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Covid-19-related seizures: A narrative review

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Abstract

Background: The Coronavirus (Sars-CoV-2, COVID-19) has been evolving its viral strains, prevalence, symptomatology, and sequelae of disease for the past three years. Although the most recognized COVID-19 symptoms involve the respiratory tract, neurological symptoms have been documented. Seizures have specifically been discussed in the literature, but remain both under-recognized and under-reported in clinical practice.

Aim: To review the literature of adult patients with COVID-19 and seizures, and integrate into clinical practice in the acute care environment from presentation to the emergency department to discharge.

Methods: A narrative literature review was conducted to identify all reported clinical studies involving adult patients with COVID-19 and de novo seizures from MEDLINE, yielding 108 relevant publication titles and abstracts. Three additional relevant studies were discovered through manual search of reference lists of included studies. After excluding non-related publications, 58 publications underwent full-text review. Reporting of results was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR; Appendix A).

Results: Data were organized into the following themes in the literature: prevalence of seizure occurrence in patients with COVID-19, electroencephalogram (EEG) findings in these patients, pathophysiology discussing possible cause, and outcomes both in and out of hospital. The reported prevalence of de novo seizures in patients who are COVID-19 positive has been reported from 0–4.44%. Several different mechanisms of pathogenesis have been hypothesized, including central nervous system dissemination and immune-mediated lesions.

Conclusion: Seizures were reported as both the presenting symptom of COVID-19 infection and a sequelae of the disease. Heterogeneity identified in both severity and pathogenesis of disease may partly account for the variability in reporting. Seizures may occur as single incidences, with no further implication to the patient, or they may occur in the context of new onset refractory status epilepticus (NORSE). Patients may require critical care for management of status epilepticus or encephalopathy with accompanying seizures. Clinician vigilance is essential in identifying COVID-19 infection in patients presenting to emergency services with seizures. Early recognition impacts patient care both in-hospital and at post-discharge follow-up.

Keywords: seizures, status epilepticus, NORSE, coronavirus, COVID-19, Sars-CoV-2, neurological manifestations, encephalopathy/encephalitis, PRES, narrative review

Introduction

Severe acute respiratory syndrome coronavirus (Sars-Cov-2), a ribonucleic acid (RNA) virus strain and its resulting coronavirus disease (COVID-19) was first reported in late 2019 in Wuhan, China (Tsai et al., 2020). Since its emergence, in its original alpha form (B 1.1.7), different COVID-19 strains have developed, each presenting with variability in symptoms (Siddiqui et al., 2022). COVID-19's most recognizable and reported clinical symptoms are those of the respiratory tract (Khatoon et al., 2022). However, an increasing number of neurological manifestations have been identified, including altered mental status, headaches, myalgias, olfactory disorders, and

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seizures (Nejad et al., 2021; Tsai et al., 2020). Several studies reported seizures as the primary presenting symptom of COVID-19 requiring medical attention (Anand et al., 2020; Emami et al., 2020; Fasano et al., 2020; Keshavarzi et al., 2021; Louis et al., 2020; Mithani et al., 2021; Nejad et al., 2021; Nichols et al., 2021). Confirmation of seizures can be done by obtaining an EEG. Jalil et al. (2021) found neurological symptoms to be especially prevalent in critically ill patients with COVID-19. There are several proposed hypotheses about the pathogenic pathways resulting in seizures associated with Sar-CoV-2 infection (Clark et al., 2021; Delorme et al, 2020; Jalil et al., 2021; Keshavarzi et al., 2021; Manganotti et al., 2021; Mithani et al., 2021; Nejad et al, 2021; Pagliari et al., 2021, Palacio-Toro et al., 2021; Sampaio Rocha-Filho et al., 2022; Siddiqui et al., 2022; Silva et al, 2021, Taquet et al., 2022; and Tsai et al., 2020). Variability exists in the severity of COVID-19 infection during seizure occurrence, timing of seizures in the disease trajectory, outcomes of hospitalization (i.e., primary, mortality) and long-term negative sequelae (e.g., up to two years post-COVID-19 infection). Hence, a comprehensive appraisal of published literature regarding the possible association between COVID-19 and seizures is needed.

Methods

An expert medical library technician (TS) searched the MEDLINE database on January 9, 2023, for studies using search terms: "COVID-19" and "seizures." We sought to identify all research published to-date on new onset COVID-19-related seizures in the hospital setting. Search results were limited to "all adults" (≥18 years), "humans", and studies published in English or translated to English language. We included global data to ensure a broad view and increase generalizability of results. Only studies available online were included. Studies where patients had other possible pathogenesis for seizures (i.e. alcohol withdrawal) or where patients had a history of seizures (i.e., all causes) were excluded. All publication titles and abstracts were screened by the authors and reference lists from the included studies were manually checked for additional relevant studies (Appendix A). Full text of included publications were thoroughly read by the authors and data extracted, summarized and cross-referenced. This review was informed by the methods outlined by the Joanna Briggs Institute (Peters et al., 2020). Reporting was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR; Tricco et al., 2018; Appendix A).

Inclusion and exclusion criteria are presented in Table 1. The authors organized the reviewed literature into two broad classifications: Seizure Prevalence in Retrospective Literature (Appendix B) and Case Reports (Appendix C). From these groupings, topics and themes were identified.

Ethics

As this is a narrative review of published literature, no ethics approval or informed consent was required.

Research question

This review answers the following question: What is the prevalence and proposed pathogenesis of seizures in patients presenting to hospital with COVID-19 infection?

Results: Topics and themes

Overall prevalence of seizures in COVID-19 infection

After reviewing 20 retrospective analyses that included from 50 to 40,469 patients, we found significant variance in reported seizure activity in patients with COVID-19 patients. (Appendix B). In total, 58 publications were included in the results. The literature reviewed concludes that neurological findings are common in the context of COVID-19 and seizures, either as single instances or de novo status epilepticus (SE). Seizures have been documented, both retrospectively and in case reports, with SE often being formally diagnosed as new onset refractory status epilepticus (NORSE). The prevalence of acute-onset seizures in-hospital among patients who are COVID-19 positive varied in reported data from a prevalence of 0% (Lu et al., 2020) to 4.44% (Shekhar et al., 2021). Lu et al.'s (2020) retrospective cohort study of 304 patients concluded that COVID-19 poses minimal risk for seizures. The publication with the greatest prevalence of seizures occurring with COVID-19 were found in Shekar et al. (2020), who discovered a seizure prevalence rate of 4.44% (4 out of 90) in patients with COVID-19.

Although electroencephalogram (EEG) monitoring is not available or feasible in all hospital settings, the literature that reviewed patients with COVID-19 who had EEG monitoring found neurological abnormalities at prevalence rates as high as 88% (Siddiqui et al., 2022). Our summary of EEG findings is included in Appendix C. Santos de Lima et al. (2021) retrospectively reviewed 32 patients with COVID-19 and no seizure history, who underwent EEG monitoring and found four of the 32 patients had acute seizure activity. Out of 22 case studies reviewed, where EEGs were performed during the acute phase of illness and results were provided, 17 out of 22 had documented epileptiform activity on EEG. A retrospective cohort of 22 patients with COVID-19, with EEG monitoring suggested that more sporadic epileptiform discharges may be occurring in patients with COVID-19 than are labelled as seizure activity in the clinical practice (Louis et al., 2020).

Timeline of seizures in COVID-19 Infection

We found the timeline of seizures to vary in the 44 case studies we reviewed (Appendix C). Several studies identified seizure as a presenting symptom of COVID-19 in hospital settings. A retrospective case series in a tertiary care hospital in Boston documented seizure events being the symptom that prompted presentation to hospital regardless of prior symptoms of COVID-19 in seven of 1,043 patients (0.07%). Four of the seven (57.1%) seizing patients had de novo seizure events (i.e., never had a seizure in the past) and three of the seven (42.9%) had no acute preceding symptoms of COVID-19 (Anand et al., 2020). In a retrospective study of 6,147 patients with COVID-19, documented seizures were one of the presenting manifestations in four (0.07%) patients (Emami et al., 2020). Another retrospective study reported 45 of 5,872 patients (0.8%) with severe COVID-19 illness presented to the ED with seizures; 91% of these were de novo seizures (Keshavarzi et al., 2021). The authors did note, however, that not all patients with de novo seizures had fever, hypoxemia, respiratory difficulties, or medical comorbidities, which are frequently associated with seizures (Keshavarzi et al., 2021).

Case studies published early in the pandemic described similar scenarios. Karvigh et al. (2021) published in detail a patient presenting to hospital with two seizures on the day of admission. The patient had no prior history of seizures and no systemic features of COVID-19 infection. The authors did not have an explanation for the aggressive course of the epileptic activity. Fasano et al. (2020) detailed the admission of a 54-year-old male after a single seizure characterized by clonic movements in the right arm and loss of consciousness, as the first presenting symptom of COVID-19. Bhagat et al. (2021), Dixon et al. (2020), Karvigh et al. (2021), Lyons et al. (2020), and Moriguchi et al. (2020), all presented similar case studies. The authors concluded there was a possible association between seizure onset and COVID-19 infection (Fasano et al., 2020).

Hypothesized seizure pathogenesis

Several pathogenic pathways have been described in the literature to associate COVID-19 central nervous system (CNS) dissemination and seizures, including: viral trans-synaptic spread via neural cell bodies (goblet and ciliated cells) of the olfactory nerve (Nejad et al., 2021; Pagliari et al., 2021; Silva et al., 2021), dissemination through the blood-brain-barrier by infection of vascular endothelial cells, which express angiotensin-2-converting enzyme receptors (ACE2), and by transport through endothelial CNS cells (Pagliari et al., 2021; Silva et al., 2021; Supplementary Figure 1; Xiao, 2021); and lastly, immune-mediated lesions secondary to the activation of innate and acquired immunity with release of cytokines responsible for neuronal damage (Nejad et al., 2021; Pagliari et al., 2021; Silva et al., 2021; Tsai et al., 2020). One such immune mechanism is endotheliopathy causing damaged or fragile cerebral vasculature resulting in endothelial leakage (Taquet et al., 2022), or direct neuronal injury, as evidenced by increased serum neurofilament light chains (Manganotti et al., 2021). Moreover, various features of neurotropism as a mechanism of COVID-19 viral invasion have been described (Keshavarzi et al., 2021; Palacio-Toro et al., 2021).

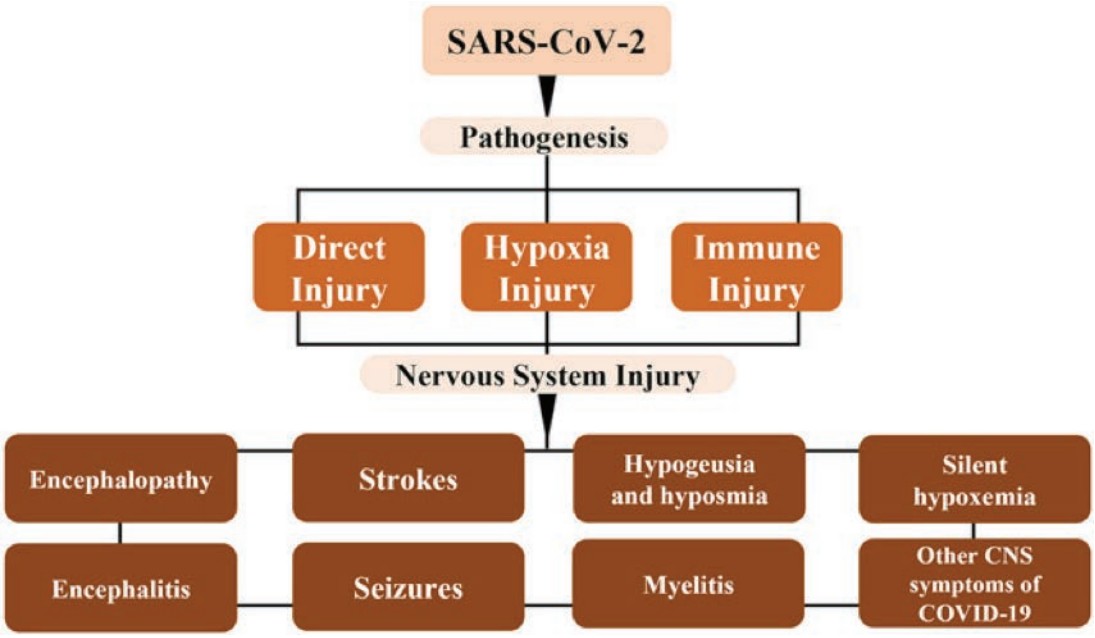
Seizures in the context of encephalopathy

Neurological manifestations in patients with COVID-19 have been increasingly reported in the literature (Silva et al., 2021) and occur in 8%–92% of hospitalized patients (Sampaio Rocha-Filho et al., 2022). More severe neurological complications, such as encephalitis or encephalopathy were found to increase patient mortality (Sampaio Rocha-Filho, 2022). A classification of encephalopathy, posterior reversible encephalopathy syndrome (PRES) was identified as one such neurological finding in multiple articles (Ioan et al., 2022; Lallana et al., 2021).

There was clear delineation in the literature reviewed between patients with COVID-19 and suspected or documented encephalitis versus those patients who were not severely ill or completely symptom-free aside from presentation with an acute-onset seizure. Features of critical illness that may be attributed to the lower seizure threshold include consequences of viral infection with acute inflammation, potential cytokine-storm, encephalitis, metabolic disturbances, vascular complications, hypoxia, and multi-organ dysfunction (Delorme et al., 2020; Pagliari et al., 2021; Sampaio Rocha-Filho et al., 2022; Tsai et al., 2020). Although temporal association may be possible between the prevalence of encephalopathy and epileptic seizures, it has not been recorded (Sampaio Rocha-Filho et al., 2022). Mithani et al. (2021) concluded that neither an association nor causation between COVID-19 infection and seizures could be established with certainty. In Appendix C, the case studies that described critically ill COVID-19 patients with seizures are identified.

Figure 1

Hypothesized Seizure Pathogenesis



(Xiao et al., 2021)

A study published in 2021 discussing new-onset seizures detailed three case studies, all of which reported systemic features of COVID-19 disease with two of the three patient cases having severe encephalopathy (Mithani et al., 2021). In a retrospective review of 198 patients with encephalitis of various etiology, seizures occurred in 67 patients (33.8%; Mithani et al., 2021). A study published in 2020 of 50 patients with COVID-19 found 11 patients with documented abnormal movements, two of whom have had documented seizure activity, confirmed on EEG in one case. All but one patient experienced encephalopathy (Clark et al., 2021). Lallana et al. (2021) investigated eight patients with COVID-19 and PRES in the Spring of 2020, where seven of the eight had documented seizures.

Patient outcomes and disease sequelae

Few studies have thus far reported in-hospital outcomes of seizures and concurrent COVID-19. In terms of in-hospital mortality, a total of 4,711 hospitalized COVID-19 patients studied, of whom had neurological manifestations, 199 were deceased (n = 1148; 17.3%; Eskandar et al., 2021). This data suggests that having neurological manifestations during an acute COVID-19 infection poses a 17.3% risk for all-cause mortality in-hospital ($p < 0.01$; Eskandar et al., 2021). The above-mentioned study also looked at seizure as a predictor of in-hospital mortality and reported a 0.4% death prevalence (five patients deceased of 1,148; Eskandar et al., 2021). However, statistical significance was not reached in this study for patients with COVID-19 who had a seizure in predicting in-hospital mortality (p = 1.00; Eskandar et al., 2021). Although this study was the largest inpatient cohort of patients with COVID-19 to date, the findings were reportedly similar to other previously completed large cohort studies (Eskandar et al., 2021). One study of 6,147 COVID-19-positive patients in Iran reported in-patient death of four patients (1.79% case fatality rate), all of whom had documented hypoxia and in-hospital seizure occurrence, but again, failed to prove cause-and-effect relationship between seizures and mortality due to the small number of patients (Emami et al., 2020).

A large, retrospective cohort study of 1,284,437 patients reported the two-year, all-cause mortality was substantial among older adults with neurological sequelae of COVID-19 infection – notably, those with seizures (Taquet et al., 2022). An Italian study that compared length of stay and mortality of patients with COVID-19 with neurological complications reported worse outcomes than those patients without neurological complications (Sampaio Rocha-Filho et al., 2022). Notably, those patients with encephalopathy had prolonged hospitalization (Relative Risk [RR] = 1.19; $p < 0.01$), as well as higher mortality (RR= 1.94; $p < 0.01$; Sampaio Rocha-Filho et al., 2022). The study also looked at seizures and the risk of prolonged hospitalisation. However, it failed to demonstrate statistical significance (Sampaio Rocha-Filho et al., 2022). Another study of 198 patients who experienced encephalitis and acute seizures in-hospital with COVID-19, demonstrated that 43 patients (29.9%) developed postencephalitic epilepsy (Mithani et al., 2021). A retrospective, cross-sectional study of 6,147 patients with COVID-19 in Iran, all of whom were critically ill with documented hypoxia and acute in-hospital seizure activity, did not require long-term anti-seizure medication (ASM) therapy unless a subsequent seizure occurred (Emami et al., 2020). Bhagat et al.(2020) noted that the majority of COVID-19-infected patients, with new onset seizures that progressed to encephalitis, recovered with minimal deficits.

Discussion

Seizures were reported as a presenting symptom to emergency departments in patients regardless of the presence of other COVID-19 symptoms. Having awareness of neurological symptoms will improve clinician recognition of COVID-19, both pre-hospital and in acute care facilities. The occurrence of seizures was also documented in critically ill patients who developed neurological symptoms progressing to encephalopathy (Hepburn et al., 2021). This is consistent with the proposed pathogenesis of the COVID-19 viral direct nervous system effect/neurotroptism or an indirect immune-mediated / para-infectious mechanism. COVID-19 may cause more significant disease complications in patients with underlying vascular pathologies, contributing to PRES and neurological sequelae (Lallana et al., 2021).

The reported prevalence of de novo seizures in patients with COVID-19 may be under-estimated due to a lack of clinician recognition of seizure activity. In Carrol et al.'s 2021 systematic review of 56 studies, 69 patients were diagnosed with seizures and seizures were the presenting symptom in 15 of them. A 2022 retrospective study of 120 patients across two cohorts; pre-pandemic (September 2019) and during the pandemic (December 2020) found a low referral rate to both acute neurology services (28%) and to the adult epilepsy team (32%; Ellis et al., 2022). Under-reporting leads to missed opportunities for specialist follow-up of patients presenting with seizures, and ultimately prevents the patients from receiving appropriate care and support (Ellis et al., 2022).

The variability in clinical management of patients with COVID-19 and seizures, along with under-reporting of seizure events to neurology services, strengthens the argument for involving specialty neurology services in order to establish a cohesive management plan. This data poses clinical implications for patients, clinicians, and health policy makers, all of whom are involved in anticipating and addressing the health burden of the pandemic (Taquet et al., 2022). Prospective studies with adequate follow-up of patients over time and reliable data collection of patients with COVID-19 and seizures may reveal a closer association.

This literature review supports educational initiatives of clinicians caring for patients presenting with COVID-19 and seizure activity (e.g., emergency medical services, acute care nurses) to ensure they are mindful of seizures as a neurological presentation of COVID-19 infection. Early identification and treatment may improve outcomes (Danoun et al., 2021; Lu et al., 2020; Sampio et al., 2022).

Strengths and limitations

The findings from this literature review were limited by the number and quality of studies published. First, given the relative novelty of COVID-19 and significant clinical constraints, the studies reviewed had variable amounts of data included (i.e. EEG confirmation of seizures, polyamerase chain reaction (PCR) confirmation of COVID-19). Second, only studies reporting on hospitalized patients were reviewed for this project. No community-based studies met our inclusion criteria. Third, the findings were limited by publication bias, as case studies were frequently published during a time when information was discovered and shared as quickly as possible. Fourth, study data heterogeneity and data quality were limited, given that all findings were retrospective and observational and peer review was inconsistent. Fifth, COVID-19 infection may be subclinical, as such it is possible that seizures occurred without investigation of COVID-19 infection status. Sixth, seizure presentation may be non-convulsive, leading to further under-recognition and documentation. Finally, this narrative review was limited to a single database search (MEDLINE). A systematic review that encompasses all database evidence would be of future research and clinical benefit.

Conclusions

The reported prevalence of de novo seizures in patients who are COVID-19 positive has been reported from 0–4.44% of patients. Reported prevalence may be underestimated due to a lack of clinician recognition of seizure activity. The proposed pathogenesis of COVID-19 contributing to seizures includes direct nervous system effect, or an indirect immune-mediated/para-infectious mechanism. Variability in severity of disease, as well as its pathogenesis may account for inconsistency in seizure events and its reporting. Further research may determine if given the relatively low reported prevalence of seizures and COVID-19 infection, if they have been largely under-recognized and under-reported (Ellis et al., 2022). It is, therefore, essential for clinicians to be increasingly vigilant to patients presenting to acute care care with seizures and COVID-19 symptoms. Recognition will impact patient care both in the emergency department, on inpatient nursing units, and in an out-of-hospital setting.

Implications for emergency nursing practice

Seizures, although not as common as other manifestations of COVID-19, can be either evident as a presenting symptom to hospital emergency rooms or during convalescence. Seizures may also occur as single events, as New Onset Status Epilepticus with COVID-19 infection, or in the context of encephalopathy secondary to critical illness, including COVID-19. Nurses who care for patients with COVID-19 at the bedside are equipped with the clinical knowledge and skills to recognize seizure activity, take the necessary steps to help cease seizure activity, and carefully document what was seen during the event. Nurses must encourage COVID-19 testing of patients who present with various neurological symptom manifestations, including seizures, and follow the necessary isolation precautions to help stop the viral spread of disease in hospital. Nurses should also encourage referral to specialty consultation to ensure proper management of neurological symptoms of patients and follow-up upon discharge.

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Conflicts of interest

None declared.

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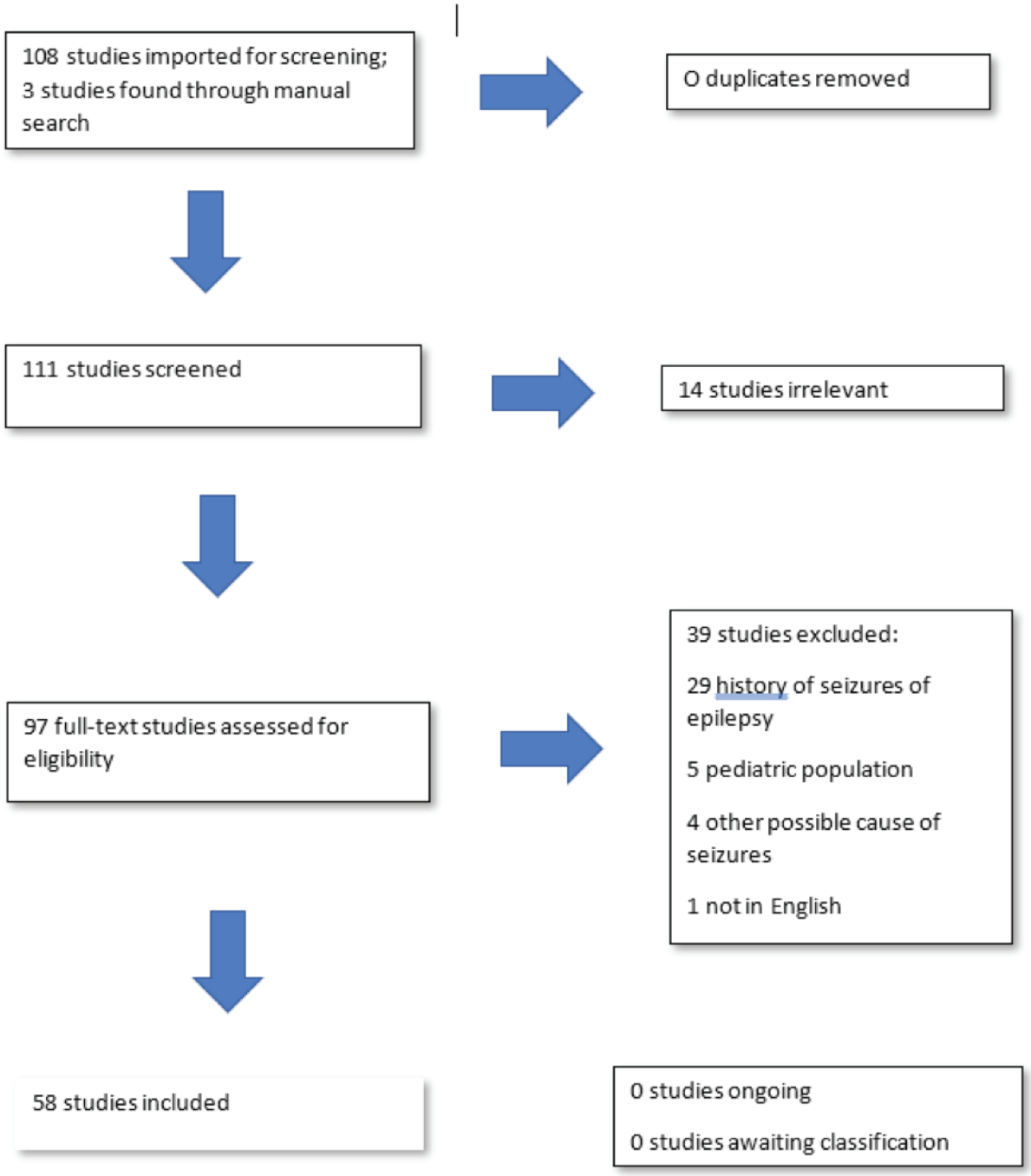
Appendix A

PRISMA-ScR



Appendix B

Retrospective Studies Reviewed

Authors	Type of study	Number of patients	Seizure prevalence	Seizure/during admission	Critical Illness	Comments
Carroll et al. (2021)	Literature review	1,182 publications	69	15/69 on presentation	NA	
Chachkhiani et al. (2020)	Retrospective analysis	256	11 (9 had surgical history; 4.3%)	NA	NA	Altered mental status very common
Clark (2021)	Retrospective case series	50	2/50 (4%)	once admitted	yes, ICU admissions	
Danoun et al. (2021)	Multi-centre retrospective	4,100	110 (2.68%)	during admission	in 70%	97.5% had no prior epilepsy
Emami et al. (2020)	Retrospective	6,147	5	in 4/5	yes in all 5	
Eskandar (2021)	Retrospective	4,711	26	once admitted	NA	
Kershavarzi et al. (2021)	Retrospective	5,872	45 (0.8%)	presenting symptom	NA	
Khedr, Abo-Elfetoh, et al. (2021)	Surveillance study	439	5	NA	6 had encephalitis	
Khedr, Shoyb, et al. (2021)	Hospital based study	439	5	NA	NA	2 had previous epilepsy
Lin et al. (2021)	Multicentre retrospective cohort study	197 who had EEG	19 (9.6%)	NA	NA	
Liotta et al (2020)		509	2	NA	NA	
Louis et al. (2020)	Retrospective cohort study	22 who had EEG	5/22 (22.7%)	NA	NA	2/5 had history of epilepsy
Lu et al. (2020)	Retrospective multicentre study	304	0 (2 with seizure like symptoms)	NA	8 with encephalopathy	
Mao et al. (2020)	Retrospective observational case series	214	1	NA	88 with critical illness	
Nalleballe et al. (2020)		40,469	258 (0.6%)			not all were inpatients; 2.3% had encephalopathy
Nejad et al., (2021)	Cross-sectional study	891	1.70%	non-specified		
Sampaio Rocha-Filho et al. (2022)	Retrospective cohort	613	2.80%	once admitted	26% requiring ventilation, 24% had encephalopathy	
Santos de Lima et al. (2021)		32	18.8% on EEG		6 severe, 16 critical	
Shekhar et al. (2020)		90	4		yes, all 4 required ICU	
Tacquet (2022)	Retrospective cohort	1,284,437				
Tsai et al. (2020)	Systemic review		1.50%			*data taken from Mao et al. and Arentz et al.
Whittaker et al. (2020)	Systematic review	38 articles	not identified			

Note. NA = not applicable; ICU = intensive care unit; EEC = electroencephalogram.

Appendix C

Case Studies Reviewed

Authors	Number of participants	Incidence of seizures	Patient demographics	When seizure occurred	NP or throat-PCR	EEG completed	Critical illness	Comments
Afshar et al. (2020)	1	1/1	39 yo F	once admitted, on day 11	NP -	unknown	yes, required intubation	acute necrotizing encephalitis
Anand et al. (2020)	7	7/7	37–88 yo	presenting symptom	NP +	2/7 had EEGs obtained; one with epileptiform discharges, one with delta		3/7 had history of epilepsy
Balloy et al. (2020)	1	1/1	59 yo M	16 days after ER presentation	NP-, tracheal suction +	suggested epileptic seizures	yes	discharged home
Bhagat et al. (2021)	1	1/1	54 yo M	presenting symptom	NP+	suggested encephalopathy	encephalitis	
Chen et al. (2020)	5	5/5	37–60, M and F	1 had "whole body shaking" pre- admission	all 5 NP +	2/5 showed epileptiform discharges	all 5	2 had SE
Delorme et al. (2020)	4	1/4	69 yo M	presenting symptom, 7 days after respiratory symptoms		lateralized periodic discharges in the right frontal lobe		SE
Dixon et al. (2020)	1	1/1	59 yo F, hx aplastic anemia	presenting symptom	NP +	unknown	yes	acute necrotizing encephalitis, expired
Dono et al. (2021)	1	1/1	81 yo M	14 days into admission	NP +	suggested SE	no	
Duong et al. (2020)	1	1/1	41 yo F	presenting symptom	unspecified +	generalized slowing, no epileptic discharges		
Efe et al. (2020)	1	1/1	35 yo F	presenting symptom		NA	encephalitis	symptom mimicked glial tumor
Farhadian et al. (2020)	1	1/1	78 yo F	after flu prodrome	NP +	not completed	no	
Fasano et al. (2020)	1	1/1	54 yo M	presenting symptom	NP -	no abnormalities	yes, encephalopathy	
Ghosh et al. (2020)	1	1/1	44yo F	flu-like illness first	NP +	none done	yes, expired	
Gomez-Enjuto et al. (2020)	1	1/1	74 yo M	once admitted, on day 15	unspecified +	unknown	PRES	
Hepburn et al. (2021)	2	2/2	76 yo M	once admitted	NP+	confirmed focal seizures	yes, encephalopathy	

continued…

" "			82 yo M	once admitted	NP +	suggested SE		
Hosseini et al. (2020)	2	2/2	46 yo M	once admitted	NP+	unknown		
" "			79 yo F	presenting symptom	NP +	unknown		
Ioan (2022)	1	1/1	38 yo M	once admitted	NP+	no epileptiform discharges	yes, PRES	
Jalil et al., (2021)	1	1/1	29 yo M	once admitted (presented with altered mental status)	NP +	generalized slowing	encephalopathy	
Karvigh et al., (2021)	1	1/1	73 yo M	presenting symptom	NP +	suggested SE	NORSE	
Koh et al. (2022)	1	1/1	20 yo F	presenting symptom	NP +	suggested SE	NORSE	
Lallana et al. (2021)	8	7/8	36-70, 50% F	once admitted	NP +	unknown	All required intubation, PRES	1-70 days for PRES to develop
Le Guennec et al. (2020)	1	1/1	69 yo M	five days into disease presentation	NP +	suggested nonconvulsive SE		
Lyons et al. (2020)	1	1/1	20 yo M	Presenting symptom	2nd NP PCR +	unknown	NORSE	
Manganotti et al. (2021)	2	2/2	37 yo M	once admitted	NP +	continuous epileptic activity	NORSE	
" "			71 yo M	once admitted	NP +	continuous epileptic activity		
Mithani et al. (2021)	3	3/3	72 yo F	once admitted, single focal seizures	NP+	sharp waves, no progression to seizures	yes, encephalopathy	
" "			48 yo M	once admitted	NP +	epileptiform discharges		
" "			30 yo M	once admitted	NP +			
Monti et al. (2020)	1	1/1	50 yo M	once admitted, on day 4	throat +	unknown	NORSE	
Moriguchi et al. (2020)	1	1/1	24 yo M	once admitted (presented with altered mental status)	NP -	unknown	yes, meningitis	
Nawfal et al. (2022)	1	1/1	21 yo F	5 weeks after covid infection	NP -	generalized slowing, intermittent lateralized periodic discharges (LPDs) over the right frontotemporal area	NORSE	though NP was -, SARS-CoV-2 IgG was present

continued…

Palacio Toro et al. (2021)	1	1/1	26 yo F	once admitted	NP +	normal 1 month after discharge	
Rezaeitalab et al. (2021)	4	4/4	56 yo F	seizures not presenting symptom	NP +	unknown	
" "			24 yo M	occurred three days after developing weakness, myalgia	NP -	unknown	
" "			65 yo F	presenting symptom	NP +	unknown	
" "			71 yo M	presenting symptom, one week after covid diagnosis	NP +	unknown	
Rodrigo-Armenteros et al. (2020)	1	1/1	62 yo M	once admitted (day 5)	NP+	continuous rhythmic epileptiform discharges	yes, encephalopathy
Siddiqui (2022)	1	1/1	middle age F	presenting symptom	NP +	suggested encephalopathy	encephalitis
Silva et al. (2021)	1	1/1	45 yo M	once admitted	NP +	no change noted	
Sohal and Mansur (2020)	1	1/1	72 yo M	once admitted, on day 3	NP +	temporal seizures, epileptogenic waves	yes, expired
Somani et al. (2020)	2	2/2	49 yo F	preadmission;	2nd NP PCR +	seizure activity	intubated
" "			73 yo F	day 1 of hospitalization	tracheal aspirate +	seizure activity	intubated dialysis, MOF, expired
Varoglu and Hosver (2022)	1	1/1	77 yo F	once admitted, on day 7	PCR +, unknown site	seizure activity	

Note. yo = years old; F = female; NP = Nurse Practitioner; EEG = electroencephalogram; M = male; ER = emergency room; SE = status epilepticus; hx = history; NA = not applicable; PRES = posterior reversible encephalopathy syndrome; NORSE = new onset refractory status epilepticus; PCR = polymerase chain reaction test; SARS-Cov-2 = severe acute respiratory syndrome coronavirus (COVID-19); IgG = immunoglobulin G, LPD = lymphoproliferative disorder; MOF = multiple organ failure.