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## **Prevalence of long-COVID-19 syndrome among patients of MMC, Mardan: A descriptive study**

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**Abstract**---Introduction: The COVID-19 is an upper respiratory tract infection caused by the SARS-COV-19 virus. As of 2022, 504M cases have been reported globally with a substantial death toll of 6.2M. Although the conventional symptoms remain the same at the time of onset, the post-recovery symptoms vary. The cause of these diverse symptoms and their trigger is still under research. We have conducted this research in order to find out the post-infection sequelae among patients. Objectives: 1) To identify the post-COVID-19 manifestations; 2) To address the stigma associated with COVID-19 infection. 3) To determine the different environmental and social aspects of COVID-19 infection; 4) To find the effects of COVID-19 infection on overall quality of life. Methodology: A descriptive study was conducted among 50 COVID-19 recovered

patients in Mardan Medical complex. Data was collected from pathology laboratory, Mardan Medical complex. Data was analyzed using SPSS version 24.0 and was presented in the form of frequencies and percentages. Results: Among the most common symptoms, Fatigue presented with the most occurrence with over 70% presentation followed by generalized joint pain with over 50% presentation 6% of individuals experienced severe deforming pain and discomfort whereas 3.9% experienced some form of anxiety or depression 55.5% of individual have had been careful in telling people about them contracting the disease. Conclusion: Everyone being treated for COVID-19 and has recovered should undergo proper checkup and screening for any post COVID manifestations.

**Keywords**---COVID-19, COVID-19 pandemic, COVID infection, Post COVID Syndrome.

## **Introduction**

COVID-19 is an upper respiratory tract infection caused by corona virus, a heterogeneous virus that manifests itself with a wide spectrum of symptoms, from asymptomatic to life-threatening and fatal disease. Initial presentation included persistent non-productive cough, a fever spiking as high as 102-degree Fahrenheit and dyspnea in mild cases to severe acute respiratory syndrome and respiratory failure in critically ill patients requiring hospitalization. Most of the infected patients completely recovered after COVID-19 infection. However, a substantial proportion of patients who have been infected with SARS-CoV-2 continue to have symptoms long past the time that they recovered from the initial phases of COVID-19 disease. These patients are said to have the long-term effects of COVID-19 “Long-Haul COVID-19” or “Long-term COVID-19” Post infection and treatment. Review identified that the most frequent symptoms of long COVID are fatigue and dyspnoea (i.e. shortness of breath). Other less typical symptoms include cognitive and mental disorders, headache, myalgia, chest and joint pains, smell and taste dysfunctions, cough, hair loss, insomnia, wheezing, rhinorrhea, sputum, and cardiac and gastrointestinal issues. These symptoms may persist for up to six months and counting after hospital discharge or symptom onset. Less common symptoms of chills, flushing, ear pain, and visual impairments associated with long COVID have also been documented. With over 504 million confirmed COVID-19 cases globally, post-COVID-19 condition risks affecting millions of people worldwide, making it an urgent research priority.

## **Literature Review**

Long-COVID-19 syndrome (referred to as post-acute sequelae of COVID-19, PASC) is a series of symptoms that continue for multiple weeks or months following infection with the coronavirus SARS-CoV-2. These symptoms can have a major negative effect on the patient’s quality of life, and reduce their ability to engage in activities. According to a study carried out by Dhaka medical college regarding the persistence of COVID symptoms beyond the viral clearance, a total of 486 patients were screened and assessed for the eligibility, 400 patients were enrolled

in the study. In total, 42 patients were lost to follow-up and 3 patients died during follow-up, 355 patients were analyzed. In total, 46% patients developed post-COVID-19 symptoms, with post-viral fatigue being the most prevalent symptom in 70% cases. Fever was present in (75%) and cough (62%), headache (20%), and lethargy 23%. Among the recruited patients, 62% patients had mild disease, 26% patients exhibited moderate disease, and 11% patients had severe disease. Some (27%) patients also had associated comorbidities (1). Another study that included systemic review and meta-analysis of one year follow on the post COVID symptoms, they searched Pub med and E base for papers reporting at least one-year follow-up results of COVID-19 survivors. Eighteen papers that reported one-year follow-up data from 8591 COVID-19 survivors were included. It was found that Fatigue/weakness (28%) was the most prevalent symptom followed by joint pain (26%),depression (23%), anxiety (22%), dyspnea (18%), and insomnia (12%) were the most prevalent symptoms at one-year follow-up (2). A study by University of Zurich Switzerland was carried out to assess the prevalence of impaired health status and physical and mental health symptoms among individuals at least six months after COVID infection. A total of 442 individuals agreed to participate and 431 were included in the analysis of total of 431 (89%) participants were symptomatic, Most commonly reported symptoms were fatigue (64%), fever (63%) and cough (50%) (3). A study was conducted by the Lung Foundation Netherland to assess whether multiple relevant symptoms recover following the onset of symptoms in hospitalized and non hospitalised patients with COVID-19.Overall a total of 112 hospitalized and 2001 non hospitalized patients were analyzed, fatigue 95% among hospitalized and 87% among the non-hospitalized and dyspnea 90% among the hospitalized and 70% among the non-hospitalized were the most prevalent symptoms during the infection and at follow-up (4). A cohort study of 100 patients carried out at Mayo clinic. Among them 23% had pre-existing respiratory disease. 34% had pre-existing depression and 19% had hypertension. The most common symptoms with which patient presented post-COVID was fatigue 80%.49% were having dyspnea and 20 %presented with headache.34% reported to have difficulty in doing daily life activities (5). A total of 958 individuals who previously suffered from COVID 19 presented to outpatient clinic of Universal Health Coverage (UHC). Out of them 442 patients were followed up till second follow up visit at 4 months and 353 were followed till their third follow up visit at 7 months. Among the patients who were followed up till 4 months, 9.7% developed fatigue and 8.6% developed shortness of breath. After a median follow-up of 7 months, 13.6% developed shortness of breath and 14.7% developed fatigue (6). A study was carried out by public health care authorities in three German regions (Kiel, Berlin, Würzburg). According to study 61.5% patients presented with neurological symptoms. 57.1% developed fatigue and sleep disturbances occurred in 57.0% of patients (7). A study of total of 207 patients was conducted at a neurology outpatient clinic in Hospital Universitário Walter Cantidio – Universidad Federal do Ceará in the state of Ceará, northeast Brazil, in order to evaluate post COVID symptoms. Insomnia was reported by 42 patients (22.2%), and these patients also complained of fatigue and depression(8).

This was a prospective cohort study conducted at Sao Paolo Hospital in Milan, Italy. A total of 377 patients were enrolled in the study. The median time from symptom onset to virological clearance was 44 (37–53) days. A diagnosis of long

COVID syndrome was made in 260/377 (69%) patients. The most common reported symptoms were fatigue (149/377, 39.5%), exertional dyspnea (109/377, 28.9%), musculoskeletal pain (80/377, 21.2%). 71/377 (18.8%) individuals developed anxiety whereas 40/377 (10.6%) patients presented symptoms of depression (9). A longitudinal, prospective cohort telephone follow-up (FU) study conducted at Careggi University Hospital for COVID-19. The patients were enrolled through telephone longitudinal FU program aimed at monitoring symptoms after 1, 3, 6, 9 and 12 months from hospital discharge. The most common (prevalence >5%) symptoms at 12-month contact were fatigue, exertional dyspnea, insomnia, confusion, fear, depression, cough, and bowel symptoms. Furthermore, different symptoms had different trends over time while somatic symptoms all decreased from month 1 to 12, emotional symptoms like fear increased up to month 6 and only afterwards decreased (10). The study comprised of patients discharged from the 7th Naval Hospital in Gdansk, north of Poland, 79 participants were included. Among them 39 were males (49.4%) and 40 were females (50.6%). After discharge, 93.7% reported at least one persistent symptom at follow-up of three months and 81% at six months. The most common symptoms were fatigue or muscle weakness (60.76% and 47.04%) and Dyspnea 21.5%. The quality of life was also affected and reported in all domains of the EQ-5D-5L questionnaire but mainly in the pain/discomfort and anxiety dimensions (11). An online prospective survey was conducted by infectious disease physicians at the Kyungpook National University Hospital located in Daegu city. The most common symptom that lasted up to 12 months was concentration difficulty (22.4%), depression in (17.8%) participants and fatigue in (16.2%) of participants. Among the total participants (1.2%) had problems with self-care and (15.4%) were having difficulty in doing their daily activities (22.0%) responders complained of pain/discomfort (12).

### ***Rationale of the study:***

The rationale study is to understand and explore the post COVID-19 sequelae in localities like Mardan and see if the complications/symptoms coincide with those observed internationally. And if they don't, what could possibly be the cause behind this fluctuating spectrum of post-infection sequelae.

### ***Objective:***

1. To identify the different post-COVID-19 manifestations.
2. To address the stigma associated with COVID-19 infection.
3. To determine the different environmental and social aspects of COVID-19 infection.
4. To find the effects of COVID-19 infection on overall quality of life.

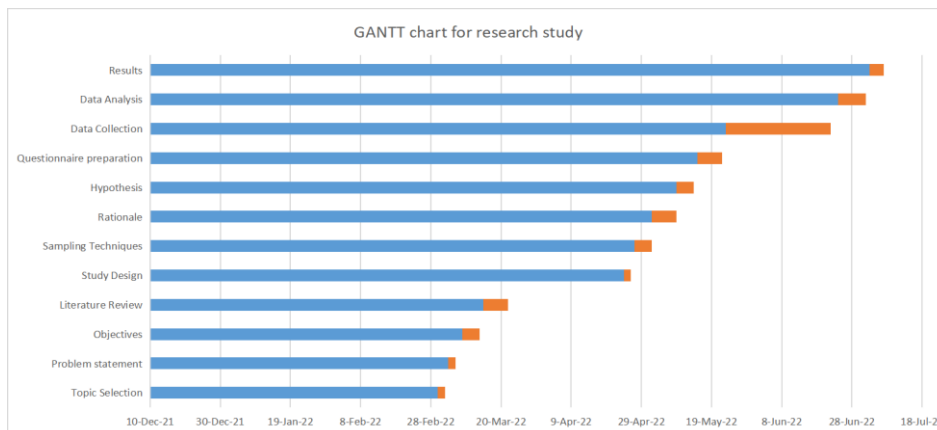
### **Materials and Methods Setting**

#### *2.1 setting:*

This study took place in MMC, Mardan. We collected data from out patients department in Mardan Medical Complex, Mardan. These OPD's included Pulmonology OPD and Medicine OPD. Furthermore, we also visited the respective wards.

## 2.2 Duration:

The time duration of this research span over a duration of 4 months.



## 2.3 Study design:

A descriptive, cross-sectional, questionnaire-based study was conducted among 50 COVID-19 recovered patients, whose information was obtained from OPDs/Wards of Pulmonology and Medicine departments of Mardan Medical Complex. The questionnaire consisted of four sections: sociodemographic data, post-COVID-19 manifestations, questions relating to the stigma, and the Quality of life (QoL) of the recovered COVID-19 patients.

For questions related to the stigma, we used ten questions from the stigma questionnaire by Dar et al., consisting of a total of 15 items (13). A 4-point Likert scale (1: strongly disagree, 2: disagree, 3: agree, 4: strongly agree) was used to score each of these questions (14). We used the EuroQol five-dimension five-level questionnaire to assess the QoL (15), while the modified BG Prasad Socioeconomic Classification updated for 2019 was employed to determine the socioeconomic status of the participants. Data was analyzed using SPSS version 24.0. Data was presented in the form of frequencies and percentages.

## 2.4 Sample Size:

We calculated the sample size through the OpenEpi.com sample size calculator. Using an anticipated frequency (p) of 90.89%, a confidence interval (CI) of 95%, and a 5% degree of precision, the estimated sample size was 128.

## 2.5 Sampling Technique:

We carried out a convenience sampling technique among 128 patients of MMC, Mardan.

### *2.6 Inclusion criteria:*

1. Participants >18 years of age or <60 years of age from either gender were selected.
2. Our study included COVID-19 survivors with a negative-reverse transcription-polymerase chain reaction (RT-PCR) in the last 20-90 days.

### *2.7 Exclusion criteria:*

1. Participants <18 years of age or >60 years of age from either gender were excluded.
2. We excluded any COVID-19 patient who has not tested positive and/or negative by an RT-PCR. Moreover, any COVID-19 survivors with a history of psychiatric illness were also excluded from the study.

### *2.8 Data Analysis:*

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 24.0. Descriptive statistics, such as frequencies, percentage were employed for the presentation of categorical variables. The chi-square test was used for categorical variables. A p-value of <0.05 was considered statistically significant.

## **Results**

The study included 128 individuals selected through convenience sampling. Out of 128 individuals, 68.8% were between the ages of 20-30 years, 22.7% between 30-50 years, 8.6% between 50-60 years. 63.3% of the individuals were unemployed whereas 36.7% were employed. 83.6% had no co-morbidities. Hypertension peaked in co-morbidities having a percentage of 5.5, diabetes mellitus 3.1%, multiple co-morbidities existing at the same time corresponded to 1.6%. 83.6% of the individuals were not taking any medications for their co-morbidities. Anti-hypertensives comprised 5.5% of the medications with anti-diabetes a close second having 3.1% intake. In Post-Covid Manifestations, Fatigue Post-treatment exhibited the most with 72.7% occurrence. Depression occurred in 32.8%. 53.1% of the individuals experienced shortness of breath. 33.6% of the individuals developed persistent cough. Joint pain was experienced by 53.9%. 43.8% of the individuals had complaints of trouble falling asleep. 46.9% of the individuals had headaches post-treatment. 29.7% of people did not take any medicines to relieve any of these conditions. Among the medicines that were taken, paracetamol was used the most with a percentage of 36.7 followed by Aspirin, Bromazepam, Montelukast, Naproxen, Antibiotics having an intake of 0.8%, 0.8%, 0.8%, 1.6%, 0.8% respectively. Multiple intakes corresponded to a total of 28.9%. 33.6% of the individuals agreed to have been hurt by people learning about their COVID infection. 18% individuals agreed to have lost friends because of COVID disease. 55.5% of the individuals agreed to have been careful in telling whoever about their disease. 22.7% of the individuals agreed to have felt guilty that they contracted the disease. 5.5% of the individuals agreed that having had COVID infection made them a bad person. Of the 128, 42.2% agreed that

people would often look down upon someone who has been a COVID patient. Regarding mobility, 68.8% of the individuals did not experience any problems walking whereas 4.7% of the individuals were unable to walk about post-treatment. 79.9% of the individuals had no problem washing or dressing themselves whereas 2.3% were unable to wash or dress themselves. Regarding Day-to-Day activities, 62.5% of the individuals had no problem going about their usual activities whereas 7.8% were unable to do any activity at all. Upon asking about pain/discomfort, 57% did not experience any pain whereas 8.6% of the individuals had severe pain/discomfort. 54.7% of the individuals had no signs of anxiety/depression whereas 3.9% experienced extreme anxiety and depression.

Tables:

		Frequency	Percentage
Age	20-30 years	88	68.8
	30-50 years	29	22.7
	50-60 years	11	8.6
Employment status	Unemployed	81	63.7
	employed	47	36.3
Family Members	1-5	42	32.8
	6-10	68	52.1
	11-15	13	10.2
	16-20	4	3.1
	21-25	1	.8
Family Income	10000-20000	12	9.4
	30000-50000	32	25
	>50000	84	65.5

Comorbidities And Medicine For Comerbidities			
		Frequency	Percent
Comorbidities	No	107	83.6
	Hypertension	7	5.5
	Diabetes Mellitus	4	3.1
	Hypertension and Diabetes mellitus	8	6.3
	Multiple	2	1.6
Medicine	No	107	83.6
	Anti-diabetics	7	5.5
	Anti-hypertensive	4	3.1
	Multiple	10	7.8

Post-COVID Manifestations			
		Frequency	Percent
Fatigue	Yes	35	27.3
	No	93	72.7
Feeling Depressed	Yes	86	67.2
	No	42	32.8
Shortness of breath	Yes	60	46.9
	No	68	56.1
Cough	Yes	85	66.4
	No	43	34.6
Joint Pain	Yes	59	46.1
	No	69	56.9
Trouble falling asleep	Yes	72	56.3
	No	56	43.7
Headaches	Yes	68	53.1
	No	60	46.9

Stigma associated with COVID Infection			
		Frequency	Percent
Hurt by people learning I had COVID	Agree	85	66.4
	Disagree	43	33.6
Lost friends because I had COVID	Agree	125	82
	Disagree	23	18
Feel guilty because I was COVID Positive	Agree	99	77.3
	Disagree	29	22.7
Feeling that I'm a bad person	Agree	121	94.5
	Disagree	7	5.5
People would look down upon someone who has had COVID	Agree	74	57.8
	Disagree	54	42.2

Implication of COVID Infection on quality of life			
		Frequency	percent
Mobility	I have no problem in walking about	87	68
	I have moderate problem in walking about	35	27.3
	I'm unable to walk	6	4.7



Self care	I have no problem washing or dressing myself	101	78.9
	I have moderate problem	24	18.8
	I'm unable to wash or dress myself	3	2.3
Usual Activities	I have no problem doing my usual activity	80	62.5
	I have moderate problem	38	29.7
	I'm unable to do my usual activity	10	7.8
Pain/discomfort	No pain or discomfort	73	57
	Moderate pain	44	34.7
	Extreme pain or discomfort	11	8.3
Anxiety/depression	No anxiety or depression	70	54.7
	Moderate anxiety or discomfort	53	41.4
	Extreme anxiety or depression	5	3.9

## Discussion

In our study, we found out that most patients tended to have a similar spectrum of post COVID manifestations where fatigue predominated with a staggering prevalence of 72.7% which was consistent with the findings by a study conducted by Kamal et al.(16) who also found out fatigue to be the most predominant symptom with a percentage of 72.8%. These findings were followed by joint pain with a percentage of 53.9%. Study by Kamal et al. (16) found out that 31.4% of the subjects had joint pain. Shortness of breath corresponded to a percentage of 53.1%. In a study conducted by Dinah V Parum (17), 88% of the subjects experienced shortness of breath. The varying occurrence of symptoms corresponding to different age groups seemed to display a specific pattern with most symptoms being exhibited by those in the 50-60 age group. Some symptoms, like depression and anxiety seemed to predominate in those 20-50 years of age. In our study, depression was seen in 32.8% of the subjects. In a study by Valentina Bucciarelli et al.(18) 52.4% of the participants met the criteria for major depressive disorder. In our study we found out that 43.8% of the subjects had trouble falling asleep. Andrea Pilotto et al.(19) found out that 30.8% of the subjects had trouble falling asleep. We also found out that 29.7% of the subjects did not take any medicines to relieve any of these conditions. Among the medicines that were taken, paracetamol had the highest percentage of 36.7%. Symptoms relating to the quality of life were mostly exhibited by the elderly, in whom questions regarding stigma related to COVID-19 were also mostly agreed upon.

## Conclusion

Patients recovered from COVID-19 manifested sequelae after the last negative PCR that ranged from mild symptoms like fatigue, joint pain and headache to more serious like major depressive disorders and mobility associated problems. The most reported symptoms were fatigue, joint pain, anxiety and headache. The severity of these manifestations were correlated to the presence any co-morbidities including hypertension, diabetes, hepatitis B, C and tuberculosis.

The presence of these manifestations suggest that all patients who have recovered from COVID-19 infection should undergo screening for the presence any post infection manifestation.

## References

1. Mahmud R, Rahman MM, Rassel MA, Monayem FB, Sayeed SKJB, Islam MS, et al. Post-COVID-19 syndrome among symptomatic COVID-19 patients: A prospective cohort study in a tertiary care center of Bangladesh. *PloS One*. 2021;16(4):e0249644.
2. Han Q, Zheng B, Daines L, Sheikh A. Long-Term Sequelae of COVID-19: A Systematic Review and Meta-Analysis of One-Year Follow-Up Studies on Post-COVID Symptoms. *Pathog Basel Switz*. 2022 Feb 19;11(2):269.
3. D M, T B, A A, He A, A D, Js F, et al. Burden of post-COVID-19 syndrome and implications for healthcare service planning: A population-based cohort study. *PloS One* [Internet]. 2021 Jul 12 [cited 2024 May 30];16(7). Available from: <https://pubmed.ncbi.nlm.nih.gov/34252157/>
4. Goërtz YMJ, Van Herck M, Delbressine JM, Vaes AW, Meys R, Machado FVC, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res*. 2020 Oct;6(4):00542–2020.
5. Vanichkachorn G, Newcomb R, Cowl CT, Murad MH, Breeher L, Miller S, et al. Post-COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at Mayo Clinic and Characteristics of the Initial Patient Cohort. *Mayo Clin Proc*. 2021 Jul;96(7):1782–91.
6. Augustin M, Schommers P, Stecher M, Dewald F, Gieselmann L, Gruell H, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. *Lancet Reg Health Eur*. 2021 Jul;6:100122.
7. Bahmer T, Borzikowsky C, Lieb W, Horn A, Krist L, Fricke J, et al. Severity, predictors and clinical correlates of Post-COVID syndrome (PCS) in Germany: A prospective, multi-centre, population-based cohort study. *EClinicalMedicine*. 2022 Sep;51:101549.
8. Moura AEF, Oliveira DN, Torres DM, Tavares-Júnior JW, Nóbrega PR, Braga-Neto P, et al. Central hypersomnia and chronic insomnia: expanding the spectrum of sleep disorders in long COVID syndrome - a prospective cohort study. *BMC Neurol*. 2022 Nov 9;22(1):417.
9. Bai F, Tomasoni D, Falcinella C, Barbanotti D, Castoldi R, Mulè G, et al. Female gender is associated with long COVID syndrome: a prospective cohort study. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis*. 2022 Apr;28(4):611.e9-611.e16.
10. Fumagalli C, Zocchi C, Tasseti L, Silverii MV, Amato C, Livi L, et al. Factors associated with persistence of symptoms 1 year after COVID-19: A longitudinal, prospective phone-based interview follow-up cohort study. *Eur J Intern Med*. 2022 Mar;97:36–41.
11. Och A, Tylicki P, Polewska K, Puchalska-Reglińska E, Parczewska A, Szabat K, et al. Persistent Post-COVID-19 Syndrome in Hemodialyzed Patients-A Longitudinal Cohort Study from the North of Poland. *J Clin Med*. 2021 Sep 28;10(19):4451.

12. Kim Y, Bitna-Ha null, Kim SW, Chang HH, Kwon KT, Bae S, et al. Post-acute COVID-19 syndrome in patients after 12 months from COVID-19 infection in Korea. *BMC Infect Dis.* 2022 Jan 27;22(1):93.
13. Dar SA, Khurshid SQ, Wani ZA, Khanam A, Haq I, Shah NN, et al. Stigma in coronavirus disease-19 survivors in Kashmir, India: A cross-sectional exploratory study. *PLOS ONE.* 2020 Nov 30;15(11):e0240152.
14. Sullivan GM, Artino AR. Analyzing and Interpreting Data From Likert-Type Scales. *J Grad Med Educ.* 2013 Dec;5(4):541–2.
15. McCaffrey N, Kaambwa B, Currow DC, Ratcliffe J. Health-related quality of life measured using the EQ-5D–5L: South Australian population norms. *Health Qual Life Outcomes.* 2016 Sep 20;14(1):133.
16. Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. *Int J Clin Pract.* 2021 Mar;75(3):e13746.
17. Parums DV. Editorial: Long COVID, or Post-COVID Syndrome, and the Global Impact on Health Care. *Med Sci Monit Int Med J Exp Clin Res.* 2021;27:e933446.
18. Bucciarelli V, Nasi M, Bianco F, Seferovic J, Ivkovic V, Gallina S, et al. Depression pandemic and cardiovascular risk in the COVID-19 era and long COVID syndrome: Gender makes a difference. *Trends Cardiovasc Med.* 2022 Jan;32(1):12–7.
19. Pilotto A, Cristillo V, Cotti Piccinelli S, Zoppi N, Bonzi G, Sattin D, et al. Long-term neurological manifestations of COVID-19: prevalence and predictive factors. *Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol.* 2021 Dec;42(12):4903–7.