



## Headache in a group of SARS-COVID-19 patients: an observational prospectical study

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Despite the recent outbreak of SARS-COVID-19 is mainly characterized by respiratory symptoms, neurological involvement has been reported in several cases, in which extended review, Ling Mao and colleagues [1] have described different neurological symptoms, with an involvement of the central nervous system (CNS), the peripheral nervous system (PNS), and the skeletal muscular injury. Headache is present in 13% of these patients, but the authors do not specify its characteristics and its relationship with the clinical features of COVID-19 [2, 3].

In this study, we report the findings of a small group of patients that have been hospitalized in order to better characterize the specific type of their cephalic pain. We have evaluated 73 patients in total (mean age 69.75), 52 of whom were males (mean age: 70.55) and 21 were females (mean age: 67.66). The patients have been treated with oxygen at different flow depending on their clinical state, drugs as antibiotics when necessary, antimalarial drug (hydroxychloroquine) and steroids when needed, but most importantly they have been asked multiple questions in order to better characterize their type of headache (we left out all the patients that were unable to provide reliable answers). No one has been evaluated with CT scan, but all patients had a normal neurological

examination: they did not have any clinical sign of impairment of the CNS/PNS or any other neurological symptom.

In the male group, 49 subjects did not complain about having headache (67.1%), while 3 patients reported headache during hospitalization (5.7%): 2 men suffered from tension type headache (TTH) only during hospitalization, whereas 1 patient complained about migraine without aura (MO) both during hospitalization and at home.

In the female group, 5 patients had pain during hospitalization (23.8 %): MO was present in 2 of them (9.5%), whereas TTH was reported by the other 3 (14.28%). Among these 5 women, 3 complained about pain also at home (1 MO/1 TTH/1 with MO and TTH).

Seven women out of 21 complained about pain at home: 5 referred pain with TTH characteristics (one of them suffered from both type of pain MO and TTH while one suffered only from MO).

All patients but two manifested headache during their first day of recovery, usually at low intensity with disappearance after 3–4 days without the need of any treatment.

Among the patients that were suffering from headache during their hospitalization, all subjects had either a chest CT scan or a Rx, which was indicative of interstitial pneumoniae or other findings related to this disease, swab was positive in 6 (3M/3F) negative in 1 female and not reported in 1 female.

Five subjects were treated with hydroxychloroquine (1M/4F): 1 man with antiretroviral therapy (Kaletra®), 3 with antibiotics, and 1 with steroid (desametasone).

Even if the mean age of our sample is older than the usual age of patients with primary headache, which may be related to the advanced age of COVID patients, the number of females still remains greater than the number of men (23.6% vs 5.7%).

Although the small size of our sample does not allow us to draw any conclusion, we can state that TTH is the prevalent type of headache. To date, the characteristics of headache

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during SARS-COVID-19 pandemic is lacking in literature, also in studies that are bigger than ours.

Our data are in line with those described in many different surveys: in China, Huang [2] has reported headache in 8% of the patients (41 subjects), while Ling Mao (1) has described the clinical characteristics of 214 subjects, 13.1% of whom had headache. Rodriguez-Morales has made a systematic review and a meta-analysis showing headache in 5.6% of 126 cases [3].

We know that our sample is too little to make relevant assumptions; however, the first impression is that headache is not a significant finding in SARS-COVID-19 disease, and TTH is the most present type of pain. This result may be caused by a stressful situation (hospitalization, solitary confinement of patients, inability to have anyone contact with their relatives), rather than being a primary symptom of the disease. Recent hypothesis has interestingly proposed that the engagement of cortical areas involved in breathing control, like for example the insular cortex, may be responsible for a reduced perception of hypoxaemia that is commonly observed in this subjects: this mechanism may perhaps also explain the low perception of headache in these patients and thus the reduced reported frequency of the pain. The same authors have proposed that a dysfunction of C fibers related to COVID may also contribute to a derangement of breathing observed in the SARS-COVID pneumonitis. Further studies with a larger number of patients will be required to better understand whether headache is a primary or a secondary symptom in SARS-COVID19 disease and also to characterize the pathogenetic mechanism of this important illness.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical standards** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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