



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



# Acute symptomatic seizures and COVID-19: Hospital-based study

Eman M. Khedr<sup>a,\*</sup>, Ahmed Shoyb<sup>b</sup>, Mahmoud Mohammaden<sup>c</sup>, Mostafa Saber<sup>b</sup>

<sup>a</sup> Department of Neuropsychiatry, Faculty of Medicine, Assiut University, Egypt

<sup>b</sup> Department of Neuropsychiatry, Faculty of Medicine, Aswan University, Egypt

<sup>c</sup> Department of Neuropsychiatry, Faculty of Medicine, South Valley University, Egypt

## ARTICLE INFO

### Keywords:

COVID-19  
Seizure  
Cerebrovascular stroke  
Epilepsy  
CNS  
Encephalitis

## ABSTRACT

**Background and purpose:** Post COVID-19 seizures are relatively rare. The aim of the present study was to estimate the frequency of acute symptomatic seizures among patients with COVID-19 and to discuss possible pathophysiological mechanisms.

**Material and methods:** Out of 439 cases with COVID-19 that were admitted to Assiut and Aswan University hospitals during the period from 1 June to 10 August 2020, 19 patients (4.3 %) presented with acute symptomatic seizures. Each patient underwent computed tomography (CT) or magnetic resonance imaging (MRI) of the brain and conventional electroencephalography (EEG). Laboratory investigations included: blood gases, complete blood picture, serum D-Dimer, Ferritin, C-reactive protein, renal and liver functions, and coagulation profile.

**Results:** Of the 19 patients, 3 had new onset seizures without underlying pathology (0.68 % out of the total 439 patients); 2 others (0.46 %) had previously diagnosed controlled epilepsy with breakthrough seizures. The majority of cases (14 patients, 3.19 %) had primary pathology that could explain the occurrence of seizures: 5 suffered a post COVID-19 stroke (3 ischemic and 2 hemorrhagic stroke); 6 patients had COVID-related encephalitis; 2 patients were old ischemic stroke patients; 1 patient had a brain tumor and developed seizures post COVID-19.

**Conclusion:** acute symptomatic seizure is not a rare complication of post COVID-19 infection. Both new onset seizures and seizures secondary to primary brain insult (post COVID encephalitis or recent stroke) were observed.

## 1. Introduction

In addition to systemic and respiratory symptoms, it has recently been reported that 36.4 % (78/214) of patients with COVID-19 develop neurological symptoms (Mao et al., 2020), of which anosmia and headache are the most common whereas seizures and stroke are relatively rare (Whittaker et al., 2020). The proposed mechanisms of CNS involvement could be attributed to retrograde movement from the olfactory nerve, entry into CNS through circulating lymphocytes or entry through permeable blood brain barrier (BBB) (Moriguchi et al., 2020; Ye et al., 2020).

Given that patients with COVID-19 may have hypoxia, multiorgan failure, and severe metabolic and electrolyte derangements, it is plausible to expect clinical or subclinical acute symptomatic seizures to occur in some cases (Emami et al., 2020; Nalleballe et al., 2020; Romero-Sánchez et al., 2020). Only a few studies had been conducted to investigate the underlying mechanism of seizures associated COVID-19

(Emami et al., 2020; Hepburn et al., 2020; Nikbakht et al., 2020; Sohal and Mansur, 2020).

The aim of the present study is to estimate the frequency of seizures among Egyptian patients with COVID-19 and to discuss possible pathophysiological mechanisms.

## 2. Material and methods

This was an observational, retrospective cohort study sampled from all patients with suspected COVID-19 who were sufficiently ill to be admitted during the period of 1 June to 10 August 2020 to the largest two University hospitals in Upper Egypt (Assiut University Hospitals and Aswan University hospital). Evidence of SARS-CoV-2 infection was defined as: 1- Cases with definite COVID-19 if patients came with clinical symptoms of infection and PCR of respiratory samples (eg, nasal or throat swab) was positive. 2- Cases with probable COVID-19 if clinical symptoms and chest CT was consistent with COVID-19 plus one or 2

\* Corresponding author at: Department of Neuropsychiatry, Faculty of Medicine, Assiut University Hospital, Assiut, Egypt.

E-mail addresses: [emankhedr99@yahoo.com](mailto:emankhedr99@yahoo.com), [emankhedr99@aun.edu.eg](mailto:emankhedr99@aun.edu.eg) (E.M. Khedr).

laboratory investigations were positive (lymphopenia, high serum ferritin and D-Dimer Level) but PCR was negative or unavailable. Unfortunately it was not possible to sample CSF in these situations.

All patients who had “seizure” as a presenting manifestation of their illness were recruited and included in the study. The data of clinical manifestations of COVID-19 and the associated comorbidities were recorded. A chest CT was taken to demonstrate the ground-glass opacities of the lungs with consolidation and laboratory investigations including blood gases, complete blood picture, serum D-Dimer, Ferritin, C-reactive protein, renal, liver functions, coagulation profile. CT and/or MRI brain scan and EEG were performed in each patient.

### 2.1. The primary outcome

- 1 Estimation of the frequency of seizures either primary or secondary.
- 2 Determination of the type of seizures associated with COVID-19, complications with serial seizures or status epilepticus and correlation with laboratory and imaging studies.

### 2.2. Consent

Written informed consent was obtained from conscious patients or from first degree relatives of the others. The Local Ethical Committee of the Faculty of Medicine, Assiut and Aswan University/Egypt approved the study.

### 2.3. Statistical analysis

Data was coded, tabulated and recorded on a PC using the Statistical package for Social Science (SPSS 25). Number and percent or means ± standard deviation (SD) were used to represent data. The level of significance was set at  $P < 0.05$ .

## 3. Results

Among 439 confirmed or probable COVID-19 patients (337 (76.7 %)

recruited from Assiut university hospitals, and 102 (23.3 %) from Aswan university hospital, 19 (4.3 %) presented with seizures. The median age was 47 [IQR; 35–65] years; 7 (36.8 %) were males and 12 (63.2 %) were females.

Only 3 patients presented with new onset seizures without underlying pathology (0.68 %), another 2 patients had previously diagnosed, controlled epilepsy with breakthrough seizures (0.46 % of the total sample of patients). The other 14 patients had primary pathology that could account for the seizures (3.19 %). Five patients had a recent post COVID-19 stroke (ischemic or hemorrhagic stroke); 6 patients had COVID-19 related encephalitis; 2 patients had a previous stroke before developing COVID-19, and 1 patient had an old brain tumor and developed new onset seizures post COVID-19. See Fig. 1 flow chart. Details of all cases are presented below and in the Tables.

#### 3.1. Post-COVID-19: new onset seizure without underlying pathology

Three patients developed new onset seizures post COVID-19. All had fever, fatigue, dyspnea and gastrointestinal symptoms (GIT) for 3–5 days before developing generalized tonic-clonic convulsions. One patient had DM, the second had DM, hypertension (HTN) and a history of hepatic disease and the third patient had no comorbid disorders. Two patients had a positive PCR for COVID-19 and showed ground-glass opacity in CT chest; the remaining patient had a normal CT chest. One patient had anemia, thrombocytopenia, one had lymphopenia and the third one had normal laboratory data (Table 1).

#### 3.2. Post COVID-19: previously diagnosed, controlled epilepsy with breakthrough seizures

Two patients had a history of previously diagnosed, controlled epilepsy and had been seizure-free for up to 2 years prior to infection but had a recurrence of their seizures post COVID-19. One of them had fever, fatigue, cough, dyspnea and confusion for 4 days followed by serial seizures. The other one had fever for only 2 days before developing generalized seizures. Details of PCR and CT chest and laboratory data

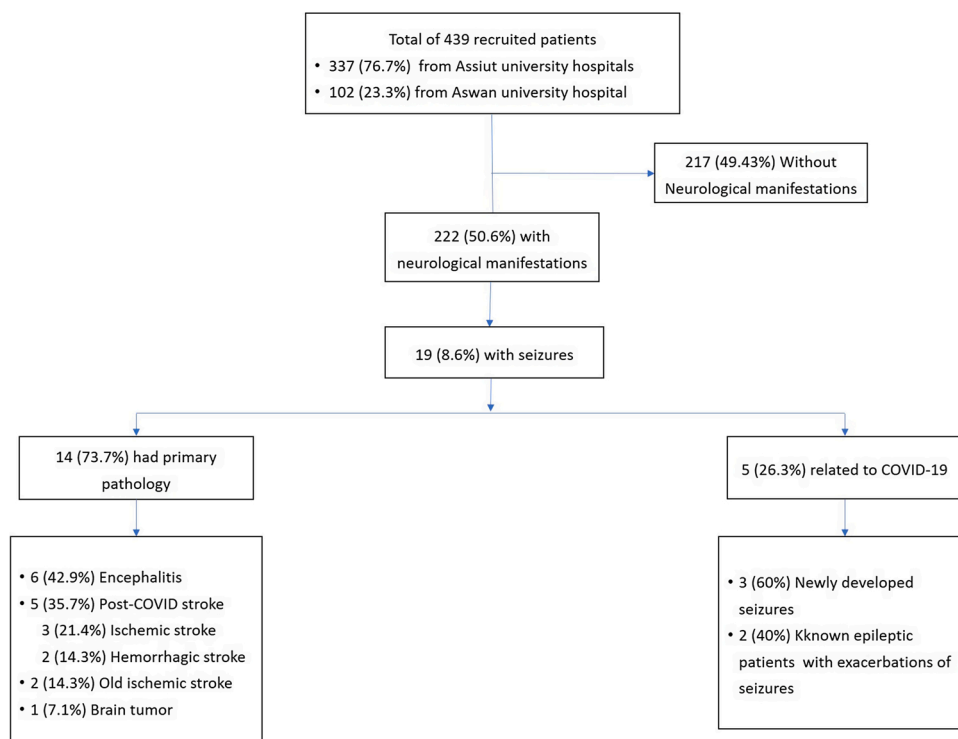


Fig. 1. The flowchart of all confirmed or probable COVID-19 patients (439) presented with seizures (19 patients).

**Table 1**

Post-COVID-19: new onset seizures without underlying pathology and in previously diagnosed, controlled epilepsy with breakthrough seizures.

Patient Number	Age (years)s)	Constitutional symptoms and duration of it	Type of seizures	CT Chest	PCR	Laboratory data	Comorbidity disorders
1	Mid 50 s	Fever, fatigue, diarrhea and confusion. 3 days	Generalized seizures (GTCC)	Not available	Positive	Normal	DM
2	late 40s	Fever, fatigue, dyspnea, abdominal pain and confusion. 5 days	Generalized seizures (GTCC)	Bilateral ground-glass opacity.	Negative	Normal	No
3	Mid 80s	Fever, cough and DCL. 3 days	Generalized seizures (myoclonus)	Normal	Positive	Anemia, thrombocytopenia	HTN, DM, Hepatic. Epilepsy
4	late 10s	Fever, fatigue, cough, dyspnea and confusion 4 days	Generalized seizures (GTCC) complicated by serial seizures	Bilateral ground-glass opacity.	Positive	Raised liver enzymes, low PO <sub>2</sub> , anemia, leukocytosis, lymphopenia.	
5	late 60s	Fever, for 2 days	Generalized seizures (GTCC)	Bilateral ground-glass opacity.	Positive	Low PO <sub>2</sub> , anemia and lymphopenia.	Epilepsy, HTN and DM.

PCR; polymerase reaction; GTCC; generalized tonic clonic seizures, HTN; hypertension, DM; diabetes Mellitus; DCL; disturbed level of consciousness; CT; computer tomography.

are illustrated in [Table 1](#).

### 3.3. Post-COVID-19: acute stroke (ischemic and hemorrhagic stroke as documented by CT/MRI brain) presenting with seizure onset

Three patients had a recent ischemic stroke with seizure onset after COVID-19 infection. All had fever, cough and sputum; one had additional dyspnea as constitutional symptoms for 3–7 days. Onset of seizure was coincident with stroke in all cases. One patient had generalized seizures and the other 2 had focal seizures with secondary generalization. Two patients had HTN and cardiovascular disease (CVD); one of them also had renal impairment. The third patient had raised liver enzymes. All 3 patients had a negative PCR for COVID-19 but they had bilateral ground-glass opacities on chest CT. All patients had raised D-dimer, anemia and leukocytosis; 2 of them had lymphopenia.

Of the two patients who had acute cerebral hemorrhage, one had fever, myalgia, cough and headache for 2 days followed by repeated

focal seizures and disturbed consciousness with and left hemiplegia. The other patient had fever, headache, cough, dyspnea and confusion for 3 days before having generalized seizures and left hemiplegia. Other details are illustrated in [Table 2](#).

### 3.4. Post-COVID-19 encephalitis with seizure onset

Six patients developed seizures in the context of COVID-19 related encephalitis. All of them had fever and 5 of them had headache and cough; these constitutional symptoms lasted between 2–6 days before seizures developed. One patient had visual hallucinations and another one had meningeal signs. All 6 patients had generalized seizures and 2 of them developed status epilepticus; one of these had serial seizures. All were transferred to ICU. MRI brain scans with contrast showed a combination of diffuse cerebral oedema, leptomeningeal enhancement with T2 and FLAIR hyper-intensities in the frontal lobes and/or bilateral medial temporal lobes and thalami. One patient had a comorbid pineal

**Table 2**

Post-COVID-19: acute stroke (ischemic or hemorrhagic) associated with seizure onset.

Patient Number	Age (years)	Constitutional symptoms and duration (days) of it Symptoms and signs of stroke (Type of stroke)	Type of seizures	CT Chest	PCR	Laboratory data	Comorbidity disorders
6	mid 50s	Fever, cough, sputum. 7days DCL, recent left hemiplegia and seizures. (Ischemic stroke)	Focal seizures with secondary generalization.	Bilateral ground-glass opacity.	Negative	Hypoalbuminemia, raised liver enzymes, increased PT, decreased PC, raised D dimer, anemia, leukocytosis and lymphopenia.	No
7	late 60s	Fever, cough and sputum. 5 days Double stroke, recent right hemiplegia, mixed aphasia and seizures. (Ischemic stroke)	Generalized seizures (GTCC)	Bilateral ground-glass opacity.	Negative	Raised PH (alkalosis), low PO <sub>2</sub> , raised D dimer, anemia, leukocytosis and lymphocytosis.	HTN, CVD and old left hemiplegia.
8	early 70s	Fever, cough, sputum and dyspnea. 3 days DCL, recurrent left hemiplegia and seizures. (Ischemic stroke)	Focal seizures with secondary generalization.	Bilateral ground-glass opacity.	Negative	Hypoalbuminemia, raised blood urea and creatinine, low PO <sub>2</sub> and PCO <sub>2</sub> , raised D dimer, anemia, leukocytosis and lymphopenia.	HTN, CVD and renal impairment.
9	mid 30s	Fever, myalgia and cough. 2 days. Headache and neck stiffness, DCL, left hemiplegia and seizures. (Hemorrhagic stroke)	Focal seizures	Bilateral ground-glass opacity.	Positive	Raised PH (alkalosis), low PO <sub>2</sub> and PCO <sub>2</sub> and leukocytosis.	Asthmatic.
10	Early 40s	Fever, headache, cough, dyspnea. 3 days	Generalized seizures (GTCC)	Not available	Positive	Raised creatinine, leukocytosis, neutrophilia and lymphopenia.	No

PCR; polymerase reaction; GTCC; generalized tonic clonic seizures, HTN; hypertension, DM; diabetes Mellitus; DCL; disturbed level of consciousness; CT; computer tomography; CVD; cerebrovascular disease; PCO<sub>2</sub>; partial pressure oxygen; PCO<sub>2</sub>; partial pressure carbon dioxide; PT; prothrombin time; PC; prothrombin concentration.

body tumor and hydrocephalus. EEG showed diffuse slowing of the background activity with bilateral periodic sharp waves and epileptiform discharges. One patient was 4 months pregnant. Other details are illustrated in Table 3.

### 3.5. Post-COVID-19: seizures in patients with old neurological disorders (2 ischemic stroke/ one brain tumor)

Two patients had a history of old ischemic stroke confirmed by CT brain. One patient had fever, cough and dyspnea as constitutional symptoms for 4 days while the other had no constitutional symptoms. One patient presented with focal seizures with secondary generalization and the other presented with generalized seizures complicated by serial seizures. The remaining patient had an old parafalcine meningioma as documented by brain MRI. After admission to hospital she had disturbed consciousness for 1 day and then developed frequent generalized seizures complicated by status epilepticus. PCR, comorbidities, CT chest and laboratory data are illustrated in Table 4.

## 4. Discussion

Severe acute respiratory syndrome Coronavirus-2 (SARS)-CoV-2 was first reported in Wuhan, China and officially named COVID-19 by the WHO on February 2020. The primary target cells for SARS-CoV-2 are the epithelial cells of the respiratory and gastrointestinal tract, which contain angiotensin converting enzyme 2 (ACE2), which is the portal of the virus to enter the cell (Li et al., 2020b). The ACE2 is expressed in the brain, particularly in the brain stem and in the regions responsible for regulation of cardiovascular function; expression of ACE2 has been found in both neurons and glia (Gowrisankar and Clark, 2016). In present study we found 19 (4.3 %) patients who presented with seizures mostly after constitutional symptoms of COVID-19, which was higher than other studies (Romero-Sánchez et al., 2020). In a study from Spain, during March 2020, of 841 patients hospitalized with confirmed COVID-19, seizures occurred in 6 (0.7 %) patients, 2 of which followed

intracranial hemorrhages; 1 patient had encephalitis and 1 patient was previously diagnosed with epilepsy (Romero-Sánchez et al., 2020). In Wuhan, China, from January to February 2020, of 214 patients with confirmed COVID-19, seizures occurred in only 1 (0.5 %) patient. In the USA, from January to June 2020, of 40,469 patients with confirmed COVID-19, only 258 (0.6 %) patients had seizures (Nalleballe et al., 2020). All these cases were newly-developed seizures "without underlying pathology" or occurred in known epileptic patients, or were secondary to primary brain injury (ischemic or hemorrhagic stroke) post COVID-19.

In the present study; only 3 patients (0.68 %) developed new onset seizures without underlying pathology. It could be contributed to direct entry of the virus to the CNS via olfactory nerve or the affected sensory or motor neurons lead to release of pro-inflammatory cytokines (TNF- $\alpha$ , IL-6, IL-1B), nitric oxide, prostaglandin E2, and free radicals, and causes chronic inflammation neural hyper-excitability, seizure, and death (Huang et al., 2020a; Tufan and Avanoğlu Güler, 2020). SARS-CoV-2 triggers a systemic inflammatory storm (peripherally) with a massive release of cytokines, chemokines, and other inflammation signals which causes a significant disruption of the blood brain Barrier (BBB) leading to neuroinflammation, neuronal apoptosis and seizures (Steardo et al., 2020). The accumulation of inflammatory markers also may lead to local cortical irritation that precipitates seizures (Hepburn et al., 2020). High levels of glutamate released from ischemic or hypoxic cells into the extracellular spaces may activate AMPA and NMDA receptors leading to neuronal apoptosis or death (Prentice et al., 2015). Decreased GABA receptors may also lead to hyper-excitability of neural networks and seizure (Galanopoulou, 2008). In the present study the 2 (0.46 %) patients who previously had well-controlled epilepsy and experienced breakthrough seizures. Seizures exacerbation in controlled epileptic patients could be attributed to factors such as fever and hypoxemia which may trigger the seizures and sometimes introduce complications such as serial seizures or status. Stress also might be an independent precipitant for triggering seizures in some epileptic patients (Huang et al., 2020b).

**Table 3**  
Post-COVID-19 encephalitis with seizure onset.

Patient Number	Age (years)	Constitutional symptoms and duration in days and symptoms of encephalitis	Type of seizures	CT Chest	PCR	Laboratory data	Comorbid disorders
11	late 10s	Fever, headache, cough, dyspnea and tachycardia for 6 days followed by DCL seizures	Generalized seizures (GTCC) Complicated by status epilepticus.	Bilateral ground-glass opacity.	Positive	Hypoalbuminemia, increased PT, raised PH (alkalosis), low PCO <sub>2</sub> , anemia, neutrophilia, lymphopenia.	No
12	early 20s	Fever, headache, nausea, cough, dyspnea and tachycardia for 4 days followed by DCL, and meningeal signs, and seizures	Generalized seizures (GTCC) Complicated by status epilepticus	Bilateral ground-glass opacity.	Positive	Raised liver enzymes, increased PT, increased blood urea and creatinine, raised PH (alkalosis), low PO <sub>2</sub> and PCO <sub>2</sub> , anemia, neutrophilia and lymphopenia.	Pineal body tumor and hydrocephalus.
13	mid 40s	Fever, fatigue, bone pain, cough, dyspnea, nausea for 4 days followed by confusion seizures	Generalized seizures (GTCC)	Bilateral ground-glass opacity.	Positive	Increased creatinine, leukocytosis, neutrophilia and lymphopenia.	No
14	mid 60s	Fever for 2 days followed by confusion and seizures	Generalized seizures (GTCC)	Bilateral ground-glass opacity.	Positive	Hypoalbuminemia, raised liver enzymes, increased PT, increased blood urea and creatinine, low PO <sub>2</sub> , anemia, leukocytosis, neutrophilia and lymphopenia.	No
15	early 40s	Fever, cough, visual for 5 days followed by hallucination and behavioral changes and seizures	Generalized seizures (GTCC)	Normal	Positive	Hypoalbuminemia, raised AST, raised PH (alkalosis), low PO <sub>2</sub> and PCO <sub>2</sub> , anemia, neutrophilia, lymphopenia and thrombocytopenia.	Pregnancy ( $\pm$ 4 months)
16	early 20s	Fever, headache, cough, dyspnea for 6 days followed by confusion and seizures	Generalized seizures (GTCC) Complicated by serial seizures	Bilateral ground-glass opacity.	Positive	Hypoalbuminemia, low PO <sub>2</sub> , anemia, leukocytosis, lymphopenia	Epilepsy

PCR; polymerase reaction; GTCC; generalized tonic clonic seizures, HTN; hypertension, DM; diabetes Mellitus; DCL; disturbed level of consciousness; CT; computer tomography; CVD; cerebrovascular disease; PCO<sub>2</sub>; partial pressure oxygen; PCO<sub>2</sub>; partial pressure carbon dioxide; PT; prothrombin time; PC; prothrombin concentration.

**Table 4**

Post-COVID-19 seizure in old neurological disorders (2 ischemic stroke patients + one had brain tumor “meningioma”).

Patient Number	Age (years)	Constitutional symptoms and duration of it	Type of seizures	CT Chest	PCR	Abnormal Laboratory data	Comorbid disorders
17	early 50s	Fever, cough and dyspnea for 4 days followed by DCL and seizures	Focal seizures with secondary generalization.	Bilateral ground-glass opacity.	Negative	Raised AST, low PO <sub>2</sub> , anemia, neutropenia and lymphocytosis	HTN, DM and old CVD.
18	early 40s	No constitutional symptoms. 0 day	Generalized seizures (GTCC) complicated by serial seizures.	Bilateral ground-glass opacity.	Positive	Low PH (acidosis) and lymphocytosis.	Tramadol dependence and old CVD.
19	early 50s	Fever for one day followed by DCL and seizures	Generalized seizures (GTCC) Complicated by status epilepticus.	Bilateral ground-glass opacity.	Negative	Leucocytosis.	Brain tumor

PCR; polymerase reaction; GTCC; generalized tonic clonic seizures, HTN; hypertension, DM; diabetes Mellitus; DCL; disturbed level of consciousness; CT; computer tomography; CVD; cerebrovascular disease; PCO<sub>2</sub>; partial pressure oxygen; PCO<sub>2</sub>; partial pressure carbon dioxide; PT; prothrombin time; PC; prothrombin concentration.

On the other hand the incidence of seizure following acute stroke is rare, in the present study 5 patients had post-COVID-19 acute stroke (3 ischemic and 2 hemorrhagic) associated with seizure onset. The Incidence of acute ischemic stroke was approximately 5% in hospitalized patients with severe disease in Wuhan, China (Li et al., 2020a). COVID-19 leads to hypoxemia and excessive secretion of inflammatory cytokines, which contributes to the occurrence of ischemic stroke (Zhai et al., 2020) and increases the incidence of seizure (Hepburn et al., 2020). The incidence of seizures following spontaneous intracerebral hemorrhage reportedly ranges from 2.8 to 18.7% (Woo et al., 2012). Seizures after hemorrhagic strokes are thought to be due to irritation by products of blood metabolism. The exact pathophysiology is unclear, but an associated ischemic area secondary to hemorrhage is thought to play a part. Hemosiderin deposits are thought to cause irritability after a hemorrhagic stroke (Silverman et al., 2002). About 11.5 % of stroke patients are at risk of developing post-stroke seizures within five years (Myint et al., 2006). The occurrence of seizure in old stroke patients could occur due to changes in neuronal excitability and gliotic scarring (Myint et al., 2006). In present study, 2 patients had a history of old stroke and newly-developed seizures following COVID-19. The occurrence of seizure in old stroke patients in the present study may be unrelated to COVID-19 infection, but one patient had fever and hypoxemia and the other was dependent on tramadol and stopped suddenly while in the hospital which could potentially explain seizure occurrence.

The occurrence of seizures associated encephalitis or brain tumors are common. The incidence of encephalitis related to SARS-CoV-2 is debated, with only case reports available (Moriguchi et al., 2020; Pilotto et al., 2020; Wong et al., 2020) but this also emphasizes the neuroinvasive potential of the virus. In our study, 6 (1.37 %) patients developed seizures in the context of encephalitis with COVID-19 infection. Two of them developed status epilepticus and one developed serial seizures; one patient had neck stiffness suggesting meningioencephalitis and another one developed behavioral changes and visual hallucinations associated with disturbance of consciousness. The clinical manifestation, EEG findings and brain imaging supported diagnosis of encephalitis. An immunologic response induced by SARS-CoV-2 may cause inflammatory injury and edema and may lead to alterations in consciousness and seizures (Wu et al., 2020). Only 1 patient with old parafalcine meningioma as documented by MRI brain developed seizures post COVID-19. About 20–40 % of all brain tumor patients develop seizures (Glantz et al., 2000). Seizures exacerbation in patient with brain tumor could be attributed to fever and hypoxemia of COVID-19 which may trigger the seizures.

## 5. Conclusion

seizure is not a rare complication of post covid-19 infection. We observed both newly-developed seizures and seizures secondary to primary brain insult (post COVID-19 encephalitis or post COVID acute

stroke as well as old stroke). Central and peripheral accumulation of cytokines, fever, and hypoxia could contribute to the occurrence of seizures.

## References

- Emami, A., Fadakar, N., Akbari, A., Lotfi, M., Farazdaghi, M., Javanmardi, F., Rezaei, T., Asadi-Pooya, A.A., 2020. Seizure in Patients With COVID-19, pp. 1–5.
- Galanopoulou, A.S., 2008. GABA(A) receptors in normal development and seizures: friends or foes? *Curr. Neuropharmacol.* 6, 1–20.
- Glantz, M.J., Cole, B.F., Forsyth, P.A., Recht, L.D., Wen, P.Y., Chamberlain, M.C., Grossman, S.A., Cairncross, J.G., 2000. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 54, 1886–1893.
- Gowrisankar, Y.V., Clark, M.A., 2016. Angiotensin II regulation of angiotensin-converting enzymes in spontaneously hypertensive rat primary astrocyte cultures. *J. Neurochem.* 138, 74–85.
- Hepburn, M., Mullaguri, N., George, P., Hantus, S., Punia, V., Bhimraj, A., Newey, C.R., 2020. Acute symptomatic seizures in critically ill patients with COVID-19: is there an association? *Neurocrit. Care* 1–5.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J., Cao, B., 2020a. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England)* 395, 497–506.
- Huang, S., Wu, C., Jia, Y., Li, G., Zhu, Z., Lu, K., Yang, Y., Wang, F., Zhu, S., 2020b. COVID-19 Outbreak: The Impact of Stress on Seizures in Patients With Epilepsy.
- Li, Y., Li, M., Wang, M., Zhou, Y., Chang, J., Xian, Y., Wang, D., 2020a. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Stroke Vasc. Neurol.* 5, 279–284.
- Li, Y.C., Bai, W.Z., Hashikawa, T., 2020b. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J. Med. Virol.* 92, 552–555.
- Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li, Y., Hu, B., 2020. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 77, 683–690.
- Moriguchi, T., Harii, N., Goto, J., Harada, D., Sugawara, H., Takamino, J., Ueno, M., Sakata, H., Kondo, K., Myose, N., Nakao, A., Takeda, M., Haro, H., Inoue, O., Suzuki-Inoue, K., Kubokawa, K., Ogihara, S., Sasaki, T., Kinouchi, H., Kojin, H., Ito, M., Onishi, H., Shimizu, T., Sasaki, Y., Enomoto, N., Ishihara, H., Furuya, S., Yamamoto, T., Shimada, S., 2020. A first case of meningitis/encephalitis associated with SARS-coronavirus-2. *Int. J. Infect. Dis.* 94, 55–58.
- Myint, P.K., Staufenberg, E.F., Sabanathan, K., 2006. Post-stroke seizure and post-stroke epilepsy. *Postgrad. Med. J.* 82, 568–572.
- Nalleballe, K., Reddy Onteddu, S., Sharma, R., Dandu, V., Brown, A., Jasti, M., Yadala, S., Veerapaneni, K., Siddamreddy, S., Avula, A., Kapoor, N., Mudassar, K., Kovvuru, S., 2020. Spectrum of neuropsychiatric manifestations in COVID-19. *Brain Behav. Immun.* 88, 71–74.
- Nikbakht, F., Mohammadkhanzadeh, A., Mohammadi, E., 2020. How does the COVID-19 cause seizure and epilepsy in patients? The potential mechanisms. *Mult. Scler. Relat. Disord.* 46, 102535.
- Pilotto, A., Odolini, S., Masciocchi, S., Comelli, A., Volonghi, I., Gazzina, S., Nocivelli, S., Pezzini, A., Focà, E., 2020. Steroid-Responsive Encephalitis in Coronavirus Disease 2019.
- Prentice, H., Modi, J.P., Wu, J.Y., 2015. Mechanisms of neuronal protection against excitotoxicity, endoplasmic reticulum stress, and mitochondrial dysfunction in stroke and neurodegenerative diseases. *Oxid. Med. Cell. Longev.* 2015, 964518.
- Romero-Sánchez, C.M., Díaz-Maroto, I., Fernández-Díaz, E., Sánchez-Larsen, A., Layos-Romero, A., García-García, J., González, E., Redondo-Peñas, I., Perona-Moratalla, A. B., Del Valle-Pérez, J.A., Gracia-Gil, J., Rojas-Bartolomé, L., Fera-Vilar, I., Monteagudo, M., Palao, M., Palazón-García, E., Alcahut-Rodríguez, C., Sopenana-

- Garay, D., Moreno, Y., 2020. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. *Neurology* 95, e1060–e1070.
- Silverman, I.E., Restrepo, L., Mathews, G.C., 2002. Poststroke seizures. *Arch. Neurol.* 59, 195–201.
- Sohal, S., Mansur, M., 2020. COVID-19 presenting with seizures. *IDCases* 20, e00782.
- Steardo, L., Steardo Jr., L., Zorec, R., 2020. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol. (Oxf)* 229, e13473.
- Tufan, A., Avanoğlu Güler, A., 2020. COVID-19, immune system response, hyperinflammation and repurposing antirheumatic drugs. *Turk. J. Med. Sci.* 50, 620–632.
- Whittaker, A., Anson, M., Harky, A., 2020. Neurological manifestations of COVID-19: a systematic review and current update. *Acta Neurol. Scand.* 142, 14–22.
- Wong, P.F., Craik, S., Newman, P., Makan, A., Srinivasan, K., Crawford, E., Dev, D., Moudgil, H., Ahmad, N., 2020. Lessons of the month 1: a case of rhombencephalitis as a rare complication of acute COVID-19 infection. *Clin. Med. Lond. (Lond)* 20, 293–294.
- Woo, K.M., Yang, S.Y., Cho, K.T., 2012. Seizures after spontaneous intracerebral hemorrhage. *J. Korean Neurosurg. Soc.* 52, 312–319.
- Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., Liu, C., Yang, C., 2020. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav. Immun.* 87, 18–22.
- Ye, M., Ren, Y., Lv, T., 2020. Encephalitis as a clinical manifestation of COVID-19. *Brain Behav. Immun.* 88, 945–946.
- Zhai, P., Ding, Y., Li, Y., 2020. The impact of COVID-19 on ischemic stroke. *Diagn Pathol* 15, 78.