



## **Seizures in Pediatrics with COVID-19 Disease: A Case Series of 5 Patients**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author FZ was the main writer of the manuscript. Authors AK and SB did the patient management. Author BM reviewed the literature. All authors read and approved the final manuscript.*

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**Case Study**

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### **ABSTRACT**

In December 2019, the outbreak of coronavirus started in China, and after a while, it spread worldwide. These diseases can appear with respiratory and gastrointestinal symptoms in pediatrics, but neurological symptoms like seizures are uncommon. Furthermore, there is no specific data about the nervous system manifestation in children. This case series study is aimed to diagnose COVID-19 in children with nervous system manifestation.

**Keywords:** *Seizure; pediatrics; neurological symptoms; coronavirus; COVID-19.*

### **1. INTRODUCTION**

In December 2019, in Wuhan, China, a new coronavirus named severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2), caused a new disease [1].

The mean incubation period of the SARS-CoV-2 virus is estimated to be five days [2]. The initial manifestations of this COVID-19 disease are fever, dry cough, shortness of breath and fatigue; this disease can also cause neurological symptoms. The neurological manifestations

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divided into two groups of the central nervous system and peripheral nervous system. Central nervous system involvement includes headache, dizziness, ataxia, encephalitis, stroke, and seizures [3,4]. Central nervous system symptoms such as headache (13.1%) and dizziness (16.8%), encephalopathy, and delirium, are the most common neurological symptoms in these patients [5,6].

In this study, we report five coronavirus infected children referred to Besat hospital in Sanandaj, Iran, from April to July 2020.

## 2. CASE PRESENTATIONS

### 2.1 Case 1

An 18 month-old boy with a consecutive bilateral tonic-clonic seizure attack (status) was admitted to Besat hospital. He had a three-day history of fever and diarrhea (3-4 per day); he did not experience vomiting and cough; he also had a history of contact with a coronavirus infected patient. On the third day, he experienced five consecutive bilateral tonic-clonic seizures attacks.

He had cardio-respiratory arrest at presentation, and his pupils were double mydriatic; therefore, cardiopulmonary resuscitation (CPR) was started for him, He was also intubated. Patient was resuscitated after five minutes of CPR and was transferred to the pediatric intensive care unit (PICU) where he received phenytoin, phenobarbitone, ceftriazone and vancomycin.

This patient had a past medical history of seizures at four month of age and had been on Sodium Valproate.

His initial laboratory results showed lymphopenia and elevated ESR and CRP (Table 1). Chest CT Scan result revealed bilateral ground glass opacity. Nasopharyngeal PCR was positive for coronavirus, so Hydroxychloroquine and Kaletra (Lopinavir/Ritonavir) were added to his treatment but in spite of this patient's condition

deteriorated and he died three days later from Covid 19 complications.

### 2.2 Case 2

A 53 day-old infant with no past medical history of a specific disease was admitted to the hospital with a consecutive generalized tonic seizure attack (status). He had a two-day history of fever; with no gastrointestinal symptoms or cough. On the second day, he experienced four consecutive generalized tonic seizure attacks.

His primary vital signs were elevated temperature of 39.8°C, a tachycardia of 130 beats/ minute and oxygen saturation of 96%. Patient was transferred to the Pediatric intensive care unit after achieving seizure control. He received P. henobarbitone, Vancomycin and Cefotaxime.

His primary lab results showed elevated CRP (Table 1).

Also, a lumbar puncture performed and showed a normal CSF result.

Patient started coughing on the second day of admission, so a chest CT scan and PCR of nasopharyngeal samples were done to rule out coronavirus infection. In his chest CT, generalized GGO was seen in both lungs and his PCR was positive for coronavirus. He was asked to continue on antibiotics therapy because of the positive findings in support of Coronavirus infection and was eventually discharged home in a good general condition.

### 2.3 Case 3

A 3-year-old boy with a history of febrile convulsion attack was admitted to the hospital with consecutive bilateral tonic-clonic seizure attacks. He had a three-day history of fever and cough without gastrointestinal symptoms and a history of contact with a coronavirus infected patient. On the third day of admission, he experienced four episodes of continuous bilateral tonic-clonic seizure attacks.

**Table 1. Patients primary laboratory results**

	WBC( $\mu$ l)	Neut%	Lymph%	Hb(g/dL)	Plt(/ $\mu$ l)	CRP	ESR(mm/hr)
Case 1	7700	90	10	10	110000	2+	25
Case 2	10600	60	40	13.6	256000	3+	10
Case 3	3000	92	8	10	120000	2+	30
Case 4	6600	90	10	11	200000	NEG	12
Case 5	21100	40	60	11.2	284	NEG	5

He had cardio-respiratory arrested at the first of admission. Patient died despite resuscitation measures.

His laboratory results showed leukopenia, lymphopenia, and elevated levels of CRP (Table 1). The PCR test of nasopharyngeal samples was positive for Coronavirus infection.

#### 2.4 Case 4

A 36 month-old boy was admitted into Besat hospital on account of reduced level of consciousness following continuous bilateral tonic-clonic seizure attacks.

He had a four-day history of fever and cough and on the fourth day, he experienced three consecutive generalized tonic clonus seizure attacks.

He had a birth history of preterm (he had been born at a gestational age of 34 weeks) and had been on hospitalization at the neonatal intensive care unit (NICU) for two weeks. Also he had a past medical history of one febrile convulsion attack when he was two months old.

On admission, patient had a low Glasgow Coma Scale of 8/15, so had to be intubated and transferred to the PICU where he was given Phenytoin, Phenobarbitone, Vancomycin and Ceftriazone. His full blood count result showed lymphopenia (Table 1).

Lumbar puncture was performed, and the laboratory result of CSF fluid was normal.

A chest CT scan and PCR of nasopharyngeal samples were done. The chest CT scan was normal but the PCR test results were positive for coronavirus, so Kaletra was added to his treatment. After 48 hours of admission, the patient became conscious, and was extubated.

He was finally discharged in good general condition after eight days of admission.

#### 2.5 Case 5

A 75 day-old infant with no past medical history of any specific disease was admitted to the hospital with fever and atonic seizures. He had two days history of fever and no gastrointestinal symptoms or cough. On the second day, he experienced three atonic seizure episodes with 5 minutes' intervals; each attack lasting for 10 seconds.

He had a history of close contact with coronavirus infected patients. He was in the same room with the infected patient for 3 hours, and the patient had played with the baby.

His primary vital signs were temperature 38°C, oxygen saturation of 97% and a heart rate of 140 beats/min. He was transferred to the pediatric intensive care unit (PICU) where he received with phenobarbital, vancomycin, and cefotaxime.

His primary lab results showed elevated C-reactive protein (CRP) (Table 1).

In addition, lumbar puncture was performed, and the laboratory result of CSF fluid was normal.

Chest CT was normal, but PCR of nasopharyngeal sample was positive for Coronavirus. He was therefore asked to continue on antibiotics therapy and was finally discharged from the hospital after 14 days with a good general condition.

- Brain CT scan of all cases was normal and had no abnormal findings.

### 3. DISCUSSION

Our study reported five children admitted to Besat hospital in Sanandaj, Iran, with positive PCR tests for COVID-19 disease. Their primary symptoms were fever, cough, vomiting, and diarrhea, and all of them had experienced consecutive generalized tonic/clonic seizure attacks (status) before referring to the emergency department. The mean duration of symptoms before admission was 3.4 days.

Previous studies showed that other types of CoV like MERS-CoV<sup>1</sup> could cause neurological manifestations like intracerebral hemorrhage and polyneuropathy secondary to systemic complications and extended ICU stay [7].

Angiotensin-converting enzyme 2 (ACE2) receptor on human body cells can bind to SARS-CoV-2, so the virus can affect the organs. This receptor is expressed on many organs like the brain, kidneys, small intestine, lung parenchyma, and airways [8,9]. Therefore, SARS-CoV-2 is a neuro-invasive virus found in the brain or cerebrospinal fluid [10].

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<sup>1</sup>Middle East respiratory syndrome-related coronavirus

Many studies have been done on adult patients to evaluate nervous system manifestations of COVID-19. A recent review study concluded that anosmia, ageusia<sup>2</sup>, and headache are the most common neurologic complaints in infected patients. Also, other neurological diagnoses like stroke, impairment of consciousness, seizures, and encephalopathy are reported [11].

Aravinthan et al. did one study in 2020 on 153 patients with a mean age of 71 years old to evaluate the neurological and neuropsychiatric complications of COVID-19; the results showed that the prevalence of cerebrovascular events was 62%; ischemic stroke was the most common cerebrovascular event with the prevalence of 74%, intracerebral hemorrhage occurred in 12%, and CNS vasculitis in 1% [12]. Guillain-Barré syndrome and Miller Fisher syndrome were also reported in coronavirus infected patients [13,14].

Cerebrovascular diseases, encephalopathy, and Guillain-Barré syndrome are life-threatening conditions in coronavirus infected patients [15]. Moreover, the overall quality of life can be affected by CNS involvement in COVID-19 [16].

There is no specific data on the nervous system manifestation of COVID-19 in children. McAbee et al. in 2020 reported one case of an 11-Year-Old Child with encephalitis associated with COVID-19 infection [17]. In 2020, Abdel-Mannan et al. reported four coronavirus infected children with central and peripheral neurological symptoms, and signs such as weakness and encephalopathy were common and were reported in all the cases; other symptoms were headaches, dysarthria, dysphagia, meningism, and cerebellar ataxia, and reduced reflexes. None of them experienced respiratory symptoms [18].

In our study, gastrointestinal and respiratory symptoms appeared before neurologic symptoms. Furthermore, considering that two out of 5 reported patients who had neurological manifestations died, it can be concluded that brain involvement and the appearance of neurological symptoms are factors affecting mortality in children.

The mortality rate in children is very low, and it is 0.69% [19]. There is no data on the factors affecting mortality in pediatrics up till now. However, male sex, advanced age, and past medical of hypertension, diabetes mellitus,

cardiovascular disease, and cerebrovascular disease can increase the risk of mortality in infected adult patients [20].

#### 4. CONCLUSION

According to our study, we can conclude that neurological symptoms can be one of the COVID-19 symptoms but do not manifest as early symptoms of COVID-19 in children. In addition, seizures in the context of coronavirus infection are likely to be more severe and are life threatening in children predicting poor prognosis. Therefore, seizures should be considered a severe manifestation of COVID-19 in children. Early assessment of neurological symptoms in these children is recommended.

#### CONSENT

As per international standard or university standard, patients' gurdians' written consent has been collected and preserved by the author(s).

#### ETHICAL APPROVAL

It is not applicable.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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<sup>2</sup>loss of taste functions of the tongue

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