



## **Negative influence on tension headache during acute crisis and after Covid-19 infection: a systematic review**

*"The Negative Interference in Voltage-Type Headache During the Acute Phase and After COVID-19 Infection: A Systematic Review"*

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### **SUMMARY:**

In 2019, the SARS-CoV-2 pandemic began. The highly contagious coronavirus, which transmits COVID-19, reached global proportions. Numerous symptoms were reported during the symptomatic phase, with headache reported in approximately 6-15% of patients, and in preliminary studies, it reached approximately 60% of cases, being highly associated with fever. The pathophysiology is interconnected with direct mechanisms of viral injury, such as inflammatory processes, and can persist beyond the acute phase, with cases of persistence after a long period of infection, with moderate to severe intensity. This article is a systematic review conducted using databases with eligibility criteria consisting of complete studies published in the last three years, focusing primarily on COVID-19 infection, accentuating previous tension-type headache attacks and those developed during the acute phase. The studies revealed the ineffectiveness of neuroradiological and laboratory tests, as they revealed no changes in the pathophysiological mechanisms involved. Headache in the early phase of infection was associated with a previous history of migraine, thus having a greater chance of persisting after COVID-19 infection. Therefore, it is concluded that COVID-19 infection exacerbates headache attacks, with tension headache being one of the most prevalent symptoms, especially in women, during SARS-CoV-2 infection. It is also more prevalent in patients with a previous history of headache and migraine, and is a persistent symptom post-COVID-19.

**Keywords:** Tension Headache. Covid-19. Acute attacks. Systematic Review.

### **ABSTRACT:**

In 2019, the SARS-CoV-2 pandemic began, a coronavirus with a high capacity for spread and transmitter of COVID-19, reaching global levels. With reports and descriptions of numerous during the symptomatic phase, headache was reported in about 6-15% of patients, and in preliminary studies reached about 60% of cases, being highly associated with febrile conditions. Pathophysiology is interlinked with direct mechanisms of viral injury, such as inflammatory processes, and may last beyond the acute phase, with cases of persistence after a long period of infection with moderate to severe intensity. This article is about a Systematic Review made by means of databases with eligibility criteria being complete studies published in the last 3 years, whose main focus is COVID 19 infection accentuating previous tension headache crises and developed during the acute phase. The studies showed that neuroradiological and laboratory tests were ineffective, as there were no changes in them about the pathophysiological mechanisms involved. Headache in the early stages of infection was associated with a history of migraine progression, thus having a higher chance of enduring post-COVID-19 infection. It is therefore concluded that COVID-19 infection accentuates

headache attacks, noting tension headache as one of the most prevalent symptoms, mainly in females, during SARS-CoV-2 infection, and is more prevalent in patients with a previous history of headache and migraine, being a persistent symptom after COVID-19.

**Keywords:** Tension headache. Covid-19. Acute seizures. Systematic Review.

## 1. INTRODUCTION

In 2019, the SARS-CoV-2 pandemic began, a coronavirus with high capacity for dissemination and transmission of the COVID-19 disease, reaching levels global. There are reports and descriptions of numerous symptoms during the symptomatic phase, headache has been reported in about 6%-15% of patients, and in preliminary studies it has reached approximately 60% of cases, being highly associated with fever. However, although frequent, the description of the characteristics of headache symptoms can be nonspecific and raise doubts about the origin of the pain. Differential diagnosis should consider underlying pathologies, such as primary headaches, pain of functional origin such as the increased use of PPE (personal protective equipment), in addition to related conditions anxiety and other factors (PORTA-ETESSAM et al, 2022).

Pain in younger patients is more frequent, and patients who have underlying medical conditions Previous headache-causing conditions, such as migraines and tension headaches, also present greater chances of persistent pain after SARS-CoV-2 infection. pathophysiology is possibly associated with direct mechanisms of viral injury, processes inflammatory, hypoxemia, coagulopathies and endothelial involvement, and the pain may last longer than the acute phase of the disease, with cases where it persists even after long periods after infection (ROCHA-FILHO, 2022).

Although COVID-19 related headache should be classified as "headache" origin of viral infection" its symptoms can be very similar to migraine or tension headache, without a clear predominance of a pattern (FERNÁNDEZ-DE-LAS-PEÑAS et al, 2021). The pain is usually bilateral, of compressive quality, and can be moderate to severe in intensity, associated with nausea, vomiting and photophobia (DONO et al, 2021).

In view of the recent pandemic, and because there is still a lack of studies on the relationship between intensity of tension headache and SARS-COV-2 infection in exposed patients and

patients not exposed to COVID-19, it is clear that there is a need for further studies on the cases described, and the observation of the quality of their results, since it is a high-risk pathology incidence and the impact it can have on the quality of life of those affected, it is necessary this systematic literature review to clarify whether exposure to COVID-19 can be considered a risk of harm to patients with tension headache.

## 2. MATERIAL AND METHOD

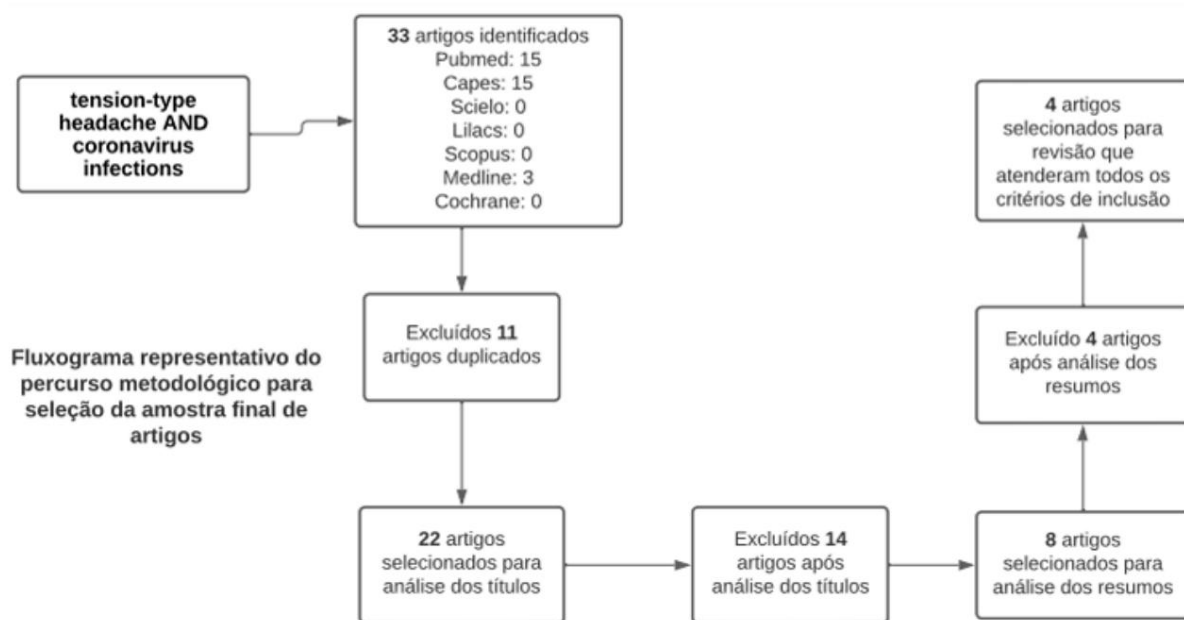
This is a Systematic Review carried out in the period from August two thousand and twenty and two on November 1 of the same year. This type of study summarizes the results of primary studies using strategies that reduce the occurrence of random errors and systematic. This way, it is possible to have comprehensive and reliable access to results of numerous works already published on a given topic (ROEVER, 2017). Furthermore, Roever (2017) further defines Systematic Review as:

(...) Process of researching, selecting, evaluating, synthesizing and reporting the clinical evidence on a particular question and/or topic. In Nowadays, systematic review is considered a more effective way rational and less biased way of organizing, evaluating and integrating scientific evidence (ROEVER, 2017).

This review was prepared using the recommended steps for systematic reviews - PRISMA checklist -, which contains twenty-seven items, divided into seven categories, including: title, abstract, introduction, methods, results, discussion and funding (PAGE et al, 2021). The research was carried out through the Scielo, Pubmed, Capes, Medline, Scopus, Lilacs and Cocharane with the following descriptors: headache tension-type AND coronavirus infections in DESC and tension-type headache AND coronavirus infections in MESH. 33 articles were identified and after excluding these duplicates, 22 remained for title analysis. After carrying out this verification, they were 8 articles were selected for abstract analysis and 4 for review, as demonstrated in flowchart below:

3

**Flowchart representing the methodological path for sample selection  
end of articles**



Source: prepared by the authors.

Eligibility criteria were full studies published in the last three years (2020-2022) in English and Portuguese. Exclusion criteria were publications made in other languages, not complete and published more than three years ago or that did not address the topic, mainly those who associated tension headache with infections other than COVID 19. Furthermore, the review was based on case-control, cohort and case report studies, which had as their main focus the COVID 19 infection, accentuating headache attacks tensional. To correlate the studies, a table with codes was created, aiming identify each article individually. Therefore, each article received a code to citation during the study.

TÍTULO DO ARTIGO	CÓDIGO
New <u>daily persistent headache after SARS-CoV-2 infection: a report of two cases</u>	A1
The <u>presence of headache at onset in SARS-CoV-2 infection is associated with long-term post-COVID headache and fatigue: A case-control study</u>	A2
<u>Headache Attributed to SARS-CoV-2 Infection or COVID-19 Related Headache — Not Migraine-like Problem-Original Research</u>	A3
<u>Spectrum of Headaches Associated With SARS CoV-2 Infection: Study of Healthcare Professionals</u>	A4

Source: prepared by the authors.

### 3 THEORETICAL FRAMEWORK

#### 3.1 SYMPTOMATOLOGY OF HEADACHE IN ACUTE SARS-COV2 CRISIS

From the selected and analyzed articles A2 and A3, we can infer based on the sample of cases monitored that the emergence of headache, especially tension and migraine type, was one of the most common symptoms in patients who were infected with the SARS-CoV-2, reaching more than 50% of the total number of patients monitored, meeting with the findings in the literature (ROCHA FILHO, 2022). Furthermore, it provided new analyses as being even more prevalent in patients who already had previous headache symptoms and patients who developed headache symptoms in the acute phase of the disease. In these patients, the symptoms lasted longer and more persistently (KACPRZAK, MALCZEWSKI, DOMITRZ, 2021) (FERNANDEZ-DE-LAS-PÉÑAS, 2021).

#### 3.2 HIGHER PREVALENCE OF TENSION HEADACHE IN FEMALES

Studies A2 and A4 also demonstrate a greater predominance in females compared to males, in the proportion of 6 to 4 (60%) in study A2 and 8 to 4 (60%) in study A2.

to 2 (81%) in study A4. Regarding the duration of headache symptoms tensional, studies have shown a reduction over time, although it can last for more than 180 days, especially in patients who had headache symptoms prior to the COVID-19 infection. Comparing the data obtained through the analysis and interpretation of studies cited with the findings in the literature regarding the higher prevalence in the sex female, it can be correlated to the fact that women have a higher incidence and previous prevalence of headache, especially tension-type and migraine, which corroborates also the findings that patients who had a history of headache prior to infection by the virus had more pronounced headache symptoms during the acute phase of the disease and sequelae that lasted longer (GARCÍA-AZORÍN et al, 2021). About 83% of patients who had migraine prior to the SARS-CoV-2 virus reported the development of a tension-type headache as a new post-infectious symptom (KACPRZAK, MALCZEWSKI, DOMITRZ, 2021). It is also worth noting that in no of the selected studies there was any type of conflict of interest.

### 3.3 ETIOLOGY OF HEADACHE IN ACUTE SARS-COV2 CRISIS

According to study A1, which both patients followed were undergo a complete clinical and neuroradiological evaluation in addition to a blood sample with research on inflammatory biomarkers also having been carried out, no findings were revealed no pathological change, the cause being then maintained as idiopathic, however according to with the literature, the pathophysiology of headache in the covid 19 crisis suggests that it arises through mechanisms resulting from systemic involvement of the disease and not from a primary invasion of the central nervous system and of an inflammatory nature (SIQUEIRA, BRAGA, PAGLIA, 2022).

## 4. RESULTS AND DISCUSSION

The search process in the aforementioned databases resulted in a total of 33 articles. The articles found were compiled using the EndNote platform, thus allowing the identification and exclusion of 11 duplicate articles. Of the remaining 22 articles In the end, 4 articles that met the inclusion criteria were selected.

### Variables analyzed in the reviewed studies



Artigo selecionado	Número de participantes	Ano de publicação	País	Autor	Desenho do estudo	Nível de evidência - GRADE
A1	2	2021	Itália	DONO, et al	Relato de caso	Muito Baixo
A2	615	2021	Espanha	FERNANDEZ-LAS-PEÑAS, et al	Caso controle	Baixo
A3	100	2021	Polônia	KACPRZAK, MALCZEWSKI, DOMITRZ	Caso controle	Baixo
A4	112	2020	Espanha	PORTA-ETESSAM, et al	Coorte	Moderado

Source: prepared by the authors.

Study A1 is a case report study, which followed 2 patients with persistent headache and Sars-CoV-2 infection, who underwent a clinical evaluation and complete neuroradiological examination, as well as blood tests. In case 1, it was monitored and performed the anamnesis of a 49-year-old woman who sought care due to a headache persistent that began 10 days before admission and that had started symptoms 4 days after the onset of respiratory symptoms associated with the Sars-CoV-2 virus in which it was the serology test was performed with a positive result. The tests were carried out neuroradiological and blood tests, without any type of alteration or presence of inflammation. The Table 2 below shows the timeline showing the correlation between the emergence of symptoms of the Sars-CoV-2 virus and the subsequent appearance of headache, which proved to be persistent.

In case 2, a 41-year-old woman was followed up and admitted to the emergency room. with sudden onset of asthenia and hypoesthesia on the left side, his anamnesis was not any previous headache symptoms were found in a 5-year period. A nasopharyngeal swab test for SARS-CoV-2, which was positive. A head CT scan was performed and blood tests, both without alterations. On the twentieth day of follow-up, the patient still had a persistent headache that did not respond to pharmacological treatment. In study A2 of the case-control type, the study was carried out with 615 patients hospitalized during the first wave of SARS-CoV-2, separating 2 groups, a group of 205 patients who presented headache symptoms during the acute phase and a second group of 410 patients who did not present headache symptoms during the acute phase, and after 7 months of discharge from the hospital interviews were conducted by calling patients and a questionnaire was completed about of symptoms related to SARS-CoV-2, resulting in patients with headache at baseline had a higher number of post-COVID symptoms (incidence rate:

1.16, 95% CI: 1.03–1.30). Headache at onset was associated with a previous history of migraine (Odd Ratio: 2.90, 95% Confidence Interval: 1.41–5.98) and with the development of persistent tension-type headache as a new symptom post-COVID (Odd Ratio: 2.65, CI 95%: 1.66–4.24). Study A3, a case-control study, involved 100 health workers randomly selected individuals who presented symptoms associated with COVID-19 disease, 96 were confirmed with positive serology in the last 3 months and a questionnaire to focus on primary headache disorder and its comparison with the characteristics of headache in COVID-19. In which 83% of participants reported headache as one of the post-COVID symptoms of moderate to severe intensity and an average duration of 7-8 hours as shown in the table below, this being the most frequent predominant symptom.

### Headache characteristics, accompanying features, and responses to treatment

Table 2

Headache characteristics, accompanying features, and treatment responses of patients experiencing.

Headache Characteristics	Number of Participants Reporting Symptom
Tension-type headache (squeezing pain)	36 (43%)
Pulsating headache	14 (17%)
Unilateral headache	5 (6%)
Whole head localization	41 (49%)
Frontal lobe localization	24 (29%)
Occipital lobe localization	8 (10%)
Length of headache episode	From 1h headache to 7 day headache; mean episode length 7 h 53 min.
Accompanying nausea/vomiting	26 (31%)
Accompanying photophobia/phonophobia	12 (14%)
Escalation by physical effort	39 (47%)
Migraine aura preceding headache	6 (7%)

Source: KACPRZAK, MALCZEWSKI, DOMITRZ, 2021.

In the A4 cohort study, headache characteristics were observed in healthcare professionals with clinically diagnosed SARS-CoV-2 infection and/or confirmed serologically, through self-administered questionnaires with the aim of characterize the type, duration and presence of headache associated with other symptoms. It was



a total of 112 questionnaires were answered, with 29 of the participants reported headache symptoms taking about 3.9-6 days to appear after the diagnosis of SARS-CoV-2. The following table compares the clinical features of headache in individuals with and without a history of migraine. Respondents with a history of migraine showed frequently reported exacerbation with activity, nausea, and vomiting; none of these differences was statistically significant.

## FINAL CONSIDERATIONS

Thus, it is concluded that yes, COVID-19 infection accentuates the crises of headache since the appearance of headache was one of the most common symptoms in affected by the SARS-CoV-2 virus infection. It has become even more prevalent in patients who had previous headache symptoms and in those who developed the symptoms of headache in the acute phase of the disease. In addition, around 6 to 45% of patients, according to the aforementioned articles, who complained of headache in the acute phase of the disease, headache persisted beyond the symptomatic phase. Furthermore, the headache was initially related to a previous history of migraine, leading to persistent tension-type headache as a product and a new post-covid symptom, in which it was added that the reported intensity of the headaches were considered moderate to severe, and lasted an average of 7 to 8 hours. Thus, it is concluded that infection by the SARS-CoV-2 virus acts to exacerbate headache attacks tensional affect them both in intensity and/or duration.

## REFERENCES

DONO, F. et al. New daily persistent headache after SARS-CoV-2 infection: a report of two cases. **Neurol Sci** 42. 3965–3968. 2021.

FERNÁNDEZ-DE-LAS-PENAS C, et al. The presence of headache at onset in SARS CoV-2 infection is associated with long-term post-COVID headache and fatigue: A case-control study. **Cephalalgia**.41(13):1332-1341. 2021.

GARCÍA-AZORÍN, D. et al. Frequency and phenotype of headache in covid-19: a study of 2194 patients. **Sci Rep** 11, 14674 (2021).



KACPRZAK, A.; MALCZEWKI, D.; DOMITRZ, I. Headache Attributed to SARS-CoV-2 Infection or COVID-19 Related Headache—Not Migraine-like Problem-Original Research. **Brain Sci.** 11, 1406. 2021.

PAGE, Matthew J. et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. **The BMJ.** V. 372, n. 71, p. 1-9, Jan. 2021.

PORTA-ETESSAM, J. et al. Spectrum of Headaches Associated With SARS-CoV-2 Infection: Study of Healthcare Professionals. Headache. **The Journal of Head and Face Pain**, 60: 1697-1704. 2020.

ROCHA-FILHO, S. Headache associated with COVID-19: Epidemiology, characteristics, pathophysiology, and management. Headache. 2022 Jun;62(6):650 656. **Epub.** 2022.

ROEVER, L. Understanding systematic review studies. **Rev Soc Bras Clin Med.** 15(2):127-30, Apr-Jun 2017.

SIQUEIRA, LFA; BRAGA, IP; PAGLIA, BAR Headaches and their relationships to Covid-19. **Research, Society and Development.** v.11, n.13. 2022.