pre -test.
- Results of control and study group were compared to the pretest results to evaluate the effect of strength and balance training on fatigue in patients with multiple sclerosis.

4. Results:

Table (1) shows that, approximately two third of control and study group (64.4 % and

66.7%) respectively ranged between 20 to less than 30 years old. Regarding gender, more than two third (68,9%) of the control and 73.3% of the study group were females. In relation to marital status, 66.7% of control group and 73.3% of study group were single. Concerning educational level, 64.4 % and 66.7% of control and study group respectively have university education. As regards occupation, 84.4 % of the control and 77.8% of the study group weren't working. This table demonstrates that, no statistically significant difference between the two groups as regard demographic data ($p > 0.05$).

Figure (1) Demonstrates that there was no significant difference between pre and post modified fatigue impact scale(MFIS) among control group, where the mean score of modified fatigue impact scale at the beginning of the study was 51.24 ± 9.38 and after 12 weeks of the study was 53 ± 3.91 meanwhile, there was a significant reduction in the total score of modified fatigue impact scale among the study group after 12 weeks of the performance of the strength and balance training (SBT) where the mean score of modified fatigue impact scale at the beginning of the study was 52.64 ± 5.33 and after 12 weeks of SBT was 40.58 ± 6.46 .

Figure (2): Illustrates that there was no significant difference in the modified fatigue impact scale (MFIS) between the control and study group at the beginning of the study where the mean score of MFIS among control & study group was (51.24 ± 9.38) (52.64 ± 5.33) respectively $P > 0.05$, but the end of the study shows significant difference between the two groups where the mean score of MFIS among control group became (53 ± 3.91) while the study group was (40.58 ± 6.46) $P < 0.05$.

Regarding the subscales of the modified fatigue impact scale, there was a significant difference in both physical and psychosocial sub scales between the control and study group $P < 0.05$ meanwhile, there was no significant difference in the cognitive subscale $P > 0.05$.

Figure (3) Shows that majority of the study group (82.2%) performed all the exercises of strength and balance training, while 17.8% of them had some limitations in the performance of some exercises

Figure (4): Illustrates that, there was a significant negative correlation between the performance of strength and balance training & modified fatigue impact scale among study group.

Table (1): Demographic data of the studied patients

	Control group (n = 45)		Study group (n = 45)		χ ²	P
	No	%	No	%		
Age						
From 20<30	29	64.4%	30	66.7%	0.128	0.988
From 30<40	10	22.2%	10	22.2%		
From 40<50	5	11.1%	4	8.9%		
From 50<60	1	2.2%	1	2.2%		
Gender						
Male	14	31.1%	12	26.7%	0.216	0.642
Female	31	68.9%	33	73.3%		
Marital status						
Single	30	66.7%	33	73.3%	0.476	0.490
Married	15	33.3%	12	26.7%		
Level of Education						
Read and write	0	0%	1	2.2%	1.150	0.563
Secondary school	16	35.6%	14	31.1%		
University education	29	64.4%	30	66.7%		
Occupation						
Requires effort	3	6.7%	3	6.7%	0.941	0.625
Doesn't requires effort	4	8.9%	7	15.6%		
Doesn't work	38	84.4%	35	77.8%		

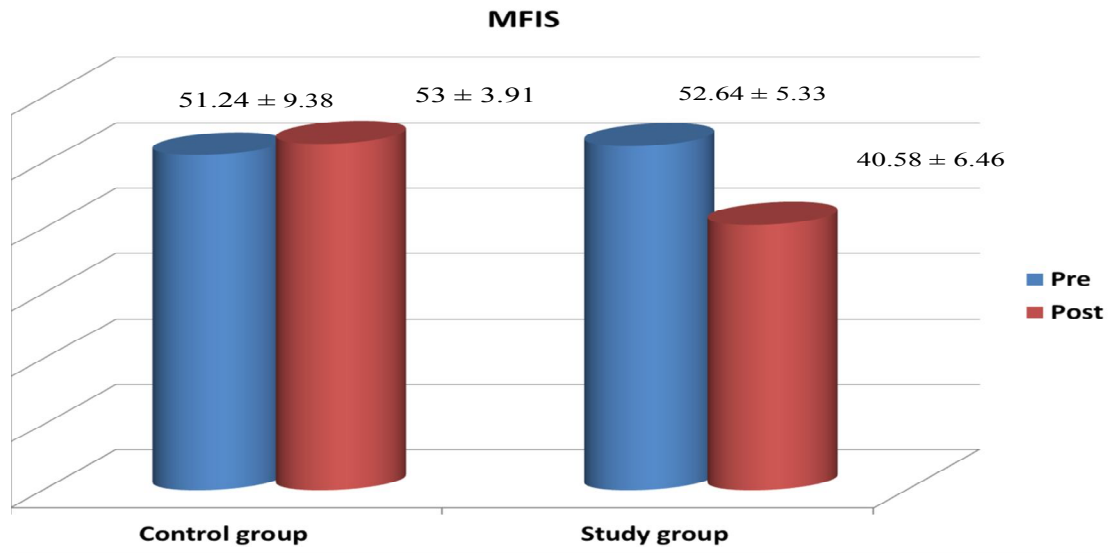


Figure 1: - Comparison between pre & post modified Fatigue impact Scale among control and study group

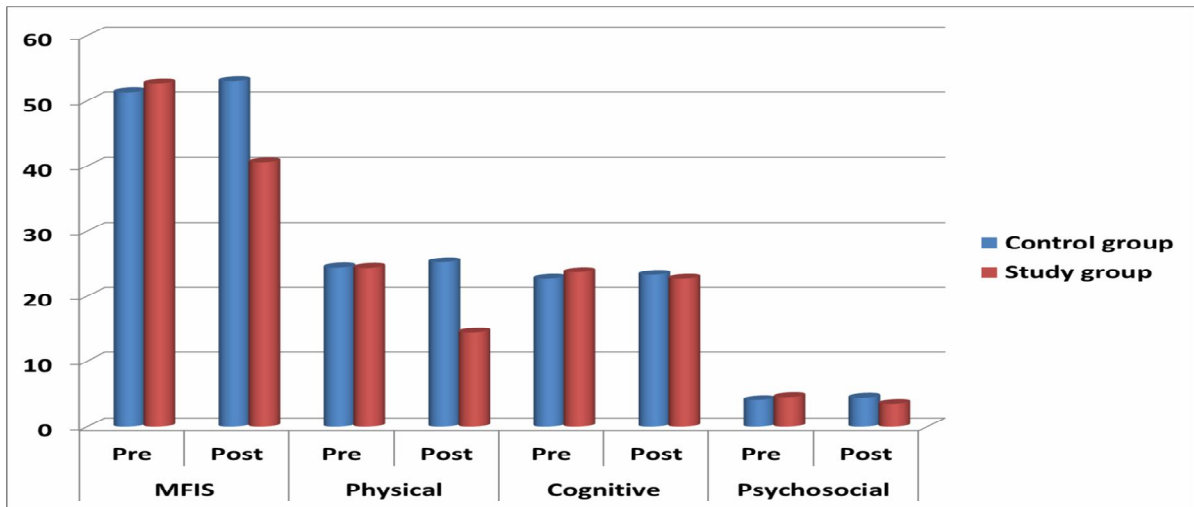


Figure 2: Comparison between the control and study group as regard Modified Fatigue Impact Scale χ^2 : chi-square test

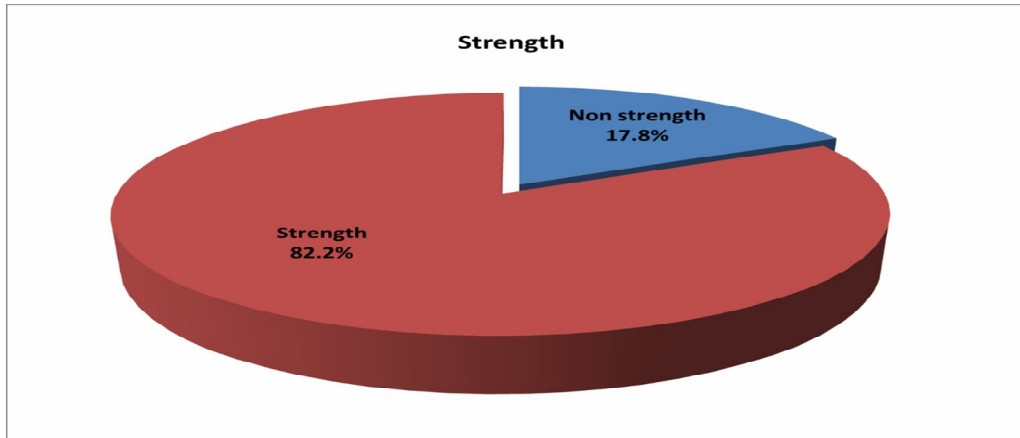


Figure 3: Performance of strength and balance training in the study group

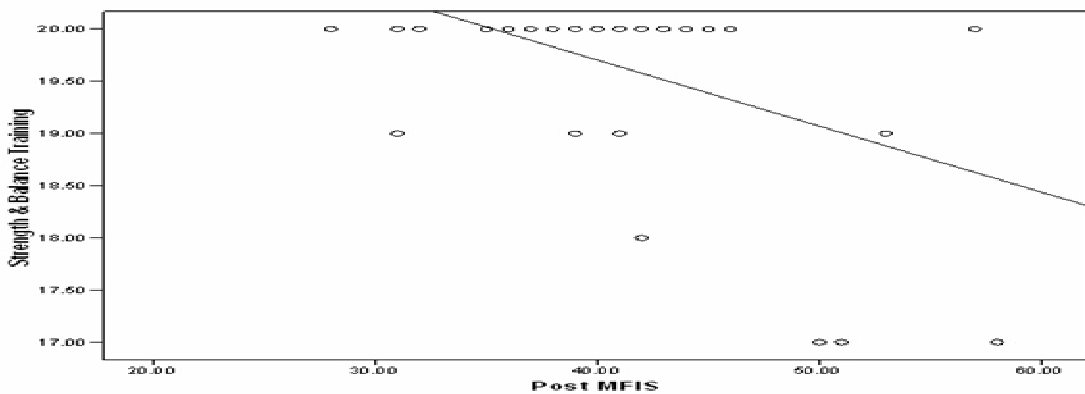


Figure 4: The correlation between the performance of strength and balance training & modified fatigue impact scale of the study group

5. Discussion

Multiple sclerosis (MS) is one of the most common autoimmune diseases of the central nervous system (CNS) occurring in young adult

with many and different symptoms. One of the most prominent and disabling symptoms of MS is fatigue which occurs in 75-95% of patients with multiple sclerosis (Adamopoulou et al., 2019).

The nurse should consider a full spectrum of effective fatigue management interventions, from exercises such as strength and balance training to educational strategies in conjunction with medication. Therefore, the aim of this study was to evaluate strength and balance training on fatigue in patients with multiple sclerosis

The results of the present study revealed that approximately two-thirds of control and study group were at second decade of age. This finding was in line with **Zakaria et al., (2016)** who found that the mean age of MS patients was in the same decade. This may be due to the younger adult are more affected with MS than older age (**Govindarajan, Liu, Parra Corral, Bangiyev, Krupp, Charvet& Duong, 2021**). However, these findings contradict with the results of **Braakhuis et al., (2019)** who reported that the mean age of MS patients was in the fourth decade of age.

Concerning gender, the present study showed that less than three quarter of the study group and more than two third of control group were females. These results were similar with **Ben-Zacharia, (2020)** who told that majority of MS patients were females. In contrast, these results disagree with **Borji, Taghinejad & Salimi, (2018)** Who stated majority of the MS participants in study and control group were male.

Regarding educational level, the current study showed that approximately mostly of control and study group have higher education. This result was near to the result of **Abdullah, Badr & Manee, (2018)** who found that a majority of the MS participants have higher education. But this result was not consistent with **Bjørnevik et al., (2016)** who stated that the higher level of education was associated with decreased MS risk.

Concerning the occupation, the findings of the present study noticed that majority of the studied participants in both groups were not working. This finding agrees with **Matesic& Marcinko, (2020)** who said that majority of MS patients don't work. Although this finding disagrees with **Shahrbanian, Duquette& Mayo, (2018)** who said that majority of the MS patients were employee.

Concerning fatigue, the results of this study revealed that, there is a significant reduction in fatigue among study group who practiced regular exercise in the form of strength and balance training than control group who didn't practice it. These results were in an agreement with **Kasch, (2021)** who noticed that there was an average reduction in fatigue among MS patients who

performed the training. Also, this finding came in accordance with **Novotna et al., (2019)** who noted that 12 weeks of progressive resistance circuit training were associated with improvement in fatigue complaint. This improvement in fatigue may be due to the effective strength and balance training and adherence of the participants to the planned sessions of it.

From the researcher's point of view, one of the reasons for the success of strength and balance training in this study was the opportunity to implement the training in the winter season. It has been scientifically proven that overheating in the training rooms affects the response of MS patients to exercise, as it leads to excessive fatigue and makes them less able to complete the exercises. This fact supported by **Grover et al., (2017)** who stated that exercising in a cooler temperature is more effective than hooter and would prevent post-exercise perceived fatigue among MS patients.

But these results contradict with **Bahmani, Razazian, Farnia, Alikhani, Tatari& Brand, (2019)** who found that there was no change on fatigue complaint among MS patients after practicing exercise.

Regarding the subscales of modified fatigue impact scale (MFIS), the current study noticed that there was significant reduction in both physical and psychosocial subscales of MFIS mean while there was no significant difference in the cognitive subscale. These results were congruent with **Stroud& Minahan, (2009)** who reported that the Physical and Psychosocial components, and overall score of the MFIS were significantly improved in patients who practiced exercise than who don't while there was no improvement in the cognitive component. This came in accordance with **MS DeLuca, Chiaravalloti & Sandroff, (2020)** who proved that exercise training is associated with beneficial outcomes in all domains except cognition in MS. This may be due to the greater burdens of MS disease on the cognitive function which is persistent and progressive including learning and memory and attention (**Mollison et al., 2017**).

As regarding the correlation between strength and balance training (SBT) and modified fatigue impact scale (MFIS), the results of the present study showed that there is a significant negative correlation between the performance of SBT and MFIS where it was found that increased physical activity in patients with multiple sclerosis led to a decrease in their fatigue scale. This finding was consistent with **Rzepka Toś, Boron, Gibas & Krzystanek, (2020)** who noted that higher scores

of fatigues in FSS and MFIS were inversely correlated with the intensity of physical activity and MS patients with lower physical activity have a higher severity of fatigue, which negatively affects cognitive, psychosocial, and physical functioning.

This finding also supported by Mayo, Miksche, Attwell-Pope & Gawryluk, (2019) who found that there was a significant negative correlation between physical activity and fatigue. In contrast, these findings disagree with Selukar, (2015) who stated that there was not any correlation between fatigue and physical activity. And the correlation between them remains unclear.

From the researcher point of view, this finding may be due to increased level of disability among those participants, as where disable patients have limitations in practicing any exercise. In addition to fear of performing any effort to avoid increased the perception of fatigue which lead to deconditioning and the last one increase fatigue perception. The reason for the inverse correlation between exercise and fatigue in the current study was that the study participants had a minimal disability and their commitment to the strength and balance training which began gradually to avoid their feeling of fatigue as a result of exercise.

6. Conclusion: This study indicates that strength and balance training is a simple nonpharmacological and cost-effective intervention. It is Effective in reducing fatigue among patients with multiple sclerosis

7. Recommendations: Based upon findings of the present study, the following suggestions can be recommended:

- Neurology Units should support the nonpharmacological intervention like strength and balance training in managing fatigue in the routine care for MS patients.
- Arabic, colored booklet about the practice of strength and balance training should be available for all MS patients who have fatigue

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9. Reference:

- Abdullah, E. J., Badr, H. E., & Manee, F. (2018). MS people's performance and

satisfaction with daily occupations: implications for occupational therapy. *OTJR: occupation, participation and health*, 38(1), 28-37.

- Adamopoulou, F., Alikari, V., Zyga, S., Tsironi, M., Tzavella, F., Giannakopoulou, N., & Theofilou, P. (2019). The effect of fatigue and pain self-efficacy on health-related quality of life among patients with multiple sclerosis. *Materia socio-medica*, 31(1), 40.
- Al Abbad, B. K. N. (2020). Self-management support for people with Multiple Sclerosis (Doctoral dissertation, Keele University).
- Al-Abdullah, M., & Siddiqui, A. (2018). Demographic and disease characteristics of multiple sclerosis in the Southwest Region of Saudi Arabia. *Neurosciences (Riyadh, Saudi Arabia)*, 23(4), 320.
- Amiri, M. (2021). Multiple sclerosis in Iran: An epidemiological update with focus on air pollution debate. *Journal of Clinical and Translational Research*, 7(1), 49.
- Bahmani, D. S., Razazian, N., Farnia, V., Alikhani, M., Tatari, F., & Brand, S. (2019). Compared to an active control condition, in persons with multiple sclerosis two different types of exercise training improved sleep and depression, but not fatigue, paresthesia, and intolerance of uncertainty. *Multiple sclerosis and related disorders*, 36, 101356.
- Ben-Zacharia, A. B. (2020). The Association Between Body Mass Index, Brain Volume and Cognitive Function in Adult Patients with Relapsing-Remitting Multiple Sclerosis (Doctoral dissertation, New York University).
- Børnevik, K., Riise, T., Cortese, M., Holmøy, T., Kampman, M. T., Magalhaes, S., ... & Pugliatti, M. (2016). Level of education and multiple sclerosis risk after adjustment for known risk factors: The EnvIMS study. *Multiple Sclerosis Journal*, 22(1), 104-111.
- Borji, M., Taghinejad, H., & Salimi, A. H. (2018). The effect of motivational interviewing on fatigue in patients with multiple sclerosis. *Archives of Neuroscience*, 5(3).
- Braakhuis, H. E. M., Berger, M. A. M., Van Der Stok, G. A., Van Meeteren, J., De Groot, V., Beckerman, H., & Bussmann, J. B. (2019). Three distinct physical behavior types in fatigued patients with multiple

- sclerosis. *Journal of neuroengineering and rehabilitation*, 16(1), 1-9.
- Callesen, J., Cattaneo, D., Brincks, J., & Dalgas, U. (2018). How does strength training and balance training affect gait and fatigue in patients with Multiple Sclerosis? A study protocol of a randomized controlled trial. *Neuro Rehabilitation*, 42(2), 131-142.
 - DeLuca, J., Chiaravalloti, N. D., & Sandroff, B. M. (2020). Treatment and management of cognitive dysfunction in patients with multiple sclerosis. *Nature Reviews Neurology*, 16(6), 319-332.
 - El-Tallawy, H. N., Farghaly, W. M., Badry, R., Metwally, N. A., Shehata, G. A., Rageh, T. A., ... & Kandil, M. R. (2016). Prevalence of multiple sclerosis in Al Quseir city, Red Sea governorate, Egypt. *Neuropsychiatric disease and treatment*, 12, 155.
 - Fisk, J., Ritvo, P., & Archibald. (1994). Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clinical Infectious Diseases*, 18(Supplement_1), S79-S83.
 - Govindarajan, S. T., Liu, Y., Parra Corral, M. A., Bangiyev, L., Krupp, L., Charvet, L., & Duong, T. Q. (2021). White matter correlates of slowed information processing speed in unimpaired multiple sclerosis patients with young age onset. *Brain Imaging and Behavior*, 15(3), 1460-1468.
 - Grover, G., Ploughman, M., Philpott, D. T., Kelly, L. P., Devasahayam, A. J., Wadden, K., ... & Button, D. C. (2017). Environmental temperature and exercise modality independently impact central and muscle fatigue among people with multiple sclerosis. *Multiple Sclerosis Journal—Experimental, Translational and Clinical*, 3(4), 2055217317747625.
 - Guillamó, E., Cobo-Calvo, Á., Oviedo, G. R., Travier, N., Álamo, J., Niño-Mendez, O. A., ... & Javierre, C. (2018). Feasibility and effects of structured physical exercise interventions in adults with relapsing-remitting multiple sclerosis: a pilot study. *Journal of sports science & medicine*, 17(3), 426.
 - Kasch, S. (2021). Improvements in Timing Variables for the Timed Up and Go and Its Subphases Following A Progressive Resistance Training Program.
 - Kratz, A. L., Atalla, M., Whibley, D., Myles, A., Thurston, T., & Fritz, N. E. (2020). Calling out MS fatigue: feasibility and preliminary effects of a pilot randomized telephone-delivered exercise intervention for multiple sclerosis fatigue. *Journal of Neurologic Physical Therapy*, 44(1), 23-31.
 - Matesic, I., & Marcinko, I. (2020). Identifying the relevant determinants of MS related fatigue: The role of the clinical indicators of disease and personality. *Multiple sclerosis and related disorders*, 42, 102054.
 - Mäurer, M., Schuh, K., Seibert, S., Baier, M., Hentschke, C., Streber, R., ... & Pfeifer, K. (2018). A randomized study to evaluate the effect of exercise on fatigue in people with relapsing–remitting multiple sclerosis treated with fingolimod. *Multiple Sclerosis Journal—Experimental, Translational and Clinical*, 4(1), 2055217318756688.
 - Miller, A. (Ed.). (2017). *Handbook of relapsing-remitting multiple sclerosis*. Springer.2
 - Miller, P., & Soundy, A. (2017). The pharmacological and non-pharmacological interventions for the management of fatigue related multiple sclerosis. *Journal of the neurological sciences*, 381, 41-54.
 - Moghaddam, V. K., Dickerson, A. S., Bazrafshan, E., Seyedhasani, S. N., Najafi, F., Hadei, M., ... & Sarmadi, M. (2021). Socioeconomic determinants of global distribution of multiple sclerosis: an ecological investigation based on Global Burden of Disease data. *BMC neurology*, 21(1), 1-11.
 - Mollison, D., Sellar, R., Bastin, M., Mollison, D., Chandran, S., Wardlaw, J., & Connick, P. (2017). The clinico-radiological paradox of cognitive function and MRI burden of white matter lesions in people with multiple sclerosis: A systematic review and meta-analysis. *PloS one*, 12(5), e0177727.
 - Novotna, K., Sucha, L., Kalincik, T., Reznicek, P., Sobisek, L., Hoskovcova, M., & Kubala Havrdova, E. (2019). Circuit Training Can Have Positive Impact on Muscle Strength, Balance, Depression and Fatigue in Multiple Sclerosis Patients: A Randomized Controlled Study. *United Journal of Physical Medicine & Rehabilitation*, 1(1), 1-8.
 - Penner, I. K., McDougall, F., Brown, T. M., Slota, C., Doward, L., Julian, L., ... & Miller, D. (2020). Exploring the impact of fatigue in progressive multiple sclerosis: a mixed-

- methods analysis. *Multiple Sclerosis and Related Disorders*, 43, 102207.
- Sands, W., Wurth, J., & Hewitt, J. (2012). Basics of strength and conditioning manual. *The National Strength and Conditioning Association's* (NSCA).
 - Seguin, R., Epping, J., Buchner, D., Bloch, R., & Nelson, M. (2002). Growing stronger; strength training for older adults.
 - Shahrbanian, S., Duquette, P., & Mayo, N. E. (2018). Impairment, disability and fatigue in multiple sclerosis. *Caspian journal of internal medicine*, 9(3), 244.
 - Stroud, N. M., & Minahan, C. L. (2009). The impact of regular physical activity on fatigue, depression and quality of life in persons with multiple sclerosis. *Health and quality of life outcomes*, 7(1), 1-10.
 - Tramonti, C., Di Martino, S., Foglia, A., & Chisari, C. (2020). Perceived fatigue, lower limb muscle force and performance fatigability after a rehabilitation program in Multiple Sclerosis. *European Journal of Translational Myology*, 30(4).
 - Yamout, B. I., Assaad, W., Tamim, H., Mrabet, S., & Goueider, R. (2020). Epidemiology and phenotypes of multiple sclerosis in the Middle East North Africa (MENA) region. *Multiple Sclerosis Journal-Experimental, Translational and Clinical*, 6(1), 2055217319841881.
 - Zakaria, M., Zamzam, D. A., Hafeez, M. A. A., Swelam, M. S., Khater, S. S., Fahmy, M. F., ... & Gadallah, M. (2016). Clinical characteristics of patients with multiple sclerosis enrolled in a new registry in Egypt. *Multiple sclerosis and related disorders*, 10, 30-35.
 - Zeydan, B., Atkinson, E. J., Weis, D. M., Smith, C. Y., Gazzuola Rocca, L., Rocca, W. A., ... & Kantarci, O. H. (2020). Reproductive history and progressive multiple sclerosis risk in women. *Brain Communications*, 2(2), fcaa185.