

NEUROPATHIC PAIN IN COVID-19 INFECTION: A SYSTEMATIC REVIEW

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Abstract: Introduction: Neuropathic pain is a symptom present in COVID-19 infections. It is known that patients infected by the virus develop some type of neurological impairment, so neuropathic pain may appear as a possible manifestation of the disease. With this, this article aims to demonstrate how this symptom appears in the sick and emphasize the importance of the topic act since it is a new and still poorly understood disease. **Methodology:** Systematic review of studies published from March, 2019 to January, 2020 from the Scielo, Lilacs and PubMed databases. **Results:** A sample of articles was performed after implementing the inclusion and exclusion criteria. The studies were published between 2021 and 2022. All articles were found on Pubmed, while other sources from sources such as Scielo and Lilacs did not bring results. The presence of several neuropathies between 7.69%-24.8% in the selected studies. Depression presented a possible relationship with our patients. Most of the patients were in the intensive care unit. **Conclusions:** A strong relationship was observed between COVID-19 infection and some type of pain syndrome. Neuropathic pain was not very present.

Keywords: Neuropathic pain, COVID-19, SARS-CoV-2, Chronic pain

INTRODUCTION

Pain can be defined as “an unpleasant sensory and emotional experience associated with, or similar to that associated with, actual or potential tissue damage” (RAJA, et al., 2020). It is known that in several cases of COVID, pain is a symptom that can be accompanied and that its chance of recurrence increases as the patient is kept in intensive care units. (KEMP., CORNER., COLVIN, 2020) COVID is associated with several types of pain, but neuropathic pain,

due to its tendency to chronification, deserves to be treated in a more thorough way.

Chronic pain has been shown to be related to psychological stressors, viral infection and the consequences of admission to the intensive care unit. In addition, it is known that COVID has a tendency to cause central and/or peripheral neurological complications, due to the direct invasion of the virus into the central nervous system or through an immune system response to fight the infection, hence the pain. neuropathic can become a common complaint. Therefore, the purpose of this review is to correlate neuropathic pain with COVID infection (ATTAL; MARTINEZ; BOUHASSIRA, 2021)

METHODS

This is a Systematic Review of the literature that went through the following steps: elaboration of the review protocol, formulation of the research question, search for studies, selection and evaluation of studies after application of predetermined inclusion and exclusion criteria. The platforms Pubmed, Scielo, Lilacs were used as a database for the research. We included in this study articles searched between the dates of March 2020 and January 2022. The search was carried out using descriptors in English and Portuguese and their correlates. We use the terms “COVID” and “Neuropathic pain” as descriptors. In the search, 82 articles were found and 6 of them were selected. As inclusion criteria, we used patients over 18 years of age, clinical studies in indexed journals. We excluded articles that were reviews, case reports, articles that addressed treatment issues.

RESULTS

A sample of 6 articles was obtained after implementing the inclusion and exclusion

criteria. The studies were published between 2021 and 2022. All articles were found on Pubmed, while other research sources such as Scielo and Lilacs did not bring results. All articles are in English. Among the selected articles are cohort, case-control and cross-sectional studies. The number of participants in each study ranges from 9 to 1320 patients and the age ranges from 18-87 years.

Table 01 contains data on the articles analyzed regarding the order of organization, main author, year of publication, date of publication, title and type of study.

Regarding the main results of the studies, all addressed neuropathic pain in COVID-19 infection. Some of them brought possible risk factors related to the occurrence of neuropathic pain. Others spoke more about the number of cases of patients complaining of neuropathic pain after infection. Data related to the main findings of the articles can also be seen in table 01:

Of the selected studies, 4 evaluated the percentage of patients with complaints compatible with neuropathic pain, mainly through the application of questionnaires such as DN4 and NTSS. Among these studies, the percentage of neuropathic pain ranged between 7.69%-24.8%. In the study conducted by OJEDA, Antonio et al., 2021, patients who were in the ICU for more than 10 days or with APACHE II greater than 14 were chosen, that is, patients with greater chances of presenting pain symptoms and evaluated the occurrence of pain. pain of recent origin in them. Of these, 65 patients were selected for the study, with 50.8% (33 patients) reporting recent-onset pain; 38.5% clinically significant pain, 16.9% neuropathic pain. 10 of 33 (30%) patients with pain of recent origin had pain compatible with neuropathic origin.

In another study conducted by JENA, Debasish et. al, 2022, the occurrence of pain

TITLE	REFERENCE / YEAR	DATABASES	KIND OF THE ARTICLE	MAIN FOUND
Characteristics and influence on quality of life of new-onset pain in critical COVID-19 survivors	OJEDA, Antonio et al., 2021	December 6, 2021, Pubmed	COHORT STUDY	Of 65 patients, 16.9% reported neuropathic pain:
Insight into pain syndromes in acute phase of mild-to-moderate COVID-19: Frequency, clinical characteristics, and associated factors	OGUZ-AKARSU, Emel et al., 2021	October 8, 2021, Pubmed	SECTIONAL STUDY	Of 222 study participants, 159 reported at least one type of pain syndrome. Among those analyzed, 55 patients (24.8%) reported neuropathic pain.
Cohort study protocol to characterize the incidence and severity of neuropathic pain in patients with severe acute syndrome coronavirus 2 infection/ April 2021	ODOZOR U., Chioma et al., 2021	April 20, 2021, Pubmed	COHORT STUDY	An increase in the incidence of new-onset neuropathic pain is expected after COVID-19 illness along with an increase in severity experienced by COVID-19 patients with pre-existing chronic pain.
Musculoskeletal and neurological pain symptoms among hospitalized COVID-19 patients	JENA, Debasish et. Al, 2022	January 19, 2022 Pubmed	CROSS-SECTIONAL STUDY	Neuropathic pain was present in 14 (7.69%) of 182 patients evaluated.
Multisystem Involvement in Post-Acute Sequelae of coronavirus Disease 19	NOVAK, Peter et. Al, 2022	January 18, 2022 pubmed	COHORT STUDY	Patients with PACS and POTS reported neuropathic pain, fatigue, and dyspnea
Characteristics and risk factors of persistent neuropathic pain in recovered covid-19 patients	MAGDY, Rehab et al., 2021	December 21 , 2021 pubmed	CASE CONTROL	Depression, longer and more severe illness, and increased ferritin levels as risk factors for neuropathic pain

TABLE 01.

in patients with covid 19 was evaluated, which showed rates of neuropathic pain even lower than those found by OJEDA, Antonio et al. 2021. We included 182 patients who were hospitalized for covid-19 with a mean age close to 48 years. Pain symptoms were reported in 61.54% of patients, most were related to myalgia with 32.96%, while pain of neuropathic origin was present in only 14 patients (7.69%).

In addition to hospitalization in the intensive care unit, other possible risk factors were taken into account when talking about neuropathic pain in covid infection. One of the selected studies was a case control conducted by MAGDY, Rehab et al, 2021, in which they took two different groups. A group that had covid and did not evolve with pain and a second group that had the infection and evolved with pain. All patients who scored at least 4/10 on DN4 were included in this study. In the results, it was observed that patients who had neuropathic pain had more depression, increased disease duration, more severe cases and increased ferritin levels than control cases.

In addition, a painful syndrome can be found in most individuals who have had covid-19, and this can be observed in the study carried out by OGUZ-AKARSU, Emel et al., 2021, in which they tried to analyze how these syndromes behave. In it, of 222 participants, 159 reported at least some type of pain. Among these, only 55 patients (24.8%) reported neuropathic pain while 110 (49.6%) reported myalgia.

DISCUSSION

Pain related to COVID-19 infection is extremely common and occurs in some patients in the acute phase or even weeks after infection. This pain can manifest itself in different ways, behaving as a simple myalgia or through a neuropathic involvement. This

was described by JENA, Debasish et. al, 2022, in which 61.54% of COVID patients reported some type of pain syndrome.

Neuropathic pain is a symptom that must be frequent, mainly due to the tropism of COVID for affecting the central nervous system. However, its incidence was low (7.24%), when compared to the number of people with myalgia, for example (32.96%), as described by JENA, Debasish et. al, 2022.

It is known that prolonged hospitalizations in intensive care units can increase the risk of chronic pain, since most patients undergo invasive procedures and are exposed to moments of continuous stress. However, comparing the observed studies, the rate of patients with pain of neuropathic origin still remains low, even in those with long duration in the ICU as described by OJEDA, Antonio et al., 2021, in which only 16.9% of patients reported pain compatible with neuropathic origin.

In addition, the occurrence of neuropathic pain depends not only on the degree of systemic and inflammatory involvement, but also on the occurrence of external factors such as anxiety and depression. It is noticed that patients with a tendency to depressive disorders are more likely to develop chronic pain, such as neuropathic pain. This is reinforced by the study conducted by MAGDY, Rehab et al, 2021, in which patients who had neuropathic pain had more depression than when compared to controls.

Although there is some degree of relationship between the onset of neuropathic pain in patients who have had the COVID-19 infection, more studies still need to be conducted. It is known that COVID, like other viruses, can have some degree of neurological involvement and this must be further explored in the coming years. Because it is still a new disease, we do not know how the incidence of infection-related

neuropathic pain will impact in the future. However, it is expected that the number of people living with pain will increase, hence the importance of this study.

Furthermore, the ideal would be for future studies on the subject to address patients in different contexts, both in outpatient and hospital settings, so that more concrete information can be obtained on the subject.

CONCLUSION

A high correlation of COVID-19 with some type of pain syndrome was observed, being present in up to (70%) of patients. Myalgia was the most frequent pain of recent origin (32%). A low incidence rate of neuropathic pain was found in studies with variations between (7.24% - 24.8%). Most of the studies were conducted in intensive care unit settings. A relationship was observed between patients with symptoms of neuropathic pain and depression.

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