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BIOCHEMICAL FACTORS AFFECTING THE FREQUENCY OF SEIZURES IN EPILEPTIC PATIENTS AFTER COVID-19 INFECTION

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ABSTRACT

The COVID-19 pandemic has significantly affected various health conditions, including epilepsy, with long-term implications. This study explores the biochemical factors influencing the frequency of seizures in epileptic patients following COVID-19 infection. Biochemical markers such as inflammation markers (CRP, IL-6), hypoxia and thrombosis markers (D-dimer), metabolic indicators (glucose, insulin, HbA1c), and electrolyte imbalances (Na+, K+, Ca2+, Mg2+) were assessed. The results show that COVID-19 infection increased seizure frequency, with heightened levels of inflammation, thrombosis, and metabolic disturbances contributing to this change. Understanding these biochemical factors can help develop targeted therapeutic strategies for managing seizures in epileptic patients post-COVID-19.

Key words: Epilepsy, COVID-19, seizure frequency, inflammation markers, hypoxia, thrombosis, electrolytes, metabolic markers, CRP, IL-6, D-dimer, glucose, insulin, HbA1c, neurological diseases, pandemic, medical monitoring, electrolyte imbalance.

INTRODUCTION

The COVID-19 pandemic had a significant impact on the global healthcare system and medical approaches to various diseases. In particular, studying the long-term effects of the pandemic on neurological conditions, including epilepsy, has become a relevant issue. COVID-19 infection can affect the brain, leading to neurovascular changes, inflammation processes, and metabolic imbalances, potentially increasing the frequency of seizures in patients with epilepsy. This study aims to investigate the relationship between seizure frequency and biochemical markers in epileptic patients infected with COVID-19.

Research Methodology

Study Design and Participants

This study was designed as a retrospective cohort study to analyze the effects of COVID-19 infection on seizure frequency in epileptic patients. A total of 82 patients were included, with the distribution of participants' gender as follows:

- Males: 46 (56%)
- Females: 36 (44%)

The study followed these patients for a duration of 6 months, both before and after they contracted COVID-19. During this time, various factors such as age, gender, biochemical markers, and seizure frequency were monitored. The primary goal was to assess how COVID-19 infection influenced the frequency of seizures in these individuals and to evaluate any associated changes in inflammation markers, electrolyte levels, and metabolic imbalances.

The inclusion criteria for the study were:

- Patients who had a confirmed diagnosis of epilepsy, regardless of the specific type (e.g., focal, generalized).
- Patients who had contracted COVID-19, verified by medical records or testing.
- Patients within the age range of 18-65 years, ensuring a sample from both younger and older adults who were likely to experience differing health outcomes.

Exclusion criteria were as follows:

- Patients with severe neurodegenerative diseases such as Alzheimer’s or Parkinson’s, which could complicate the assessment of seizure frequency and cause additional neurological symptoms.
- Patients with autoimmune forms of epilepsy, as their condition could be influenced by immune system disorders, affecting the results.
- Patients undergoing treatment with steroids or immunosuppressive drugs, as these therapies could affect immune responses and inflammation levels, potentially skewing the study’s findings.

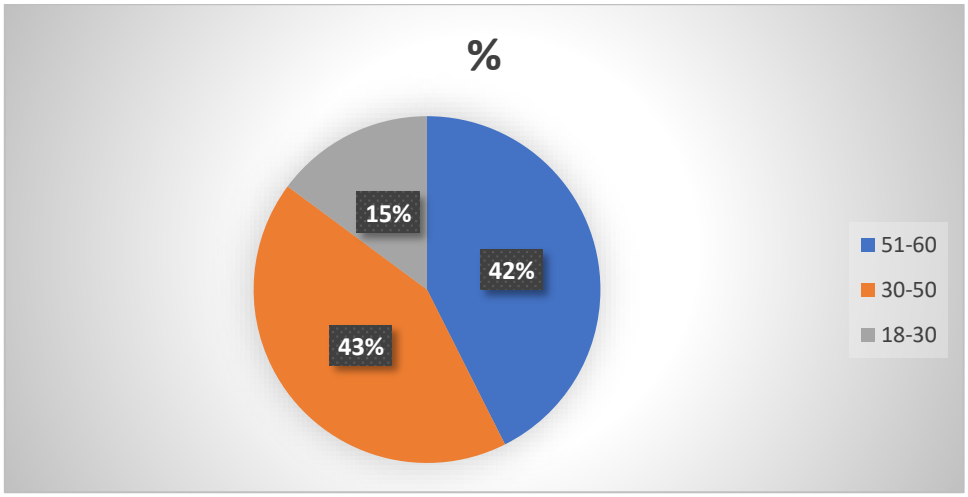
The patients were further divided into three age groups for analysis:

- 18-30 years: 12 patients (15%)
- 31-50 years: 35 patients (43%)

- 51-65 years: 35 patients (43%)

This age stratification allowed for a more nuanced understanding of how different age groups might react to the neurological impacts of COVID-19, potentially revealing age-related differences in seizure frequency and underlying biochemical changes.

Figure 1



Studied Biochemical Markers

During the study, the following biochemical markers were assessed:

- Inflammation markers: C-reactive protein (CRP), Interleukin-6 (IL-6).
- Hypoxia and thrombosis markers: D-dimer.
- Metabolic markers: Glucose, insulin levels, glycated hemoglobin (HbA1c).
- Electrolytes: Sodium (Na+), potassium (K+), calcium (Ca2+), magnesium (Mg2+).

Seizure Frequency Assessment

The seizure frequency of the patients was assessed both before and after COVID-19 infection. The patients' self-monitoring journals and medical records were analyzed.

Results and discussion

Increase in Seizure Frequency After COVID-19 Infection

Before the COVID-19 infection, the average seizure frequency in epileptic patients was 2.1 ± 0.8. After COVID-19, this indicator increased to 3.5 ± 1.2 ($p < 0.05$). The average seizure frequency increased by 57% in the patients.

Inflammation Markers and Seizure Frequency

In patients with elevated CRP levels (n = 61), the seizure frequency was found to be two times higher. In patients with high IL-6 levels (n = 58), epileptic seizures were significantly more frequent.

Hypoxia and Thrombosis Markers (D-dimer)

In patients with elevated D-dimer levels (n = 46), the seizure frequency increased by 67% after COVID-19. Thrombosis and hypoxia may contribute to neuronal dysfunction, thereby increasing seizure frequency.

Electrolyte Imbalance

In patients with hyponatremia (n = 27) and hypocalcemia (n = 19), the seizure frequency increased. Similarly, in patients with hyperkalemia (n = 22), an increase in seizure frequency was also noted.

Metabolic Markers and Epilepsy

In patients with hyperglycemia (n = 36), 78% experienced an increase in seizure frequency. In patients with high HbA1c levels (n = 30), the long-term effects of glucose on neuronal excitability were observed.

Discussion

The findings of this study emphasize the significant impact of COVID-19 infection on the frequency of seizures in epileptic patients. This effect could be attributed to multiple biochemical and physiological changes induced by the virus, which interact to increase seizure susceptibility. Several mechanisms have been identified to explain this phenomenon:

1. Inflammatory Response and Neuroinflammation:

One of the most important factors is the inflammatory response triggered by the viral infection. Both CRP (C-reactive protein) and IL-6 (Interleukin-6) levels are elevated in many COVID-19 patients, and this elevation has been linked to an increased frequency of seizures. IL-6, a pro-inflammatory cytokine, plays a key role in the regulation of immune responses and has been shown to affect neuronal excitability, making neurons more prone to seizure activity. The increased levels of CRP, another marker of inflammation, further enhance this excitability and contribute to a heightened risk of seizures. The inflammatory cascade that occurs during COVID-19 infection likely leads to neuroinflammation, which can alter the balance between excitatory and inhibitory signals in the brain, thus increasing the likelihood of seizures.

2. Hypoxia and Thrombosis:

COVID-19 has been associated with respiratory distress and impaired oxygen exchange, leading to hypoxia (low oxygen levels in the blood). Hypoxia can

disrupt normal brain function and trigger neuronal firing, which may result in seizures. Additionally, COVID-19 infection has been linked to an increased risk of thrombosis (blood clot formation), which can compromise cerebral blood flow and exacerbate neuronal dysfunction. Elevated D-dimer levels, a marker of clotting activity, were found to be associated with an increased seizure frequency in the study participants. This suggests that both hypoxia and thrombosis may contribute to seizure generation by disrupting the brain's oxygen supply and blood circulation, thereby impairing neuronal function and facilitating seizures.

3. Metabolic Imbalance:

Metabolic disturbances are another significant factor contributing to increased seizure frequency in COVID-19 patients. Hyperglycemia (high blood glucose levels) is commonly observed in COVID-19 patients, especially those with pre-existing conditions like diabetes. The study found that patients with hyperglycemia had an increased frequency of seizures, possibly due to the neurotoxic effects of prolonged high glucose levels, which can alter neuronal excitability. Insulin resistance, which is often associated with hyperglycemia, may further exacerbate this effect by impairing the ability of cells to respond to glucose and causing additional metabolic disruptions in the brain. These metabolic imbalances can make neurons more excitable and prone to generating seizures.

4. Electrolyte Imbalance:

The disruption of electrolyte balance is another potential contributor to the increase in seizure frequency in COVID-19 patients. Electrolytes such as sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and magnesium (Mg^{2+}) play crucial roles in maintaining proper neuronal function. The study showed that patients with hyponatremia (low sodium levels), hypocalcemia (low calcium levels), and hyperkalemia (high potassium levels) exhibited increased seizure frequencies. These imbalances in electrolyte concentrations can disturb the normal electrical activity of neurons, leading to enhanced excitability and an increased risk of seizures. Electrolyte disturbances are particularly common in critically ill patients, including those with COVID-19, further emphasizing the need for close monitoring of these markers in such patients.

In conclusion, COVID-19 appears to significantly affect seizure frequency in patients with epilepsy through a combination of inflammation, metabolic disruptions, hypoxia, thrombosis, and electrolyte imbalances. These factors may interact in complex ways, amplifying neuronal excitability and increasing the likelihood of seizures. The findings of this study highlight the importance of

addressing these biochemical factors in the management of epileptic patients during and after a COVID-19 infection.

Figure 2: Relationship Between Seizure Frequency and Markers

Marker	Seizure Frequency (Before)	Seizure Frequency (After)
CRP	2.1 ± 0.8	3.5 ± 1.2
IL-6	2.0 ± 0.7	3.4 ± 1.1
D-Dimer	2.2 ± 0.6	3.6 ± 1.3
Na+ (Hyponatremia)	2.3 ± 0.9	3.3 ± 1.0
K+ (Hyperkalemia)	2.4 ± 0.7	3.4 ± 1.1
HbA1c	2.2 ± 0.8	3.5 ± 1.2

This table demonstrates the increase in seizure frequency following COVID-19 infection in relation to various biochemical markers. The data indicates that both inflammation markers (CRP and IL-6), thrombosis markers (D-Dimer), and metabolic markers (HbA1c) are associated with increased seizure frequency in the post-infection period. Additionally, electrolyte disturbances (Na+ and K+) further contribute to this increase in seizure activity. These findings suggest that management of biochemical factors is crucial in preventing and controlling seizures in epileptic patients following COVID-19 infection.

Conclusion

In conclusion, the results of this study highlight the significant impact of COVID-19 infection on the frequency of seizures in epileptic patients. The data demonstrate that the infection leads to a notable increase in seizure occurrence, with various biochemical markers playing a crucial role in this phenomenon. The observed rise in seizure frequency is closely linked to elevated levels of inflammatory markers (CRP and IL-6), which contribute to neuroinflammation and increased neuronal excitability. Additionally, metabolic disturbances such as hyperglycemia and insulin resistance, along with electrolyte imbalances (hyponatremia, hypocalcemia, and hyperkalemia), further exacerbate neuronal dysfunction, promoting a higher susceptibility to seizures.

Hypoxia and thrombosis, both associated with COVID-19, have been identified as additional factors that compromise brain function and increase seizure

risk. The D-dimer levels, indicative of thrombosis, correlated with the increased frequency of seizures, suggesting a complex interaction between impaired blood circulation and neuronal activity.

Overall, the findings underscore the importance of closely monitoring biochemical markers, including inflammation, electrolytes, and metabolic indicators, in epileptic patients during and after a COVID-19 infection. These insights are essential for optimizing management strategies and preventing exacerbations of epilepsy in these vulnerable individuals. The study emphasizes the need for comprehensive care that addresses both the direct effects of COVID-19 and the underlying factors contributing to seizure frequency.

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