The Impact of COVID-19 Pandemic on Physical Activity and Health Measures in Patients With Multiple Sclerosis

Mahan Shafie[1], Abdorreza Naser Moghadasi[2], Sina Kazemian[3,4], Mahsa Mayeli[1], Narges Shakerian[5,6], Mohaddeseh Azadvari[7,8]

[1] *School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Multiple Sclerosis Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran*

[3] *Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran*

[4] *Cardiac Primary Prevention Research Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran*

[5] *Rehabilitation Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

[6] *Department of Physiotherapy, School of Rehabilitation Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

[7] *Department of Physical Medicine and Rehabilitation, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran*

[8] *Urology Research Centre, Tehran University of Medical Sciences, Tehran, Iran*

Received: 19 Oct. 2022; Accepted: 01 Jun. 2023

Abstract- The COVID-19 pandemic restrictions may have significant implications for patients with multiple sclerosis (MS). The objective of this study is to explore the impact of the pandemic on physical activity levels and health outcomes among MS patients, as well as to examine potential associations between these factors. In this cross-sectional study, 197 patients with confirmed MS diagnosis were included. Physical activity and health status were assessed using international physical activity questionnaire-long form (IPAQ-LF) and short form 36 health survey questionnaire (SF-36) during the period of restrictions. The relationship between clinical characteristics, physical activity levels and health status parameters were examined. A total of 45 participants (22.8%) scored low, 73 (37.1%) scored moderate, and 79 (49.1%) achieved a high level of physical activity during the COVID-19 pandemic. We observed no significant association between total physical activity and any domains of SF-36 health status, except for pain. However, correlations were found between IPAQ and SF-36 domains. Specifically, walking showed positive correlations with physical functioning, physical limitation, general health, and physical component summary score. Vigorous activity demonstrated a negative correlation with social functioning, while moderate activity displayed a positive correlation with energy levels. Despite the challenges of home isolation and quarantine, most of our participants managed to achieve a moderate to high level of physical activity, while their overall health status was found to be moderate. Additionally, significant correlations were identified between the domains of health status and different types of physical activity, particularly walking. Further studies are warranted to optimize the care and support provided to patients with MS.

Acta Med Iran 2023;61(7):399-407.

Keywords: COVID-19; Health status; International physical activity questionnaire; Multiple sclerosis; Physical activity; Short form 36 health survey questionnaire

Introduction

The global impact of the coronavirus disease 2019 (COVID-19) has been a significant concern, as countries continuously encountering the challenge posed by emerging variants (1). As a result, in response to the COVID-19 pandemic, numerous countries worldwide implemented rigorous preventive measures, including the implementation of national lockdowns and the imposition of social restrictions (2,3). Several studies have

Corresponding Author: M. Azadvari
Department of Physical Medicine and Rehabilitation, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 2163120000, E-mail address: drazadvari@yahoo.com

demonstrated that the implementation of restrictions and self-isolation measures has led to a significant increase in sedentary behavior and a decline in physical activity participation (4). This shift in lifestyle was particularly observed among individuals with chronic disorders, who generally exhibit lower levels of physical activity (5-7). Notably, a systematic review and meta-analysis examining the impact of the COVID-19 pandemic on physical activity among individuals with chronic diseases revealed a remarkable decline in activity levels compared to pre-pandemic levels (8).

Multiple sclerosis (MS) is a chronic and autoimmune neurological disease that causes various physical and psychosocial problems (9). Patients with MS often experience limitations in physical activity due to factors such as impaired mobility, fatigue, fear of falling, and walking difficulties. Consequently, their overall level of physical activity tends to be lower compared to that of healthy individuals. It has been shown that the intensity and duration of physical activity tend to reduce with increasing disability levels measured by expanded disability status scale (EDSS) in patients with MS (10). However, research has indicated that supervised and individualized physical activity programs can have a positive impact on the health status of MS patients (11,12). Although some studies showed that MS is not a specific risk factor for COVID-19 infection, the sedentary lifestyle seemed to be extended in this population during home isolation and restrictions due to COVID-19 pandemic (11,13,14). In this regard, a number of studies have reported a decrease in physical activity levels among this group of patients during the pandemic (15). However, it is worth noting that some studies have found no specific change (6), which adds a level of controversy to the topic.

Understanding the impact of these restrictions on physical activity levels and the potential consequences for individuals with chronic neurological disorders is of utmost importance. Developing strategies to promote and facilitate physical activity within the constraints of these restrictions can help mitigate the adverse effects on the overall health and well-being of this vulnerable population. Hence, in this study, we evaluated the level of physical activity of people with MS during the pandemic by applying international physical activity questionaries (IPAQ) and the health status based on the short form 36 health survey questionnaire (SF-36). Additionally, we explored the potential association between physical activity levels and health status parameters within this population.

Materials and Methods

Study design and participants

In this cross-sectional study, we included 197 patients aged between 18 to 65 years old with a confirmed diagnosis of MS according to the McDonald 2017 criteria for MS diagnosis (16) during March and April 2021. We have enrolled 197 patients through a nonprobabilistic convenience sampling. All participants were selected from the multiple sclerosis research center in Sina Hospital, a referral center for MS in Tehran, Iran, affiliated with Tehran University of Medical Sciences, Tehran, Iran. The long format of the Persian-validated IPAQ (17) was used to evaluate the physical activity level of participants. To evaluate the health status, we used the Persian-validated version of the SF-36 questionnaire (18). The data for the study was gathered online by using Google forms. All participants were requested to participate using e-mail or WhatsApp messenger before sending the questionnaires. Data were collected by trained independent medical staff.

Questionnaires

The IPAQ questionnaire investigates physical activity in five separate parts: work, transportation, domestic/garden, leisure time, and sitting. There are specific questions in each domain to evaluate vigorous-intensity, moderate-intensity, and walking activities. After weighting different activities by their energy requirement, we reported collected data for each type of activity in MET-minutes/week. An overall total physical activity MET-minutes/week score was computed by adding all vigorous, moderate, and walking scores. Data cleaning and inclusion/exclusion criteria were defined based on the latest IPAQ guidelines (19).

We used the SF-36 questionnaire to evaluate the health status of participants. There are 36 multiple choice questions that score on a scale from 0 to 100. All questions are categorized into eight scales: physical functioning (10 items), role limitations due to physical health (4 items), role limitations due to emotional problems (3 items), energy/ fatigue (4 items), emotional well-being (5 items), social functioning (2 items), pain (2 items), and general health (5 items) based on the RAND health care guidelines. The Physical Component Summary (PCS) and the Mental Component Summary (MCS) scores from the SF-36 questionnaire were calculated using predefined scoring algorithms. These scores are derived by weighting and summing responses to specific sets of questions within the SF-36: the PCS score primarily reflects responses to questions pertaining

to physical functioning, role physical, bodily pain, and general health, while the MCS score predominantly reflects responses to questions related to vitality, social functioning, role emotional, and mental health (20).

Ethical considerations

The protocol of this study corresponded to the 2013 Helsinki declaration and was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.IKHC.REC.1400.131). Written informed consent was obtained from all participants before inclusion in the study. The people participating in the study were considered anonymous and all data were registered confidentially with no personal information.

Statistical analysis

We evaluated and scored each questionnaire based on published protocol. Categorical variables are presented as numbers (percentages), and continuous variables are demonstrated as mean±standard deviation and median. To compare physical activity and health status among demographic groups, we utilized the Mann-Whitney U and Kruskal-Wallis tests. Furthermore, we employed linear regression analysis to evaluate the association of numerical baseline variables with physical activity and health status. Given that the assessed parameters were non-parametric, we employed Spearman's Rho test to assess the correlation between physical activity and health status. All statistical analyses were performed using IBM Corp, released 2016 IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY: IBM Corp. $P \leq 0.05$ was considered statistically significant.

Results

A total of 197 patients with MS participated in this study. Baseline characteristics of the studied population are presented in Table 1. The age range of the participants in this study was between 15 and 65 years, with a mean age of 36.8±9.4 years. The duration of MS diagnosis varied among the participants, with a mean of 8.2±6.8 years (range: 1-49 years) and 85 (43.1%) individuals had a diagnosis duration of ≥8 years. In terms of the clinical type of the disease, the majority of patients (70.1%) had relapsing-remitting MS, followed by secondary progressive MS (25.4%), neuromyelitis optica (2.5%), and primary progressive MS (2.0%). The median EDSS score was 2.5, with an interquartile range of 1.5 to 4.5, while 92 (46.7%) patients had EDSS score ≥3.

Table 1. Baseline characteristics of the study population

Characteristic*		Total (n=197)
Age		36.8±9.4
Sex	**Female**	154 (78.2%)
	Male	43 (21.8%)
Marital status	**Single**	85 (43.1%)
	Married	112 (56.9%)
	Divorced	0
Education	**Some high school**	6 (3.0%)
	Post-secondary certificate or diploma	59 (29.9%)
	Bachelor's degree	84 (42.6%)
	Master's degree	40 (20.3%)
	Professional or doctorate	8 (4.1%)
Occupation status	**Employed**	77 (39.1%)
	Unemployed	120 (60.9%)
Type of multiple sclerosis	**Primary Progressive**	4 (2.0%)
	Secondary Progressive	50 (25.4%)
	Relapsing Remittent	138 (70.1%)
	Neuromyelitis Optica	5 (2.5%)
Years since diagnoses		8.2±6.8
Years since diagnoses ≥8 years		85 (43.1%)
EDSS		2.5 [1.5-4.5]
EDSS ≥3		92 (46.7%)

* Data are presented as mean±standard deviation, number (%), and median [Interquartile Range].
EDSS; Expanded Disability Status Scale

The findings of the physical activity and health status assessments are provided in Table 2. According to the categorization of patients using the IPAQ protocol, 45 participants (22.8%) scored low, 73 (37.1%) scored moderate, and 79 (49.1%) achieved a high level of physical activity during the COVID-19 pandemic.

The relationship between clinical characteristics and physical activity and health status is outlined in Table 3. Age did not show a significant correlation with IPAQ domains; however, it was found to be associated with

physical functioning, physical limitations, pain, and general health in the SF-36 health status assessment. Marital status had a notable impact on various domains of physical activity and health status. Married patients exhibited significantly higher rates of total physical activity and total moderate physical activity (*P*=0.046 and *P*<0.001, respectively), while also having significantly lower scores for total walking and sitting (*P*=0.004 and *P*=0.008, respectively). Moreover, married patients demonstrated significantly lower scores in PCS score, physical functioning, physical limitations, and pain within the health status domains. In the multivariable regression analysis, after adjusting for age and education level as potential confounders, marital status remained an independent predictor of moderate activity (*P*:0.030), walking (*P*:0.032), and sitting (*P*:0.009) according to IPAQ scores.

Table 2. Descriptive statistics of physical activity (MET-minutes/week) and health status of study populations

Questionnaire	Scale	Items	Minimum	Maximum	Mean±SD	Median
IPAQ	Vigorous activity	2	0	20160	1175.8±2610.7	80.0
	Moderate activity	3	0	18600	2961.9±4153.4	1000.0
	Walk	3	0	24024	829.3±2022.4	297.0
	Total physical activity	8	0	42084	4967.0±5677.0	2922.0
	Sitting time	1	30	750	382.1±165.3	390.0
SF-36	Physical functioning	10	0	1000	716.2±281.9	800.0
	Role limitations due to physical health	4	0	400	179.7±157.8	100.0
	Role limitations due to emotional problems	3	0	300	139.1±124.7	100.0
	Energy/fatigue	4	0	400	189.3±73.2	180.0
	Emotional well being	5	0	480	276.2±100.9	280.0
	Social functioning	2	0	200	127.5±47.5	125.0
	Pain	2	0	200	130.0±51.3	130.0
	General health	5	0	500	268.1±130.5	250.0
Physical component summary score			170	2100	1294.1±525.7	1340.0
Mental component summary score			65	1380	732.2±285.6	690.0

MET: Metabolic Equivalent of Task, EDSS; Expanded Disability Status Scale, SD: Standard Deviation

Table 3. Association between baseline characteristics and physical activity and health status parameters.

		Baseline characteristics*									
		Age	Sex	Marital status	Education	Occupation status	Type of multiple sclerosis	MS Duration	MS Duration ≥8 years	EDSS	EDSS ≥3
IPAQ	Vigorous activity	NS	NS	NS	NS	NS	NS	NS	0.044	NS	NS
	Moderate activity	NS	0.016	<0.001	NS	NS	NS	NS	NS	NS	NS
	Walk	NS	NS	0.004	NS	NS	NS	NS	NS	NS	NS
	Total physical activity	NS	NS	0.046	NS	NS	NS	NS	NS	NS	NS
	Sitting	NS	NS	0.008	NS	NS	NS	NS	NS	NS	NS
SF-36	Physical functioning	<0.001	NS	0.003	0.027	NS	<0.001	<0.001	<0.001	<0.001	<0.001
	Role limitations due to physical health	0.001	NS	0.003	0.021	NS	<0.001	0.003	0.023	<0.001	<0.001
	Role limitations due to emotional problems	NS	NS	NS	NS	NS	0.002	NS	NS	0.011	0.018
	Energy/ fatigue	NS	NS	NS	NS	NS	0.014	NS	NS	NS	NS
	Emotional well being	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	Social functioning	NS	NS	NS	NS	NS	0.005	NS	NS	0.002	0.003
	Pain	0.030	NS	0.009	0.022	NS	0.001	0.007	NS	<0.001	0.002
	General health	0.001	NS	NS	NS	NS	<0.001	0.001	0.003	<0.001	<0.001
PCS score		<0.001	NS	0.002	0.024	NS	<0.001	<0.001	<0.001	<0.001	<0.001
MCS score		NS	NS	NS	NS	NS	0.005	NS	NS	0.029	0.047

* Numerical variables were compared using linear regression analysis, while categorical variables were compared using the Mann-Whitney U and Kruskal-Wallis tests. All significant *P* are presented

EDSS; Expanded Disability Status Scale, MCS: mental component summary, NS: Not Significant *P*, PCS: physical component summary

Although there was no significant association between MS type and physical activity scores, associations were observed between MS type and SF-36 domains, including physical functioning, role limitations due to physical activity and emotional problems, energy/fatigue, social functioning, pain, and general health, and both PCS and MCS scores. The duration of MS did not show a relationship with IPAQ domains; however, correlations were noted between disease duration and physical functioning, role limitations due to physical activity, pain, and general health within the SF-36 domains.

While EDSS did not exhibit correlations with any IPAQ domains, it showed associations with physical functioning, role limitations due to physical activity and emotional problems, social functioning, pain, and general health within the health status assessment.

The correlation between physical activity and health status measures is presented in Table 4. Our findings revealed that total physical activity did not show a significant association with any domains of SF-36 health status, except for the pain domain. Furthermore, the following correlations were identified between IPAQ and SF-36 domains. Walking demonstrated a positive correlation with physical functioning, physical limitation, and general health, and PCS score. Vigorous activity exhibited a negative correlation with social functioning, while moderate activity displayed a positive correlation with energy levels.

Table 4. Spearman's Rho correlations of physical activity and health status

Questionnaires		IPAQ				
		Vigorous activity	Moderate activity	Walk	Total physical activity	Sitting
SF-36	Physical functioning	-0.064	0.083	0.187**	0.066	-0.073
	Role limitations due to physical health	-0.110	-0.026	0.159*	-0.080	0.004
	Role limitations due to emotional problems	-0.031	0.044	0.073	-0.011	-0.018
	Energy/fatigue	-0.054	0.154*	0.082	0.124	-0.032
	Emotional well being	-0.041	0.123	0.074	0.076	-0.076
	Social functioning	-0.190**	0.092	0.006	-0.024	-0.017
	Pain	-0.074	-0.101	0.075	-0.160*	0.017
	General health	-0.088	0.122	0.198**	0.058	-0.124
Physical component summary score		-0.079	0.065	0.214**	0.023	-0.068
Mental component summary score		-0.091	0.112	0.069	0.039	-0.028

* Correlations with two-tailed $P<0.05$
** Correlations with two-tailed $P<0.01$

Discussion

The aim of this study was to investigate the levels of physical activity and health status using the IPAQ and SF-36 questionnaires, as well as explore potential associations between these variables in patients with MS during the COVID-19 pandemic. The demographic characteristics and clinical profiles of our study population were consistent with previous studies examining MS during the COVID-19 pandemic (21). Our findings revealed that 77.2% of the participants reported moderate to high levels of physical activity. In comparison to a study conducted in Spain that assessed physical activity in MS patients during the COVID-19 pandemic using the IPAQ, our participants had higher scores for total physical activity, vigorous activity, and moderate activity. However, they reported lower levels of activity in the walking domain (6). Moreover, our data revealed elevated physical activity levels in most of the domains compared to other studies (13,15). In terms of sitting time during a week, our participants had a slightly lower mean time spent sitting compared to the study conducted by Moti *et al*., which examined this value among MS patients in the USA (22). Similarly, our findings showed that the sitting time of our sample was lower compared to other relevant studies (6,13,23). In a recent study conducted by Ozkeskin *et al*., a comparison was made between MS patients with and without COVID-19 in terms of fatigue, sleep quality, physical activity, quality of life, and psychological status. The findings indicated that COVID-19 had a negative impact on the physical activity levels of MS patients and also

influenced fear parameters related to the coronavirus. Specifically, the results revealed that MS patients who tested positive for COVID-19 had significantly lower IPAQ total scores compared to COVID-19 positive patients without MS (13).

Despite the lockdown and social restrictions due to the pandemic, these data specified a higher level of physical activity among Iranian MS patients during this period. It should be considered that this study was conducted on 197 MS patients in March and April 2021 when strict restrictions were imposed to confront a new wave of COVID-19 outbreak. Moderate and high degree of physical activity despite of these strict and obligatory restrictions compared to previous studies might suggest the possible role of desensitization. However, further works are required to illustrate better, the possible correlation between time passing and the physical activity during a pandemic. In addition, participants in our study displayed a comparatively younger age distribution and lower disability levels when compared to similar investigations. Moreover, we noted a relatively elevated proportion of employed individuals in our study compared to other studies (21,24). These observations suggest that higher levels of disability could potentially contribute to unemployment, indirectly impacting physical activity levels (25,26). Interestingly, we found that higher levels of physical activity were observed specifically in the work and transport domains, with similar trends observed in the overall measure of total physical activity. Therefore, higher levels of physical activity, despite pandemic conditions, may also be related to younger participants and a lower level of disability. It is important to acknowledge that over the past two decades, a significant body of evidence has consistently highlighted the positive impact of physical activity on various aspects of multiple sclerosis (MS). Notably, the dissemination of these findings through social media and health system networks has played a crucial role in raising awareness among patients. This widespread dissemination has motivated individuals with MS to prioritize and sustain their physical activity levels, even in challenging circumstances such as the extraordinary atmosphere created by the pandemic (27,28).

The utilization of SF-36 as a measure of health status offers the advantage of detecting various aspects of the disease beyond the natural clinical progression of the disease. This questionnaire can effectively highlight specific areas of health that may require particular attention. While a dedicated control group was not included in this study for a direct comparison of SF-36 health status, the scores obtained were consistent with previous studies involving a similar population (29).

Analyzing the physical activity and health status scores in relation to demographics and clinical characteristics yielded significant results. Our observations revealed a significant impact of marital status on total physical activity, moderate physical activity, walking, and sitting scores among our participants. Interestingly, a study examining the association between marital status and physical activity among American men and women found that single individuals expended less energy in overall physical activity, while engaging more in leisure-time activities (30). Although this study was conducted on a healthy population in non-COVID situations, results are equivalent and comparable to ours. We must emphasize that potential confounding factors associated with marital status and both IPAQ and SF-36 scores could include variables such as age, socioeconomic status, and education level. Age can influence both IPAQ and SF-36 scores, as younger individuals may be more physically active (leading to higher IPAQ scores) and have fewer health issues (thus, higher SF-36 scores), and age is often correlated with marital status. Socioeconomic status is another key confounder: individuals of higher status may have more resources and access to health-promoting activities and healthcare, contributing to higher IPAQ and SF-36 scores, while also being related to marital status. Education level is a further potential confounder, with more educated individuals likely having a better understanding of health benefits associated with physical activity and better health-seeking behaviors, which could influence both their IPAQ and SF-36 scores. Moreover, education level could influence marital status, as more educated individuals might marry later due to spending more years in education. In this study, after adjustment with age and education level, we found that marital status remained an independent predictor of moderate activity, walking, and sitting according to IPAQ scores. Besides, age was a major contributor to health status using linear regression analysis. Age was negatively correlated with physical functioning, physical limitation, pain, and general health, which was in line with previous studies (31).

Furthermore, we found that the type of MS was associated with nearly all SF-36 health status domains. This association can be attributed to the distinct clinical courses of different MS types. The more progressive course of MS, which is an unfavorable prognostic factor, was notably associated with lower scores in the assessment of health status. These findings are in the same line with previous studies. A study by Ford *et al*.,

evaluating health status and quality of life among MS patients concluded that patients with progressive disease courses experience greater levels of impairment and disability and lower scores of health status than other groups (32). Moreover, we identified correlations between the duration of MS disease and SF-36 domains. Typically, as the disease progresses over the years, symptoms tend to become permanent, which may influence the overall health status of individuals. Therefore, the duration of MS can also contribute to the assessment of health status (33). There was no association between EDSS and IPAQ physical activity scores while it was correlated with SF-36 physical functioning. Among our patients, the median of EDSS was 2.5 [1.5-4.5] which is relatively low. Since most of our patients had low EDSS, these observations remained consistent throughout the study.

In our final analysis, we explored the correlation between IPAQ scores and SF-36 domains. Notably, among the various physical activity scales, walking demonstrated the most significant influence on health status as determined by SF-36. Participants who achieved higher scores in walking demonstrated significantly improved general health and physical functioning. Additionally, they experienced fewer restrictions caused by physical health issues, and higher scores for the physical component summary. Another noteworthy finding was the significant negative correlation between the total score of physical activity and pain, which holds valuable implications for MS patients. These associations suggested that specific types and intensities of physical activity may have differential impacts on various aspects of health status, including pain, physical functioning, social functioning, and overall well-being. These results align with both clinical observations and theoretical studies, reinforcing the idea that physical activity can have a substantial impact on health status and psychological well-being in individuals with MS, even in unique circumstances such as the COVID-19 pandemic (11,12,34).

The current study had some limitations. First, it was an online and anonymous survey that accelerated the data gathering process and eliminated applying systematic samplings. Second, due to the cross-sectional design of the study and its inherent biases, some consideration must be taken before interpreting the results and analyses. Third, the studied population displayed a comparatively younger age distribution with lower disability levels, which could affect the results. Additionally, the COVID-19 pandemic had fluctuations over time. Hence, the time frame of the study might have an impact on the observations. Evaluating patients in different periods could be a valuable strategy for further studies with a longitudinal evaluation model to compare the results more comprehensively.

This study aimed to assess the level of physical activity and health status among MS patients in Iran during the COVID-19 pandemic. Despite the home isolation and quarantine, the majority of our participants obtained a high or moderate level of physical activity, and the overall health status was moderate among our patients. Age, education, and marital status were the remarkable demographic contributors regarding both physical activity and health status. Significant correlations were observed between the SF-36 health status domains and the type of physical activity, particularly walking. These findings have implications for the management of MS patients, particularly in the context of a pandemic. However, further research is needed to investigate the potential effects of physical activity on various aspects of MS, with a focus on improving quality of life and physical as well as socio-psychological well-being in these patients. Such studies would provide valuable insights for optimizing the care and support provided to individuals living with MS in unique circumstances such as the COVID-19 pandemic.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382:727-33.
2. Ciotti M, Ciccozzi M, Terrinoni A, Jiang WC, Wang CB, Bernardini S. The COVID-19 pandemic. Crit Rev Clin Lab Sci 2020;57:365-88.
3. Shafie M, Mayeli M, Hosseini H, Ashoorkhani M. Medical Sciences' Students Responses During the Late Phase of the COVID-19 Pandemic in Iran: A Comprehensive Investigation of the Risk Perception and Information Exposure. Acta Med Iran 2021;59:704-12.
4. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet 2020;395:912-20.
5. Kang C, Yang S, Yuan J, Xu L, Zhao X, Yang J. Patients with chronic illness urgently need integrated physical and psychological care during the COVID-19 outbreak. Asian J Psychiatr 2020;51:102081.
6. Reguera-García MM, Liébana-Presa C, Álvarez-Barrio L, Alves Gomes L, Fernández-Martínez E. Physical Activity, Resilience, Sense of Coherence and Coping in People with Multiple Sclerosis in the Situation Derived from COVID-

19. Int J Environ Res Public Health 2020;17:8202.
7. Ghasemi H, Kazemian S, Nejadghaderi SA, Shafie M. Takotsubo syndrome and COVID- 19: A systematic review. Health Sci Rep 2023;6:e972.
8. Pérez-Gisbert L, Torres-Sánchez I, Ortiz-Rubio A, Calvache-Mateo A, López-López L, Cabrera-Martos I, et al. Effects of the COVID-19 Pandemic on Physical Activity in Chronic Diseases: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2021;18:12278.
9. Oh J, Vidal-Jordana A, Montalban X. Multiple sclerosis: clinical aspects. Curr Opin Neurol 2018;31:752-9.
10. Pedullà L, Santoyo-Medina C, Novotna K, Moumdjian L, Smedal T, Arntzen EC, et al. Physical Activity in Multiple Sclerosis: Meeting the Guidelines at the Time of the COVID-19 Pandemic. J Neurol Phys Ther 2023;47:112-21.
11. Halabchi F, Alizadeh Z, Sahraian MA, Abolhasani M. Exercise prescription for patients with multiple sclerosis; potential benefits and practical recommendations. BMC Neurol 2017;17:185.
12. Sadeghi Bahmani D, Kesselring J, Papadimitriou M, Bansi J, Pühse U, Gerber M, et al. In Patients With Multiple Sclerosis, Both Objective and Subjective Sleep, Depression, Fatigue, and Paresthesia Improved After 3 Weeks of Regular Exercise. Front psychiatry 2019;10:265.
13. Özkeskin M, Özden F, Karaman B, Ekmekçi Ö, Yüceyar N. The comparison of fatigue, sleep quality, physical activity, quality of life, and psychological status in multiple sclerosis patients with or without COVID-19. Mult Scler Relat Disord 2021;55:103180.
14. Willis MD, Robertson NP. Multiple sclerosis and the risk of infection: considerations in the threat of the novel coronavirus, COVID-19/SARS-CoV-2. J Neurol 2020;267:1567-9.
15. Kalron A, Dolev M, Greenberg-Abrahami M, Menascu S, Frid L, Avrech-Shezifi S, et al. Physical activity behavior in people with multiple sclerosis during the COVID-19 pandemic in Israel: Results of an online survey. Mult Scler Relat Disord 2021;47:102603.
16. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018;17:162-73.
17. Vasheghani-Farahani A, Tahmasbi M, Asheri H, Ashraf H, Nedjat S, Kordi R. The Persian, last 7-day, long form of the International Physical Activity Questionnaire: translation and validation study. Asian J Sports Med 2011;2:106-16.
18. Montazeri A, Goshtasebi A, Vahdaninia M, Gandek B. The Short Form Health Survey (SF-36): translation and validation study of the Iranian version. Qual Life Res 2005;14:875-82.
19. Di Blasio A, Di Donato F, Mazzocco C. Guidelines for the data processing and analysis of the International Physical Activity Questionnaire; 2016.
20. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 health survey. Manual and interpretation guide. Boston: The Health Institute, New England Medical Center, 1993:10-6.
21. Louapre C, Collongues N, Stankoff B, Giannesini C, Papeix C, Bensa C, et al. Clinical Characteristics and Outcomes in Patients With Coronavirus Disease 2019 and Multiple Sclerosis. JAMA Neurol 2020;77:1079-88.
22. Motl RW, Sasaki JE, Cederberg KL, Jeng B. Validity of sitting time scores from the International Physical Activity Questionnaire-Short Form in multiple sclerosis. Rehabil Psychol 2019;64:463-8.
23. Hubbard EA, Motl RW, Manns PJ. The descriptive epidemiology of daily sitting time as a sedentary behavior in multiple sclerosis. Disabil Health J 2015;8:594-601.
24. Matysiak M, Siger M, Walczak A, Ciach A, Jonakowski M, Stasiołek M. The influence of COVID-19 pandemic lockdown on the physical activity of people with multiple sclerosis. The role of online training. Mult Scler Relat Disord 2022;63:103843 .
25. Employment and Community Living Issues for People with Multiple Sclerosis. Work 2015;52:723-4.
26. Krause JS, Dismuke-Greer CE, Jarnecke M, Li C, Reed KS, Rumrill P. Employment and Gainful Earnings Among Those With Multiple Sclerosis. Arch Phys Med Rehabil 2019;100:931-937.e1.
27. Dennett R, Gunn H, Freeman JA. Effectiveness of and User Experience With Web-Based Interventions in Increasing Physical Activity Levels in People With Multiple Sclerosis: A Systematic Review. Phys Ther 2018;98:679-90.
28. Flachenecker P, Bures AK, Gawlik A, Weiland AC, Kuld S, Gusowski K, et al. Efficacy of an Internet-Based Program to Promote Physical Activity and Exercise after Inpatient Rehabilitation in Persons with Multiple Sclerosis: A Randomized, Single-Blind, Controlled Study. Vol. 17, Int J Environ Res Public Health 2020;17:4544.
29. Riazi A, Hobart JC, Lamping DL, Fitzpatrick R, Freeman JA, Jenkinson C, et al. Using the SF-36 measure to compare the health impact of multiple sclerosis and Parkinson's disease with normal population health profiles. J Neurol Neurosurg Psychiatry 2003;74:710-4.
30. Sobal J, Hanson K. Marital status and physical activity in US adults. Int J Sociol Fam 2010;36:181-98.
31. Hopman WM, Towheed T, Anastassiades T, Tenenhouse A, Poliquin S, Berger C, et al. Canadian normative data for the SF-36 health survey. CMAJ 2000;163:265-71.

32. Ford HL, Gerry E, Johnson MH, Tennant A. Health status and quality of life of people with multiple sclerosis. Disabil Rehabil 2001;23:516-21.
33. Inojosa H, Proschmann U, Akgün K, Ziemssen T. A focus on secondary progressive multiple sclerosis (SPMS): challenges in diagnosis and definition. J Neurol 2021;268:1210-21.
34. Krüger T, Behrens JR, Grobelny A, Otte K, Mansow-Model S, Kayser B, et al. Subjective and objective assessment of physical activity in multiple sclerosis and their relation to health-related quality of life. BMC Neurol. 2017;17:10.