Objective: Neurological manifestations associated with coronavirus disease-2019 (COVID-19) are broad and heterogeneous. Although the predominant clinical presentation is respiratory dysfunction, concerns have been raised about the neurological hallmarks. Many reports suggest some findings on electroencephalography (EEG) can be relevant to COVID-19.

Materials and Methods: Patients with COVID-19 admitted to hospital and referred for EEG from March 1, 2020 to February 15, 2021, were retrospectively enrolled. When research databases were queried with the terms “COVID-19 (ICD code: 10: U07.3) and “EEG”, total number of patients obtained was 32. Number of patients excluded due to unconfirmed diagnose with COVID-19 was 12. Twenty adult patients with certain diagnose of COVID-19 who underwent 21-electrode routine EEG during the outbreak with neurological deterioration were identified.

Results: Background abnormalities was evident in one of fourth patients (n=5, 25%). Mild diffuse slowing (n=3, 15%) and focal slowing (n=3, 15%) with left frontotemporal tendency (n=2, 10%) were observed. Epileptiform abnormalities and seizures were detected showing focal (n=4, 20%) or generalized onset (n=1, 5%).

Conclusion: Here we performed a retrospective single-centre study to evaluate the electroencephalographic findings in patients diagnosed with COVID-19 since it remains unknown. It needs to be more clarified with increasing number of recordings.

Keywords: COVID-19, electroencephalography, epilepsy

Electroencephalographic Findings in Patients with COVID-19: A Single-center Experience

Introduction

Coronavirus disease-2019 (COVID-19) is a severe public health threat that primarily targets the human respiratory system. However, it is also associated with neurological manifestations, including seizures, altered mental state, and headache (1,2). People with COVID-19 may continue to suffer from persistent neurological symptoms, even after apparent resolution of respiratory illness. 

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symptoms, including anosmia, taste loss, fatigue, anxiety, cognitive impairment, or “brain fog”. Several pieces of evidence showed that neurotropic and neuroinvasive capabilities of coronaviruses may prompt seizures, convulsions, mental status changes, encephalitis, or encephalomyelitis (3). Several studies have tried to describe the typical manifestations of COVID-19 and its neurological consequences, but it remains unknown. Patients with COVID-19 may propose an increased risk with neurological deteriorations with cognitive changes or seizure-like events. However, the extent to which COVID-19 is associated with seizures is unknown. Some recent reports described the association between COVID-19 and neurological symptoms in electroencephalography (EEG) abnormality as a common feature, including background activity slowing, periodic and rhythmic activity, and epileptiform discharges (4).

New-onset seizures in a patient with COVID-19 are another important unexplored feature of this pandemic. Overall changes and outcomes of these patients and specific hallmarks of COVID-19 are still unexplored, most probably, due to the restricted number of diagnostic utilities. After more than a year of confirmation with the worldwide pandemic, we have conducted a study to evaluate the potency of EEG in patients with COVID-19-related symptoms.

Material and Methods
The Local Institutional Ethics Committee at Necmettin Erbakan University approved this study of human subjects that review the EEG and other clinical data (no: 2021/5135). For this observational and descriptive study, patients with COVID-19 who are admitted to Necmettin Erbakan University Meram Faculty of Medicine Hospital neurology department from March 1, 2020, to February 15, 2021, were retrospectively enrolled. Databases that were queried with the terms “COVID-19” (ICD code:10:U07.3) and “EEG” revealed a total number of 32 patients. A total of 12 patients were excluded due to unconfirmed COVID-19 diagnoses. Thus, 20 adult patients with certain COVID-19 diagnoses who underwent 21-electrode routine EEG (rEEG) for neurological deterioration were identified. Exclusion criteria were younger than 18 years old and were infused with anesthetics or sedating agents during or before the rEEG to avoid their confounding effects on EEG. EEGs were accomplished with the Nihon-Kohden EEG acquisition system with 32 channels. This is a standardized digital EEG recording with time-locked video. EEGs were recorded over 20 min with scalp electrodes placed according to the International 10-20-system, and portions of this record are reviewed using bandpass filters of 10-35 Hz with a sensitivity of 10 mV/mm. Hyperventilation and intermittent photic stimulation were performed as an activating procedure and their effects were noted. EEGs are independently evaluated by two different neurologists and a clinical neurophysiologist to bring homogeneity using the American Clinical Neurophysiology Society’s guideline for documentation (5). EEGs were categorized into normal or abnormal, regarding the background rhythm, periodic or rhythmic discharges, and epileptiform abnormalities. The characteristic of periodic discharges and epileptiform abnormalities as spikes and waves and periodic or rhythmic discharges were identified.

Statistical Analysis
Descriptive statistics (mean, frequency, and standard deviation) and Student’s t-test on parametric data showing normal distribution were evaluated using the Statistical Package for the Social Sciences for statistical analysis.

Electronic medical records, laboratory, and radiologic testing for all patients were retrospectively reviewed. Data on age, sex, co-existing diseases, and conditions like altered mental status, headache, stroke, smell or taste changes, and neuroimaging findings (brain tomography or magnetic resonance) were collected. Any missing or uncertain records were clarified through direct communication with these patients, their health caregivers, or their families.

Results
A total of 20 adult patients with COVID-19 who underwent rEEG after neurological deterioration were identified, who were aged 22-72 years (mean: 46.8±3.3), including 7 males (35%) and 13 females (65%). Positive severe acute respiratory syndrome coronavirus 2 nucleic acid polymerase chain reaction test on preadmission was determined in 75% (15 out of 20) of cases and the rest were diagnosed according to the chest-computed tomography (20%) and positive anti-body test result (5%). Of these 20 patients, one had prior epilepsy and is taking antiseizure medication (ASM). EEGs were abnormal in half of the patients, which were classified into three subgroups as follows: 1) Background abnormalities in the quarter of patients (n=5, 25%). They were further categorized into mild diffuse slowing (n=3, 15%) or focal slowing (n=3,15%) with left frontotemporal tendency (n=2, 10%). 2) Epileptiform changes and seizures were categorized into focal (n=4, 20%) or generalized. Control EEGs were concordant with the previous one in all patients (4/4). 3) Periodic or rhythmic patterns of intermittent rhythmic discharges are obtained in patients who present with new-onset seizure (n=1, 5%) (Figure 1).

Patient demographics, COVID-19-specific diagnostic studies, history, chief complaints, and comorbidities of patients are summarized in Table 1. Brain MRI was performed in 17 out of 20 patients, of which 1 had consistent findings with an ischemic stroke with bilateral watershed infarcts (Figure 2), 1 had a lobar meningioma, and 8 (47%) was normal. The investigation for the reasons for referrals revealed that the most common was cognitive changes (n=5, 25%) followed by seizure-like events (n=5, 25%). Memory disturbance (n=4, 20%), confusion (n=1, 5%), and attention deficit (n=1, 5%) were counted as a single category and described as cognitive changes. New-onset seizure, myoclonic jerks, and recently developed opsoclonus-myoclonus without any suspicious underlying etiology other than COVID-19 were the most interesting subjects in this study (n=3, 15%) and will be discussed later on. Prolonged headache (n=2, 15%), temporary numbness or burning sensations on hands and feet (n=3, 15%), myalgia (n=1, 5%), and unpleasant smell sensation or loss of taste/smell (n=2, 10%) were the resting reasons for rEEG investigations.

Discussion
This study aimed to evaluate and assess the utility of EEG in emerging COVID-19-associated symptoms and define the presenting epileptiform abnormalities. To our knowledge, this is the first systematic study in Turkey that highlights the electroencephalographic findings with COVID-19.
Table 1. Summary of demographic features, history, diagnostic method, and complaints with electroencephalography indication and features

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age</th>
<th>History</th>
<th>COVID-19 diagnostic method</th>
<th>Patients’ complaint after COVID-19</th>
<th>EEG abnormalities</th>
<th>Control EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>P 1</td>
<td>F/22</td>
<td>None</td>
<td>Chest CT +</td>
<td>New-onset seizure</td>
<td>IRD</td>
<td>Focal ED (left frontotemporal)</td>
</tr>
<tr>
<td>P 2</td>
<td>M/43</td>
<td>None</td>
<td>PCR +</td>
<td>Opsoclonus-myoclonus</td>
<td>No abnormality</td>
<td>Focal ED (left frontal)</td>
</tr>
<tr>
<td>P 3</td>
<td>F/62</td>
<td>DM, mucormycosis</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>Focal ED (right temporal)</td>
</tr>
<tr>
<td>P 4</td>
<td>M/29</td>
<td>None</td>
<td>Chest CT +</td>
<td>Confusion</td>
<td>Focal ED (left frontal)</td>
<td>Focal ED (left frontal)</td>
</tr>
<tr>
<td>P 5</td>
<td>F/31</td>
<td>None</td>
<td>Chest CT +</td>
<td>Confusion</td>
<td>Focal ED (right temporoparietal)</td>
<td>Focal ED (right temporal)</td>
</tr>
<tr>
<td>P 6</td>
<td>F/40</td>
<td>None</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>Focal ED (right temporal)</td>
</tr>
<tr>
<td>P 7</td>
<td>F/50</td>
<td>HT, AF</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>Focal ED (right temporal)</td>
</tr>
<tr>
<td>P 8</td>
<td>F/64</td>
<td>CVD, left parietal meningioma</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>Focal ED (right temporal)</td>
</tr>
<tr>
<td>P 9</td>
<td>F/31</td>
<td>MS</td>
<td>PCR +</td>
<td>Loss of taste and smell</td>
<td>No abnormality</td>
<td>-</td>
</tr>
<tr>
<td>P 10</td>
<td>F/61</td>
<td>HT, CVD, CKD</td>
<td>PCR +</td>
<td>Myoclonic jerks on the hands and legs</td>
<td>Focal slowing (Left frontotemporal)</td>
<td>-</td>
</tr>
<tr>
<td>P 11</td>
<td>M/65</td>
<td>Dementia</td>
<td>PCR +</td>
<td>Memory deficits</td>
<td>Mild diffuse slowing</td>
<td>-</td>
</tr>
<tr>
<td>P 12</td>
<td>M/72</td>
<td>DM, HT, CAD, delirium</td>
<td>PCR +</td>
<td>Memory deficits, delirium</td>
<td>Mild diffuse slowing</td>
<td>-</td>
</tr>
<tr>
<td>P 13</td>
<td>F/43</td>
<td>CVD</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>-</td>
</tr>
<tr>
<td>P 14</td>
<td>M/37</td>
<td>None</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>-</td>
</tr>
<tr>
<td>P 15</td>
<td>F/39</td>
<td>Epilepsy</td>
<td>Anti-body +</td>
<td>Increased seizure frequency</td>
<td>Mild diffuse slowing+ generalized ED</td>
<td>-</td>
</tr>
<tr>
<td>P 16</td>
<td>F/35</td>
<td>None</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>-</td>
</tr>
<tr>
<td>P 17</td>
<td>M/60</td>
<td>None</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>-</td>
</tr>
<tr>
<td>P 18</td>
<td>F/34</td>
<td>MG</td>
<td>Chest CT +</td>
<td>Memory deficits</td>
<td>No abnormality</td>
<td>-</td>
</tr>
<tr>
<td>P 19</td>
<td>M/58</td>
<td>DM</td>
<td>PCR +</td>
<td>Emotional expression changes, increased laughter, and Ischemic CVD Prolonged headache</td>
<td>Focal ED (right temporoparietal)</td>
<td>-</td>
</tr>
<tr>
<td>P 20</td>
<td>F/60</td>
<td>HT</td>
<td>PCR +</td>
<td>Memory deficits</td>
<td>No abnormality</td>
<td>-</td>
</tr>
</tbody>
</table>

Seizure-like events and cognitive changes were almost the main reason to investigate an rEEG (50%) according to the study, and abnormal EEG was reported in half of the subjects. Altered mental status (including attention deficit, memory disturbances, confusion, and delirium) even in the absence of sedating agents was reported in one-fourth of the subjects (5/20, 25%) after excluding the case with preexisting dementia. Antony and colleagues showed that altered mental status (61.7%) and seizure-like events (31.2%) were the most common reasons for EEG investigation in a systematic review (4). The incidence of altered mental status was disparate from our study, which is probably related to their older age population (The median age of their participants was 61.3 years).

Follow-up EEGs were discordant with the first one showing high reliability (4/4). The main abnormality on EEG includes background slowing with the diffuse or focal distribution. The sporadic epileptiform abnormalities were not rare (25%), predominantly showing focal tendency that correlated with the clinical presentation. Patients with prior epilepsy have abnormal EEG (55%) or epileptiform discharges (30%). Follow-up EEGs were available in 20% of patients with the same features. Focal epileptiform discharges with frontotemporal dominancy (left > right) were the main features of these analyses.

Acute symptomatic seizures with ongoing seizure activity without prior epilepsy in COVID-19 infection are increasingly reported (6,7). Furthermore, recent systematic reviews suggest that patients with preexisting neurological disorders, like epilepsy, may develop neurological problem exacerbations in the setting of COVID-19 (8). Subjects with new-onset seizures in this study presented with intermittent rhythmic discharges on admission with a frequency of >1 Hz, which is known to correlate with increased seizure risk (9,10). Subsequent EEG revealed focal epileptiform discharges with frontotemporal lateralization. (Figure 1) Subject was seizure-free with medication.

Another subject among these patients with COVID-19 who were diagnosed with acute ischemic stroke was presented concomitant acute symptomatic seizure. Seizure control is maintained with levetiracetam at 500 mg twice a day with gradual ASM cessation. Several days after, the patient was re-admitted to the neurology outpatient clinic with increased laughter without emotional intensity, mood changes, and attention deficit. The first and subsequent rEEG revealed right temporal epileptiform discharges in both. The patient was seizure-free in control. These first and subsequent rEEG revealed right temporal epileptiform discharges in both. The patient was seizure-free in control.

Another patient with prior epilepsy was already on ASMs (Valproic acid at 500 mg and Zonisamide at 400 mg add-on therapy) at the time of admission and presented with increased seizure frequency. This patient was discharged on the gradually increased valproic acid and decreased zonisamide. The patient remained seizure-free during the hospitalization and follow-up. Frontal EEG findings resulting from direct brain involvement in a patient with confirmed COVID-19 have been speculated, whereas more systemic involvement may lead to more diffuse changes (13). Older people are speculated to have a higher risk of developing severe manifestations with COVID-19 (13). The age of our study population ranges from 22 to 72 years, 10 of whom showed EEG abnormality (n=10, 50%). They seemed slightly older than the rest; however, the difference was not statistically proven (p=0.224).

Our study revealed that the proportion of EEG abnormality was higher in patients with cognitive changes and seizure-like events regardless of prior epilepsy. Additionally, symptoms, such as headache or burning sensations, are less likely associated with abnormal EEG.

**Conclusion**

COVID-19 may contribute to electrographic seizures and seizure detection based on continuous-EEG studies. Concerns for contamination and exposure of staff have limited the diagnostic tests among these patients, thus larger studies on EEG are relatively sparse. A need for a case-control group study among patients who are negative for COVID-19 who present with similar clinical features is the main restriction of this study.

**Acknowledgment**

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**Ethics**

**Ethics Committee Approval:** The Local Institutional Ethics Committee at Necmettin Erbakan University approved this study of human subjects that review the EEG and other clinical data (no: 2021/3135).

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**


Conflicts of Interest: No conflict of interest was declared by the authors.

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References


