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SARS-CoV-2 fecal shedding pattern in pediatric patients with acute COVID-19 or COVID-19-associated multisystem inflammatory syndrome

To the editor

The pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), broke out all over the world. Gastrointestinal symptoms, particularly vomiting, are more common in children with COVID-19 compared to adults.[1] Studies showed that a higher proportion of fecal SARS-CoV-2 RNA can be observed in patients with gastrointestinal manifestations.[2] Moreover, viral shedding through feces could continue even after clearance from the respiratory tract, which is observed to be more prevalent in children than in adults, highlighting the importance of fecal-oral transmission in pediatric cases.[3]

We evaluated the SARS-CoV-2 fecal shedding pattern in 42 children with acute COVID-19 or multisystem inflammatory syndrome in children (MIS-C) related to SARS-CoV-2 infection, who were admitted to Children's Medical Center, the hub of excellence in pediatrics in Iran, from September 2020 to April 2021. All included cases were diagnosed with SARS-CoV-2 infection by real-time reverse transcription polymerase chain reaction (rRT-PCR) of nasopharynx specimens or MIS-C based on the Centers for Disease Control and Prevention criteria.[4] This research was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.CHMC.REC.1399.180). Signed informed consent was obtained from all patients' parents or guardians. Rectal swabs were collected from all included pediatric cases on admission day or during the treatment period (initial test) and after discharge (follow-up test). The presence of SARS-CoV-2 RNA was detected by the rRT-PCR method, as previously described.[1] At least one of the following criteria was required for a severe acute COVID-19 diagnosis: SpO_2 93%, PaO_2 60 mmHg, $PaCO_2$ >50 mmHg, a respiratory rate of 70/min (in a case ≤1 year) and 50/min (in a cased >1 year), or lung infiltrates >50%; respiratory failure requiring respiratory support, septic shock development, or critical organ failure requiring intensive care unit care.[4] Moreover, disease severity of cases with MIS-C was assessed based on the vasoactive-inotropic score, degree of respiratory support, and evidence of organ injury.[5]

The median age of the patients was 5 years (range, 13 days to 15 years; interquartile range, 1.5–9.75), including 16 females (38.1%) and 26 males (61.9%). Thirteen children (31%) had underlying conditions, and 7 (16.7%) had immunodeficiency. Of the 42 patients, 19 (45.2%) were diagnosed with MIS-C, and 23 (54.8%) had acute COVID-19. Eight patients (17%) showed severe SARS-CoV-2 infection, and a mortality of 2.4% (1 case) was reported.

The detailed clinical characteristics of the children are shown in Table 1. The main presenting symptoms were fever (n=38, 90.2%), diarrhea (n=19, 45.2%), and vomiting (n=18, 42.9 %). The higher incidence of gastrointestinal symptoms in our study might be due to the inclusion of children with MIS-C as they commonly present gastrointestinal signs and symptoms. The seropositivity for IgG was 30.3% (10 out of 33) and 51.4%

Table 1. Clinical characteristics of the 42 pediatric patients with COVID-19

Characteristic	Acute COVID-19 (n=23)	MIS-C (n=19)	Total (n=42)
Underlying condition	9 (39)	4 (21.1)	13 (31)
Immunodeficiency	5 (21.7)	2 (10.5)	7 (16.7)
Severe infection	0 (0)	8 (42.1)	8 (19)
Family history of COVID-19	20 (87)	10/18 (55.6)	30/41 (73.2)
Mechanical ventilation	0 (0)	1 (5.3)	1 (2.4)
Death	0 (0)	1 (5.3)	1 (2.4)
Signs and symptoms			
Fever	19 (82.6)	19 (100)	38 (90.5)
Cough	6 (26.1)	6 (31.6)	12 (28.6)
Sore throat	1 (4.3)	2 (10.5)	3 (7.1)
Conjunctivitis	1 (4.3)	6 (31.6)	7 (16.7)
Tachypnea	3 (13)	4 (21.1)	7 (16.7)
Chest pain	2 (8.7)	2 (11.1)	4 (9.8)
Rhinorrhea	1 (4.3)	1 (5.6)	2 (4.9)
Vomiting	11 (47.8)	7 (36.8)	18 (42.9)
Headache	3 (13)	5 (26.3)	8 (19)
Abdominal pain	5 (22.7)	7 (36.8)	12 (29.3)
Diarrhea	9 (39.1)	10 (52.6)	19 (45.2)
Respiratory distress	5 (21.7)	5 (31.6)	11 (26.2)
Myalgia	2 (8.7)	1 (5.3)	3 (7.1)
Skin rash	2 (8.7)	8 (42.1)	10 (23.8)

Values are presented as number (%).
COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children

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(18 out of 35) at the initial test and follow-up test, respectively.

Five cases (12%) (4 males, 1 female) had SARS-CoV-2 RNA detected in the rectal swab, 4 at the initial test, and 2 at the follow-up test. One case had positive results both at the initial test and after discharge. The positive rectal test was observed in 2 MIS-C cases (10.5%) and 3 patients (12.5%) with acute COVID-19. MIS-C cases had positive rectal tests only at the initial test. According to the latest systematic review, the positivity rate of RNA in feces of children with positive respiratory SARS-CoV-2 RNA was 86% (95% confidence interval, 73%–96%).[3] The lower incidence of fecal RNA in our study might be due to the time of testing. In fact, we were able to identify the patient who presented with MIS-C, at an early stage. Moreover, changes or differences in treatment strategies between countries and over time may influence rectal SARS-CoV-2 shedding.

The mean duration between symptoms onset and the initial test was 7.0±1.7 days, and the mean duration between the initial test and follow-up test was 16.2±9.9 days. Studies showed that respiratory RNA was more likely to be detected during an early stage of the disease, whereas fecal RNA was more likely to be positive later on during the disease.[6-8]

In a study by Ma et al.,[2] 70% of children (n=10) with positive respiratory SARS-CoV-2 RNA showed positive results in their stool specimen on the fourth week, 40% on the fifth week, and all children tested negative on the sixth week (36–42 days). In another study, only 2 of 7 COVID-19 positive individuals (28.6%) who had been followed for more than 6 days showed rectal shedding after negative conversion of pharyngeal swabs.[9] In the systematic review by Xu et al.,[10] the mean duration of gastrointestinal viral shedding was 23.6±8.8 days from symptom onset, with a range of 10–33 days. In this study, the association between positive SARS-CoV-2 RNA test results and the duration of symptom onset to testing was not statistically significant ($P>0.1$).

The demographic characteristics, clinical symptoms, and laboratory findings of the 5 patients with positive rectal SARS-CoV-2 RNA test are sown in Supplementary 1. There were no significant differences between the positive rectal test result and any of the clinical signs or the laboratory findings. Based on the laboratory test results, a majority of the patients with positive rectal tests (4 out of 4, 100%) had elevated lactate hydrogenase (>250 U/L), prothrombin time >13.5 seconds (4 out of 4, 100%), and partial thromboplastin time >35 seconds (3 out of 4, 75%). There were no significant differences between the positive rectal test result and the severity of the disease.

Our study has some limitations. First, the size of the included cases and cases with positive rectal tests was small. Second, we tested rectal swabs of patients in only 2 time points, and we cannot determine the exact change trend in the test results of patients. Third, we did not follow up children until the point of negative results, therefore, it was not possible to determine the maximum days of viral shedding.

In conclusion, 5 of the 42 pediatric cases (12%) with acute COVID-19 or MIS-C included in our study revealed fecal viral shedding. Our results enhance the current knowledge on the COVID-19 infection in children. However, further studies with larger sample size, longer follow-up duration, evaluating the mechanism of immunomodulatory response in virus clearance and testing the viability of virus isolated from fecal samples are needed.

Setareh Mamishi, MD[1,2], Fatemeh Jalali, MD[1], Sepideh Benvari, MSc[3], Babak Pourakbari, PhD[2,4], Mohammad Reza Abdolsalehi, MD[1], Reihaneh Hosseinpour Sadeghi, MSc[2], Mohammad Shahbabaie, MD[1], Amene Navaeian, MD[1], Shima Mahmoudi, PhD[2,4,5]

[1]Department of Infectious Diseases, Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran; [2]Pediatric Infectious Disease Research Center, Tehran University of Medical Sciences, Tehran, Iran; [3]Department of Microbiology, Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran; [4]Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran; [5]Biotechnology Centre, Silesian University of Technology, Gliwice, Poland

Corresponding Author: Shima Mahmoudi, PhD
Pediatric Infectious Disease Research Center, Pediatrics Center of Excellence, Children's Medical Center Hospital, Dr. Gharib Street, Keshavarz Boulevard, Tehran, Iran
✉Email: sh-mahmoudi@sina.tums.ac.ir
https://orcid.org/0000-0003-3557-6432

Footnotes

Supplementary material: Supplementary Table 1 can be found via https://doi.org/10.3345/cep.2023.00297.

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ORCID:
Setareh Mamishi https://orcid.org/0000-0003-3557-6432
Fatemeh Jalali https://orcid.org/0000-0001-7301-8904
Sepideh Benvari https://orcid.org/0000-0003-3109-783X
Babak Pourakbari https://orcid.org/0000-0002-8956-5432
Mohammad Reza Abdolsalehi https://orcid.org/0000-0002-1991-2339
Reihaneh Hosseinpour Sadeghi https://orcid.org/0000-0003-

4022-3594
Mohammad Shahbabaie https://orcid.org/0009-0008-9105-0439
Amene Navaeian https://orcid.org/0000-0003-1372-9741
Shima Mahmoudi https://orcid.org/0000-0003-3557-6432

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