Cross-sectional study on neurological sequelae in patients with COVID 19 in AMREC and AMESC regions of Santa Catarina

Estudo transversal sobre o quadro de sequelas neurológicas nos pacientes com COVID-19 na região da AMREC e AMESC de Santa Catarina

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ABSTRACT: INTRODUCTION: COVID-long refers to the group of symptoms that persist one month after the acute phase of the disease. Fatigue, dyspnea, sensory changes, myalgia, cognitive changes stand out as the main manifestations observed. OBJECTIVE: To analyze the scenario of neurological sequelae associated with COVID-19 in the Associação de Municípios do Extremo Sul Catarinense (AMESC) and Associação dos Municípios da Região Carbonífera (AMREC) regions of Santa Catarina. METHODS: A total of 541 infected patients who were not in the acute phase of the disease participated in the survey. By means of structured telephone interviews, data regarding symptoms and treatment were obtained from these patients. RESULTS: It was found that 71.1% of the interviewed patients reported symptoms of COVID-long, mainly among women (65.4%). Cognitive changes (41.8%), anosmia (33.3%), taste alterations (27.3%) were the most frequent COVID-long neurological manifestations among the participants in the two regions surveyed. There was a significant relationship between the duration of sleep disturbance in AMREC and AMESC (p = 0.014), as well as between the duration of treatment in AMESC and no treatment in AMREC (p < 0.001). CONCLUSION: Among the neurological manifestations, there was a higher frequency of cognitive changes, anosmia, and taste disorders among individuals in the two regions studied. Moreover, the search for home treatment, primary and specialized care among AMESC patients and the lack of it among AMREC ones demonstrate significant difference between the regional scenarios. Thereby, the duration of sleep disorders, more frequent during the acute phase among AMESC participants, showed relevant distinction between the participants from the two regions, suggesting the need for more complete and prolonged studies in these populations.

KEYWORDS: COVID-19; SARS-CoV-2; Neurological Disorder; Anosmia; Disorders Sleep.

RESUMO: INTRODUÇÃO: COVID-longa refere-se ao grupo de sintomas que persistem após um mês da fase aguda da doença. Destacam-se fadiga, dispneia, alterações sensoriais, mialgia e alterações cognitivas como as principais manifestações observadas. OBJETIVO: Analisar o cenário das sequelas neurológicas associadas ao COVID-19 nas regiões da Associação de Municípios do Extremo Sul Catarinense (AMESC) e Associação dos Municípios da Região Carbonífera (AMREC) de Santa Catarina. MÉTODO: Participaram da pesquisa 541 pacientes infectados que não se encontravam na fase aguda da doença. Por meio da entrevista telefônica estruturada, foram obtidos dados referentes aos sintomas e à realização de tratamento desses pacientes. RESULTADOS: Constatou-se que 71,7% dos pacientes entrevistados relataram sintomas de COVID-longa, principalmente entre as mulheres (65,4%). Alterações cognitivas (41,8%), anosmia (33,3%), alterações do paladar (27,4%) foram as manifestações neurológicas de COVID-longa mais frequentes entre os participantes nas duas regiões pesquisadas. Demonstrou-se relação significativa entre a duração do distúrbio do sono na AMREC e AMESC (p = 0.014), assim como na realização de tratamento na AMESC e não realização de tratamento na AMREC (p < 0.001). CONCLUSÃO: Dentre as manifestações neurológicas, houve maior frequência de alterações cognitivas, anosmia e alterações do paladar entre os indivíduos das duas regiões estudadas. Além disso, a procura por realização de tratamento em ambiente domiciliar, atenção básica e especializada na região na AMESC, bem como a não realização de tratamento na AMREC, demonstrou significativa diferença entre os cenários regionais. Assim também, a duração de distúrbios do sono, com apresentação mais frequente durante a fase aguda na AMESC e a fase crônica na AMREC, apresentou relevante distinção constatada entre os participantes das duas regiões, sugerindo a realização de estudos mais completos e prolongados nessas populações.

PALAVRAS-CHAVE: COVID-19; SARS-CoV-2; Distúrbio neurológico; Anosmia; Distúrbios do sono.

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was described in December 2019 in Wuhan (China) and presented a rapid global spread. The John Hopkins University reported 30.6 million confirmed cases of the disease and 663 thousand deaths in Brazil on April the 21st, 2022. Clinically, the most common acute symptoms are fever, cough, myalgia, headache, and dyspnea. Less commonly, patients can also present gastrointestinal symptoms, such as diarrhea, vomiting, and nausea. In addition, impairment of smell (hyposmia, anosmia, and parosmia) or taste (dysgeusia) are described as sensorial disturbances presented in the coronavirus infection (COVID-19). Other neurological manifestations of the acute phase are dizziness, altered consciousness, and cerebrovascular events. The clinical condition may vary between asymptomatic, moderate symptoms to severe illness and potentially fetal.

SARS-CoV-2 may trigger, directly or indirectly, chronic manifestations. A group of symptoms that persist for more than a month is denominated as “long COVID”. Fatigue, dyspnea, sensory impairments in taste and smell, angina, myalgia, sleep disorders, and cognitive alterations are the main symptoms of long COVID. A previous study demonstrated that, up to 6 months after the acute infection, most patients continue to present at least one of their initial manifestations. Cognitive impairment and anosmia were the most prevalent after six months of infection. The persistence of these symptoms suggests a SARS-CoV-2 neurotropism highlighting the olfactory pathways as the main gateway of the virus to the central nervous system.

In the Brazilian scenario, Santa Catarina registered 20 thousand deaths and 1 million confirmed cases of COVID-19. The south region of Santa Catarina is divided into three Associations of Municipalities: AMUREL (Associação de Municipios da Região da Laguna); AMREC (Associação dos Municipios da Região Carbonífera); and AMESC (Associação dos Municipios do Extremo Sul Catarinense). The last two were the focus of this study. AMREC and AMESC represent 10% of all confirmed COVID-19 cases in the state. AMREC is comprised of 12 cities with a sum population of 400 thousand. AMESC is comprised of 15 cities with a sum population of 200 thousand.

Recognizing the Brazilian population’s chronic manifestations of SARS-CoV-2 infection is essential to develop effective therapeutic plans and strategically allocate resources to fight COVID-19. In addition, global data about these clinical repercussions are still scarce. Therefore, the present study aims to evaluate the neurological sequelae associated with COVID-19 in the AMESC and AMREC regions of Santa Catarina. It is expected that this research, with the obtained results, collaborates to identify the clinical profile of the patients affected by long COVID in the extreme south region of Santa Catarina, in addition to being a support instrument for future research on this topic.

METHODOLOGY

This study is categorized as descriptive-quantitative basic field research. The sampling process was classified as probabilistic, and the exclusion criteria were utilized systematically. The inclusion criteria were the following: infection to SARS-CoV-2 between March 2020 and July 2021; older than 18 years old; both sexes; that were treated in the COVID care facilities from the studied regions; that answered the first phone call; accepted to participate in the research, signed the informed consent form; and that lived in the cities that authorized the access to phone data from individuals infected with COVID-19. Patients not meeting the inclusion criteria described above were excluded from the study.

The probabilistic sampling approach was best for representing the study population, considering the randomly assigned data processing aspect. The data collection method of this research was phone interviews because of the difficulty of accessing outlying towns and complying with social distancing rules stated during the pandemic. Initially, all municipal health departments from AMRED and AMESC were contacted. After the authorization to conduct the study, the compliance terms for data collection were sent. Posteriorly, the list of patients infected by COVID-19 between March 2020 and July 2021 was obtained by consulting each city’s database, along with each individual’s telephone contact. From this, the sample size described below was divided proportionally to the size of the population of each city and the number of infected individuals.

The calculation of sample size was performed using the methodology proposed by Medronho, $P (0.50)$ is the value that maximizes the sample size, and $\varepsilon (0.05)$ is the maximum sampling error. The study included 541 patients, 388 from the AMREC region and 153 from the AMESC region, infected with COVID-19 who were no longer in the acute phase of the disease. Patients were selected randomly by an electronic sorter with the phone date collected previously. The phone calls were made according to a data collection instrument that was structured and approved, along with the rest of the research, by the Ethics Committee for Research with Humans (Comité de Ética em Pesquisa com Seres Humanos - CEPSH/UFSC), under protocol number 5.019.542.

The data collection instrument initially contained basic information such as the name and sex of the patients. Next, the interviewers asked about the presence of symptoms presented during and after the SARS-CoV-2 infection and their duration. The symptoms were headache, smell and taste alterations, dizziness, fatigue, dyspnea, cough, myalgia, fever, palpitations, alteration in


consciousness, cognitive impairment, and sleep disorders. The response was considered positive if the patient reported episodes of these symptoms during and after the acute phase of the COVID-19 infection. For some patients, the symptom had to be explained to facilitate understanding. Also, to ask about alterations in smell, taste, consciousness, cognitive, and sleep patterns, the question “Did you notice a change in your sleep pattern during or after the COVID-19 infection?” was asked. The response was considered positive if the patient reported any change in their usual pattern, such as episodes of nocturnal awakening, excessive daytime sleepiness, insomnia, and difficulty waking up even after long periods of sleep.

As for cognitive impairment, the response was computed when the patient reported significant deficits in attention, short-term memory, concentration, and emotional processing. Syncope episodes and coma were considered alterations in consciousness. As for taste and smell alterations, the description of hypogeusia, ageusia, hyposmia, and anosmia were computed. In addition, the questionnaire ended with a question about the treatment, only the symptoms of long COVID reported by the patient. If the individual with long COVID performed any form of intervention in the home environment, they were questioned if they sought care in the municipal primary care, if they needed specialized evaluation in the private sector, if they sought a rehabilitation center, if they chose not to perform any form of treatment or, finally, if they sought some therapeutic measure in a place not mentioned above. The individuals were not asked which specific therapeutic procedures they were submitted to.

RESULTS

Table 1 shows the symptoms evaluated with the questions asked, including headache, sleep disorder, changes in consciousness, cognitive changes, myalgia, fever, palpitations, fatigue, dyspnea, cough, dizziness, anosmia, and taste alterations. The duration of these symptoms was divided into periods of 1 to 4 weeks, 1 to 10 months, and 10 months or more. The analysis of the two regions revealed that AMESC patients presented sleep disorder, mainly in the acute phase of the disease (66.7% in the period of 1-4 weeks), while individuals from AMREC report this disorder in the chronic phase of the disease (33.3% in the period between 1-10 months), and this comparison was significant between the two populations analyzed (p = 0.014).

Regarding the neurological symptoms, when grouped, cognitive impairments stood out (55.2% in the AMREC region vs. 68.5% in the AMESC region), anosmia (45.8% in the AMREC vs. 48.3% in the AMESC), taste alterations (35.5% in AMREC vs 47.2% in AMESC) as the most common neurological manifestations of long COVID among participants with persistent symptoms of the two regions studied. Symptoms such as fatigue, myalgia, and headache were the most frequently reported by patients in both regions, respectively. In the analysis of the duration of symptoms, cognitive impairments were more frequent in the 10 months or more period among patients from AMREC (67.2%) and AMESC (78.1%).

Table 1 - Duration of symptoms among patients residing in the AMESC and AMREC regions.

<table>
<thead>
<tr>
<th>Duration of Symptoms</th>
<th>Regions, n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMREC (388)</td>
<td>AMESC (155)</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>n=252 (64,9)</td>
<td>n=104 (68,0)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>12 (7,0)</td>
<td>13 (12,5)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>24 (9,3)</td>
<td>5 (4,8)</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>n=60 (15,5)</td>
<td>n=21 (13,7)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>19 (31,7)</td>
<td>14 (66,7)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>20 (33,3)</td>
<td>2 (9,5)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>21 (35,0)</td>
<td>5 (23,8)</td>
</tr>
<tr>
<td>Consciousness impairments</td>
<td>n=25 (6,4)</td>
<td>n=17 (11,1)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>23 (92,0)</td>
<td>15 (88,2)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>1 (4,0)</td>
<td>1 (5,9)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>1 (4,0)</td>
<td>1 (5,9)</td>
</tr>
<tr>
<td>Cognitive impairments</td>
<td>n=177 (45,6)</td>
<td>n=64 (41,8)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>12 (6,8)</td>
<td>3 (4,7)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>46 (26,0)</td>
<td>11 (17,2)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>119 (67,2)</td>
<td>50 (78,1)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>n=281 (72,4)</td>
<td>n=107 (69,9)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>219 (77,9)</td>
<td>85 (79,4)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>32 (11,4)</td>
<td>15 (14,0)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>30 (10,7)</td>
<td>7 (6,5)</td>
</tr>
<tr>
<td>Fever</td>
<td>n=201 (51,8)</td>
<td>n=77 (50,3)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>201 (100,0)</td>
<td>77 (100,0)</td>
</tr>
<tr>
<td>Heart palpitations</td>
<td>n=96 (24,7)</td>
<td>n=36 (23,5)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>72 (75,0)</td>
<td>21 (58,3)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>15 (15,6)</td>
<td>6 (16,7)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>9 (9,4)</td>
<td>9 (25,0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>n=302 (77,8)</td>
<td>n=123 (80,3)</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>159 (52,6)</td>
<td>74 (60,2)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>87 (28,8)</td>
<td>33 (26,8)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>56 (18,5)</td>
<td>16 (13,0)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>n=164 (42,3)</td>
<td>n=60 (39,2)</td>
</tr>
</tbody>
</table>
In addition to the information presented in Table 1, it was found that 71.7% (388) of the total number of participants manifested at least one symptom in a period longer than one month, with 299 in the AMREC region and 89 in the AMESC. Furthermore, the mean age of the participants was 41.33 ± 13.66 years. When comparing genders, women represented 65.5% (254) of the total number of long-term COVID-19 patients. Also, for females, cognitive impairment (49.2%), anosmia (45.3%), and fatigue (42.9%) were persistent symptoms most observed among participants in both regions.

Table 2 demonstrates the three most frequent neurological symptoms of long COVID: cognitive impairment, anosmia, and taste alterations. These manifestations were analyzed according to the duration of the symptom associated with the treatment. There was no statistically significant association between the duration of symptoms and treatment for the three neurological manifestations.

In cognitive impairment, the average symptom lasted 8.41 ± 3.02 months. It was noted that, among patients who did not undergo treatment, 71.6% of them had the symptom for 10 months or more. On the other hand, among those who were treated, primary care represented the main setting for clinical evaluation.

Regarding anosmia and taste alterations, it was observed that, in both symptoms, among patients that did not undergo treatment, the duration range between 1-10 months was the most frequent (49.6% in anosmia vs. 3% in taste alterations). Although only 14.5% of patients with anosmia seen in primary care had symptoms for 10 months or more, this facility represented the leading choice for undertaking treatment. A similar frequency was found in taste alterations, present in 14.9% of the patients who were seen in primary care, with symptoms lasting for 10 months or more.

Table 3 shows patient treatment according to the AMREC and AMESC regions, only for patients with long COVID. A significant association was observed between undertaking treatment at home, in primary and specialized care in the AMESC region, and not undertaking treatment in the AMREC region (p = < 0.001).

### Table 2 - Treatment for taste alterations, cognitive impairments, and anosmia.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Treatment, n(%)</th>
<th>p-value&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At home</td>
<td>Primary Care</td>
</tr>
<tr>
<td>Cognitive impairments</td>
<td>n=31</td>
<td>n=48</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>2 (6,5)</td>
<td>2 (4,2)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>11 (35,5)</td>
<td>7 (14,6)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>18 (58,1)</td>
<td>39 (81,3)</td>
</tr>
<tr>
<td>Anosmia</td>
<td>n=36</td>
<td>n=69</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>20 (55,6)</td>
<td>33 (47,8)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>12 (33,3)</td>
<td>26 (37,7)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>4 (11,1)</td>
<td>10 (14,5)</td>
</tr>
<tr>
<td>Taste alterations</td>
<td>n=33</td>
<td>n=67</td>
</tr>
<tr>
<td>1 – 4 weeks</td>
<td>21 (63,6)</td>
<td>36 (53,7)</td>
</tr>
<tr>
<td>1 – 10 months</td>
<td>9 (27,3)</td>
<td>21 (31,3)</td>
</tr>
<tr>
<td>10 months or more</td>
<td>3 (9,1)</td>
<td>10 (14,9)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Value obtained after likelihood-ratio test. Source: Study data, 2022.

<sup>2</sup>Value obtained after Pearson’s chi-squared test. Statistically significant value after residual analysis. Source: Study data, 2022.
This is the first study to identify symptoms of long COVID in the southern region of Santa Catarina, and the data showed that most patients had at least one of the symptoms. After analyzing the 541 patients, this research found that patients with long-term COVID-19 were common in both regions, and it was present in periods longer than 10 months after the diagnosis of the disease. 44.2% continued to present the symptoms, and this high frequency is in line with the literature. After a survey of 3800 patients, the frequency of a persistent symptom after 35 weeks of diagnosis is around 92%. Previous studies suggest that SARS-CoV-2 can induce a prolonged inflammatory state responsible for the main manifestations of long COVID. In addition, differences in this immunological response can be observed between females and males, indicating lower production of interleukins after viral infections in women who would explain the higher prevalence of long COVID in this population.

Long COVID was more frequent among women (65.5%). This finding was observed in other studies that identify the female sex as a risk factor for long COVID. As for neurological symptoms, it was found that the frequency of anosmia and alterations in taste during long COVID was surprisingly high among the patients analyzed since 80% of these dysfunctions are usually recovered within two weeks. On the other hand, this study demonstrated that 41.8% of the interviewed patients presented cognitive impairments that persist after a month or more (according to Table 1), which is consistent with studies that highlight “brain fog” as one of the primary neurological manifestations present during the long COVID. Premaraj et al. found that, in the first three months after the acute phase of the disease, about one-third of the patients had deficits in memory and concentration. However, when the period evaluated is seven months, this index can reach 72% of patients.

Sleep alterations were also found in the study through the report of episodes of nocturnal awakening, excessive daytime sleepiness, insomnia, and difficulties in waking up even after long periods of sleep, characterizing it as a sleep disorder. Such alterations can be explained by the loss of specific cells located in the lateral hypothalamus due to the neurotropism of SARS-COV-2. In the AMESC region, sleep alterations were also observed in most patients during the acute phase of the disease (66.7%). Similar results were found in a study carried out by the University College London, which showed that 78.6% of 3203 patients reported sleep disorders in the first weeks.

On the other hand, in the AMREC region, about one-third of the patients reported sleep disorders in the chronic phase of the disease. This significant difference (p = 0.014) possibly occurred due to the reverse geographic distribution between the two regions since AMESC has a larger population in rural areas, while AMREC is predominantly urban. Therefore, people residing in urban areas are more likely to develop stress due to nighttime routines, excessive work, and poor diet, which are risk factors for reduced sleep quality. In contrast, people residing in rural areas perform manual work, outdoors activities, and are exposed to greater exposure to daylight, which could be related to better sleep quality. Fragmented sleep patterns can cause significant impacts on the daily activities of these patients, from reduced performance at work to the necessity to seek more health services, as sleep disorders may be associated with a variety of chronic diseases, such as diabetes mellitus and arterial hypertension. Furthermore, the worsening of this disorder can trigger narcolepsy, a disabling hypersomnia disorder.

Cognitive impairments represented the main neurological manifestation observed in this study in patients with long COVID in the AMREC and AMESC, especially in those who persisted with symptoms after 10 months or more, which aligns with previous literature. Cognitive impairments are understood as significant deficits in at-
tention, short-term memory, concentration, and emotional processing\textsuperscript{32,33}. In international studies, the term “brain fog” is used to refer to these alterations\textsuperscript{42} and the neurotropism of SARS-CoV-2 is attributed as the cause of this disorder since when it enters the central nervous system (CNS) through the olfactory nerve, the virus settles especially in the hippocampus, impairing cognitive processes\textsuperscript{33-37}.

This intellectual dysfunction significantly reduces the patients’ quality of life, especially in their work routine\textsuperscript{21,38}. Thus, 86% of employees feel unable to work after 7 months due to cognitive impairments\textsuperscript{51}. These observations highlight the importance of long-term care for these patients, with adjustments in the work environment, such as telecommunication, flexible hours, and gradual return, which allow adequate recovery time\textsuperscript{21}. In addition, multidisciplinary follow-ups are indicated for these patients, especially with occupational strategies for intellectual strengthening, such as mental repetition exercises, relaxation techniques, and screening of the areas of greatest deficit. Regarding drugs, there is evidence that Luteolin attenuates cognitive impairment, but other prolonged clinical studies need to be carried out\textsuperscript{38}.

As for smell and taste alterations, the literature described that the duration of these symptoms varied between 7 and 14 days\textsuperscript{40}, that most of these patients showed improvement between one and three weeks\textsuperscript{39}, and 98% of the patients studied recovered from anosmia and dysgeusia in 28 days\textsuperscript{40}. However, the results of this study demonstrated the prolonged persistence of these symptoms in both regions, with 8.13% of the patients presenting anosmia and 6.47% of dysgeusia in the period of 10 months or more. Although there is currently no specific treatment for this clinical condition\textsuperscript{42,43}, there is a need to supervise those patients with more prolonged symptoms in both regions.

The mechanism attributed to anosmia is related to the direct aggression of SARS-CoV-2 to the sustaining cells of the olfactory bulb, causing an interruption in the signaling of olfactory sensory neurons and, consequently, loss of sensorineural cilia\textsuperscript{44}. As for dysgeusia, due to the angiotensin 2 receptors (ACE-2) present in the salivary glands and in the back of the tongue, these regions are early targets for the virus, causing local inflammatory reactions that generate the disorder\textsuperscript{45,46}.

There are few studies that address the use of health services by patients from the regions surveyed with long-term COVID\textsuperscript{47-49}. This study found that 98.8% of the patients with persistent symptoms in the AMESC region sought some medical care, a higher percentage than the study carried out by Menges et al.\textsuperscript{47}, who highlighted the search for medical assistance by about 40% of patients. It is also noted that at AMESC, the main option chosen by patients was primary care, which is in accordance with the literature\textsuperscript{48}, which reinforces the relevance of public health as a space for empathetic acceptance of patients’ complaints\textsuperscript{49,51}.

This search for medical care demonstrates that evaluating patients with long-term COVID-19 tends to be a significant challenge for health services\textsuperscript{52}. The association between the chronic phase of the infection and the worsening of patient’s quality of life indicates the need for the development of specialized services for the care of patients with post-COVID syndrome, especially with a tendency to increase the total number of cases worldwide. In that regard, to develop public strategies aimed at these patients, it is essential to delimit the symptoms during the chronic period of SARS-CoV-2 infection\textsuperscript{53}. Thus, this research demonstrates relevant evidence for understanding the symptoms and the development of investigation protocols in the two regions studied.

Specific treatment recommendations are still scarce\textsuperscript{54}, and a multidisciplinary, individualized, longitudinal approach is indicated to search for warning signs for specialized evaluation and monitor the recovery progress\textsuperscript{55}. Rehabilitation should be patient-centered and adapted to their needs, focusing on symptomatic intervention, educational measures, and improving quality of life\textsuperscript{56}. On the other hand, the study significantly demonstrated that 57.2% of patients with long COVID in the AMREC region did not undergo treatment, conduct that does not coincide with the general recommendations for long-COVID\textsuperscript{56}. Thus, self-medication, the immediate need to return to the work environment, and the lack of information about symptoms and treatment stand out as factors for distancing these patients from health services\textsuperscript{57,58}.

Monitoring, medical evaluation, and rehabilitation are essential to ensure the visibility of this population affected by long-term COVID-19\textsuperscript{59,60}. In addition, due to the possible association between SARS-CoV-2 infection and the occurrence of comorbidities such as diabetes mellitus and arterial hypertension, which are frequent in urban environments\textsuperscript{59}, the present study suggests prolonged follow-up of patients at AMREC by health professionals from each city that integrates the association.

LIMITATIONS

The present study found, as a limitation, the use of self-reports to assess symptoms. Thus, data on the duration and presentation of manifestations may be overestimated or neglected. In addition, telephone contact with patients is a limitation, evidenced by the high rate of unsuccessful calls. Finally, literature on long COVID are still scarce in national database, making these studies encouraging instruments in Brazilian territory.

CONCLUSION

Cognitive impairments, fatigue, and anosmia were the most persistent symptoms in the two regions studied. It was observed that, among the neurological symptoms,
cognitive impairments, anosmia, and taste alterations were the most frequent in patients with long COVID in the studied population. In addition, differences in the treatment and duration of sleep disorders were observed between participants from the AMREC and AMESC regions. Therefore, further studies should focus on both regions so that they are prepared for treating the symptoms observed in the patients, reducing the quality of life impact on the population.

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