Effect of COVID-19 Related Lockdown on Nonmotor Symptoms of Parkinson’s Disease

Sir,

The coronavirus disease 2019 (COVID-19) pandemic, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a worldwide crisis. To limit the spread of the disease, social distancing has been advocated strongly, and several countries including India have imposed lockdown with suspension of daily outdoor activities. This lockdown situation would appear to be especially difficult for Parkinson’s disease (PD) patients to cope with. It is challenging for the PD patients to adjust to these changes owing to their cognitive and motor inflexibility.[1] There is an increase in anxiety and stress, as well as worsening of motor symptoms.[2] Another important concern was the reduced access to health services and procurement of medications during the lockdown,[2] which could aggravate both motor and nonmotor symptoms (NMS) in PD. We undertook this study to evaluate the changes of NMS of PD patients during the COVID-19 lockdown situation.

This study recruited PD patients under regular follow-up at the Movement Disorders clinic of Bangur Institute of Neurosciences, Kolkata, India, who were enrolled in an ongoing study approved by the institutional ethics committee. According to institute protocol, we contacted the patients/caregivers over telephone for routine follow-up. We included patients who had visited our institute at least once during the 3 months preceding the beginning of lockdown, and were on a stable dosing of anti-Parkinsonian medications not requiring any change on their last visit. We compared this baseline data with that obtained from our telephonic interview (done in May–June 2020). We collected demographic details, enquired regarding COVID-19 and difficulties faced during the lockdown, and asked about any change in the motor and nonmotor symptoms of PD. For NMS, we used the 30-item NMS Questionnaire (NMSQuest),[3] and additionally enquired for fatigue. Duration of disease was noted and the pre-lockdown modified Hoehn and Yahr (HY) staging was utilized.

Out of total 55 patients, 78.2% were male. Every responder had some knowledge about COVID-19. 52.7% had an overall perception of deterioration during lockdown, and 9.1% said that their condition improved. None of the patients had COVID-19 or a known history of close contact with a patient of COVID-19. All the patients were continuing their medications, although, 10.9% had some difficulty procuring medicines in the initial stages of lockdown. Patients reported deterioration of motor symptoms such as an increase in slowness (41.8%), stiffness (25.5%), or tremor (30.9%). There was significant increase in prevalence of total NMS per patient (P = <0.001), as well as several individual NMS such as, anxiety, impaired concentration, loss of interest, weight loss, and pain [Table 1]. Other NMS also showed increased prevalence during lockdown except, vomiting, bowel incontinence, hyposmia, sexual problems, double vision, and delusion. NMS which were already present pre-lockdown, showed an increase in severity except double vision and bowel incontinence. Taking together the appearance of new symptoms and increase in severity of pre-existing symptoms, the NMS could be grouped as follows- >40% increase- impaired concentration, weight loss, anxiety, loss of interest, fatigue, and pain; 20–39% increase- depression, daytime somnolence, restless legs, forgetfulness, constipation, insomnia, dizziness, and urinary urgency; <20% increase- rest of the NMS. Younger patients experienced greater overall worsening of NMS ($r_s = -0.293$, $P = 0.03$), and of loss of interest in particular ($P = 0.003$). Worsening of impaired concentration was associated with longer duration of disease ($P = 0.025$). There was no significant difference in increase of NMS regarding gender and HY staging of the patients. There was also no association between worsening of the motor symptoms and increase in NMS.

52.7% of patients deteriorated during lockdown. An Indian study has documented worsening in 28% of PD patients,[2] whereas a Spanish study reported deterioration in 65.7% patients.[4] The limitations imposed by lockdown including social isolation, restriction of physical activity, and sudden change in lifestyle, along with the anxiety and uncertainty regarding COVID-19, contribute to the aggravation of symptoms in PD patients.[1] A study showed that worsening of

Table 1

| Symptom            | Pre-Lockdown | Post-Lockdown | Change |
|--------------------|--------------|--------------|--------|
| Anxiety            | 10%          | 25%          | +15%   |
| Fatigue            | 20%          | 30%          | +10%   |
| Impaired concentration | 30%      | 40%          | +10%   |
| Weight loss        | 10%          | 20%          | +10%   |
| Depression         | 0%           | 10%          | +10%   |
| Daytime somnolence | 5%           | 10%          | +5%    |
| Restless legs      | 10%          | 20%          | +10%   |
| Forgetfulness      | 5%           | 15%          | +10%   |
| Constipation       | 0%           | 5%           | +5%    |
| Insomnia           | 0%           | 5%           | +5%    |
| Dizziness          | 0%           | 2%           | +2%    |
| Urinary urgency    | 0%           | 5%           | +5%    |

Sources:
[1] Kanner AM, Ribot R, Mazarati A. Bidirectional relations among common psychiatric and neurologic comorbidities and symptoms in PD. Neurosciences, Kolkata, India, who were enrolled in an ongoing study approved by the institutional ethics committee.
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Table 1: Increase of Nonmotor Symptoms during Lockdown

| NMS                        | Frequency of NMS | Increase of NMS during lockdown |
|----------------------------|------------------|---------------------------------|
|                            | Pre-lockdown (N) | Post-lockdown (N) | p      | Age | Sex | HY | Duration |
| Impaired concentration     | 32               | 43                | 0.024* |     |     |     |          |
| Weight loss                | 38               | 47                | 0.041* |     |     |     |          |
| Anxiety                    | 35               | 46                | 0.017* |     |     |     |          |
| Loss of interest           | 25               | 37                | 0.021* |     |     |     |          |
| Fatigue                    | 47               | 50                | 0.376  |     |     |     |          |
| Unexplained pain           | 21               | 36                | 0.004* |     |     |     |          |
| Depression                 | 34               | 41                | 0.152  |     |     |     |          |
| Daytime somnolence         | 35               | 42                | 0.145  |     |     |     |          |
| Restless legs              | 40               | 47                | 0.101  |     |     |     |          |
| Forgetfulness              | 33               | 38                | 0.319  |     |     |     |          |
| Constipation               | 37               | 41                | 0.401  |     |     |     |          |
| Insomnia                   | 25               | 33                | 0.127  |     |     |     |          |
| Dizziness                  | 23               | 31                | 0.127  |     |     |     |          |
| Urinary urgency            | 32               | 37                | 0.324  |     |     |     |          |

| Total NMS per patient      | Frequency of total NMS | Increase of total NMS during lockdown |
|----------------------------|------------------------|---------------------------------------|
|                            | Pre-lockdown (Mean±SD) | Post-lockdown (Mean±SD) | p      | Mean±SD | p      | Age | Sex | HY | Duration |
|                            | 13.04±3.89             | 15.55±3.18                    | <0.001* | 6.6±3.30 | 0.03* |     |     |     |          |

*Significance level at p<0.05, *Showing NMS with ≥20% increase during lockdown

Table 2: Frequencies of increase in nonmotor and motor symptoms in patients of Parkinson’s disease and comparison with other studies

| Present study n=55 | Turkey(n=86) | Nine centers of India(n=832) | Tuscany, Italy(n=740) | USA(n=5429) |
|--------------------|--------------|------------------------------|----------------------|-------------|
| Nonmotor           |              |                              |                      |             |
| Impaired concentration | 27 (49.1) | Orthostatic hypotension          | Easy fatigability            | 209 (25.1) | Anxiety 183 (25.0) | Mood 36.5% |
| Weight loss        | 25 (45.5) | Fatigue                       | Sleep disturbances         | 199 (23.9) | Mood 181 (24.7) | Sleep 36.5% |
| Anxiety            | 23 (41.8) | Pain                          | Anxiety                  | 181 (21.8) | Inomnia 163 (22.2) | Autonomic 20.6% |
| Loss of interest   | 23 (41.8) | Daytime sleepiness            | Anxiety                  | 179 (21.5) | Cognitive 18.5% |
| Fatigue            | 22 (40)   | Anxiety                       | Depressive symptoms       | 168 (20.2) | Cognitive |
| Unexplained pain   | 22 (40)   | Cognitive impairment          | Constipation              | 163 (19.6) |
| Depression         | 20 (36.4) | Constipation                  | Forgetfulness             | 149 (17.9) |
| Daytime somnolence | 20 (36.4) | Apathy                        | Urinary problems          | 111 (13.3) |
| Restless legs      | 20 (36.4) | Urinary disorder              | Postural dizziness        | 108 (12.9) |
| Forgetfulness      | 16 (29.1) | Hallucination                 | Aggressive or             | 96 (11.5)  |
| Constipation       | 15 (27.3) | Sleep disorder                | Obsessive thoughts        | 79 (9.5)   |
| Insomnia           | 14 (25.5) | Depression                    | Visual hallucinations     | 50 (6.01)  |
| Dizziness          | 14 (25.5) | Dopamine dysregulation syndrome | Auditory hallucinations | 35 (4.2)   |
| Urinary urgency    | 12 (21.8) |                              |                         |             |

| Motor               |              |                              |                      |             |
| Slowness            | 23 (41.8)   | Bradykinesia                 | Slowness              | 259 (31.1) | Motor 217 (29.6) | Motor 47.2% |
| Tremor              | 17 (30.9)   | Tremor                       | Tremor                | 173 (20.8) |
| Stiffness           | 14 (25.5)   | Postural instability         | Stiffness             | 203 (24.4) |

*Numbers in parentheses are percentage
PD patients was dependent on the reduction of physical activity during lockdown.\textsuperscript{[9]} 15 NMS showed $\geq 20\%$ increase, and none of the NMS had an overall decrement. Previous studies have described an increase in some of these NMS during the COVID-19 pandemic, such as anxiety, stress, depression, and cognitive impairment.\textsuperscript{[6-8]} However, in addition to these symptoms, our study documented change in the wide spectrum of NMS. Other studies from around the world have also showed worsening of NMS [Table 2]. A Turkish study found maximum worsening in orthostatic hypotension,\textsuperscript{[9]} whereas an Indian multicenter study reported the highest increase in easy fatiguability followed by sleep disturbances.\textsuperscript{[10]} An Italian report showed worsening of anxiety, mood, and sleep,\textsuperscript{[11]} and an American study also documented significant involvement of these NMS domains along with autonomic and cognitive impairment.\textsuperscript{[12]} We found comparable worsening of these symptoms; however, the greatest increase was for impaired concentration, weight loss, anxiety, and loss of interest. Hence, although there were some differences regarding the magnitude of worsening of the various NMS, there was a similar trend in most of these studies.

Worsening of NMS was greater in younger patients. The younger patients were likely to be more active prior to the lockdown and probably engaged in jobs which were restricted because of the lockdown. This might lead to an increase in NMS, especially anxiety and depression, and explain the loss of interest. Impaired concentration, loss of interest, and forgetfulness might be linked to increased depression and anxiety, although, disruption of daily routine and difficulty of coping with the sudden change of lifestyle may cause cognitive stress that exacerbates or unmasks cognitive impairment. Lack of regular exercise and physical activity possibly aggravated pain and fatigue. However, fatigue may be a manifestation of viral infections including COVID-19, although none of them tested positive for COVID-19 in our study. None of our patients developed new onset hyposmia, and both patients with increased severity of pre-existing hyposmia had tested negative for COVID-19.

To conclude, this study documented worsening of motor and several nonmotor symptoms in PD patients during the COVID-19 pandemic related lockdown in India.

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**Conflicts of interest**

There are no conflicts of interest.

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