COCID-19 AND SEIZURE/EPILEPSY

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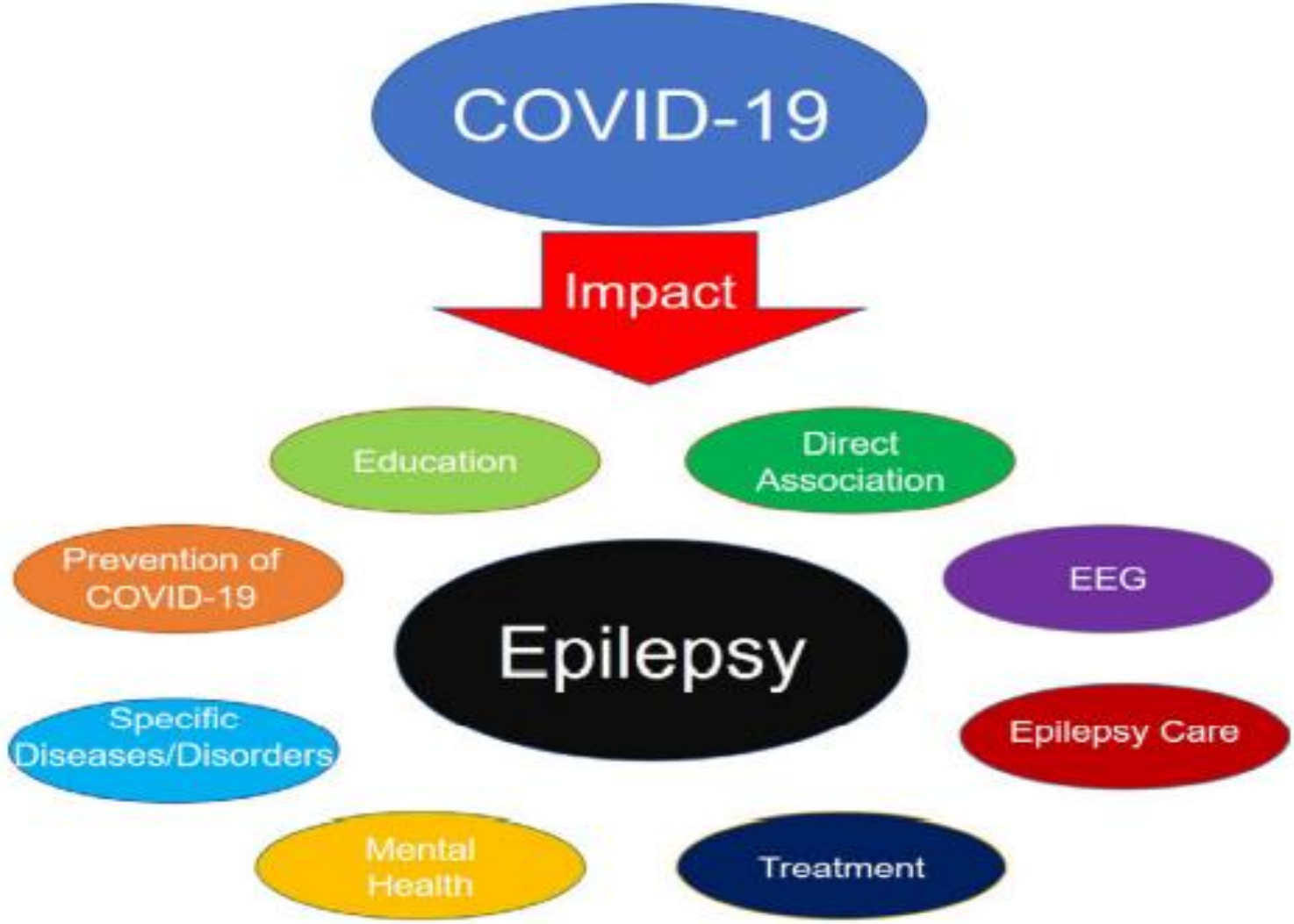

Fig. 1. Epilepsy and associated issues that may be affected by COVID-19. COVID-19, coronavirus disease 2019.

Associations between COVID-19 and epilepsy/seizure

- Based on the **limitations of studies**, it is probably **too early** to determine that **epilepsy is a risk factor for COVID-19**. A systematic review article showed that the rate of COVID-19 severity in people with epilepsy(PWE) **is lower than** other neurological disorders

- In addition, epilepsy is not a single disease and research **looking at different groups of epileptics** is also needed to determine which patients with epilepsy are truly at higher risk

Could COVID-19 cause acute symptomatic seizures?

- Various studies have reported the **incidence** of acute symptomatic seizures due to COVID-19 as **less than 1%.** This is lower than the seizure rates previously reported for SARS (2.7%) and MERS (8.6%)
- In fact, **acute symptomatic seizure has not been mentioned** in several studies that summarized the symptoms of a large sample of COVID-19 patients

Worsening of seizures during the COVID-19 crisis

- According to those studies, the proportion of patients experiencing **increased seizures varied from 8–35%,** and may reflect factors such as the status of COVID-19 infection in different locations and the proportion of individuals with an at-risk background (e.g., **older age**)

- In a study involving three epilepsy centers in Italy and Spain, **no significant changes in seizure frequency** were reported during the COVID-19 emergency
- One explanation was that **stay-at-home** orders or **quarantine** due to COVID-19 would allow patients with epilepsy to live a **regular life**
- On the other hand, increased stress and lack of access to physicians or medication refills, particularly during the **early months of service shutdowns**, would likely have **worsened** seizure control during the COVID-19 crisis

Comorbidity of patients with epilepsy and COVID-19

- **Elderly**: high risk for severe COVID-19 illness
- **Stroke in elderly**: high risk for severe illness
- **Pediatric with epilepsy and neurodisability:** are more likely to develop pneumonia or other respiratory complications

Epilepsy as a neurological complication of COVID-19

- The incidence of epilepsy caused by COVID-19 is **not yet known**, and any such investigation will **require a sufficient follow-up period**

Mechanisms of seizures in COVID-19

Direct mechanism

- SARS- COV-2 is able to **directly enter and infect CNS**, causing meningitis and encephalitis, and thereby causing seizures
- **Bloodstream**: **ACE-2 receptors** (on the cardio-respiratory neurons of the brainstem, glial cells, basal ganglia, motor cortex, raphe, and endothelial cells of the brain)
- **Through the olfactory nerve**: causing **inflammation and demyelinating reactions** with potential subsequent seizures

Indirect mechanism

- **1-** The overloading of ACE-2 receptors by SARS- COV-2 results in the **down-regulation of ACE-2 expression**, leads to dysfunction of the renin-angiotensin system and **elevated production of angiotensin II**
- This results in a cascade of interactions that promote **brain degeneration** with the possibility of **resulting in seizures**

- **2- Cytokine storm** an immune-mediated life-threatening disease which is caused by **impaired NK and cytotoxic T-cell function**
- This impaired function results in **excessive secretion of pro-inflammatory cytokines** such as TNFα, and IL 1, 4, 6, 8, 10, and 18 and then leads to **multi-organ damage**

- **3- Hypoxia and hypoxia:** COVID-19 can cause **pneumonia** and result in devastating hypoxia (**potentiate hypoxic encephalopathy and seizures**)
- Ischemic brain injury also contributes to **cerebral tissue hypoperfusion** and may lead to seizures

Exacerbation of seizure in PWE

- The effects of COVID-19 on PWE still **remain unclear**. The importance of maintaining control of epilepsy with ASMs
- **provoked seizures** by sepsis, fever, sleep deprivation, electrolyte
- **Drug-drug interactions** between ASMs and the anti-COVID therapy

EEGs during the COVID-19 crisis

- **No COVID-19-specific findings** that would lead to suspicion of COVID-19 infection based on EEG testing
- A **large multicenter study is needed** to investigate the characteristics of EEG findings in COVID-19 patients

Impact of COVID-19 on epilepsy care

- **1- Restriction** of clinical care due to COVID-19
- **2- Utility and strengths/weaknesses of telemedicine** for patients with epilepsy: **decreased risk of exposure, no physical exam**, and less likely to make **use of telemedicine services in male** patient

Treatment for PWE during the COVID-19 crisis

1-Anti-Seizure Medications

- - **The combination** of eslicarbazepine /lacosamide and atazanavir/lopinavir/ritonavir can cause potentially **fatal arrhythmias**
- - CBZ, PHT, and Pb, should be used with caution when in combination with **remdesivir**

2- Diet therapy

- patients may experience substantial **obstacles to maintaining specific diets (KD)** under the COVID-19 crisis
- The possibilities of **telemedicine** in terms of providing nutritional guidance are also promising

3- Epilepsy surgery

- In March–April of 2020, some authorities recommended that elective surgeries be postponed as much as possible
- According to the **ILAE, frequent seizures with injuries, tonic-clonic seizures with high risk of SUDEP, and recurrent episodes of SE should be considered as urgency**
- **Video-EEG for preoperative** assessment purposes should be carefully considered during the COVID-19 crisis

- A study on surgeries as a whole found that **COVID 19-positive patients are more likely to experience post operative respiratory complications** and are at a greater risk of postoperative **mortality** within 30 days of surgery, especially for **male** patients and patients **over 70** years old

4-Immunotherapy/steroids

- Several studies have investigated whether PWE using **immunosuppressive drugs** may be at risk of severe COVID-19. In most such studies, immunosuppressive drugs **did not present an obvious risk**

Treatment for patients with SE

- A recent study found that numbers of **admissions due to SE did not differ** significantly from previous years, even if other emergency medical conditions were reduced. The authors also mentioned a trend toward **less frequent NCSE** and the **loss of female predominance** might indicate the presence of an **under-diagnosis of SE**

Mental health in patients with epilepsy

- Several reports have examined the **psychological stress** on patients with epilepsy, and such patients are reportedly more susceptible to psychological stress from COVID-19 than the general population
- mental stress can also **increase seizure frequency** and can lead to depression and other mental health problems

Difficulties in prevention of COVID-19 for PWE

1- Social distance

- While it goes without saying that social distancing is important for COVID-19 epidemic prevention, we should be aware that this can **sometimes be challenging** for individuals with epilepsy

2-Wearing masks

- One risk was discussed in which wearing a mask could **induce hyperventilation** in PWE
- Suggestion to **avoid wearing** face masks under any circumstances is probably **unreasonable** for PWE
- Wearing a face mask is probably advantageous in **crowded locations**, with **intermittent breaks in safe locations away**

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A follow-up study of patients with COVID-19 presenting with seizures

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ABSTRACT

Objective: We performed a follow-up study of patients with COVID-19 presenting with seizures.
Methods: All consecutive patients with seizures, who were referred to Namazee Hospital, Shiraz, Iran, with a diagnosis of COVID-19, from 10 August 2020 until 20 October 2020 were included in this longitudinal study. The clinical data were collected by the admitting physician. In a follow-up phone call to the discharged patients (after eight weeks or more), we inquired their seizure outcome.
Results: In total, 32 patients were studied; 28 patients were followed. Twelve patients (37.5%) presented with a single tonic-clonic seizure and nine (28.1%) had convulsive status epilepticus; one patient had functional (psychogenic) seizures. Ten patients (31.3%) had pre-existing epilepsy, eight others (25%) had pre-existing CNS problems (without epilepsy), one person (3.1%) had pre-existing functional seizures, and 13 individuals (40.1%) neither had epilepsy nor had other CNS problems. Eight patients (28.6%) reported experiencing seizure(s) after being discharged from the hospital; six of these had pre-existing epilepsy and one had pre-existing functional seizures. One patient, who had a newly developed ischemic brain infarction, reported experiencing recurrent seizures.
Conclusion: Seizures in patients with COVID-19 are either acute symptomatic (in about two-thirds) or an exacerbation of a pre-existing epilepsy/functional seizures (in about one-third). A thorough investigation of the underlying etiology of seizures in patients with COVID-19 is necessary. Seizure outcome in patients, who are hospitalized with COVID-19 and seizures, is generally good.

A follow-up study of patients with COVID-19 presenting with seizures

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- Seizures (as a presenting manifestation) in patients with COVID-19 are either **acute symptomatic seizures** (in about two thirds) or an **exacerbation** of a pre-existing epilepsy/functional seizures (in about one-third)
- **A complete investigation** of the underlying etiology of the seizure in patients with COVID-19 is necessary
- Seizure outcome in patients, who are hospitalized with COVID-19 and seizures, is **generally good** and COVID-19 does not add to the risk of developing epilepsy in the future unless a significant brain insult (e.g., CVA) happens

THANK YOU FOR YOUR ATTENTION