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Evaluation of Coronavirus Disease 2019-Positive Patients with Febrile Convulsions

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Abstract

Objective: Febrile convulsion is a common seizure type in children between 6 months and 6 years of age and is seen in 2%-5% of children.[1] Coronavirus disease 2019 spread rapidly and became a pandemic. As coronavirus disease 2019 can be seen in epilepsy patients, the relationship between coronavirus disease 2019 and seizures is not clear yet.[2] This study aimed to evaluate the characteristics of coronavirus disease 2019-positive patients with febrile convulsions and compare them with coronavirus disease 2019-negative patients with febrile convulsions regarding their clinical features.

Methods: Forty patients were included in the study. In our country, diagnosing, monitoring, and treating coronavirus disease 2019 are performed according to the Turkish Ministry of Health coronavirus disease 2019 Scientific Committee guidelines.

Results: Twelve of the patients were coronavirus disease 2019 positive, whereas 28 were coronavirus disease 2019 negative. While the rate of complex febrile convulsion was 50% in the coronavirus disease 2019-positive group, this ratio was 25% in the coronavirus disease 2019-negative patient group.

Conclusions: Seizures occur in the presence of higher-grade fever in coronavirus disease 2019-positive cases. On the other hand, the probability of seizures to occur focally and recur during the same disease period might be higher. Male gender and maternal history of febrile convulsions may be the risk factors.

Keywords: Febrile convulsion, childhood, COVID-19, infections, prognosis, simple seizure, complex seizure, treatment

INTRODUCTION

Febrile convulsion (FC) is a type of seizure accompanied by fever, occurring in children aged between 6 months and 6 years, with no intracranial infection, hypoglycemia, or acute electrolyte imbalance. It is the most common seizure type in children.[3] Environmental factors and genetics have been considered,[4] and viral diseases, vaccines, and genetic predisposition have been reported as common risk factors that might affect the developing nervous system.[5] Febrile convulsions can be classified as simple and complex. Complex FCs are fever-related unilateral seizures with focal manifestations in the foreground, lasting longer than 15 minutes and occurring more than once within 24 hours. Simple FCs are seizures that are usually generalized and with a higher course of fever, lasting less than 15 minutes.[6] The pathophysiology of FC, which is the most common seizure type in childhood, has not been identified yet.[7] Viral infections play a significant role in its etiology.

Coronavirus disease 2019 (COVID-19), which causes serious respiratory disorders, was first reported in Wuhan, the capital of China's Hubei province. The etiological agent of COVID-19 has been reported to be a new coronavirus.[8] The most common complaints regarding the disease are fever, cough, and shortness of breath.[9] Seizures related to COVID-19 have been reported in the literature. Metabolic factors, systemic disorders, and probably the direct effect of the virus can be considered among the factors that may provoke seizures in COVID-19 patients.[10]

This study aimed to evaluate the characteristics of COVID-19-positive patients with FCs and compare them with COVID-19-negative patients with FCs regarding their clinical features.

METHODS

This study was planned as a single-center, observational, and retrospective study conducted in Bursa City Hospital, a complex health center serving a population of 6 million and affiliated with the University of Health Sciences. Patients aged between 6 months and 6 years and presenting with febrile seizures were included in the study. In our country, diagnosing, monitoring, and treating COVID-19 are performed according to the Turkish Ministry of Health COVID-19 Scientific Committee guidelines. Reverse transcription-polymerase chain reaction for severe acute respiratory syndrome coronavirus-2, combined naso-oropharyngeal swabs were made in all patients admitted with fever and seizures. Complete blood count, complete urinalysis, and serum biochemical tests including electrolytes were measured in all patients. Urine and blood cultures were made in patients with a suspected bacterial infection. Cerebrospinal fluid was examined by lumbar puncture in all patients younger than 12 months and in patients between 12 months and 18 months whose central nervous system infection could not be excluded. Forty-four patients were found to present with febrile seizures. Four

patients were excluded from the study; 3 of them were diagnosed with meningitis, and the other, a 3-year-old girl, had hyponatremia-related seizures. Thus, 40 patients admitted with seizures and diagnosed with FC were included in the study. Patients diagnosed with FC were categorized into 2 groups as COVID-19-positive and COVID-19-negative. We considered prolonged seizures, focal seizures, and recurrent seizures as complex FC, whereas febrile seizures lasting less than 15 minutes as simple FC. Patients' electronic charts were evaluated, and age, gender, symptoms, clinical findings, laboratory results, neuroimaging, and elect roencephalography results were recorded as data. Electroencephalograp hy was performed 3 weeks after the seizure in all patients who had initially presented with a febrile seizure.

Ethics Disclosure

Permission for this study was granted by the Turkish Ministry of Health, General Directorate of Health Services, Scientific Research Board. Approval from the Ethics committee was obtained with that permission document (16/09/2020, Decision number: 2020-7/9).

Statistical Analysis

Statistical Package for the Social Sciences version 23.0. (IBM SPSS Corp.; Armonk, NY, USA). Comparisons between 2 independent groups regarding numerical variables were made using the Mann–Whitney *U*-test. The chi-square analysis tested differences between the rates of categorical variables in independent groups. The statistical significance level was considered as $P < .05$.

RESULTS

Forty patients were included in the study. The general characteristics of the patients included in the study are presented in Table 1. Febrile convulsion was found to be manifested at 22.6 ± 9.7 (min: 8-max: 48) months. It was more common in males when compared to females. It was determined to be most frequently manifested during upper respiratory tract infections. Twelve of the patients were COVID-19-positive, whereas 28 were COVID-19-negative (Table 2). Male gender (58.3%, 57.1%) was dominant in both groups, and there was no difference between groups ($P > .05$). Our study determined that the fever during seizures was graded higher in the COVID-19-positive group than the COVID-19-negative group, but we did not find any statistically significant difference between the 2 groups. While the rate of complex FC was 50% in the COVID-19-positive group, this ratio was 25% in the COVID-19-negative patient group (Table 2). In patients with simple FCs and complex FCs, higher fever was observed in COVID-19-positive patients. (Figure 1A and B).

Electroencephalography was normal in all patients in the study group. Magnetic resonance imaging findings were found to be normal in all patients. An arachnoid cyst was found incidentally in the posterior cerebellar region in only one patient.

MAIN POINTS

- Male gender may be a risk factor for febrile convulsion in children with COVID-19.
- Febrile convulsions seen in COVID-19 disease occur at higher fever values.
- Complex febrile convulsion type is more common in COVID-19 positive children.

Table 1. Descriptive Data of the Patients Included in the Study

Age (Mean ± SD) (Months)	22.6 ± 9.7 (Minimum: 8-Maximum: 48)	
Gender (n = 40)	n	%
Female	17	42.5
Male	23	57.5
Type of seizure		
Simple	27	67.5
Complex	13	32.5
History of febrile convulsion		
Present	16	40.0
Absent	24	60.0
COVID-19		
Positive	12	30.0
Negative	28	70.0
Upper respiratory tract infection	35	87.5
Pneumonia	2	5.0
Urinary infection	1	2.5
Acute gastroenteritis	1	2.5
Familial history of epilepsy		
Present	3	7.5
Absent	37	92.5
Maternal febrile convulsion		
Present	3	7.5
Absent	37	92.5
Paternal febrile convulsion		
Present	2	5.0
Absent	38	95.0
Total	40	100.0

Table 2. Comparison of COVID-19-Positive Group and COVID-19-Negative Group Included in the Study

	COVID-19 Positive (n = 12)	**COVID-19 Negative (n = 28)**	***P***
Age (months)	Mean ± SD	Mean ± SD	.647
	21.4 ± 9.7	22.9 ± 9.8	
	Minimum/median/maximum	Minimum/median/maximum	
	11/17.5/41	8/21.5/48	
Gender	n (%)	n (%)	
Female	5(41.7)	12 (42.9)	1.000
Male	7 (58.3)	16 (57.1)	
Type of seizure			
Simple	6 (50.0)	21 (75.0)	.154
Complex	6 (50.0)	7 (25.0)	
History of febrile convulsion			
Present	6 (50.0)	10 (35.7)	.490
Absent	6 (50.0)	18 (64.3)	
Familial history of epilepsy			
Present	1 (8.3)	2 (7.1)	1.000
Absent	11 (91.7)	26 (92.9)	
Maternal febrile convulsion			
Present	2 (16.7)	1 (3.6)	.209
Absent	10 (83.3)	27 (96.4)	
Paternal febrile convulsion			
Present	0 (0.0)	2 (7.1)	1.000
Absent	12 (100.0)	26 (92.9)	
Fever	Mean ± SD	Mean ± SD	.233
	39.6 ± 1.2	39.0 ± 0.6	
	Minimum/median/maximum	Minimum/median/maximum	
	38/39.5/42	38/39/41	

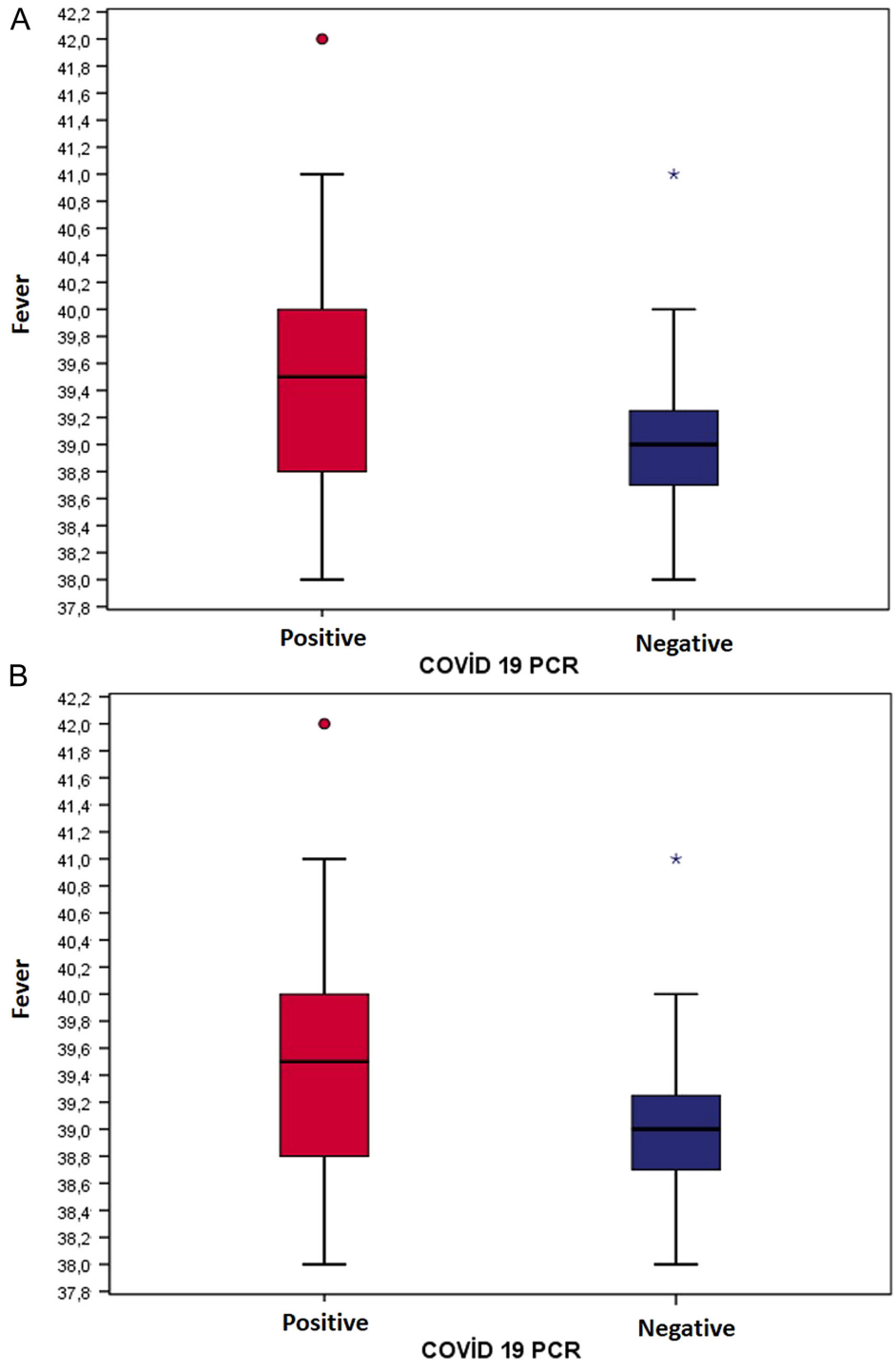

Figure 1. (A) In patients with simple febrile convulsions, higher fever was observed in COVID-19-positive patients. (B) In patients with complex febrile convulsions, higher fever was observed in COVID-19-positive patients.

DISCUSSION

This study may be the first conducted study on the association of FCs and COVID-19 in our country and the report involving the highest number of cases worldwide. Regarding the declaration of COVID-19 as a pandemic, diagnosing, monitoring, and treating COVID-19 are performed according to the guidelines published by the Turkish Ministry of Health, COVID-19 Scientific Committee.

Viral agents play a role in FCs' etiology; however, the underlying mechanisms have not been fully identified. As in other viral agents frequently reported to be associated with FC,[11,12] we do not yet know whether the direct effect of COVID-19 agent causes FC or the fever, commonly seen in COVID-19 disease course, is the etiological factor. In a limited number of articles in the literature, the relationship between seizure and COVID-19 has been examined, and it has been reported

that non-specific triggering factors for COVID-19, such as hypoxia, cytokine storm, and fever, cause seizures.[13] It is well known that fever is the most significant risk factor in FC,[14] and low-grade fever increases its recurrence compared to high-grade fever.[15] Our study determined that the fever was graded higher in the COVID-19-positive group than the COVID-19-negative group, but we did not find any statistically significant difference between the 2 groups. We did not observe any recurrence in our study. However, this might have been because recurrences could be detected during long-term follow-up. On the other hand, in our study, we observed recurrences during the same study period. In our study, the complex FC rate was 50% in the COVID-19-positive group, whereas 25% in the other group. The place and importance of fever in FCs are controversial. Antipyretic drugs have not been found to be beneficial in preventing the recurrence of febrile seizures within the same fever episode.[16] We need to consider here that even though COVID-19-positive FCs were observed at higher-grade fever, their recurrences were more frequent during the same disease period, and this was contrary to the literature because many studies had reported that its recurrence risk was higher when FC occurred in low-grade fever.

Male gender is a risk factor in FCs.[17] In our study, in both the COVID-19-positive and COVID-19-negative groups, FC was more frequently observed in males (58% and 57%, respectively), and this was consistent with the literature.

In FCs, a positive family history (mother, father, sibling) has been reported with a rate of 14%-40%.[18] In this study, maternal FC history was 16.7% in the COVID-19-positive group and 3.6% in the COVID-19-negative group.

The study was conducted in a single center. Thus, a statistically significant difference might not have been observed. We hope that, with future multi-center studies, we will be able to better identify the course of FCs, the most common seizure type in childhood, in COVID-19-positive cases.

CONCLUSION

Seizures occur in the presence of higher-grade fever in COVID-19-positive cases. On the other hand, the probability of seizures to occur focally and recur during the same disease period might be higher. Male gender and maternal history of FCs may be the risk factors.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of the Turkish Ministry of Health, General Directorate of Health Services, Scientific Research Board. Approval of the Bursa City Hospital Ethics committee was obtained with that permission document. (Date: September 16, 2020, Decision No: 2020-7/9).

Informed Consent: Written informed consent was obtained from the parents of the patients who participated in this study.

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