

Headache Incidence and Characteristics in COVID-19 Patients: A Hospital-Based Study

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Abstract

Background: Headache is one of the commonly reported symptoms of coronavirus disease-2019 (COVID-19) illness. A number of studies have been done so far focusing on headache associated with COVID-19 with variable incidence and characteristics. **Material and Methods:** This study is a prospective study conducted on 120 patients with confirmed COVID-19 illness. Critically ill and ventilated patients were excluded. Demographic data, COVID illness symptom profile, headache characteristics were documented. Patients were followed up at 2 weeks and 4 weeks. For the statistical analysis, Statistical Package for the Social Sciences (SPSS), version 24.0 was used. **Results:** 120 COVID-19 positive cases were included in the study with a mean age of 54.59 ± 14.89 years (range 21-84 years) with male-to-female ratio of 3:2. 78.33% (94) of patients had various comorbidities. 43.33% (52) cases were diabetic. The presenting symptoms were fever (65%), cough (53.33%), shortness of breath (35%) and myalgia (31.66%). 26 (21.66%) patients reported headache during the COVID illness. 18 (15%) cases had headache attributed as secondary to COVID-19 illness. Out of them, 12 cases were new onset with no past history of headache and 6 cases had a significant change in previous headache episodes. COVID-19 illness precipitated headache episodes similar to past headache type in 8 cases. Headache was the presenting symptom in 8 (6.66%) patients with COVID-19 being detected in the regular hospital screening protocol. **Conclusion:** Headache was a common symptom in COVID-19 patients. New onset headaches or change in past headache type in patients in the setting of ongoing pandemic should be screened for COVID-19.

Keywords: COVID-19, headache, pandemic

INTRODUCTION

The novel coronavirus (SARS-CoV-2; 2019-nCoV; COVID-19) pandemic has emerged as a global crisis in the early 2020. The most prevalent symptoms reported were fever (78%), cough (57%) and fatigue (31%).^[1] Headache is one of the common neurologic manifestations in COVID-19 though it is frequently neglected. Various studies conducted so far showed incidence of headache ranging from 6.5%^[2] to as high as 70.3%.^[3] There is a paucity of literature with special emphasis on headache in COVID illness with highly variable results in already published research. We aimed to determine the incidence of secondary headache due to COVID-19 illness, to describe its characteristics and temporal relation of headache with other symptoms.

MATERIAL AND METHODS

This study was a prospective cohort study conducted in a superspeciality hospital from south India, from June 2020 to December 2020. Patients with confirmed COVID-19 illness by COVID-19 reverse transcription polymerase chain reaction (RT-PCR) were included in the study. Ethics committee approval taken dated 14th May 2020. Critically ill patients with dyspnoea, hypoxia, altered sensorium, hemodynamic instability, and on ventilator support who were unable to give history were excluded from the study. All cases were evaluated for headache by a neurologist in personal protection equipment (PPE). COVID-19 hospital safety protocol was

followed for each patient. To limit the duration of exposure, demographic information was retrieved telephonically via the patient's hospital room intercom connection. Patient's demographic profile, COVID illness symptomatology, headache characteristics including location, type, severity on visual analogue scale, frequency, duration, aggravating and relieving factors were documented on a proforma. Special emphasis was given on past history of headache and whether the present headache episode was same or different from past to determine new onset of headache. Secondary headache due to COVID-19 illness has included 1) a new-onset headache occurring for the first time in close temporal relation to COVID-19 illness irrespective of its characteristics of a primary headache, 2) a pre-existing primary headache made significantly worse (usually meaning a twofold or greater

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increase in frequency and/or severity) in close temporal relation to COVID-19 illness.^[4] All patients with a positive history of headache were followed for a period of 4 weeks telephonically after discharge from hospital. Calls were made at 2 weeks and 4 weeks. For the statistical analysis, Statistical Package for the Social Sciences (SPSS), version 24.0 was used and statistics included percentage, mean and standard deviation.

OBSERVATIONS

From June 2020 to December 2020, the hospital received 175 COVID-positive cases. 55 critically ill patients were excluded from the study. 120 COVID-19 positive cases were enrolled with a mean age of 54.59 ± 14.89 years (range 21 -84 years) and male-to-female ratio of 3:2. The detailed demographic profile and COVID symptomatology has been shown in Table 1. The average COVID-19 reporting and data system (CO-RADS) score was 4.33 (range 0–5) with mean chest CT severity index of 8.03 (range 0-20). Comorbidities like hypertension, diabetes, coronary artery disease, obstructive lung disease, chronic kidney disease were present in 78.33% (94) of cases. 43.33% (52) cases were diabetic. There were three or more than three comorbidities in 11.66% (14) cases. One patient had newly retroviral state positive. The common symptoms were fever (65%), cough (53.33%), shortness of breath (35%),

myalgia (31.66%) followed by headache (21.66%). Sore throat, diarrhoea, loss of smell/taste, and fatigue were less commonly reported. None of the patients had altered sensorium, neck rigidity or focal neurological deficit. 5% of cases were on oxygen support.

Out of 120 COVID-positive cases, 26 (21.66%) reported headache during COVID illness. Out of these, 12 cases reported new-onset headache without any past history of headache. Fourteen cases had a past history of headache (7 migraine headache, 2 tension-type headache, 2 sinusitis, 1 post-traumatic headache, 2 nonspecific headache types). Among these 14, 6 cases reported a change in their character of headache from their regular headaches. So overall, secondary headache due to COVID-19 illness was reported in 18 (15%) cases and in other 8 cases, COVID illness precipitated the headache episode of past headache type [Figure 1].

Characteristics of secondary headache in 18 (15%) cases are given in Table 2. Out of 18 secondary headache cases, 8 cases (6.66%) had headache as the first presenting symptom followed by fever (1-4 days interval range) and cough (1–8 days interval range). Location of headache was mostly bilateral in the temporal and frontal region. Headache was intermittent in all cases with variable duration of 30 minutes to 3 days. Onset was sudden as well as gradual with evening predilection. Headache

Table 1: Demographic and symptoms profile of COVID-19 positive patients

Parameter	Value, % (n)
Age (y)	54.59±14.89*
Male to female ratio	3:2
CO-RADS Score	4.30 [†]
CT-SI	8.03 [†]
Comorbidities	78.33 (94)
Hypertension	38.33 (46)
Diabetes Mellitus	43.33 (52)
Coronary artery disease	10.00 (12)
Others	13.33 (16)
Symptoms and signs	
Headache	21.66 (26)
Fever	65.00 (78)
Cough	53.33 (64)
Myalgia	31.66 (38)
Sore throat	11.66 (14)
Diarrhea	1.66 (2)
Loss of smell or taste	11.66 (14)
Fatigue	5.00 (6)
Shortness of breath	35.00 (42)
Altered sensorium	0 (0)
Focal neurological deficit	0 (0)
Neck Rigidity	0 (0)
Oxygen support	5 (6)
Ventilator support	0 (0)

n=number of cases. *Data are mean±standard deviation, [†]data are mean, RAT - Rapid Antigen Test, RT-PCR- Reverse transcription polymerase chain reaction, CO-RADS - COVID-19 reporting and data system, CT-SI - CT severity index

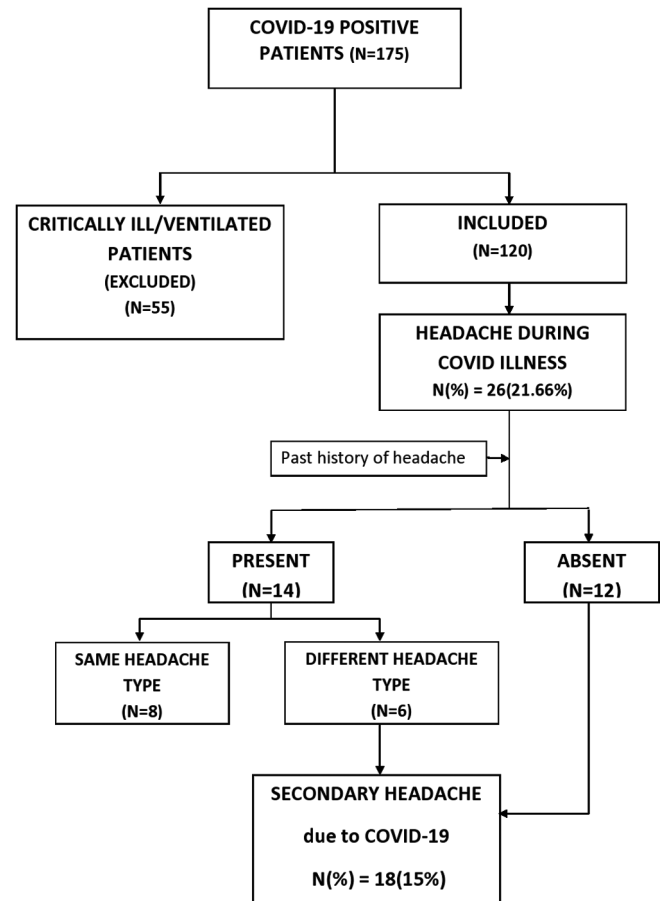


Figure 1: Flow chart showing study enrollment and headache classification

was mild (mean visual analogue scale 2.76) vague dull aching type in most of the cases. The associated features reported were nausea, vomiting, phonophobia and photophobia. Cough was a common aggravating factor followed by stress and fever. The relieving factors reported were sleep and hot beverages. Brain imaging was not done in any case. All 18 patients were

followed up telephonically for the next 1 month after discharge at 2 weeks and 4 weeks. There was complete headache relief in 8 out of 18 cases within hospital stay. Rest 10 cases were on painkillers when required and recovered within an average duration of 8.33 days after discharge. As per the international classification of headache disorders 3rd edition (ICHD-3b), only 5 out of 18 cases fit into a classical headache phenotype. 3 cases had tension-type headache and 2 cases had migraine features. Rest 13 patients were not classified.

Table 2: Characteristics of headache in COVID-19 illness

Headache characteristic	n (Total 18)
Location	
Temporal	7
Frontal	5
Occipital	2
Periorbital	2
Vertex	1
Holocranial	1
Laterality	
Bilateral	16
Unilateral	2 (right)
Nature	
Continuous	0
Intermittent	18
Onset	
Sudden	8
Gradual	10
Diurnal variation	
Morning	5
Evening	9
Afternoon	4
Quality of pain	
Vague Aching	14
Band like	3
Throbbing	1
Severity	
Mean visual analogue scale score	2.76 (range 2-6)
Associated features	
Nausea	2
Vomiting	1
Phonophobia	2
Photophobia	1
None	12
Aggravating factors	
Cough	3
Stress	2
Fever	1
Menstruation	1
None	11
Relieving Factors	
Sleep	3
Hot beverages	2
Head massage	1
None	12
Phenotype as per ICHD 3b	
Tension type headache	3
Migraine without aura	2
Non-specific	13

International classification of headache disorders 3rd edition (ICHD-3b)

DISCUSSION

Headache attributed to infection (bacterial, viral, fungal, parasitic) is one of the important subgroup in the secondary headache category as per ICHD-3b. Intracranial infection as meningitis or meningoencephalitis as well as systemic infection can lead to headache. There should be a temporal relationship between headache and infection onset to establish the causal link.^[4]

Pathophysiologically, intracranial infections cause headache via direct meningeal infiltration, inflammatory effects of the products of bacteria and by inflammatory mediators. Whereas systemic infections like influenza cause irritation of pericranial or intracranial pain-sensitive structures by direct infiltration, release of endotoxins or the immune response of inflammatory mediators. Some organisms may trigger brainstem nuclei with the end result of neurogenic inflammation and headache.^[5] COVID encephalitis has been reported in 6% of cases.^[6] In this study, none of the patients had meningoencephalitis. All new-onset headaches or headaches with a significant change in past headache type had been attributed to systemic COVID illness in view of presence of definite temporal relation between the two.

In COVID-19 illness, headache has been reported in the category of “less common symptoms” among the most prevalent ones like fever, fatigue, dry cough, myalgia and dyspnoea^[7] which is consistent with this study. But it was alarming that 8 out of 18 new-onset headache cases had headache as the first and only manifestation of COVID illness. Fever and cough followed the headache by a duration of 4- 8 days. In cases, headache preceded fever by 4 days and cough by 8 days. So in this pandemic era, any new-onset headache warrants low threshold for testing for COVID-19 resulting in early diagnosis before respiratory involvement to reduce the spread of infection.

Al-Hashel *et al.* reported 59.6% increase in migraine frequency and 64.1% increase in migraine severity during COVID era as compared to pre-pandemic period though only 4% migraine cases had COVID illness. The reasons are independent of COVID illness and multifactorial like poor follow up with neurologist, poor drug compliance, analgesic overuse, cancellation of botox sessions, poor sleep, anxiety and depression.^[8,9] Even mask-associated ‘denovo’ headache has been reported in 51.6 percent of healthcare workers.^[10] So attributing COVID-19 as the causative factor to all headache

types in COVID illness is probably not justified. Clinicians need to take the headache symptom in a broader perspective and consider other differentials even in the setting of COVID-19 illness. This study specifies that COVID illness-associated headache should be diagnosed in the setting of new-onset headache or change in past headache type in COVID illness with definite temporal relation between the two.

COVID-19 associated headache has been frequently reported as mild to moderate intensity.^[11] Uygun *et al.* 2020 found mild- and moderate-intensity headache in 74.3% vs severe and very severe headache in 25.7% COVID-19 positive patients.^[12] Various classical headache phenotypes like migraine or tension-type headache independent of past history of primary headache have been rarely reported except few studies.^[11,12] Cough was identified as a major aggravating factor.^[13] Such cases need neuroimaging to rule out possible intracranial lesions like Arnold-Chiari malformation type 1, spontaneous intracranial hypotension, carotid or vertebrobasilar diseases, middle cranial fossa or posterior fossa tumours, midbrain cyst, basilar impression, platybasia, subdural haematoma, cerebral aneurysms and reversible cerebral vasoconstriction syndrome.^[4] In this study, MRI brain was not done in any patient despite sudden onset in 8 cases and aggravation by cough in 3 cases. Because headache intensity was low on visual analogue scale in most of the cases with no focal neurological deficit on examination. There was satisfactory response to symptomatic treatment. COVID protocols for imaging in hospital also increased the threshold for MRI.

Various clinical correlates have been documented so far with headache in COVID illness. Headache has been commonly reported with anosmia/ageusia,^[11] younger age, fewer comorbidities and reduced mortality, as well as with low levels of C-reactive protein, mild acute respiratory distress syndrome, oropharyngeal symptoms,^[14] female sex and fever.^[15] Less number of positive headache patients in this study had limited us to show any particular pattern of COVID-19 associated headache, correlation of headache with various variables and effect of headache on prognosis. The second limitation of this study was inability to get brain imaging in all patients. It would have helped to rule out other secondary causes specially in current situation where cerebral thromboembolic events like ischemic stroke and cerebral venous sinus thrombosis are being frequently reported in association with COVID-19 illness. Moreover, exclusion of critically ill on ventilator patients limited us from reporting true incidence of headache in COVID illness. More data in the future will help us to better understand the headache pattern in COVID-19 patients.

CONCLUSION

Aetiology of headache during COVID pandemic can be multifactorial. But new-onset headache or change in past headache type should be considered a symptom and the threshold for COVID screening should be low in such patients

even in the absence of fever and cough. Secondary headache due to COVID illness can be described as either sudden or gradual onset, mild vague aching type, mostly in temporal or frontal location, bilateral, intermittent with variable duration and evening predilection, commonly aggravated by cough and relieved by sleep.

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Conflicts of interest

There are no conflicts of interest.

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