ORIGINAL ARTICLE

Investigating the Relationship of Age and Gender with the Prevalence of Seizure Types in Children with COVID-19: An Analytical Cross-Sectional Study in Firouzabadi Hospital

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ABSTRACT

Objectives

One of the clinical presentations of COVID-19 infection in children is seizure. Furthermore, based on other studies during the epidemy of the Omicron variant in Iran and other parts of the world, the incidence of seizure in children increased. Moreover, the distribution of different seizure types remains to be discovered due to the newness of the Omicron variant epidemic and the lack of studies in this field. Understanding the connections between demographic factors and different seizure types is crucial, as managing this disorder varies based on the type of seizure and the individual characteristics of each patient. This study aims to investigate the relationship between age and gender with the type of seizures in children under 18 years of age with the Omicron type of COVID-19.

Materials & Methods

In this this analytical cross-sectional study included 45 children diagnosed with COVID-19 and having seizures. The required information, including demographic characteristics and clinical findings of seizures, was recorded in them.

Results

No statistically significant relationship was observed between demographic characteristics and the type of seizures.

Conclusion

Although this study contains significant clinical results, more studies are needed to clarify this issue due to its limitations.

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Introduction

Since the end of 2019, the globe has witnessed a calamitous pandemic of a novel ailment known as coronavirus disease (COVID-19) instigated by the SARS-CoV2 virus. It is a rational assumption to anticipate that specific individuals diagnosed with COVID-19 may encounter seizures as a consequence of a deficiency in oxygen supply, malfunctioning of bodily organs, abnormalities in metabolic processes, interactions between various medications, or potentially even impairment to the brain that might manifest in individuals affected by COVID-19 (1).

The term febrile seizure (FS) alone does not describe an independent disease. This term can apply to any fever and seizures without encephalitis, meningitis, or any other brain disorders. FS is most common among children aged six months to six years, with a prevalence of 2-4% (2). Viral etiology is considered the most common etiology of the first episodes of fever and convulsions resulting in hospitalization in childhood (3). According to newly published studies, seizures may be one of the manifestations of the Omicron variant of COVID-19 in children. Seizures are generally divided into three categories: focal, general, and unknown. Each group includes sub-categories based on the most recent classification of seizures and epilepsies from the International League Against Epilepsy (ILAE), 2017. In this study, the distribution of seven groups of these seizures, including focal impaired aware, aware focal, focal to bilateral tonic-clonic, generalized tonic-clonic, generalized non-motor (absence), generalized and focal tonic-clonic and generalized and focal myoclonic, and their relationship with age and gender have been discussed (4).

The presence of COVID-19 has been linked to a heightened susceptibility to seizures and epilepsy compared to other infectious diseases. Reports indicate that the incidence of seizures within six months after a COVID-19 infection is 0.81% (5). In this field, there have been studies on the effect of demographic characteristics on seizures, but there have not been many studies on seizure types. Similar studies in the population of people not affected by COVID-19 show the effect of age and gender on the type of seizure.

According to studies, females were more illiterate and unemployed compared to males. Tonic-clonic seizures were more common in males.

Furthermore, recent studies indicate that tonic-clonic seizures are more common in men than in women. However, when it comes to other types of seizures, no significant difference exists between genders, except for atonic seizures (6, 7).

Moreover, another study looked at seizure types and clinical findings in children with the Omicron variant of COVID-19, which has a tiny sample size (8).

In a study involving four patients diagnosed with the Omicron variant of COVID-19, they experienced repeated seizures and even status epilepticus with a duration of 15 to 20 minutes (9).

Several scientific publications have documented cases of people with COVID-19 experiencing new-onset FS, recurrent seizures, and status epilepticus (10).

A study shows that the incidence of FS in children with Omicron disease was 25.5%, and high age, male gender, less family history, and previous medical history of seizures did not significantly affect the incidence of seizures in the group affected by COVID-19 compared to the non-infected group (11).

This study primarily aims to investigate the

relationship between age and gender with the type of seizure in children under 18 years old with the Omicron type of COVID-19.

On the other hand, this study's descriptive objectives include estimating the prevalence of age, gender, seizure type, seizure recurrence, and status epilepticus and reporting clinical findings related to COVID-19, including clinical symptoms, CT scan results, and polymerase chain reaction (PCR) test results.

A case report in 2020 discussed the occurrence of status epilepticus in children during the COVID-19 pandemic. Given the irreversible damage to the neurological system, it is essential to examine the prevalence and recurrence of seizures in this study (12).

Due to the lack of sufficient research in this field and the novelty of the issue, no documented statistics were found on the prevalence of seizures in children at the peak of the Omicron variant, the possibility of its recurrence, and how to manage these seizures. Accordingly, the current research intends to provide appropriate data on the issue.

Materials & Methods

This analytical cross-sectional study was conducted in Firouzabadi Hospital, Shahre-Rey, Tehran, Iran. The Iran University of Medical Science approved the research. The study's design and report writing were based on the equator line (STROBE).

In this analytical cross-sectional study, 45 people under the age of 18 who had both COVID-19 and seizures were included in the study.

The criteria for diagnosing COVID-19 are to have at least two of the following:

1) Positive PCR test
2) Lung pathological findings in CT scan
3) Clinical symptoms specific to Covid-19

Seizure diagnosis criteria were based on having two unprovoked seizures >24 h apart and the criteria for classifying seizures into subgroups, according to the latest ILEA guidelines and based on clinical findings.

Then, the required information about the patients was collected, including their age, sex, origin, type of seizure, recurrent seizures, status epilepticus, clinical symptoms of COVID-19 disease, pathological findings of the lung in CT scan, and PCR test results.

SPSS software version 27.0 was used for data analysis, and descriptive statistics was used to analyze the essential variables. Due to the samples' non-normal distribution, Mann-Whitney, Kruskal-Wallis, and Fisher's exact tests were also used for further data analysis. The statistical significance was considered as a P-value < 0.05.

Results

Forty-five patients were included in this study, of which 64.4% were male, and 88.4% had Iranian nationality. The mean (± SD) age of the participants was 47.73 (± 46.08) months, and 27.3% of the studied patients were in the 13—to 24-month age group. According to the obtained data, 48% of the participants experienced tonic-clonic seizures and only 2.4% experienced Myoclonic patterns. Status epilepticus was the first complaint in 45% of the patients. 75% of the patients did not experience seizures again.

COVID-19 PCR test results returned positive in 91% of patients, and 90% of the participants had clinical symptoms of COVID-19. Lung CT scan findings of 38.1% of the patients were typical for COVID-19, whereas 38.1% % had pathological findings in the CT scan that were not typical for COVID-19. Familial history and past personal history of seizure were negative in 69% and 80%

of the patients, respectively. 55.6% of patients who did not present with status epilepticus and 44.4% of patients who presented by status experienced seizures again (Table 1).

Table 1. Demographic and patient specific data

Variable		Number of cases	Percentage (%)
Gender	boy	29	64.4
	Girl	16	35.6
	Total	45	100
Nationality	Iranian	38	88.4
	Non-Iranian	5	11.6
	Total	43	100
Age (months)	12<=	7	15.9
	13.00-24.00	12	27.3
	25.00-36.00	5	11.4
	37.00-48.00	7	15.9
	49.00-60.00	2	4.5
	61.00-72.00	1	2.3
	73.00>=	10	22.7
	total	44	100
Seizure pattern	Absence	5	12.2
	Tonic-Clonic	20	48.8
	LOC	3	7.3
	Clonic	5	12.2
	Partial seizure	5	12.2
	Secondary generalized	2	4.9
	Myoclonic	1	2.4
	Total	41	100
Recurrence of seizures	Yes	10	25
	No	30	75
	Total	40	100
Status epilepticus	Yes	18	45
	No	22	55
	Total	40	100
EEG	Normal EEG	4	57.1
	Abnormal EEG	3	42.9
	Total	7	100
Lung CT scan findings	Has evidence of covid infection	8	38.1
	Doesn’t have	5	23.8
	Has pathology but non typic for COVID	8	38.1
	Total	21	100

Continued Table 1.

Clinical Presentation of Covid-19	Yes	37	90.2
	No	4	9.8
	Total	41	100
Family history of seizure	No	25	69.4
	Yes	11	30.6
	Total	36	100
Past medical history of seizure	No	32	80
	Yes	8	20
	Total	40	100

No significant relationship was found between age and seizure type (P value= 0.319)(Table 2).

51.9% of male patients and 42.9% of female patients in this study were presented with a tonic-clonic seizure pattern. Secondary-generalized seizure pattern was seen in 3.7% and 7.1% of male and female patients, respectively. The current study evaluated the relationship between gender and seizure pattern, and by applying Fisher's exact test, no statistically significant relationship was observed between seizure patterns and the gender of our participants (P value= 0.902)(Table 3).

Seizure patterns and recurrence of seizures had no statistically significant relationship in the children of our study population, according to the results of Fisher's exact test (P value = 0.335)(Table 4).

Table 2. Relationship between age and seizure pattern

Seizure pattern	Number of cases	Age* (Mean ± SD)	Nonparametric Kruskal-Wallis test
Absence	5	54.60 ± 46.39	P value = 0.319
Tonic-Clonic	19	54.47 ± 57.76	
LOC	3	65.33 ± 35.81	
Clonic	5	32.40 ± 22.96	
Partial seizure	5	55.60 ± 44.22	
Secondary generalized	2	10.50 ± 10.61	
Myoclonic	1	1.0	
Total	40	49.15 ± 47.95	

**Months of age*

Table 3. Relationship between age and seizure recurrence

Seizure recurrence	Number of cases	Mean	Standard Deviation	Nonparametric Mann-Whitney test
Yes	10	56.60	51.52	P value= 0.403
No	29	45.83	47.31	

Table 4. Relationship between seizure and gender

Seizure Pattern	Gender		Total Number (Percentage)	Fisher exact test
	Boy Number (Percentage)	Girl Number (Percentage)		
Absence	4 (14.8%)	1 (7.1%)	5 (12.2%)	
Tonic-Clonic	14 (51.9%)	6 (42.9%)	20 (48.8%)	
LOC	2 (7.4%)	1 (7.1%)	3 (7.3%)	
Clonic	3 (11.1%)	2 (14.3%)	5 (12.2%)	
Partial Seizure	3 (11.1%)	2 (14.3%)	5 (12.2%)	
Secondary Generalized	1 (3.7%)	1 (7.1%)	2 (4.9%)	P value = 0.902
Myoclonic	0 (0%)	1 (7.1%)	1 (2.4%)	
Total	27 100/0%	14 100/0%	41 100/0%	

Table 5. prevalence of PCR positive children in the population

Covid-19 PCR result	Number of cases	Percentage
Positive	41	91.1%
Negative	4	8.9%
Total	45	100%

Table 6. Relationship between seizure pattern and seizure recurrence

Seizure pattern	seizure recurrence		total	Fisher exact test
	yes	no		
Absence	3 (30%)	1 (3.6%)	4 (10.5%)	
Tonic-Clonic	4 (40%)	16 (57.1%)	20 (52.6%)	
LOC	0 (0%)	2 (7.1%)	2 (5.3%)	
Clonic	1 (10%)	3 (10.7%)	4 (10.5%)	
Partial seizure	2 (20%)	3 (10.7%)	5 (13.2%)	P value= 0.335

Continued Table 6.

Secondary generalized	0 (0%)	2 (7.1%)	2 (5.3%)
Myoclonic	0 (0%)	1 (3.6%)	1 (2.6%)
Total	10 (100%)	28 (100%)	38 (100%)

Table 7. Relationship between seizure recurrence and status epilepticus

Presented with Status epilepticus	Seizure recurrence			Fisher exact test
	Yes	No	Total	
Yes	4 (44.4%)	11 (39.3%)	15 (40.5%)	P value = 1
No	5 (55.6%)	17 (60.7%)	22 (59.5%)	
Total	9 (100%)	28 100%	37 100%	

Discussion

The study has limitations, such as the sample size, which requires more studies in this field. Additionally, no testing kit was specifically designed to diagnose the Omicron variant. However, given that the research was carried out during the peak of the Omicron outbreak, nearly all samples are believed to be contaminated with the Omicron Variant. It is essential to correctly diagnose the type of seizure because, according to ILEA reports, the first line of treatment is different for each type of drug —for example, Ethosuximide for absence seizures, Lamotrigine, and Topiramate for generalized tonic-clonic seizures.

Carbamazepine, Phenytoin, and Oxcarbazepine are the first line of treatment for FS (4).

This issue becomes even more critical when seizures arise as a complication of a persistent illness like COVID-19.

Since all the criteria for identifying COVID-19 have false positives and negatives, in this study, at least two diagnostic criteria were used to definitively diagnose COVID-19, which is more effective in the clinic.

Most patients had clinical presentations of COVID-19, such as rhinorrhea, cough, loss of appetite, and others. Besides, most of the included patients (91%) had positive COVID-19 PCR test results. Most patients had pathological findings in lung CT scans, but half did not have typical lung CT scan patterns of COVID-19, so we could state that lung involvement is a significant possibility, affecting the treatment.

In this study, no significant relationship was observed between seizure pattern, age, and sex,

confirming the results of other studies in healthy people (6).

Furthermore, according to the results, most patients have no family history and no history of previous seizures, which can be clinically vital and require more studies to prove this issue.

In this study, the prevalence of seizures in boys is higher than in girls, which is confirmed by the results of other studies in the group of people without COVID-19 (13).

Notably, seizures are most common in children aged 13 to 24 months. This is expected, given that younger patients are generally more vulnerable. This highlights the urgent need for timely treatment in this age group. The most common seizure observed was tonic-clonic, confirming the results of other studies in people not affected by COVID-19.

Also, myoclonic convulsions had the lowest prevalence in the sample size, which cannot be generalized to the population because not all types of convulsions were investigated.

It is suggested that other studies be conducted using accurate diagnostic methods such as Electroencephalogram (EEG) to ensure the type of seizure, which was not possible to perform EEG for all patients due to the limitations of this study.

Recommendation

This study can be conducted on a bigger sample size, using particular Omicron variant diagnostic kits for more accurate results.

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Authors' Contribution

Maryam kachuei conceived the study and developed the theoretical framework.

Zahra Adel performed the experiments.

Mohammad Rezazadeh analyzed the data.

Zohre Zamani contributed to the interpretation of the results.

Azita Tavasoli supervised the project and provided critical revisions to the manuscript.

All authors discussed the results and contributed to the final manuscript.

Conflicts of Interest

All authors declare that they have no conflict of interest.

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