

DOI: <https://doi.org/10.20453/rnp.v89i3.6835>

Characteristics of epileptic seizures in COVID-19 patients during the first year of the pandemic: a systematic review

Características de las crisis epilépticas en pacientes con COVID-19 durante el primer año de la pandemia: una revisión sistemática

Bruno Miceli Gonzalez Nogueira ^{1, a} , Cláudia Cecília da Silva Rêgo ^{1, 2, b} ,
Valéria Coelho Santa Rita Pereira ^{2, b} , Jorge Paes Barreto Marcondes de Souza ^{1, 3, c} ,
Soniza Vieira Alves-Leon ^{1, 2, d} 

ABSTRACT

In March 2020, the World Health Organization declared COVID-19 a pandemic. Epileptic seizures were described in different cohorts as being associated both with the acute phase and with long COVID-19. The objective of this review was to identify the incidence and characteristics of seizures in patients infected with SARS-CoV-2 in cohort studies published between December 2019 and December 2020. According to the PRISMA statement, a search in nine databases was conducted. One hundred and twenty-two articles were included in the final analysis. Of 9,285 patients, 328 (3.53%) adults and 22 (0.24%) pediatric patients had seizures during and/or after COVID-19. Of these, 71/328 (21.65%) adults and 5/22 (22.73%) pediatric patients had been diagnosed with epilepsy or had had an episode of seizure before infection. Among the classified seizures in adults, 14.33% (n = 47) were myoclonic, 14.02% (n = 46) generalized tonic-clonic seizures (GTCS) and 10.67% (n = 35) focal motor seizures. Of the pediatric patients, 10 (45.45%) had GTCS and 6 (27.27%) had status epilepticus with predominant motor symptoms. In 98.48% of the adults and in all 22 pediatric patients, the seizure occurred during the acute phase. The incidence of seizures was 3.6% in adults and 13.58% in pediatric patients. In adults, *de novo* seizures were approximately 3.1 times more incident than recrudescences; in pediatric patients, seizures in those without prior history were exactly three times more incident. Among the classified seizures, the most common was myoclonic in adults and GTCS in pediatric patients.

Keywords: COVID-19; SARS-CoV-2; epileptic seizures; seizures; epilepsy.

Cite as:

Nogueira BMG, Rêgo CCS, Pereira VCSR, Souza JPB, Alves-Leon SV. Characteristics of epileptic seizures in COVID-19 patients during the first year of the pandemic: a systematic review. *Rev Neuropsiquiatr.* 2026; 89(3): 320-341. DOI: 10.20453/rnp.v89i3.6835

Received: 2025, July 28

Accepted: 2026, June 11

Online: 2026, September 25

Correspondence:

Bruno Miceli Gonzalez Nogueira

✉ bmicgonza@gmail.com



Open access article, distributed under the terms of the Creative Commons Attribution 4.0 International License.

© The authors

¹ Federal University of the State of Rio de Janeiro, Biomedical Institute, Department of Morphological Sciences. Rio de Janeiro, Brazil.

² Clementino Fraga Filho Teaching Hospital, Department of Neurology, Epilepsy Center. Rio de Janeiro, Brazil.

³ Clementino Fraga Filho Teaching Hospital, Department of Neurosurgery, Epilepsy Center. Rio de Janeiro, Brazil.

^a MSc in Molecular and Cellular Biology.

^b PhD in Neurology.

^c PhD in Medicine (General Surgery).

^d PhD in Medicine/Internal Medicine/Neurology.

RESUMEN

En marzo de 2020, la Organización Mundial de la Salud declaró la COVID-19 como pandemia. Las crisis epilépticas se han descrito en diferentes cohortes como asociadas tanto con la fase aguda de la infección como con la COVID-19 prolongada. El objetivo de esta revisión fue identificar la incidencia y las características de las crisis epilépticas en pacientes infectados por SARS-CoV-2 en estudios de cohorte publicados entre diciembre de 2019 y diciembre de 2020. Se realizó una búsqueda en nueve bases de datos siguiendo los lineamientos de PRISMA. Se incluyeron 122 artículos en el análisis final. De 9285 pacientes, 328 (3,53 %) adultos y 22 (0,24 %) pediátricos tuvieron crisis convulsivas durante y/o después de la COVID-19. De estos, 71/328 (21,65 %) adultos y 5/22 (22,73 %) pediátricos fueron diagnosticados con epilepsia o presentaron un episodio de crisis antes de la infección. Entre las crisis clasificadas en adultos, 47 (14,33 %) fueron mioclónicas, 46 (14,02 %) crisis tónico-clónicas generalizadas (CTCG) y 35 (10,67 %) crisis motoras focales. De los pacientes pediátricos, 10 (45,45 %) presentaron CTCG y 6 (27,27 %) evidenciaron estado epiléptico con síntomas motores predominantes. En el 98,48 % de los adultos y en los 22 pediátricos, la crisis ocurrió durante la fase aguda de la infección por COVID-19. La incidencia de crisis fue de 3,6 % en adultos y 13,58 % en pediátricos. En adultos, las crisis *de novo* fueron aproximadamente 3,1 veces más incidentes que las recrudescencias; en pediátricos, las crisis en pacientes sin antecedentes fueron exactamente tres veces más incidentes. Entre las crisis clasificadas, la mioclónica fue la más encontrada en adultos, mientras que en pediátricos fue la CTCG.

Palabras clave: COVID-19; SARS-CoV-2; crisis epilépticas; crisis convulsivas; epilepsia.

INTRODUCTION

On March 11, 2020, Coronavirus Disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (1). By March 10, 2023, over 6.8 million deaths had occurred worldwide (2). Common symptoms of the disease included cough, fever, chills, dyspnea, fatigue, anorexia, myalgia, headache, anosmia and ageusia/dysgeusia. Other non-specific symptoms, such as sore throat, nasal congestion or runny nose and gastrointestinal manifestations (nausea, vomiting, or diarrhea), have also been reported (3). Manifestations of the nervous system by COVID-19 have been widely reported and this involvement is associated with the severity of the disease (4-9). Epileptic seizures are frequent manifestations in the course of the infections that affect the central nervous system (CNS) and have been described in published cohorts of patients with COVID-19 (10-27).

Epileptic seizures may arise from another primary disease process. In this context, infections represent an important role in triggering acute and remote symptomatic seizures in the acute phase or in the later phases of CNS infections (28). These seizures are triggered through mechanisms that include

inflammatory phenomena, dysfunction in excitatory and inhibitory signaling, and synaptopathy resulting from alterations in the circuits and molecules that participate in neuronal excitability, as shown by our group in animal models and in human astrocyte culture (29-31).

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and the emergence of seizures in individuals with and without a prior history of epilepsy (32-47) motivated us to investigate how often this phenomenon occurs and the characteristics of these patients. In this study, we aim to identify: epidemiological factors, such as age, sex, and ethnicity, that were associated with reports of seizures during SARS-CoV-2 infection or in the post-infection period; the incidence and types of seizures that recrudescened during or after infection in patients with a previous history of epilepsy; the incidence and types of seizures that arose during infection or in the post-COVID-19 period in patients without a previous history of epilepsy (patients experiencing *de novo* seizures); whether the onset of the seizure manifestation was during the acute phase or after infection; the associated symptoms and comorbidities; the clinical outcomes; and the probable causes for the seizure manifestation.

We use the expression “with a previous/prior history of epilepsy/seizure” to refer both to patients who had been diagnosed with epilepsy before the infection, and to patients who had not been previously diagnosed with epilepsy, but who had a history of having had at least one seizure episode prior to the infection.

MATERIALS AND METHODS

A systematic review was conducted following the guidelines of the PRISMA statement (<http://prisma-statement.org/>) (48). Since this study is only a literature review and does not involve actual human participants, biological materials or individual, personal human data, it is exempt from approval by a research ethics committee.

Selection of Studies and Eligibility Criteria

A bibliographic search for papers published between December 2019 and December 21, 2020, was conducted in the following databases: *Portal Regional da Biblioteca Virtual em Saúde (BVS)*, PubMed/MEDLINE, EMBASE (Elsevier), Scopus (Elsevier), COVID-19 Global Literature on Coronavirus Disease, Coronavirus Research Database (ProQuest), PsycInfo, The Cochrane Library and Web of Science (WoS). The following descriptors were used: “SARS-CoV-2,” “COVID-19,” “epilepsia,” “crises epilépticas,” “crises convulsivas,” and synonyms in Portuguese, mapped in the Health Sciences Descriptors (DeCs), and “SARS-CoV-2,” “COVID-19,” “epilepsy,” “epileptic seizures,” “seizures,” and synonyms in English, mapped in MESH Terms and Emtree. Of the total number of references retrieved, duplicates were excluded. The remaining references were reviewed by three of the authors, who excluded certain articles based on their title, keywords and abstract. The complete texts of relevant articles were then acquired and these authors performed a new selection by evaluating the full text, applying the same eligibility criteria. Clinical trials, studies involving animals, those addressing therapy with antiepileptic drugs, pharmacological treatment for COVID-19, and any other articles that did not include cases of patients with COVID-19 and seizures during the acute phase or after infection were excluded. The following types of articles in English, Portuguese and Spanish were included: case reports, case series and observational, retrospective or prospective cohort studies describing cases of patients with a confirmed diagnosis of COVID-19, with or without a previous history of epilepsy/seizure, who had experienced seizures during the acute phase and/or after the infection. Two distinct groups of patients were included:

adults ≥ 19 years of age and pediatric patients from 0.07 to 216 months.

Data Extraction and Statistical Analysis

Three of the authors extracted the data onto Microsoft Excel spreadsheets. For all cases of confirmed COVID-19 with manifestation of seizures, the following data were recorded: age, sex and ethnicity; total number of patients with previous history of epilepsy/seizure whose seizures recrudescened during and/or after the SARS-CoV-2 infection; total number of patients without prior history of epilepsy/seizure who experienced *de novo* seizures during the infection and/or in the post-infection period; number of cases that presented with seizures during the acute phase, cases presenting with seizures after recovering from the infection and cases that presented with seizures both during the acute phase and in the post-COVID-19 phase. In addition, data were recorded on associated comorbidities; probable causes for the manifestation of the seizure; outcome; symptoms during the acute phase of COVID-19 and types of seizures. In compliance with the criteria for a systematic review, all the articles selected by reading the full text would be included for the qualitative evaluation stage. Nevertheless, we decided that articles presenting case reports alone or case series would be selected without qualitative assessment since they did not present elements that could confuse the intended selection. The systematic review was developed based on the publications selected after having been read in their entirety.

Microsoft Excel was used to analyze all the data. Two independent databases of patients’ quantitative and qualitative characteristics were constructed, one for adults and one for the pediatric cohort. Descriptive statistics were performed. The mean, sample standard deviation (SD) of the mean and median ages were calculated, with the mean and median in months for pediatric patients with seizures and in years for adult patients.

Additionally, comparisons between adult and pediatric patients’ characteristics were performed using the Pearson’s chi-square test or Fisher’s exact test, as appropriate, with the aim to determine if there are some statistical differences between both cohorts. The characteristics compared were distribution by sex, types of seizure, time of onset of the seizure manifestation, comorbidities, symptoms during the acute phase of the infection, clinical outcomes and probable causes for the seizure manifestation. Fisher’s

exact test was preferentially used due to the small sample size of the pediatric group. A p value < 0.05 was considered statistically significant.

RESULTS

A total of 1,606 papers published between December 2019 and 21 December 2020 were initially identified in the literature search: 20 in the Portal Regional da Biblioteca Virtual em Saúde (BVS), 266 in PubMed/MEDLINE, 642 in EMBASE (Elsevier), 324 in Scopus

(Elsevier), 187 in COVID-19 Global Literature on Coronavirus Disease, 40 in the Coronavirus Research Database (ProQuest), 18 in PsycInfo, 5 in The Cochrane Library and 104 in WoS.

After all duplicated papers had been removed, the titles, keywords and abstracts of the 773 remaining publications were evaluated, resulting in 217 articles to be read in their entirety. Of these, 122 articles met the inclusion criteria for the final analysis. All the steps in the selection process are shown in Figure 1.

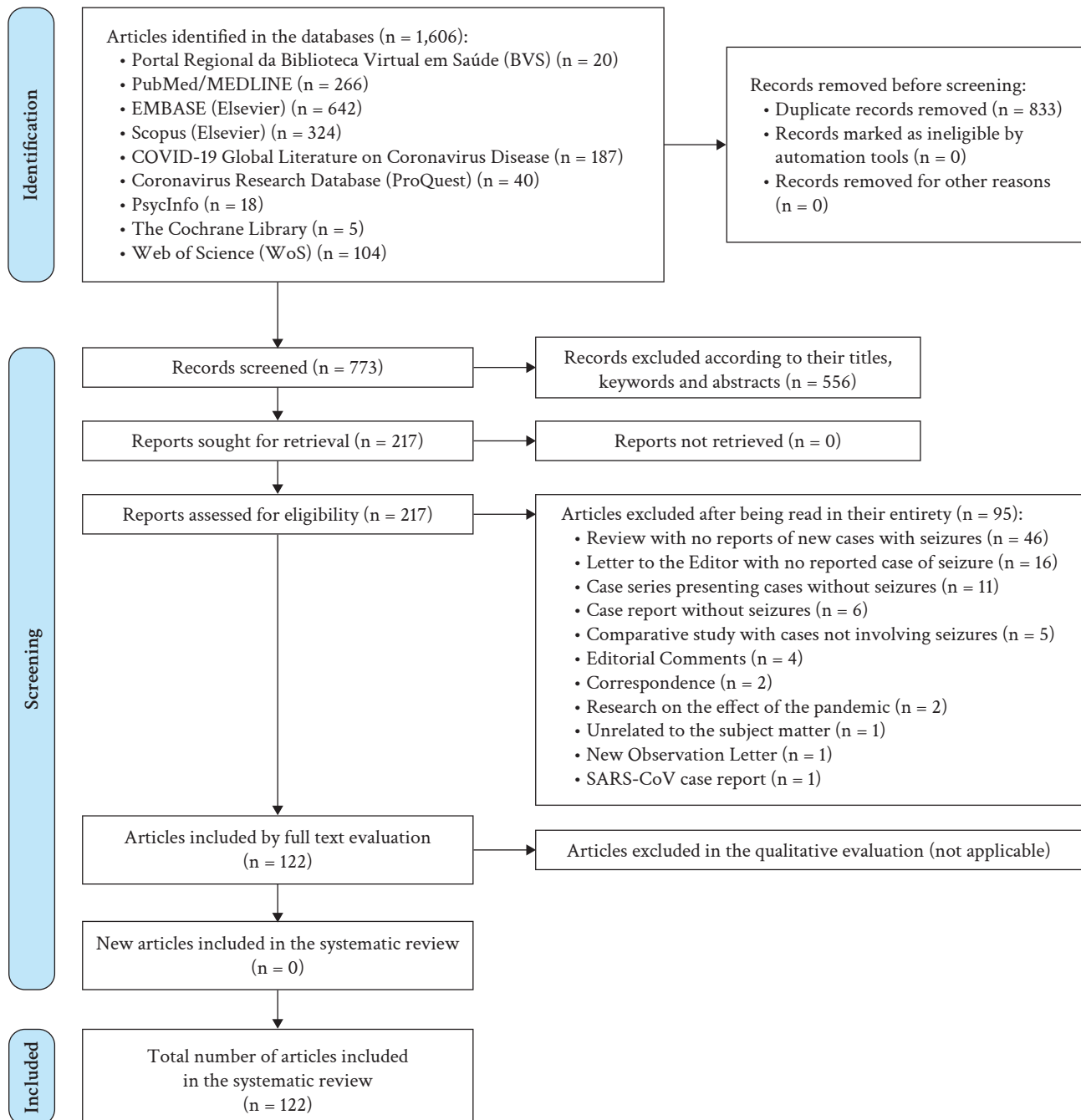


Figure 1. Flowchart of the process used to search for and select articles in accordance with the PRISMA statement guidelines (48) (<http://prisma-statement.org/>).

Based on these 122 articles, a cohort of 9,285 SARS-CoV-2 patients was obtained: 9,123 adults (98.25%) and 162 (1.74%) children and adolescents. Of those

quantitatives, 328 adults (3.6%) and 22 pediatric patients (13.58%) had seizures during and/or following the infection, respectively (Figure 2).

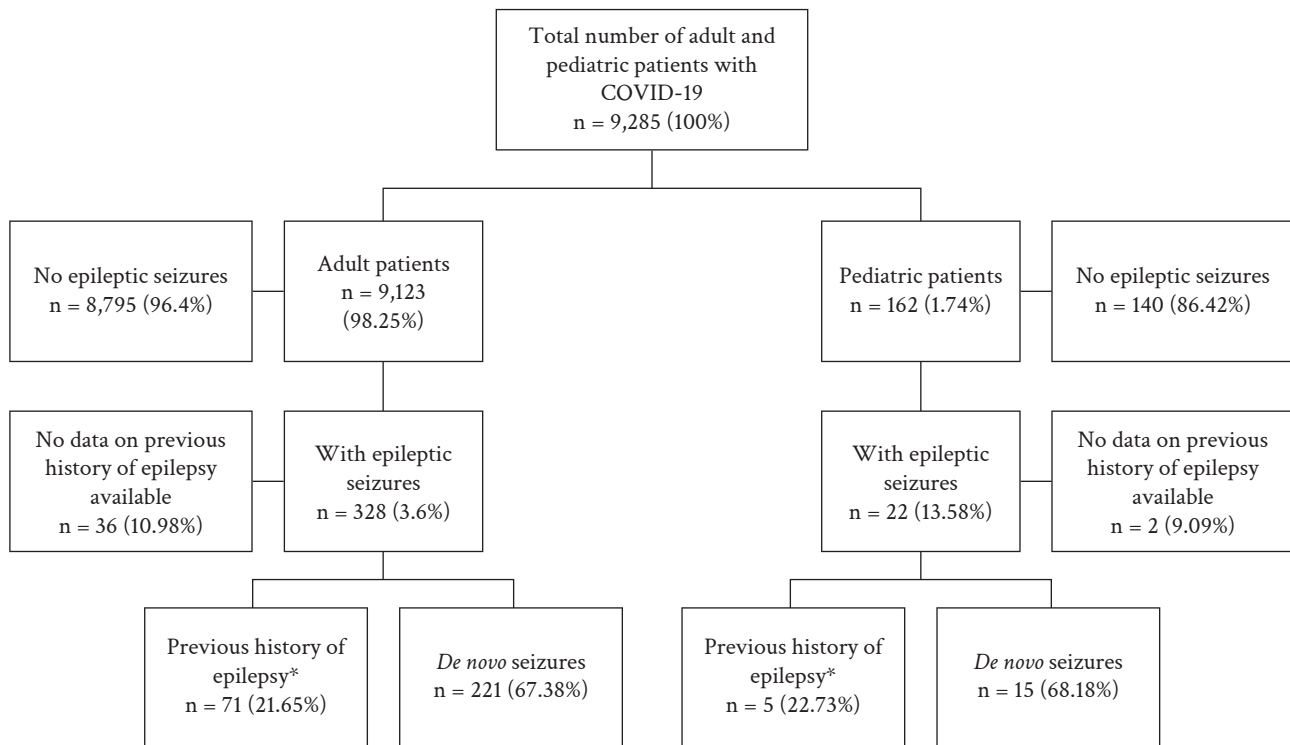


Figure 2. Flowchart of the cohorts of adult and pediatric patients. * One patient in the cohort of 71 adults and one in the cohort of 5 pediatric patients had no previous history of epilepsy but had experienced a single episode of seizure prior to the infection.

Data on patients' sex were available for 181 adults (55.18% of 328), which were 114 male (62.98% of 181) and 67 female (37.02%), and for 20 pediatric patients (90.91% of 22), which were 10 male (50% of 20) and 10 female (50%). Ethnicity was only recorded in 10 adult cases (3.05% of 328): four Afro-descendant women (40% of 10), two Afro-descendant men (20%), one Caucasian woman (10%) and three Caucasian men (30%). And in pediatric patients, ethnicity was recorded in two cases (9.09% of 22): an Afro-descendant baby (50% of 2) and a Caucasian baby (50%), both female. Mean age in the adult cohort was 58.54 years (SD 15.96; range 20-88 years; median 62 years) (n = 151). And mean age in the pediatric cohort was 83.54 months (SD 81.59; range 0.07-216 months; median 48 months) (n = 20).

The distribution by sex was statistically compared between the 181 adults and the 20 pediatric patients, it means, all the cases with sex not reported in both cohorts were excluded. The Pearson's chi-square test was used to perform this comparison, and no significant differences were observed in sex distribution between

the adult and pediatric patients with sex reported ($\chi^2 = 0.79$; $p = 0.37$).

Of the 328 adult patients, 221 (67.38%) individuals experienced a *de novo* seizure during or following the COVID-19 infection, and 71 (21.65%) individuals had a previous history of epilepsy/seizure and experienced recrudescence of their seizures during or after the infection, while no information if they had or not prior history of epilepsy/seizure was available in 36 (10.98%) cases that presented with seizure during the acute phase or in the post-infection period. This information was missing for 2/22 (9.09%) pediatric patients who had seizure during the acute phase, while 15 (68.18%) children and adolescents experienced a *de novo* seizure during or following the infection, and 5 (22.73%) who had a previous history of epilepsy/seizure experienced recrudescence of their seizures during the acute phase of the infection (Figure 2).

In the adult cohort, 174 patients (53.05%) presented with unclassified seizures (49). Among those classified, myoclonic seizure was the most common

(n = 47; 14.33% of 328); followed by generalized tonic-clonic seizure (GTCS) (n = 46; 14.02%); focal motor seizure (FMS) (n = 35; 10.67%); status epilepticus with predominant motor symptoms (convulsive status epilepticus, CSE) (49) (n = 24; 7.32%); status epilepticus without predominant motor symptoms (non-convulsive status epilepticus, NCSE) (50) (n = 13; 3.96%); unclassified status epilepticus (n = 4; 1.22%);

tonic seizure (n = 2; 0.61%; of these two patients, one of them manifested, only during the acute phase of the infection, episodes of generalized tonic seizures); atonic seizure (n = 1; 0.3%); clonic seizure (n = 1; 0.3%); and absence seizure with eyelid myoclonus (ASEM) (n = 1; 0.3%). Twenty patients (6.1%) of the cohort had more than one type of seizure during the acute phase and/or after the infection (Figure 3).

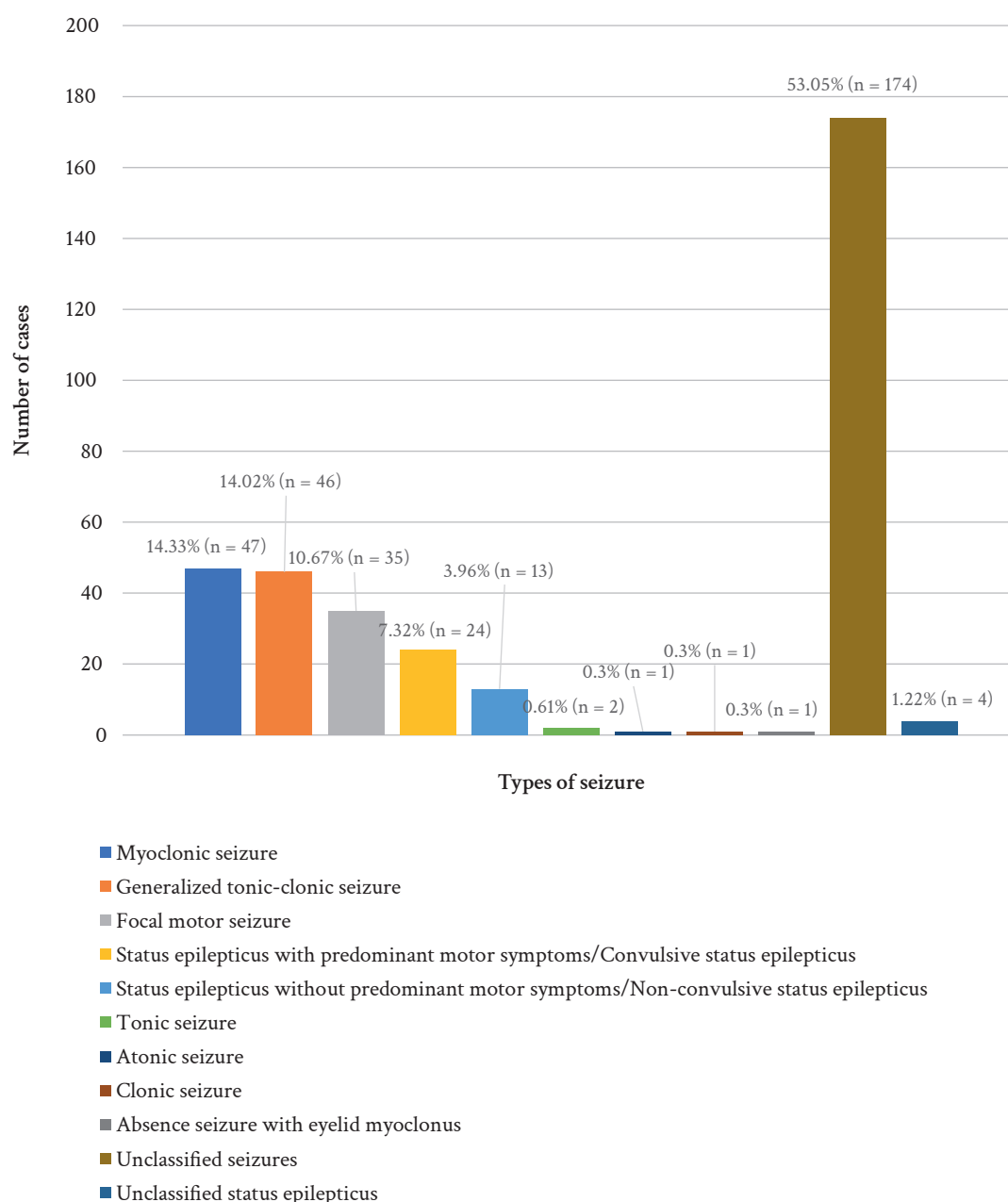


Figure 3. Frequency of seizure types among adult patients (n = 328).

In the pediatric cohort, GTCS was the most common (n = 10; 45.45%) followed by CSE (n = 6; 27.27%), subentrant seizures (n = 2; 9.09%), FMS (n = 2; 9.09%), myoclonic seizure (n = 1; 4.54%) and NCSE

(n = 1; 4.54%). Three patients (13.64%) had more than one type of seizure and in three cases (13.64%) seizures were not classified (Figure 4).

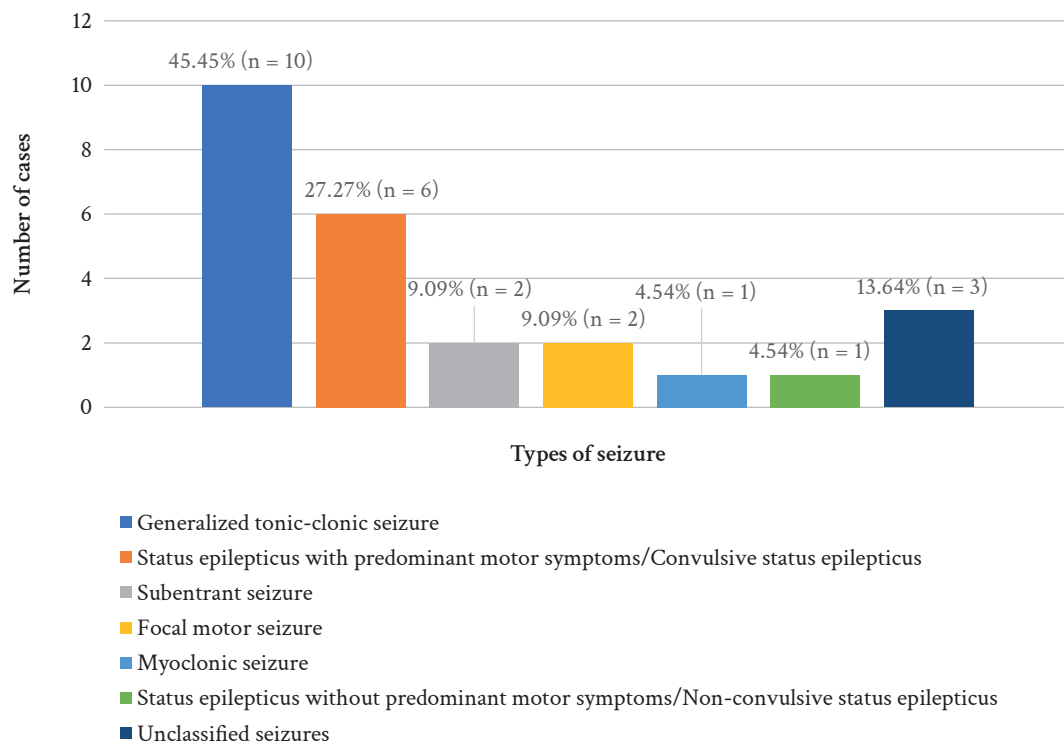


Figure 4. Frequency of seizure types among pediatric patients (n = 22).

Due to the small pediatric sample size, the low expected number of cases in several seizure categories, and the presence of expected values < 5 , seizure types were grouped according to clinical similarity to allow for valid statistical analysis. The Fisher's exact test was applied, considering $p < 0.05$ as statistically significant, to perform the statistical comparison between adult and pediatric patients regarding the types of seizure. A statistically significant difference in seizure semiology was observed between the two cohorts. Generalized tonic-clonic seizures were significantly more incident in the pediatric patients than in adults (45.45% vs. 14.02%; $p < 0.001$). Status epilepticus, including cases

with and without predominant motor symptoms (CSE and NCSE) and unclassified status epilepticus, was also significantly more prevalent in the pediatric cohort (31.82% vs. 12.50%; $p = 0.021$), also reaching statistical significance. In contrast, unclassified seizures, excluding unclassified status epilepticus, were significantly more common among adults (53.05% vs. 13.64%; $p < 0.001$), reflecting greater clinical heterogeneity or diagnostic limitations in this group. No statistically significant difference was observed between cohorts regarding focal or other motor seizure types (26.52% in adults vs. 22.73% in pediatric patients; $p = 0.78$) (Table 1).

Table 1. Comparative distribution of the seizure types.

Seizures group	Adults		Pediatric patients		p-value
	n	%	n	%	
Generalized tonic-clonic seizure	46	14.02	10	45.45	<0.001
Status epilepticus*	41	12.5	7	31.82	0.021
Focal/other motor seizure types#	87	26.52	5	22.73	0.78
Unclassified seizures§	174	53.05	3	13.64	<0.001

* Status epilepticus: this group includes cases with and without predominant motor symptoms (CSE and NCSE), and also includes unclassified status epilepticus. # Focal/other motor seizure types: this group includes, in the adult cohort, myoclonic seizures, focal motor seizures, tonic seizures, atonic seizures, clonic seizures, and absence seizures with eyelid myoclonus; in the pediatric cohort, it includes focal motor seizures, myoclonic seizures, and subentrant seizures. Rare seizure types observed exclusively in adults (tonic, atonic, clonic seizures and absence seizures with eyelid myoclonus) were grouped together for statistical analysis, due to their very low number of cases and absence in the pediatric cohort. § Unclassified seizures: this group does not include unclassified status epilepticus.

In the 71 adult patients with a previous history of epilepsy/seizure, unclassified seizures were recorded in 59 (83.1%), FMS in 5 (7.04%), GTCS in 5 (7.04%), NCSE in 2 (2.82%), myoclonic seizure in 1 (1.41%) and CSE in 1 (1.41%). All these seizure episodes occurred only during the infection. Two patients (2.82%) had more than one type of seizure during the acute phase of the infection.

In the 5 pediatric cases with a prior history, CSE was recorded in 3 (60%), GTCS in 1 (20%) and NCSE in 1 (20%). The episodes were restricted to the acute phase of the infection in all these patients.

In the 221 adult patients with no prior history of epilepsy/seizure, unclassified seizures were recorded in 105 (47.51%), GTCS in 38 (17.19%), myoclonic seizure in 33 (14.93%), FMS in 26 (11.76%), CSE in 22 (9.95%), NCSE in 7 (3.17%), tonic seizure in 2 (0.9%), atonic seizure, ASEM and unclassified status epilepticus in 1 each (0.45% in each case). Most episodes occurred only during the infection; however, in two cases (0.9%) a myoclonic seizure occurred only following the infection and in one case (0.45%) it occurred both during and after the infection. Other types of seizure occurring only after the infection were: FMS in 1 case (0.45%); CSE in two cases (0.9%), NCSE in 1 (0.45%) and atonic seizure in 1 (0.45%). Fifteen patients (6.79%) had more than one type of seizure during the acute phase and/or after the infection.

In the 15 pediatric patients with no prior history, GTCS was recorded in 9 (60%), CSE in 3 (20%), subtrant seizures in 2 (13.33%), FMS in 2 (13.33%), unclassified seizure in 1 (6.67%) and myoclonic seizure in 1 (6.67%). Almost all the seizure episodes occurred exclusively during the acute phase of the infection, with two exceptions: in the only patient in whom a myoclonic seizure was recorded, it occurred both in the acute phase and after infection (6.67%). And since this same patient also manifested GTCS, only in this patient (6.67%) did GTCS coincidentally also occur both during the acute phase and after infection. Two patients (13.33%) had more than one type of seizure exclusively during the acute phase of the infection, and 1 (6.67%) had more than one type of seizure both during the acute phase and following the infection.

Overall, 321 (97.87%) adult patients had a seizure exclusively during the acute phase of the infection. Of the 174 (54.21% of 321) for whom sex was recorded, 111 (63.79%) were male. Five of the 328 patients (1.52%) had seizures only after the infection and three of these

(60%) were male. Two patients (0.61% of 328), both female (100%), had seizures both during and after the infection.

Twenty-one of the pediatric patients (95.45%) had seizures only during the acute phase of the infection, with 9 of these (42.86% of 21) being female and 10 (47.62%) male. The sex of the other two patients (9.52%) was not reported. None of the 22 pediatric patients (0%) had a seizure only after the infection. Only one (4.54%), female (100%), had seizures both during and following the infection.

When comparing adult and pediatric patients regarding the time of onset of seizure manifestation, using the Pearson's chi-square test, no statistically significant difference was observed between the groups ($\chi^2 = 4.07$; $p = 0.13$). A secondary analysis using a dichotomized variable (acute phase versus non-acute phase) and Fisher's exact test also showed no significant difference ($p = 0.41$).

The frequency of comorbidities in the entire cohort of 350 patients (including adult and pediatric patients) with seizures was 51.43% ($n = 180$). Of the 328 adults, 34 (10.37%) had no comorbidities. In 124 cases (37.8%), the presence of comorbidities was not reported, while in 170 cases (51.83%) at least one comorbidity was present. Of these, 73 (42.94%) were male and 47 (27.65%) were female; however, in 50 cases (29.41%) sex was not reported.

The most prevalent comorbidities were a previous history of epilepsy/seizure ($n = 71$; 21.65% of 328), systemic arterial hypertension (SAH) ($n = 52$; 15.85%), diabetes ($n = 28$; 8.54%); chronic kidney disease (CKD) ($n = 18$; 5.49%); and cerebrovascular accident (CVA) ($n = 14$; 4.27%). Other comorbidities included Human Immunodeficiency Virus (HIV) infection ($n = 6$; 1.83%), obesity ($n = 6$; 1.83%), traumatic brain injury ($n = 6$; 1.83%), lipid disorders ($n = 5$; 1.52%), alcohol consumption/alcoholism ($n = 5$; 1.52%); asthma ($n = 4$; 1.22%) and cardiovascular disease ($n = 4$; 1.22%) (Figure 5).

Seven of the 22 pediatric patients (31.82%) had no comorbidities. In five (22.73%) cases, comorbidities were not reported and in the remaining 10 (45.45%) cases at least one comorbidity was present in each. Of these, 5 (50%) were male and 5 (50%) were female, with the most prevalent comorbidities being a prior history of epilepsy/seizure ($n = 5$; 22.73% of 22) and premature delivery/birth ($n = 2$; 9.09%) (Figure 6).

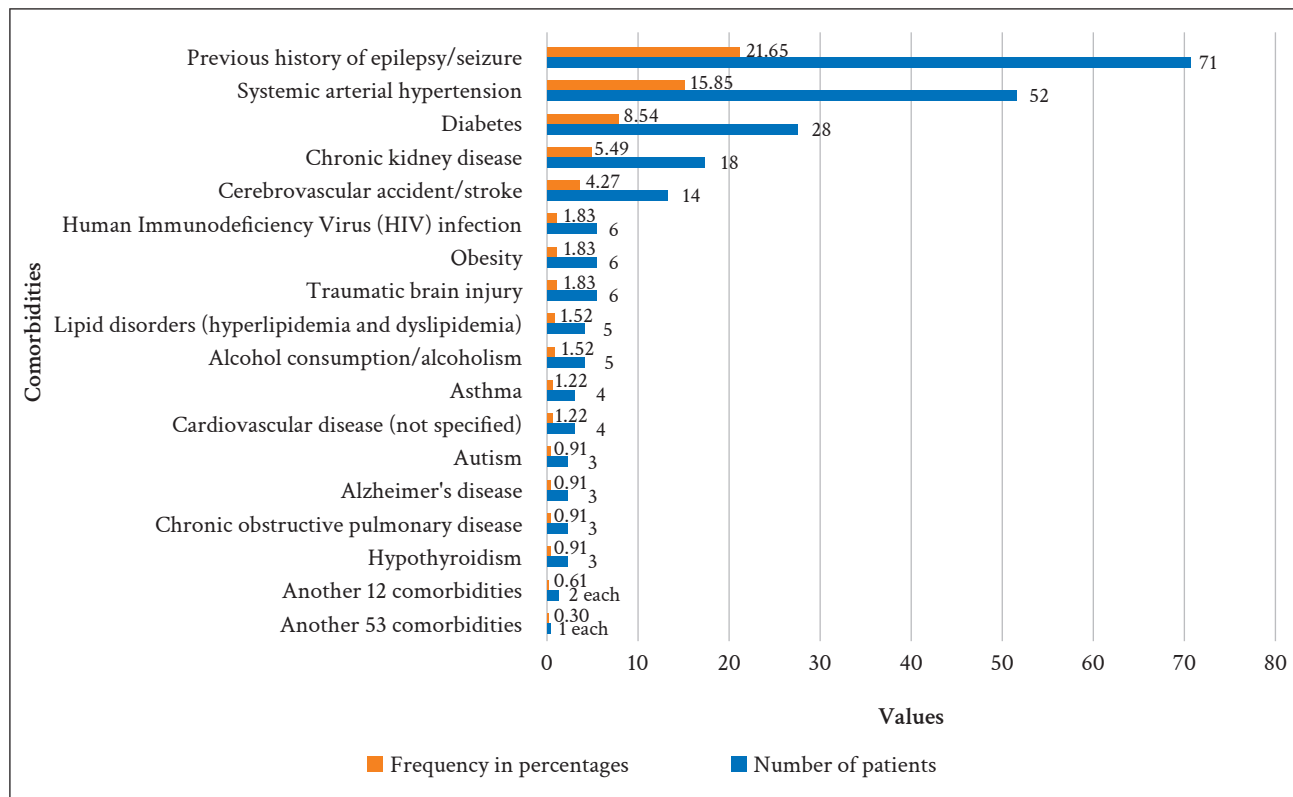


Figure 5. Number and percentage of adult patients (n = 328) for each comorbidity documented in the cohorts studied.

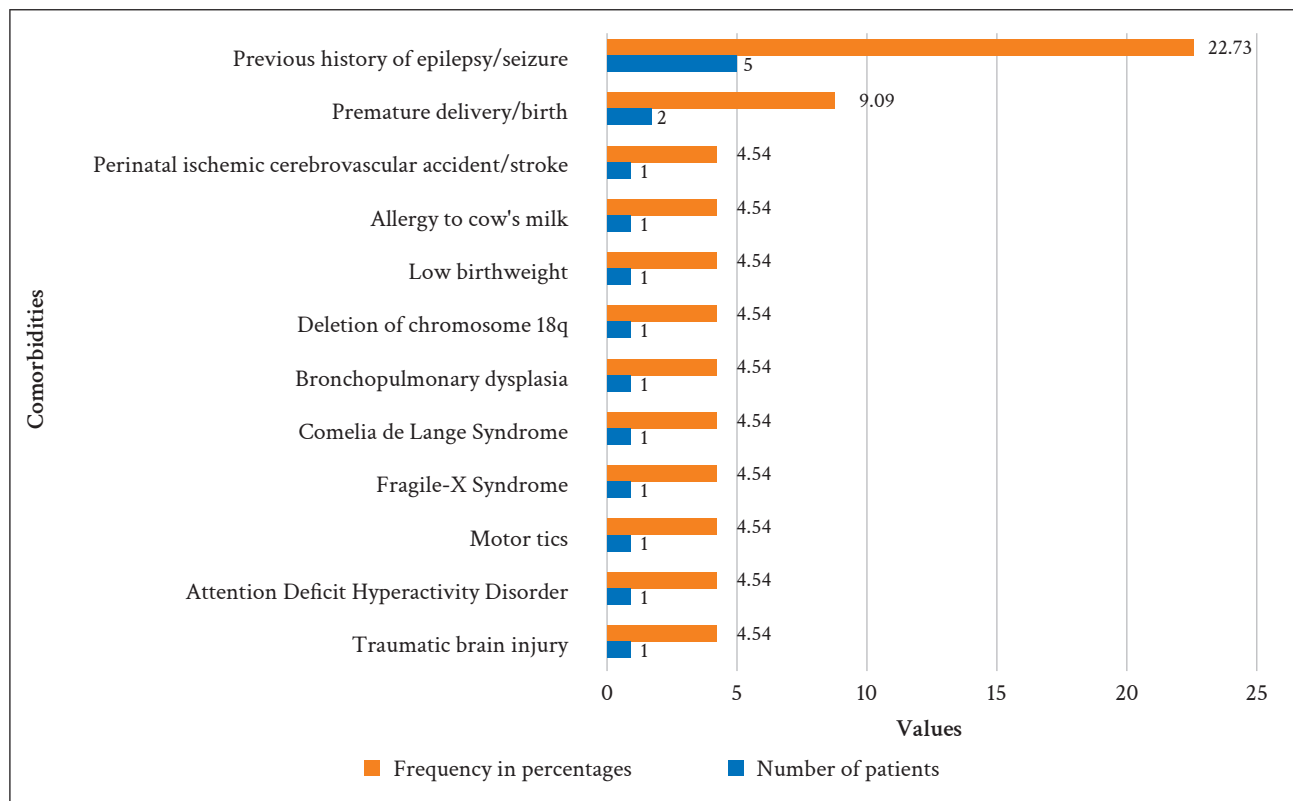


Figure 6. Number and percentage of pediatric patients (n = 22) for each comorbidity documented in the cohorts studied.

When comparing comorbidities between adult and pediatric patients, a statistically significant difference was observed in the overall presence of comorbid conditions, with pediatric patients more frequently presenting no comorbidities than adults (31.82% vs. 10.37%; $p = 0.038$). This reflects a lower burden of chronic diseases in pediatric patients. The prevalence of a prior history of epilepsy/seizure was similar between adult and pediatric patients (21.65% vs. 22.73%, respectively), with no statistically significant difference between groups ($p = 0.91$), suggesting a comparable clinical profile with respect to this specific factor. Additionally, missing comorbidity data were more frequent among adults compared to pediatric patients (37.8% vs. 22.73%; $p = 0.041$). This higher proportion of missing data in adults is possibly related to the greater clinical complexity and extensive medical history in this age group. Qualitative analysis revealed distinct clinical profiles, with adults predominantly presenting chronic, cardiovascular and metabolic conditions (for example: SAH, diabetes, CKD, CVA, HIV, neurodegenerative diseases), whereas pediatric patients more frequently exhibited perinatal, genetic, and neurodevelopmental disorders (for example: prematurity, low birth weight, genetic syndromes, Attention Deficit Hyperactivity Disorder). This difference is clinically relevant, even when some categories do not allow for formal statistical testing due to low frequency.

During the acute phase of COVID-19, adults most frequently presented fever, followed by cough and mental confusion. Several respiratory manifestations (including respiratory failure, hypoxia and anoxia, and dyspnea) were also common. Less frequent symptoms encompassed other neurological manifestations, gastrointestinal complaints, cardiovascular alterations, musculoskeletal symptoms, other respiratory symptoms, and sensory symptoms. Detailed frequencies are presented in Table 2.

Among pediatric patients, fever was the predominant symptom. Respiratory manifestations (hypoxia, cough, dyspnea, and respiratory failure) and gastrointestinal symptoms (nausea, vomiting, and diarrhea) were also frequent. Neurological, behavioral/psychological, and miscellaneous symptoms occurred less commonly. Detailed frequencies are provided in Table 3.

Table 2. Symptoms presented by the adult patients during the acute phase of COVID-19.

Symptoms	n	%
Fever	99	30.18
Cough	64	19.51
Mental confusion	53	16.16
Respiratory failure	52	15.85
Hypoxia and anoxia	47	14.33
Dyspnea	43	13.11
Disorder of consciousness	31	9.45
Fatigue	25	7.62
Headache	23	7.01
Nausea	23	7.01
Vomiting	22	6.71
Tachycardia	18	5.49
Somnolence and hypersomnia	15	4.57
Tachypnea	12	3.66
Myalgia	11	3.35
Anosmia	10	3.05
Diarrhea	10	3.05
Arterial hypertension	10	3.05
Delirium	8	2.44
Chest pain	7	2.13
Dizziness	6	1.83
Ageusia/dysgeusia	5	1.52
Chills	5	1.52

A statistical comparison, using the Fisher's exact test, was performed between adult and pediatric cohorts regarding the main symptoms, that is, the most relevant clinical symptoms, which are: fever, hypoxia/anoxia, respiratory failure, cough, mental confusion, nausea, vomiting, diarrhea, and fatigue. Pediatric patients presented a significantly higher frequency of fever (72.73% vs. 30.18%; $p < 0.001$), hypoxia (31.82% vs. 14.33%; $p \sim 0.03$), nausea (22.73% vs. 7.01%; $p \sim 0.01$), vomiting (22.73% vs. 6.71%; $p < 0.01$), and diarrhea (18.18% vs. 3.05%; $p < 0.01$), when compared with adults. No statistically significant differences were observed between the two cohorts regarding cough, respiratory failure, mental confusion, or fatigue.

Table 3. Symptoms presented by the pediatric patients during the acute phase of COVID-19.

Symptoms	n	%
Fever	16	72.73
Hypoxia	7	31.82
Nausea	5	22.73
Cough	5	22.73
Vomiting	5	22.73
Diarrhea	4	18.18
Dyspnea	4	18.18
Respiratory failure	4	18.18
Mental confusion	3	13.64
Tachycardia	3	13.64
Tachypnea	3	13.64
Nasal congestion	2	9.09
Dysarthria	2	9.09
Disorder of consciousness	2	9.09
Abdominal pain	2	9.09
Hypotension	2	9.09
Lethargy	2	9.09
Somnolence	2	9.09
Psychomotor agitation	1	4.54
Anxiety	1	4.54
Apathy	1	4.54
Abdominal distension	1	4.54
Chest pain	1	4.54
Macular eruption	1	4.54
Fatigue	1	4.54
Diffuse muscle weakness	1	4.54
Right hemiparesis	1	4.54
Loss of appetite	1	4.54
Insomnia	1	4.54
Irritability	1	4.54
Myalgia	1	4.54
Strange behavior changes	1	4.54
Pruritus	1	4.54
Urinary retention	1	4.54
Rhinitis	1	4.54
Rhinorrhea	1	4.54
Influenza-like syndrome	1	4.54

To ensure methodological robustness and clinical relevance, statistical comparisons were focused on the most prevalent and clinically meaningful symptoms, while rare manifestations with very low frequencies were not individually tested, in order to avoid unreliable estimates due to sparse data.

In 189 adult patients (57.62% of 328), the outcome was not reported. Sex was also not reported for 135 (71.43% of 189) patients, while 17 (8.99%) were women and 37 (19.58%) were men. Eighty patients (24.39% of 328) were discharged from hospital, 37 (46.25% of 80) females and 33 (41.25%) males. For the 10 (12.5%) remaining cases, sex was not reported. Forty-two patients (12.8% of 328) died in hospital, 7 (16.67% of 42) females and 33 (78.57%) males. In the two (4.76%) remaining cases, sex was not reported. Another 17 patients (5.18% of 328), 6 (35.29% of 17) females and 11 (64.71%) males, remained hospitalized.

Of the pediatric patients, 17 (77.27% of 22) were discharged from hospital. Six of these (35.29% of 17) were female and nine (52.94%) were male. In two (11.76%) cases, there was no report on sex. Three patients (13.64% of 22) died in hospital: two (66.67% of 3) girls and one (33.33%) boy. One patient (4.54% of 22), a girl (100%), remained in hospital, and in the case of another girl (4.54% of 22) outcome was not reported.

Of the 350 adult and pediatric patients, 97 (27.71%) were discharged from hospital: 42 (43.3% of 97) males and 43 (44.33%) females, with no data on sex being available in 12 (12.37%) cases. Forty-five patients (12.86% of 350) died in hospital: 34 (75.56% of 45) males, 9 (20%) females and 2 (4.44%) other patients for whom data on sex were unavailable. Eighteen patients (5.14% of 350) remained hospitalized: 11 (61.11% of 18) males and 7 (38.89%) females. In 190 cases (54.29% of 350), outcome was not reported: 37 (19.47% of 190) males, 18 (9.47%) females and 135 (71.05%) cases in which sex was not reported.

The main clinical outcomes, it means, hospital discharge, death, and remaining hospitalized, were compared between adult and pediatric patients. "Not reported" cases were excluded from the analysis, according to standard statistical practice. Therefore, only 139 adult cases ($n = 80$ (57.6%), $n = 42$ (30.2%), and $n = 17$ (12.2%)) and 21 pediatric cases ($n = 17$ (81%), $n = 3$ (14.3%), and $n = 1$ (4.7%)) were considered for this comparison. The Pearson's chi-square test was applied, and the comparison showed no statistically significant differences between adult and pediatric

patients regarding the distribution of the clinical outcomes ($\chi^2 = 4.20$; $p = 0.123$). Although pediatric patients tended to present higher discharge rates and lower mortality, these differences did not reach statistical significance.

Probable causes of the different types of seizure in the adult cohort varied. The SARS-CoV-2 infection itself and a prior history of epilepsy/seizure were the most common causes ($n = 72$; 21.95% of 328 and $n = 71$; 21.65%, respectively). Next, cytokine storm

syndrome induced by SARS-CoV-2 ($n = 67$; 20.43%), fever ($n = 61$; 18.6%), metabolic and hydroelectrolyte disorder ($n = 52$; 15.85%), hypoxia or anoxia ($n = 43$; 13.11%), encephalitis caused by SARS-CoV-2 ($n = 31$; 9.45%), CKD or kidney failure ($n = 29$; 8.84%), and encephalopathy due to the SARS-CoV-2 infection ($n = 19$; 5.79%) (Table 4). In 41 cases (12.5%) with no previous history of epilepsy/seizure and in another 4 cases (1.22%) for which there was no report on whether or not they had a prior history of epilepsy/seizure, the probable cause of the seizure was not reported.

Table 4. Probable causes of the seizure during the acute phase of the infection and/or after the infection in adult patients for whom this information was available.

Probable causes	n	%
SARS-CoV-2 infection itself	72	21.95
Prior history of epilepsy/seizure	71	21.65
Cytokine storm syndrome induced by SARS-CoV-2	67	20.43
Fever	61	18.6
Metabolic and hydroelectrolyte disorder	52	15.85
Hypoxia or anoxia	43	13.11
Encephalitis by SARS-CoV-2	31	9.45
Chronic kidney disease or kidney failure	29	8.84
Encephalopathy due to SARS-CoV-2 infection	19	5.79
Acute Respiratory Distress Syndrome	15	4.57
Hypoxic encephalopathy	12	3.66
Hemorrhagic cerebrovascular accident	10	3.05
Posterior Reversible Encephalopathy Syndrome	9	2.74
Ischemic cerebrovascular accident	8	2.44
Neuroactive drugs	7	2.13
Traumatic brain injury and subdural hematoma	7	2.13
Autoimmune encephalitis by SARS-CoV-2 or post-infection with SARS-CoV-2	6	1.83
Previous history of cognitive decline	6	1.83
Advanced age	6	1.83
Presence of autoantibodies in serum	6	1.83
Septic shock	4	1.22
Meningoencephalitis due to SARS-CoV-2	4	1.22
Venous thromboembolic disease and cerebral venous thrombosis and coagulopathy with multiple thrombotic events	3	0.91
Side effect of hydroxychloroquine	3	0.91
Hypoxic-ischemic encephalopathy	3	0.91
Cerebral venous sinus thrombosis induced by the SARS-CoV-2 infection	3	0.91

PRES: Posterior Reversible Encephalopathy Syndrome.

Table 4. (Continuation).

Probable causes	n	%
Ischemic stroke with hemorrhagic transformation	2	0.61
Encephalitis/meningitis secondary to SARS-CoV-2	2	0.61
Subarachnoid hemorrhage	2	0.61
Obesity	2	0.61
Lacunar stroke due to COVID-19	1	0.3
Long-standing aneurysm	1	0.3
Obstructive sleep apnea	1	0.3
Cerebral endothelial damage caused by the SARS-CoV-2 infection	1	0.3
Encephalitis with herpes simplex virus 1	1	0.3
Acute hemorrhagic necrotizing encephalitis secondary to SARS-CoV-2 infection	1	0.3
Encephalomalacia secondary to long-standing traumatic brain injury and SARS-CoV-2 infection	1	0.3
Metabolic encephalopathy	1	0.3
Acute necrotizing encephalopathy due to Covid-19	1	0.3
Encephalopathy due to ischemic stroke	1	0.3
Epilepsy secondary to long-standing stroke/cerebrovascular accident exacerbated by SARS-CoV-2 infection	1	0.3
Acute exacerbation caused by Covid-19 in a chronic degenerative bone marrow condition	1	0.3
COVID-19 exacerbation of Acute Disseminated Encephalomyelitis	1	0.3
Infiltration of allograft and meningoencephalitis by SARS-CoV-2	1	0.3
Grade III anaplastic astrocytoma	1	0.3
Demyelinating lesions induced by SARS-CoV-2	1	0.3
Acute hemorrhagic leukoencephalomyelitis secondary to SARS-CoV-2 infection	1	0.3
Acute, PRES-type leukoencephalopathy with multifocal hemorrhage related to COVID-19	1	0.3
Delayed post-hypoxic necrotizing leukoencephalopathy associated with COVID-19	1	0.3
Leukoencephalopathy due to COVID-19	1	0.3
Subtherapeutic levels of anticonvulsant	1	0.3
Cardiorespiratory arrest	1	0.3
Acute reaction to stress	1	0.3
Inflammatory response following SARS-CoV-2 infection	1	0.3
Syndrome of Inappropriate Antidiuretic Hormone Secretion secondary to SARS-CoV-2 infection	1	0.3
Dural venous sinus thrombosis due to SARS-CoV-2	1	0.3
Cyst in the occipital region	1	0.3

PRES: Posterior Reversible Encephalopathy Syndrome.

In the pediatric patients, fever was the most common probable cause of the seizures (n = 12; 54.54% of 22), followed by the SARS-CoV-2 infection itself (n = 7; 31.82%), metabolic disorder (n = 6; 27.27%), hypoxia, a previous history of epilepsy/seizure,

cytokine storm syndrome induced by SARS-CoV-2 (n = 5 each; 22.73%), and pediatric multisystem inflammatory syndrome associated with the SARS-CoV-2 infection (n = 3; 13.64%). Proinflammatory and vasoconstrictive effects due to the upregulation

of components of the renin-angiotensin-aldosterone system and encephalopathy due to the SARS-CoV-2 infection were found in two cases each (9.09%), with hemorrhagic CVA, ischemic CVA, coagulopathy and other causes in one case each (4.54%) (Table 5).

Table 5. Probable causes of the seizure during the acute phase of the infection and/or after the infection in pediatric patients for whom this information was available.

Probable causes	n	%
Fever	12	54.54
SARS-CoV-2 infection itself	7	31.82
Metabolic disorder	6	27.27
Hypoxia	5	22.73
Prior history of epilepsy/seizure	5	22.73
Cytokine storm syndrome induced by SARS-CoV-2	5	22.73
Pediatric multisystem inflammatory syndrome associated with SARS-CoV-2 infection	3	13.64
Proinflammatory and vasoconstrictive effects due to upregulation of components of the renin-angiotensin-aldosterone system	2	9.09
Encephalopathy due to SARS-CoV-2 infection	2	9.09
Liver failure	2	9.09
Acute renal failure	2	9.09
Myocardial lesion	2	9.09
Hemorrhagic cerebrovascular accident	1	4.54
Ischemic cerebrovascular accident	1	4.54
Coagulopathy	1	4.54
Antibody-negative autoimmune encephalitis due to SARS-CoV-2 infection	1	4.54
Hypoxic encephalopathy	1	4.54
Ganglioglioma	1	4.54
Traumatic subdural hemorrhage	1	4.54
Acute Respiratory Distress Syndrome	1	4.54
Pathogenic frameshift variant and SARS-CoV-2 infection itself	1	4.54

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2.

A comparative statistical analysis between adults and pediatric patients regarding the probable causes of seizures was performed using Fisher's exact test. The analysis focused on the most prevalent probable causes in both cohorts, as these are the only causes with acceptable minimum statistical power. These probable causes were: fever, SARS-CoV-2 infection itself, metabolic disorders, hypoxia/anoxia, prior history of epilepsy/seizure, and cytokine storm syndrome induced by SARS-CoV-2. When performing the statistical comparison, fever was significantly more frequent in the pediatric patients (54.54% vs. 18.6%; $p < 0.001$). No statistically significant differences were observed between cohorts regarding seizures attributed to SARS-CoV-2 infection itself, metabolic disorders, hypoxia, prior history of epilepsy/seizure, or cytokine storm syndrome induced by SARS-CoV-2 (all $p > 0.05$). A similar distribution between cohorts was observed regarding seizures attributed to prior history of epilepsy/seizure (21.65% vs. 22.73%; $p > 0.99$). Pediatric multisystem inflammatory syndrome associated with SARS-CoV-2 infection and some systemic complications were observed exclusively in the pediatric cohort, precluding formal statistical comparison.

DISCUSSION

This study appears to be unique in that the period covered was the first year of the pandemic when most COVID-19 features remained largely unknown. In this period, almost nothing was known about the neurological impact of SARS-CoV-2 – particularly its relationship with seizures – including whether or not individuals with epilepsy would experience a recrudescence of their seizures; whether new cases would arise during the infection, and, if so, what the most common types of seizure and their characteristics would be. The findings strongly suggest that COVID-19 may precipitate both new-onset seizures and exacerbations of pre-existing epilepsy at rates higher than expected in the general population. This supports the hypothesis that SARS-CoV-2 can act as an acute epileptogenic trigger.

In the cohort of 9,285 patients, 350 (3.77%) of these presented with seizures, whose percentage corresponds to an incidence around 3.5 times greater than the percentage of people with epilepsy in the worldwide population, which ranges from 0.5 to 1.0% (51, 52). In a meta-analysis, Hussaini et al. (53) found similar values, with seizures being recorded in 255/11,526 patients (2.2%). Consequently, these data

lead us to conclude that there appears to have been an emergence of new cases of seizures/epilepsy and recrudescence of seizures due to COVID-19.

There was a predominance of males in the adults with seizures cohort, with 62.98% of the adults for whom data on sex were available being male. In the study conducted by Finsterer, however, 64.1% of the cohort was female (54). Neither sex predominated in the pediatric cohort of our study, with 50% of patients of each sex in the 20 patients with data on sex reported. Kim et al. (55), however, reported a predominance of males in their cohort. The males corresponded to 53.1%.

The age of the adults who presented with seizures was ≥ 60 years in 53.64% of the cases for which this information was available ($n = 151$). In a study conducted by Sun et al. (56), 52.17% of the patients who had seizures ($n = 12$) were aged ≥ 60 years, suggesting that the incidence and recrudescence of the seizures were greater in older patients. Of the pediatric patients whose accurate age was reported and who had seizures ($n = 20$), 65% were over one year old. Similar results were reported by Han et al. (57) in children < 60 months old. Of a total of 33,457 children, 64 (0.19%) presented with seizures. Mean age of these cases was 36.7 months, suggesting that in pediatric patients the occurrence of seizures during the acute phase of the infection increases after the first year of life. Therefore, our study and other studies have shown that older adults and children above one year of age appeared more susceptible to seizure occurrence, indicating age-dependent vulnerability to COVID-19-related neurological complications.

Of the ten adults with seizures (3.05%) for whom ethnicity was reported, 60% were Afro-descendants. According to Somani et al. (58), patients with Afro-descendant ethnicity constitute a cohort that presents higher mortality from COVID-19. In the present study, 66.67% of the Afro-descendant adults were discharged from the hospital, which contradicts this statement. Nevertheless, due to the extremely small number of adult patients, with COVID-19 and seizures, and with ethnicity reported as Afro-descendant, included in this study, more studies are needed to evaluate the clinical outcomes of a much larger n of adults with COVID-19, with ethnicity reported as Afro-descendant, and who have presented with seizures, so that this hypothesis by Somani et al. (58) whether actually contradicted or corroborated.

Of the adult patients who had seizures but no previous history of epilepsy/seizure and for whom sex was

reported ($n = 140$; 63.35% of 221), 85 (60.71%) were male. This emergence of *de novo* seizures in men could be linked to the greater number of male patients in this cohort of 328 adults. Furthermore, 60 men (42.86% of 140) had other comorbidities, while this was found in 39 (27.86% of 140) women. Therefore, associated comorbidities could explain not only the greater number of cases of SARS-CoV-2 infection, but also the fact that there were more cases of seizures in males in this cohort. In the pediatric cohort, 5 patients (22.73%) were reported to have a previous history of epilepsy/seizure and 15 (68.18%) to have had seizures for the first time during the infection and/or in the post-infection period. This suggests that it is likely that there are more children and adolescents with no prior history of epilepsy/seizure presenting with *de novo* seizures during the acute phase or after the infection than those with a prior history suffering a recrudescence of the seizures. The study by Han et al. (57) corroborates this hypothesis, since, of the 33,457 patients of ≤ 60 months of age with COVID-19, 71 (0.21%) presented with febrile seizures. Of those, 7 patients (0.02% of 33,457 and 9.86% of 71) had a previous history of epilepsy/seizure, while 64 (0.19% of 33,457 and 90.14% of 71) did not and were diagnosed with febrile seizure associated with COVID-19. In the present study, of the 5 patients with a previous history of epilepsy/seizure, four (80%) had fever during the infection. And of the 15 without prior history, the majority ($n = 10$; 66.67%) had fever during the acute phase of the infection. This means that fever is an almost always present symptom in pediatric patients infected with SARS-CoV-2 who experience seizures, and the presence of this symptom in 14 of the 22 patients shows a similarity between the cohort of pediatric patients with COVID-19 and seizure manifestation from the present study and the cohort of 71 patients from the study conducted by Han et al. (57).

Although seizure types varied widely in the cohort of 328 adults, the type of seizure was unclassified in most cases. Classification was often incomplete in published reports, reflecting limitations in case documentation during the early pandemic. This high proportion of unclassified seizures underscores the challenges of detailed neurological assessment during a pandemic setting and highlights the need for standardized reporting in future studies.

Nonetheless, of those seizures that were classified, myoclonic seizures, generalized tonic-clonic seizures, focal motor seizures, and status epilepticus were among the most frequently described, suggesting that

COVID-19 may precipitate both focal and generalized epileptic activity. Furthermore, awareness of this classification and also of the other types of seizures described in this review, may help in the management and treatment of seizures, thus improving outcome.

Of the 22 pediatric cases, the most common types of seizure were GTCS and CSE, which suggests that, just as in adults, COVID-19 may also precipitate both focal and generalized epileptic activity in the pediatric patients. Thongsing et al. (59), in turn, reported on 16 patients aged from three months to twelve years who had the Omicron variant of COVID-19. Of those, eight (50%) had status epilepticus and six (37.5%) had seizures with focal semiology. Unlike the cohort of 328 adults, the problem of lack of seizure type classification did not occur frequently in the articles that described the cases of the 22 pediatric patients included in this review, as only three of these patients presented with seizures that were not classified.

In the 221 adult patients with no prior history of epilepsy/seizure, excluding unclassified seizures, numerous seizure types were recorded. Since there wasn't the factor prior history of epilepsy/seizure exercising a main role, the most probable triggers for these various seizure types in these patients were the SARS-CoV-2 infection itself, cytokine release syndrome induced by the virus, fever, metabolic or electrolyte disorders, and hypoxia or anoxia.

Also in the 15 pediatric patients with no prior history of epilepsy/seizure, excluding unclassified seizures in one patient, many different seizure types were recorded. In the cases of these patients, since there was not the factor previous history of epilepsy/seizure in this group, possible causes for the manifestation of the seizure types recorded in them include pediatric multisystem inflammatory syndrome associated with the SARS-CoV-2 infection, encephalopathy due to SARS-CoV-2, hypoxia and/or fever.

Timing of seizure onset provides additional support for a causal relationship. Almost all the adult cases (323/328; 98.48%) and the entire cohort of pediatric cases (100%) had seizures during the acute phase of the infection. Irrespective of age and sex, this appears to be the moment at which these neurological manifestations predominantly occur. This predominance of seizures occurring during the acute phase of infection suggests that active viral replication, systemic inflammation, and acute physiological stressors play a central role in seizure precipitation. And the infection appears to play an important role in triggering seizures

through different epileptogenic mechanisms, with proinflammatory cytokine storms being one of the most relevant (60, 61).

In the 328 adult's cohort, more than half the number of patients had at least one comorbidity, indicating that comorbidities are present in most adults with COVID-19 who have seizures and that the comorbidities contribute to the seizures and to increasing their incidence. These results are supported by the findings of Beghi et al. (62), who evaluated 1,523 adult patients, 1,213 (79.64%) of whom presented with neurological manifestations during the infection, with 126 (8.27% of 1,523 and 10.39% of 1,213) having seizures, including status epilepticus. Of that cohort, 83 patients (65.87%) had at least one non-neurological comorbidity, suggesting that, as in the present review, the comorbidity also contributed to increasing the incidence of seizures in the 126 adults. Of the 170 adults in the present study who had comorbidities, more than 70 were men and less than 50 were women, indicating that the comorbidity may contribute more often to seizures in male patients.

In the 22 pediatric patients' cohort, in turn, almost half the number of patients had at least one comorbidity. Choi et al. (63) evaluated 612 children in Korea. Of those, 59 (9.64%) had seizures during the infection, with 27 (45.76%) having chronic underlying diseases and 25 (42.37%) having neurological disorders. Therefore, it cannot be inferred that comorbidities are generally present in most pediatric patients with COVID-19 who have seizures, nor that the comorbidity contributes to a greater incidence of seizures, as it appears to do in adults. Further studies with larger cohorts of pediatric patients are required to clarify any associations.

The two most common symptoms recorded during the acute phase of COVID-19 in adults were fever ($n = 99$; 30.18%), and cough ($n = 64$; 19.51%). Conversely, Beghi et al. (62) reported that headache ($n = 61$; 48.41%) and dyspnea ($n = 56$; 44.44%) were the most common symptoms found in their cohort of 126 patients. In any case, fever and headache are not only typical symptoms of COVID-19, they are also related symptoms, and represent strong triggers for seizures during infection. Cough and dyspnea, in turn, are respiratory symptoms, also very common in infection.

Among the pediatric patients, the most common symptom during the infection was fever ($n = 16$; 72.73%), followed by hypoxia ($n = 7$; 31.82%), nausea,

cough, and vomiting ($n = 5$; 22.73% in each case). Other gastrointestinal (diarrhea), respiratory (dyspnea, respiratory failure, tachypnea and nasal congestion), neurological (mental confusion), cardiovascular (tachycardia), and psychological (psychomotor agitation, anxiety and apathy) symptoms were also recorded (12, 64). Salleh et al. (65) conducted a study with 649 patients, 29 of whom (4.47%) had febrile seizures due to the infection. The most common symptoms during the acute phase were fever ($n = 29$; 100%), lack of appetite ($n = 8$; 27.59%) and cough ($n = 7$; 24.14%). As in the present review, the most common symptom was fever, in line with its role as a strong trigger for seizures in both adult and pediatric patients.

At least 12.8% of the 328 adult patients in the present study died, with a predominance of male deaths ($n = 33$; 10.06% compared to $n = 7$; 2.13% for women). This may have been due to the greater number of comorbidities found in men. Boz et al. (66) also reported more deaths in men compared to women ($n = 17$; 37.78% of 45 versus $n = 7$; 15.56% of 45, respectively). Those authors analyzed a cohort of 17,806 adult patients with COVID-19, 45 (0.25%) of whom presented with seizures during the infection. Of those, 24 (53.33%) died in hospital. The present findings corroborate data from the international literature (67-71), showing that the presence of neurological manifestations in COVID-19 is associated with more severe disease progression.

Notably, 29 of the 42 adult patients who died (69.05%) had at least one documented comorbidity, again suggesting that the presence of a comorbidity contributed to a poorer prognosis and to an increased number of deaths (72). Similar conclusions could be reached regarding the study conducted by Boz et al. (66) in which, of the 45 adults with seizures, 24 died, and of those, 23 (95.83%) had at least one recorded comorbidity. Considering the number of deaths per sex, both in that study and in the present study, an association can be made between the greater number of comorbidities and poorer outcome in adult males.

Three of the 22 pediatric patients died. Conversely, in the study conducted by Salleh et al. (65), none of the 29 pediatric patients died. The few deaths in the pediatric cohort must be related to the fact that the children and adolescents had few comorbidities and did not have a severe form of the disease, thus not being as severely ill from COVID-19.

Regarding possible triggers of the seizures in the adult patients, the major factors were the SARS-CoV-2 infection itself, cytokine release syndrome induced by the virus and fever. This is in line with many of the studies included in this review, showing that the onset of *de novo* seizures in patients with no prior history of epilepsy/seizure could be due to a possible direct invasion of SARS-CoV-2 into the CNS (15), as well as an intense inflammatory reaction with breakdown of the blood-brain barrier (70). The second most frequent factor was a previous history of epilepsy/seizure, which, in itself, contributed to recrudescence of seizures during the acute or post-COVID-19 phases (73).

In the pediatric cohort, fever was the main probable cause of the seizure, followed by the SARS-CoV-2 infection itself and metabolic disorder. These findings show that, in both the adult and pediatric patient cohorts, fever and SARS-CoV-2 infection itself are among the top four probable causes of seizures in these patients from both cohorts, due to the high probability of these two factors triggering this neurological manifestation.

Further research is required regarding a possible neuroinvasion of SARS-CoV-2. Notwithstanding, seizures can be triggered by other mechanisms and pathological consequences of COVID-19, including cerebrovascular events, encephalitis, hypoxia, electrolyte disorders, renal disease and neuroinvasive drugs, all of which should be considered when managing such patients (74, 75).

Certain limitations of this review must be taken into consideration, since most articles identified failed to provide data on sex, ethnicity, age, comorbidities, symptoms, types of seizure and outcome. This hampered data collection and may have resulted in biases.

Conversely, the moment of seizure onset was documented in each case, both in the adult and pediatric cohorts, enabling the incidence of this neurological manifestation to be analyzed during the acute phase and after the infection, and constituting a strongpoint. In addition, all the probable causes of the seizure were documented in each case and the most common causes were analyzed for each cohort. Considering the scarcity of such data in case studies in the literature, we believe that the present systematic review contributes to current knowledge on the manifestation of epileptic seizures during and/or after COVID-19.

CONCLUSIONS

The incidence of seizures was 3.6% in adults and 13.58% in the pediatric cohort. Although a higher number of men among adults with seizures was found, in the pediatric cohort with seizures, we did not see this difference, the number of patients for each sex was exactly the same ($n = 10$ for each). Nevertheless, any affirmation in relation to the predominance of sex, either in the adult or pediatric cohort, would be premature. Data on ethnicity were practically unavailable (10/328 adults and 2/22 pediatric patients), hampering any analysis. Taking into account that, in the cohort of adults, 221 patients without a previous history of epilepsy/seizure experienced seizures for the first time, while 71 with a prior history presented with a recrudescence of seizures, the incidence of epileptic seizures was approximately 3.1 times higher in adults with no previous history ($221/71 = 3.11$). Likewise, considering that, in the pediatric cohort, 15 patients without a prior history of epilepsy/seizure presented with seizures for the first time, while 5 with a previous history presented with a recrudescence of seizures, it is clear that the incidence of epileptic seizures was exactly 3 times higher in pediatric patients with no prior history ($15/5 = 3$). Among the classified seizures, myoclonic seizure was the most common in the adults and GTCS in the pediatric patients. Additionally, almost all the adult and pediatric patients had seizures during the acute phase of the infection. In the adult cohort, the most common underlying comorbidities were a previous history of epilepsy/seizure, systemic arterial hypertension, diabetes, CKD and CVA. Excluding unclassified seizures, the symptoms recorded during the acute phase of the infection were fever, cough and mental confusion. In the pediatric cohort, the predominant underlying comorbidity was a previous history of epilepsy/seizures, and the symptoms recorded during the acute phase of the infection were fever and hypoxia. Further studies with larger cohorts of adult and pediatric patients with confirmed COVID-19 and seizures are required to confirm these findings. However, the present results may help guide future studies, as well as the management and treatment of these patients in clinical practice.

Conflicts of interest: The authors declare that there are no conflicts of interest associated with this work.

Funding: This study was conceived and conducted by the authors themselves, with no need for any institutional support or the participation of any third parties. The authors designed the study, performed the

literature review, screened and selected the articles, interpreted the data, wrote the report and took the decision to submit this manuscript for publication.

Authors' contributions:

BMGN: conceptualization and study design, search strategy, bibliographic research, collection and compilation of the data, statistical analysis and data interpretation, writing of the manuscript, critical review of the initial versions and approval of the final version. **CCSR:** conceptualization and study design, search strategy, collection and compilation of the data, statistical analysis and data interpretation, writing of the manuscript, critical review of the initial versions and approval of the final version. **VCSR, JPBMS:** conceptualization and study design, writing of the manuscript, critical review of the initial versions and approval of the final version. **SVAL:** conceptualization and study design, search strategy, statistical analysis and data interpretation, writing of the manuscript, critical review of the initial versions and approval of the final version.

Acknowledgements: The authors would like to thank the Coordination for the Improvement of Higher Education Personnel (CAPES) for providing a master scholarship that enabled this study to be performed, including the study design, research, analysis and interpretation of the data, and preparation of the manuscript for publication. We would also like to thank the team at the Laboratory of Translational Neurosciences (LabNet), who contributed with valuable input to the development of this study.

REFERENCES

1. Meca-Lallana V, Aguirre C, Río B, et al. COVID-19 in 7 multiple sclerosis patients in treatment with ANTI-CD20 therapies. *Mult Scler Relat Disord*. 2020;44:102306. doi:10.1016/j.msard.2020.102306
2. Johns Hopkins University & Medicine. Coronavirus Resource Center: COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University & Medicine [database on the Internet]. JHU; [n. d.] [cited on March 10, 2023]. Available from: <https://www.coronavirus.jhu.edu/map.html>
3. Ministério da Saúde (BR). Covid-19 [Internet]. Gov.br; [n. d.] [cited on May 17, 2025]. Available from: <https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/c/covid-19>
4. Benameur K, Agarwal A, Auld SC, et al. Encephalopathy and encephalitis associated

- with cerebrospinal fluid cytokine alterations and coronavirus disease, Atlanta, Georgia, USA, 2020. *Emerg Infect Dis.* 2020;26(9):2016-21. doi:[10.3201/eid2609.202122](https://doi.org/10.3201/eid2609.202122)
5. Cai X, Ma Y, Li S, et al. Clinical characteristics of 5 COVID-19 cases with non-respiratory symptoms as the first manifestation in children. *Front Pediatr.* 2020;8:258. doi:[10.3389/fped.2020.00258](https://doi.org/10.3389/fped.2020.00258)
6. Dixon L, Varley J, Gontsarova A, et al. COVID-19-related acute necrotizing encephalopathy with brain stem involvement in a patient with aplastic anemia. *Neurol Neuroimmunol Neuroinflamm.* 2020;7(5):e789. doi:[10.1212/NXI.0000000000000789](https://doi.org/10.1212/NXI.0000000000000789)
7. Etemadifar M, Salari M, Murgai AA, et al. Fulminant encephalitis as a sole manifestation of COVID-19. *Neurol Sci.* 2020;41(11):3027-9. doi:[10.1007/s10072-020-04712-y](https://doi.org/10.1007/s10072-020-04712-y)
8. Farias EC, Justino MC, Mello ML. Multisystem inflammatory syndrome in a child associated with Coronavirus Disease 19 in the Brazilian Amazon: fatal outcome in an infant. *Rev Paul Pediatr.* 2020;38:e2020165. doi:[10.1590/1984-0462/2020/38/2020165](https://doi.org/10.1590/1984-0462/2020/38/2020165)
9. Munhoz RP, Pedrosa JL, Nascimento FA, et al. Neurological complications in patients with SARS-CoV-2 infection: a systematic review. *Arq Neuro-Psiquiatr.* 2020;78(5):290-300. doi:[10.1590/0004-282X20200051](https://doi.org/10.1590/0004-282X20200051)
10. Anand P, Al-Faraj A, Sader E, et al. Seizure as the presenting symptom of COVID-19: a retrospective case series. *Epilepsy Behav.* 2020;112:107335. doi:[10.1016/j.yebeh.2020.107335](https://doi.org/10.1016/j.yebeh.2020.107335)
11. Besnard S, Nardin C, Lyon E, et al. Electroencephalographic abnormalities in SARS-CoV-2 patients. *Front Neurol.* 2020;11:582794. doi:[10.3389/fneur.2020.582794](https://doi.org/10.3389/fneur.2020.582794)
12. Canham LJW, Staniaszek LE, Mortimer AM, et al. Electroencephalographic (EEG) features of encephalopathy in the setting of Covid-19: a case series. *Clin Neurophysiol Pract.* 2020;5:199-205. doi:[10.1016/j.cnp.2020.06.001](https://doi.org/10.1016/j.cnp.2020.06.001)
13. Chougar L, Shor N, Weiss N, et al. Retrospective observational study of brain magnetic resonance imaging findings in patients with acute SARS-CoV-2 infection and neurologic manifestations. *Radiology.* 2020;297(3):E313-23. doi:[10.1148/radiol.2020202422](https://doi.org/10.1148/radiol.2020202422)
14. Franke C, Ferse C, Kreye J, et al. High frequency of cerebrospinal fluid autoantibodies in COVID-19 patients with neurological symptoms. *Brain Behav Immun.* 2021;93:415-9. doi:[10.1016/j.bbi.2020.12.022](https://doi.org/10.1016/j.bbi.2020.12.022)
15. Frontera JA, Sabadia S, Lalchan R, et al. A prospective study of neurologic disorders in hospitalized patients with COVID-19 in New York City. *Neurology.* 2021;96(4):e575-86. doi:[10.1212/WNL.00000000000010979](https://doi.org/10.1212/WNL.00000000000010979)
16. Galanopoulou AS, Ferastraoar V, Correa DJ, et al. EEG findings in acutely ill patients investigated for SARS-CoV-2/COVID-19: a small case series preliminary report. *Epilepsia Open.* 2020;5(2):314-24. doi:[10.1002/epi4.12399](https://doi.org/10.1002/epi4.12399)
17. García-Moncó JC, Cabrera-Muras A, Collía-Fernández A, et al. Neurological reasons for consultation and hospitalization during the COVID-19 pandemic. *Neurol Sci.* 2020;41(11):3031-8. doi:[10.1007/s10072-020-04714-w](https://doi.org/10.1007/s10072-020-04714-w)
18. Koutroumanidis M, Gratwicke J, Sharma S, et al. Alpha coma EEG pattern in patients with severe COVID-19 related encephalopathy. *Clin Neurophysiol.* 2021;132(1):218-25. doi:[10.1016/j.clinph.2020.09.008](https://doi.org/10.1016/j.clinph.2020.09.008)
19. Louis S, Dhawan A, Newey C, et al. Continuous electroencephalography characteristics and acute symptomatic seizures in COVID-19 patients. *Clin Neurophysiol.* 2020;131(11):2651-6. doi:[10.1016/j.clinph.2020.08.003](https://doi.org/10.1016/j.clinph.2020.08.003)
20. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol.* 2020;77(6):683-90. doi:[10.1001/jamaneurol.2020.1127](https://doi.org/10.1001/jamaneurol.2020.1127)
21. Neumann B, Schmidbauer ML, Dimitriadis K, et al.; PANDEMIC and the IGNITE study groups. Cerebrospinal fluid findings in COVID-19 patients with neurological symptoms. *J Neurol Sci.* 2020;418:117090. doi:[10.1016/j.jns.2020.117090](https://doi.org/10.1016/j.jns.2020.117090)
22. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, et al. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. *Neurology.* 2020;95(8):e1060-70. doi:[10.1212/WNL.00000000000009937](https://doi.org/10.1212/WNL.00000000000009937)
23. Santos de Lima F, Issa N, Seibert K, et al. Epileptiform activity and seizures in patients with COVID-19. *J Neurol Neurosurg Psychiatry.* 2021;92(5):565-6. doi:[10.1136/jnnp-2020-324337](https://doi.org/10.1136/jnnp-2020-324337)
24. Shekhar R, Sheikh AB, Suriya SS, et al. Neurological complications among native Americans with COVID-19: our experience at a tertiary care academic hospital in the U.S. *J Stroke Cerebrovasc Dis.* 2020;29(12):105260. doi:[10.1016/j.jstrokecerebrovasdis.2020.105260](https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105260)

25. Skorin I, Carrillo R, Perez CP, et al. EEG findings and clinical prognostic factors associated with mortality in a prospective cohort of inpatients with COVID-19. *Seizure*. 2020;83:1-4. doi:[10.1016/j.seizure.2020.10.007](https://doi.org/10.1016/j.seizure.2020.10.007)
26. Torres-Macho J, Ryan P, Valencia J, et al. The PANDEMYC Score. An easily applicable and interpretable model for predicting mortality associated with COVID-19. *J Clin Med*. 2020;9(10):3066. doi:[10.3390/jcm9103066](https://doi.org/10.3390/jcm9103066)
27. Vespignani H, Colas D, Lavin BS, et al. Report on electroencephalographic findings in critically ill patients with COVID-19. *Ann Neurol*. 2020;88(3):626-30. doi:[10.1002/ana.25814](https://doi.org/10.1002/ana.25814)
28. Beghi E, Carpio A, Forsgren L, et al. Recommendation for a definition of acute symptomatic seizure. *Epilepsia*. 2010;51(4):671-5. doi:[10.1111/j.1528-1167.2009.02285.x](https://doi.org/10.1111/j.1528-1167.2009.02285.x)
29. Alves-Leon SV, Cardoso MF, Pereira VC, et al. Clinical and electroencephalographic characteristics of a cohort of patients with epilepsy and absence seizures. *Arq Neuro-Psiquiatr*. 2009;67(4):986-94. doi:[10.1590/S0004-282X2009000600005](https://doi.org/10.1590/S0004-282X2009000600005)
30. Diniz LP, Almeida JC, Tortelli V, et al. Astrocyte-induced synaptogenesis is mediated by transforming growth factor β signaling through modulation of d-serine levels in cerebral cortex neurons. *J Biol Chem*. 2012;287(49):41432-45. doi:[10.1074/jbc.M112.380824](https://doi.org/10.1074/jbc.M112.380824)
31. Diniz LP, Tortelli V, Garcia MN, et al. Astrocyte transforming growth factor beta 1 promotes inhibitory synapse formation via CaM kinase II signaling. *Glia*. 2014;62(12):1917-31. doi:[10.1002/glia.22713](https://doi.org/10.1002/glia.22713)
32. Abdulsalam MA, Abdulsalam AJ, Shehab D. Generalized status epilepticus as a possible manifestation of COVID-19. *Acta Neurol Scand*. 2020;142(4):297-8. doi:[10.1111/ane.13321](https://doi.org/10.1111/ane.13321)
33. Carroll E, Neumann H, Aguero-Rosenfeld ME, et al. Post-COVID-19 inflammatory syndrome manifesting as refractory status epilepticus. *Epilepsia*. 2020;61(10):e135-9. doi:[10.1111/epi.16683](https://doi.org/10.1111/epi.16683)
34. Chen W, Toprani S, Werbaneth K, et al. Status epilepticus and other EEG findings in patients with COVID-19: a case series. *Seizure*. 2020;81:198-200. doi:[10.1016/j.seizure.2020.08.022](https://doi.org/10.1016/j.seizure.2020.08.022)
35. Emami A, Fadakar N, Akbari A, et al. Seizure in patients with COVID-19. *Neurol Sci*. 2020;41(11):3057-61. doi:[10.1007/s10072-020-04731-9](https://doi.org/10.1007/s10072-020-04731-9)
36. Farley M, Zuberi J. COVID-19 precipitating status epilepticus in a pediatric patient. *Am J Case Rep*. 2020;21:e925776. doi:[10.12659/AJCR.925776](https://doi.org/10.12659/AJCR.925776)
37. Fasano A, Cavallieri F, Canali E, et al. First motor seizure as presenting symptom of SARS-CoV-2 infection. *Neurol Sci*. 2020;41(7):1651-3. doi:[10.1007/s10072-020-04460-z](https://doi.org/10.1007/s10072-020-04460-z)
38. García-Howard M, Herranz-Aguirre M, Moreno-Galarraga L, et al. Case report: benign infantile seizures temporally associated with COVID-19. *Front Pediatr*. 2020;8:507. doi:[10.3389/fped.2020.00507](https://doi.org/10.3389/fped.2020.00507)
39. Hamidi A, Sabayan B, Sorond F, et al. A case of Covid-19 respiratory illness with subsequent seizure and hemiparesis. *Galen Med J*. 2020;9:e1915. doi:[10.31661/gmj.v9i0.1915](https://doi.org/10.31661/gmj.v9i0.1915)
40. Hepburn M, Mullaguri N, George P, et al. Acute symptomatic seizures in critically ill patients with COVID-19: is there an association? *Neurocrit Care*. 2021;34(1):139-43. doi:[10.1007/s12028-020-01006-1](https://doi.org/10.1007/s12028-020-01006-1)
41. Hwang ST, Ballout AA, Mirza U, et al. Acute seizures occurring in association with SARS-CoV-2. *Front Neurol*. 2020;11:576329. doi:[10.3389/fneur.2020.576329](https://doi.org/10.3389/fneur.2020.576329)
42. 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. doi:[10.1016/j.ijid.2020.03.062](https://doi.org/10.1016/j.ijid.2020.03.062)
43. Peña-Salazar C, López Cuiña M, Chavarría V, et al. [Convulsive status epilepticus as a possible symptom of COVID-19 in a patient with intellectual disability and autistic spectrum disorder]. *Neurologia*. 2020;35(9):703-5. doi:[10.1016/j.nrl.2020.07.010](https://doi.org/10.1016/j.nrl.2020.07.010) Spanish.
44. Saeed A, Shorafa E. Status epilepticus as a first presentation of COVID-19 infection in a 3-year-old boy; Case report and review the literature. *IDCases*. 2020;22:e00942. doi:[10.1016/j.idcr.2020.e00942](https://doi.org/10.1016/j.idcr.2020.e00942)
45. Tan YP, Tan BY, Pan J, et al. Epidemiologic and clinical characteristics of 10 children with coronavirus disease 2019 in Changsha, China. *J Clin Virol*. 2020;127:104353. doi:[10.1016/j.jcv.2020.104353](https://doi.org/10.1016/j.jcv.2020.104353)
46. Swarz JA, Daily S, Niemi E, et al. COVID-19 infection presenting as acute-onset focal status epilepticus. *Pediatr Neurol*. 2020;112:7. doi:[10.1016/j.pediatrneurol.2020.07.012](https://doi.org/10.1016/j.pediatrneurol.2020.07.012)
47. Zombori L, Bacon M, Wood H, et al. Severe cortical damage associated with COVID-19 case report. *Seizure*. 2021;84:66-8. doi:[10.1016/j.seizure.2020.11.014](https://doi.org/10.1016/j.seizure.2020.11.014)

48. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71
49. Fisher RS, Cross JH, D'Souza C, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia*. 2017;58(4):531-42. doi:10.1111/epi.13671
50. Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus. *Epilepsia*. 2015;56(10):1515-23. doi:10.1111/epi.13121
51. Costa LLO, Brandão EC, Marinho Segundo LMB. Update on epilepsy: literature review. *Rev Med*. 2020;99(2):170-81. doi:10.11606/issn.1679-9836.v99i2p170-181
52. Portaria Conjunta N° 17, de 21 de junho de 2018. Diário Oficial da União (2018, 27 June) [Internet]. Available from: https://www.gov.br/conitec/pt-br/midias/relatorios/portaria/2018/portaria_17_pcdt_de_epilepsia.pdf/@display-file/file
53. Hussaini H, Rogers S, Kataria S, et al. COVID-19-induced seizures: a meta-analysis of case series and retrospective cohorts. *Cureus*. 2022;14(8):e28633. doi:10.7759/cureus.28633
54. Finsterer J. SARS-CoV-2 associated posterior reversible encephalopathy syndrome (PRES) - a review of 82 cases. *Med J Malaysia* [Internet]. 2023;78(3):421-6. Available from: <https://www.e-mjm.org/2023/v78n3/SARS-CoV-2.pdf>
55. Kim JM, Park EG, Lee JY, et al. Characteristics of febrile seizures with SARS-CoV-2 infection in the Omicron era. *Transl Pediatr*. 2023;12(5):807-15. doi:10.21037/tp-22-579
56. Sun M, Ruan X, Li Y, et al. Clinical characteristics of 30 COVID-19 patients with epilepsy: a retrospective study in Wuhan. *Int J Infect Dis*. 2021;103:647-53. doi:10.1016/j.ijid.2020.09.1475
57. Han MJ, Heo JH, Hwang JS, et al. Incidence of febrile seizures in children with COVID-19. *J Clin Med*. 2023;12(3):1076. doi:10.3390/jcm12031076
58. Somani S, Pati S, Gaston T, et al. De novo status epilepticus in patients with COVID-19. *Ann Clin Transl Neurol*. 2020;7(7):1240-4. doi:10.1002/acn3.51071
59. Thongsing A, Eizadkhah D, Fields C, et al. Provoked seizures and status epilepticus in a pediatric population with COVID-19 disease. *Epilepsia*. 2022;63(8):e86-91. doi:10.1111/epi.17293
60. Narula N, Joseph R, Katyal N, et al. Seizure and COVID-19: association and review of potential mechanism. *Neurol Psychiatry Brain Res*. 2020;38:49-53. doi:10.1016/j.npbr.2020.10.001
61. Nikbakht F, Mohammadkhanizadeh A, Mohammadi E. How does the COVID-19 cause seizure and epilepsy in patients? The potential mechanisms. *Mult Scler Relat Disord*. 2020;46:102535. doi:10.1016/j.msard.2020.102535
62. Beghi E, Moro E, Davidescu EI, et al.; ENERGY Study Group. Comparative features and outcomes of major neurological complications of COVID-19. *Eur J Neurol*. 2023;30(2):413-33. doi:10.1111/ene.15617
63. Choi SH, Choi JH, Lee JK, et al. Clinical characteristics and outcomes of children with SARS-CoV-2 infection during the Delta and Omicron variant-dominant periods in Korea. *J Korean Med Sci*. 2023;38(9):e65. doi:10.3346/jkms.2023.38.e65
64. Enner S, Hormozdyan S, Varughese R, et al. Central apnea in an adolescent with COVID-19. *Pediatr Neurol*. 2020;110:87-8. doi:10.1016/j.pediatrneurol.2020.05.012
65. Salleh H, Soon IS, Chong VH. Frequency and risk factors for febrile seizures during COVID-19 pandemic waves: an observational study. *Eur J Pediatr*. 2023;182(7):3337-45. doi:10.1007/s00431-023-05021-0
66. Boz PB, Aslan-Kara K, Şanlı ZS, et al. Seizures in COVID-19: the relationship between biomarkers and prognosis. *Acta Neurol Belg*. 2023;123(5):1763-72. doi:10.1007/s13760-022-02054-4
67. Ghosh R, Dubey S, Finsterer J, et al. SARS-CoV-2-associated Acute Hemorrhagic, Necrotizing Encephalitis (AHNE) presenting with cognitive impairment in a 44-year-old woman without comorbidities: a case report. *Am J Case Rep*. 2020;21:e925641. doi:10.12659/AJCR.925641
68. Atakla HG, Condé K, Neishay A, et al. Cerebrovascular accidents indicative of COVID-19 infection: about 4 observations in Guinea. *Pan Afr Med J*. 2020;35(Suppl 2):65. doi:10.11604/pamj.supp.2020.35.2.23751
69. Vásquez-Colina A. Presentación neurológica severa en COVID-19. *Rev Soc Peru Med Interna*. 2020;33(2):82-4. doi:10.36393/spmi.v33i2.525
70. Young MJ, O'Hare M, Matiello M, et al. Creutzfeldt-Jakob disease in a man with COVID-19: SARS-CoV-2-accelerated neurodegeneration? *Brain Behav Immun*. 2020;89:601-3. doi:10.1016/j.bbi.2020.07.007
71. Hogan RE, Grinspan Z, Axeen E, et al. COVID-19 in patients with seizures and epilepsy: interpretation

- of relevant knowledge of presenting signs and symptoms. *Epilepsy Curr.* 2020;20(5):312-5. doi:[10.1177/1535759720948549](https://doi.org/10.1177/1535759720948549)
72. Safdarian AR, Momenzadeh K, Kahe F, et al. Death due to COVID-19 in a patient with diabetes, epilepsy, and gout comorbidities. *Clin Case Rep.* 2020;9(1):461-4. doi:[10.1002/ccr3.3557](https://doi.org/10.1002/ccr3.3557)
 73. Vollono C, Rollo E, Romozzi M, et al. Focal status epilepticus as unique clinical feature of COVID-19: a case report. *Seizure.* 2020;78:109-12. doi:[10.1016/j.seizure.2020.04.009](https://doi.org/10.1016/j.seizure.2020.04.009)
 74. Vohora D, Jain S, Tripathi M, et al. COVID-19 and seizures: Is there a link? *Epilepsia.* 2020;61(9):1840-53. doi:[10.1111/epi.16656](https://doi.org/10.1111/epi.16656)
 75. Anand P, Zakaria A, Benameur K, et al. Myoclonus in patients with coronavirus disease 2019: A multicenter case series. *Crit Care Med.* 2020;48(11):1664-9. doi:[10.1097/CCM.0000000000004570](https://doi.org/10.1097/CCM.0000000000004570)