



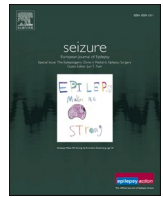
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.



Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Seizure is a rare presenting manifestation of COVID-19

Abdolkhalegh Keshavarzi^a, Ghasem Janbabaei^b, Leila Kheyrafi^b, Leila Hoseini Ghavamabad^b, Ali A. Asadi-Pooya^{c,d,*}^a Wound & Burn Healing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran^b Health and Medical Education, Tehran, Iran^c Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran^d Jefferson Comprehensive Epilepsy Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA

ARTICLE INFO

Keywords:

Coronavirus
COVID
Epilepsy
Pandemic
Seizure

ABSTRACT

Objective: The aim of the current study was to investigate whether seizure is among the presenting manifestations of COVID-19.**Methods:** All patients referred to emergency rooms anywhere in Iran between 12 and 25 April 2020 and who were sufficiently ill to require hospital admission with COVID-19, confirmed by a positive COVID-19 test, were studied. Data on the presenting manifestations were collected.**Results:** Of 5872 people, who were admitted to hospitals in Iran with COVID-19 during the study period, 45 came to the emergency room with seizures. This makes seizure as the presenting manifestation of COVID-19 in 0.8 % of all patients with a severe illness. 93 % of the patients were 15 years of age and older. Four of the individuals presenting with seizures (9%) had a past history of epilepsy. Fifteen of these individuals (33 %) had other chronic medical conditions (e.g., cancer, diabetes mellitus, heart disease, etc.).**Conclusion:** This case series provides evidence that seizures are among the presenting manifestations of COVID-19 in 0.8 % of the patients who are admitted to hospital due to a severe illness.

1. Introduction

Since late 2019, the world has been experiencing a catastrophic pandemic of the coronavirus disease (COVID-19) that is caused by SARS-CoV2 [1]. While seizures have not been frequently reported during the COVID-19 pandemic [2], affected patients may have hypoxia, multi-organ failure, and severe metabolic and electrolyte derangements [1]; hence, it is plausible to expect acute symptomatic seizures to happen in these patients. In addition, most coronaviruses share a similar viral structure and infection pathway; a growing body of evidence indicates that neurotropism is one common feature of coronaviruses [3]. Seizures were reported in previous outbreaks of coronavirus infections [e.g., during the Middle East respiratory syndrome (MERS) outbreak in 2012] [4]. In spite of the above, one retrospective study of 304 patients aimed to clarify the incidence and risk of acute symptomatic seizures in patients with COVID-19. [5]. The authors concluded that there was no evidence suggesting an additional risk of acute symptomatic seizures in patients with COVID-19 [5].

The aim of the current study was to collect the data on the presenting manifestations of COVID-19 in a nationwide study in a country that has been severely hit by the pandemic (i.e., Iran) and to clarify whether seizure is among the presenting manifestations of this viral disease.

2. Methods

Iran reported its first confirmed case of SARS-CoV2 infection on 19 February 2020. As of 24 December 2020 there was 54,156 COVID-19 related deaths with more than 1,177,004 confirmed infections in Iran [6]. Since the start of the outbreak in Iran, the Ministry of Health and Medical Education has started collecting the presenting manifestations of the patients, who referred to the emergency rooms nationwide and were admitted with a COVID-19 diagnosis. However, “seizure” as a presenting manifestation, was not among the list of the manifestations in their data collection strategy until 12 April 2020, when they included “seizure” in that list.

All patients referred to emergency rooms anywhere in Iran between

* Corresponding author at: Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.

E-mail addresses: iliakeshavarzi@yahoo.com (A. Keshavarzi), janbabai@yahoo.com (G. Janbabaei), kheyrafi@yahoo.com (L. Kheyrafi), leila200565@yahoo.com (L.H. Ghavamabad), aliasadipooya@yahoo.com (A.A. Asadi-Pooya).

<https://doi.org/10.1016/j.seizure.2021.01.009>

Received 11 June 2020; Received in revised form 8 January 2021; Accepted 10 January 2021

Available online 23 January 2021

1059-1311/© 2021 British Epilepsy Association.

Published by Elsevier Ltd.

This article is made available under the Elsevier license

(<http://www.elsevier.com/open-access/userlicense/1.0/>).

12 and 25 April 2020 and who were sufficiently ill to require hospital admission with COVID-19, confirmed by a positive COVID-19 test, were studied. All the studied patients had “seizure” as a presenting manifestation of their illness. The denominator was the total number of the patients with confirmed COVID-19 who were admitted. The presenting manifestations were collected and recorded by emergency room physicians and were entered into a national database.

The collected data included sex, age, a history of contact with a COVID-19 patient, their comorbidities, and their presenting manifestations (e.g., fever, cough, respiratory distress, seizures, etc.). No laboratory findings (other than their COVID-19 PCR test results) and no follow-up or outcome data were collected.

2.1. Standard protocol approvals, registrations, and patient consents

The Shiraz University of Medical Sciences Review Board approved this study.

2.2. Availability of data and material

The data used in this study are confidential and will not be shared.

3. Results

Of 5872 people, who were admitted to hospitals in Iran with COVID-19 during the study period, 45 came to the emergency room with seizures (with or without other manifestations). This makes seizure as the presenting manifestation of COVID-19 in 0.8 % of all patients with a severe illness. Table 1 shows the characteristics of the patients with COVID-19 and seizures (as the presenting manifestation). Just three of the patients were below 10 years of age; 93 % of the patients were 15 years of age and older. Six of the patients (13 %) were elderly people (above 65 years of age). Four of the individuals presenting with seizures (9%) had a past history of epilepsy. Fifteen of these individuals (33 %) had other chronic medical conditions (e.g., cancer, diabetes mellitus, heart disease, etc.).

4. Discussion

This study showed that seizure is rarely (< 1%) a presenting manifestation of COVID-19. Seizures happened in both sexes and all age groups and most people (91 %) had de novo seizures without a history of epilepsy, in the current study. A previous study put a question mark on the occurrence of seizures in patients with COVID-19 [5]. However, that previous study investigated a small number of patients and was retrospective in design. In addition, coronaviruses have neuroinvasion and neurotropism properties; recently, the specific SARS-CoV2 RNA was detected in the cerebrospinal fluid (CSF) in a patient with meningoencephalitis [2]. Therefore, one should anticipate to see that some patients with COVID-19 develop seizures.

In this study, we observed that not all patients with COVID-19 and seizure had fever, hypoxemia, respiratory difficulties, or medical comorbidities, including epilepsy. Therefore, it is reasonable to assume that seizures have happened due to the infection and its neurological consequences, at least in some patients. Detailed clinical, neurological, and electrophysiological investigations, particularly electroencephalography (EEG) of the patients with COVID-19 and seizures, and attempts to isolate SARS-CoV2 from the CSF may clarify the roles played by this virus in causing seizures [7,8].

New-onset seizures in patients with COVID-19 should be considered as acute symptomatic seizures and therefore, long-term antiseizure medication (ASM) therapy is usually not required, unless a subsequent seizure happens [8,9]. However, the treating physician should try to determine the etiology of the seizure and manage the cause immediately [10,11]. Furthermore, it is often necessary to start short-term ASM therapy; this is to abort prolonged seizures and also to prevent further

Table 1

Characteristics of the patients hospitalized with COVID-19 and seizures.

Characteristics	Number	Percent
Sex (Male: Female)	26: 19	58: 42
Age (years)	Median = 42; Range: 0.5–91	
History of contact with a COVID-19 patient	8	18
Fever	23	51
Cough	8	18
Respiratory distress	18	40
Oxygen saturation < 93 %	28	62
Positive chest CT scan	31 out of 36 (not done in ER in 9)	86
Admitted to (Ward: Intensive care unit)	29: 16	64: 36
	23	51
	Epilepsy: 4	9
	Hypertension: 7	16
Medical comorbidity	Diabetes Mellitus: 5	11
	Cardiac: 4	9
	Asthma: 3	7
	Others ^a : 8	13

^a 7 patients had multiple comorbidities.

seizures from happening in a patient who is already in a critical medical condition. In such circumstances, adverse effects and pharmacological properties of ASMs and also patient’s factors should be taken into account [12].

5. Limitations

This study was cross-sectional in design and the clinical data were collected at the beginning of the hospital admission of patients. First, we did not identify the etiology of seizures in these patients. Second, we did not have the follow-up data of these patients to see whether they had any more seizures and what their outcomes were. Finally, we did not have access to the whole database on all 5872 patients to compare the studied patients with those without seizures. Our data may lack generalizability to other populations; there may be significant differences between Iran and other populations with regard to their demographics, smoking rates, and prevalence of comorbidities. Therefore, this study should be replicated in other populations.

6. Conclusion

This case series provides evidence that seizures are among the presenting manifestations of COVID-19 in 0.8 % of the patients who are admitted to hospital due to a severe illness.

Role of the funding source

None.

Author contributions

Ali A. Asadi-Pooya, M.D.: Designed and conceptualized the study; analyzed the data; drafted and revised the manuscript.

Others: Data collection; revised the manuscript.

Declaration of Competing Interest

Ali A. Asadi-Pooya, M.D.: Honoraria from Cobel Daruo, RaymandRad and Tekaje; Royalty: Oxford University Press (Book publication). Others: none.

Acknowledgments

None.

References

- [1] Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun* 2020;109:102433.
- [2] Moriguchi T, Harii N, Goto J, et al. A first case of Meningitis/Encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis* 2020;94:55–8.
- [3] Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. *J Med Virol* 2020;92:552–5.
- [4] Saad M, Omrani AS, Baig K, et al. Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *Int J Infect Dis* 2014;29:301–6.
- [5] Lu L, Xiong W, Liu D, et al. New-onset acute symptomatic seizure and risk factors in corona virus disease 2019: a retrospective multicenter study. *Epilepsia* 2020;61: e49–53.
- [6] <https://www.worldometers.info/coronavirus/country/iran/> accessed on December 24, 2020.
- [7] Emami A, Fadakar N, Akbari A, et al. Seizure in patients with COVID-19. *Neurol Sci* 2020;41:3057–61.
- [8] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223):507–13.
- [9] Bergey GK. Management of a first seizure. *Continuum (Minneapolis)* 2016;22(1 Epilepsy):38–50.
- [10] Ferrarese C, Silani V, Priori A, et al. An italian multicenter retrospective-prospective observational study on neurological manifestations of COVID-19 (NEUROCOVID). *Neurol Sci* 2020;41:1355–9.
- [11] Iroegbu JD, Ifenatuoha CW, Ijomone OM. Potential neurological impact of coronaviruses: implications for the novel SARS-CoV-2. *Neurol Sci* 2020;41: 1329–37.
- [12] Asadi-Pooya AA. Seizures associated with coronavirus infections. *Seizure* 2020;79: 49–52.