Analysis of neurological disorders in people who had COVID-19 in Brazil

Análise de sintomas neurológicos em pessoas que tiveram COVID-19 no Brasil

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ABSTRACT
Introduction: After coronavirus infectious disease (COVID-19) infection, many patients have residual and persistent neurological symptoms. The severity and extent of these
Methods: Over 1 year, a virtual questionnaire was applied, using Google Forms, to people who had confirmed COVID-19 infection in Brazil, analyzing the neurological symptoms that persisted after infection, their duration and the relationship between them and the severity of the acute infection. Findings: Out of 1194 people who answered the questionnaire, 947 (79.5%) were eligible for symptoms analysis. Among these patients, 6.8% needed hospitalization (39.2% of them required oxygen therapy and 26.6% needed orotracheal intubation). The incidence of symptoms were headache (65.8%), smell dysfunction (59.6%), taste dysfunction (51.8%), muscle weakness (51.8%), memory impairment (42.8%), dizziness (37.7%), mental confusion (22.4%), difficulty walking (20%), and visual changes (9.1%). In most cases, symptoms improved within a month, despite a significant percentage of patients persisting with symptoms for several months. However, memory impairment was significantly more persistent, with 39.7% of the patients having it for more than a year. And this was frequent even in those who did not need hospitalization in the acute phase of the disease, with 24.2% of all nonhospitalized patients having this complain for more than 6 months. Interpretation: Many COVID-19 patients have persistent neurological symptoms after the acute infection has ended. In some cases the symptoms can last a long time. Despite being a self-reported study, it is very likely that there is a significant functional impact in this population and it is clear that we need to research effective therapeutic strategies for these conditions.

Keywords: COVID-19 infection, post-COVID syndrome, neurological symptoms after COVID, brain fog.

RESUMO

Introdução: Após a infecção por doença infecciosa por coronavírus (COVID-19), muitos pacientes apresentam sintomas neurológicos residuais e persistentes. A gravidade e a extensão desses sintomas ainda são desconhecidas. Métodos: Ao longo de 1 ano, um questionário virtual foi aplicado, usando o Google Forms, a pessoas que tiveram infecção confirmada por COVID-19 no Brasil, analisando os sintomas neurológicos que persistiram após a infecção, sua duração e a relação entre eles e a gravidade da infecção aguda. Resultados: Das 1.194 pessoas que responderam ao questionário, 947 (79,5%) foram elegíveis para análise dos sintomas. Dessas pacientes, 6,8% necessitaram de internação (39,2% deles necessitaram de oxigenoterapia e 26,6% de intubação orotraqueal). A incidência dos sintomas foram cefaléia (65,8%), alteração do olfato (59,6%), alteração do paladar (51,8%), fraqueza muscular (51,8%), comprometimento da memória (42,8%), tontura (37,7%), confusão mental (22,4%), dificuldade para andar (20%) e alterações visuais (9,1%). Na maioria dos casos, os sintomas melhoraram em um mês, apesar de uma porcentagem significativa de pacientes persistirem com sintomas por vários meses. No entanto, o comprometimento da memória foi significativamente mais persistente, com 39,7% dos pacientes apresentando-o por mais de um ano. E isso foi frequente mesmo naqueles que não precisaram de internação na fase aguda da doença, com 24,2% de todos os pacientes não internados apresentando essa queixa há mais de 6 meses. Interpretação: Muitos pacientes com COVID-19 apresentam sintomas neurológicos persistentes após o término da infecção aguda. Em alguns casos, os sintomas podem durar muito tempo. Apesar de ser um estudo autorreferido, é muito provável que haja um impacto funcional significativo nessa população e é claro que precisamos pesquisar estratégias terapêuticas eficazes para essas condições.
1 INTRODUCTION

Albeit primarily a disease of respiratory tract, the 2019 coronavirus infectious disease (COVID-19) has been found to have causal association with a plethora of neurological, neuropsychiatric, and psychological effects (1).

Patients recovering from a severe illness or after hospitalization may report prolonged neurologic symptoms (2). However, many patients with milder acute COVID19 symptoms who never required hospitalization for pneumonia or hypoxemia may also report persistent neurologic and systemic symptoms (3).

A possible explanation is the fact that COVID-19 infectious agent, SARS-CoV-2, has a high affinity for human angiotensin-converting enzyme 2 (ACE2) receptor. This receptor is also expressed in neurons and glial cells, which could explain the reported neurological manifestations even in patients without severe illness (4).

Little is known about long-term recovery from COVID-19 disease, especially in nonhospitalized individuals. Very few studies have prospectively assessed persistence of symptoms in these patients (5).

The understanding of how the symptoms persist and how they impact in the patient’s quality of life is important for public healthcare strategies and to measure the global impact of this disease.

This is even more important in developing countries like Brazil, with almost 30 million confirmed cases of COVID-19 infections at the end of March, 2022(6), and with serious public healthcare system limitations.

To contribute to this knowledge, we developed this study, with the objective to assess the incidence of persistent neurological symptoms in post-COVID19 patients in Brazil.

2 METHODS

We applied a web-based questionnaire where people who had COVID-19 were invited to respond, after reading and agreeing an informed consent form, with information about themselves, information about the acute disease phase and the presence or not of...
any neurological symptoms listed in the questionnaire (Figure 1). The duration of the symptom and if it was still happening was also asked.

Figure 1. List of the neurological symptoms described in the questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>Duration Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you had any kind of stroke?</td>
<td>I have not had this symptom; yes, for 2 weeks; yes, for a month; yes, for 3 months; yes, for 6 months; yes, for a year; I still have this symptom</td>
</tr>
<tr>
<td>Have you had headache? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you lost or reduced your sense of smell? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you lost or reduced your taste? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you had sight lost or alteration? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you had mental confusion? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you lost your muscle strength? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you had any difficulties in moving and/or picking up objects? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you had memory alteration? If so, for how long?</td>
<td></td>
</tr>
<tr>
<td>Have you had dizziness? If so, for how long?</td>
<td></td>
</tr>
</tbody>
</table>

Font: Created by the authors.

In all of these questions the person could answer: I have not had this symptom; yes, for 2 weeks; yes, for a month; yes, for 3 months; yes, for 6 months; yes, for a year; I still have this symptom.

The invitation to fill this questionnaire was spread by social media, stimulating people to repass it through their social groups with the objective to reach the whole Country. Data was collected from January 2021 until February 2022.

3 RESULTS

Out of 1194 people who answered the questionnaire, 947 (79.5%) were eligible for symptoms analysis, because they had a confirmatory COVID-19 test result. These captured a broad demographic (mean age 33.4 years, 13.12 SD), including individuals from all, but three, Brazilian states (Table 1).
Table 1. Demographic and clinical characteristics of COVID-19 patients of this survey

<table>
<thead>
<tr>
<th>Sex</th>
<th>% (Female)</th>
<th>% (Male)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>75.9%</td>
<td>23.8%</td>
</tr>
<tr>
<td><strong>Age</strong> (mean, Standard Deviation, range)</td>
<td>33.4, 13.2, 18-82</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Schooling</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete elementary school</td>
<td>0.4%</td>
</tr>
<tr>
<td>Complete elementary school</td>
<td>1.6%</td>
</tr>
<tr>
<td>Incomplete high school</td>
<td>2.6%</td>
</tr>
<tr>
<td>Complete high school</td>
<td>14.7%</td>
</tr>
<tr>
<td>Incomplete university education</td>
<td>26.8%</td>
</tr>
<tr>
<td>Complete university education</td>
<td>53.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospitalization</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not hospitalized</td>
<td>93.2%</td>
</tr>
<tr>
<td>1 to 7 days</td>
<td>2.9%</td>
</tr>
<tr>
<td>8 to 14 days</td>
<td>1.6%</td>
</tr>
<tr>
<td>15 to 30 days</td>
<td>1.3%</td>
</tr>
<tr>
<td>More than 30 days</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oxygen support</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not need</td>
<td>34.2%</td>
</tr>
<tr>
<td>Required, but not intubation</td>
<td>39.2%</td>
</tr>
<tr>
<td>Required intubation</td>
<td>26.6%</td>
</tr>
</tbody>
</table>

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Among patients with confirmed disease, 6.8% needed hospitalization (2.9% between 1 to 7 days, 1.6% 8 to 14 days, 1.3% 15 to 30 days, 1.1% more than 30 days). Of the hospitalized patients, 39.2% required oxygen therapy and 26.6% needed orotracheal intubation.

Headache was the most common symptom, followed by changes in smell and taste, muscle weakness, memory impairment, dizziness, mental confusion, difficulty walking, and visual changes.

Only 2 individuals reported having had a stroke (one during the acute infection phase and one after it).

Headache was reported by 65.8% (4.9% in those who needed hospitalization), with 8% persisting with this symptom at the time the questionnaire was answered. Among patients who persisted with the symptom for more than 6 months, 96.2% did not require hospitalization in the acute phase of the disease. Loss of smell and loss of taste were
reported by 59.6% and 51.8% of the individuals respectively. Only headache and loss of smell were, proportionally, more frequent in non-hospitalized patients than in hospitalized ones after 6 months (figure 2).

Figure 2. Persistence of neurological symptoms for more than 6 months between hospitalized and nonhospitalized patients

Muscle weakness was also reported by 51.8% of patients, 10.18% of those who were interned. Almost 30 percent of hospitalized patients maintained muscle weakness after 6 months. Among those not hospitalized, the frequency was 8.5%.

Memory impairment occurred in 405 (42.8%) patients. It was the 5th most common symptom, but the most persistent of all, with 25.3% still having it at the time the questionnaire was answered and 161 (39.7%) having it for more than a year. Among the 39 patients who were hospitalized, 29 (74.3%) persisted with this symptom when they completed the questionnaire. Of the patients who had memory impairment for more than 6 months, 87.3% did not have a serious illness in the acute phase, not requiring hospitalization. This represents 24.2% of all patients who did not require hospitalization in the acute phase.

The incidence of each symptom in the studied population, discriminating those who needed hospitalization at the acute phase of the disease is demonstrated in the Figure 3.
Figure 3. Incidence of neurological symptoms in post-COVID patients

The duration of each symptom and the percentage of patients, with or without a history of hospitalization, who remained symptomatic for more than 6 months are described in the Figures 2 and 4 respectively.

Figure 4. Time duration of the neurological symptoms in post-COVID patients*

* Numbers represent the absolute number

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4 DISCUSSION

The study population had a greater representation of women and young people than the distribution of the Brazilian population. The age difference may be related to access to social media and, possibly, women may be more engaged in contributing to this type of study.

The demographics being younger might put a downward bias both in cases of hospitalization and maybe even in the appearance of symptoms. Thus, it is possible that in the general population the existence of neurological symptoms is greater.

Even so, our analysis provides converging evidence to support the hypothesis that COVID-19 infection is associated with a broad spectrum of neurological symptoms that can persist long after the acute phase of the disease has ended.

Headache, smell and taste disfunctions and muscle weakness occurred in more than a half of the people, with headache being present in each 2 of 3 individuals. And, although the vast majority of headache patients improved in the first two weeks post-infection, 12.6% persisted with pain for more than 6 months, with almost all of them (96.2%) having mild cases in the acute phase of infection.

Of all the symptoms, memory impairment seems to be the most worrisome, because in addition to having a high frequency, most people reported the persistence of this symptom after 1 year. And even being more significant in cases of individuals who required hospitalization, it also occurred in those who had a milder form of the disease. As already reported, almost a quarter of all patients who did not require hospitalization (expressing mild cases) still complained of memory impairment after 6 months. This finding is in line with other robust studies that also analyzed the impact of COVID-19 on the cognitive capacity of individuals even in cases that did not require ventilatory support or hospitalization.

5 CONCLUSION

Our study does not have the statistical power to state the incidence of neurological symptoms in all COVID-19 patients, but it is useful to show a pattern of involvement of these symptoms in our population.

It also demonstrates, corroborating other publications, that symptoms can be longlasting even in mild cases of COVID-19, and are not only linked to systemic inflammatory involvement or hypoxemia present in more severe cases of the disease.
Because neurological impairments bring a lot of damage to the functionality of individuals, it is likely that such incidences have generated and still generate a great negative impact on their working abilities and quality of life. Public policy strategies must be developed to assist and rehabilitate these people.

Studies deepening the pathophysiological knowledge behind cognitive impairment in post-COVID patients are fundamental so that therapeutic strategies can be developed aiming at a functional recovery of this population

DATA SHARING STATEMENT

All data are freely available in fully anonymized format for academic researchers on request to the corresponding author.

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REFERENCES


