**Family COVID-19 cluster from an infant without respiratory symptoms**

**Abstract**

Diagnosing cases of coronavirus disease 2019 (COVID-19) with only non-respiratory symptoms has been challenging. We reported the diagnosis of a child positive for COVID-19 with abdominal pain/diarrhea and tracking his family cluster. One member of the family was COVID-19 positive by Real-Time Reverse-Transcription Polymerase Chain Reaction (RT-qPCR) and three other family members had anti-SARS-CoV-2 antibodies.

**Keywords**: asymptomatic cases, coronavirus, COVID-19, SARS-CoV-2

**Introduction**

Coronavirus disease 2019 (COVID-19), an emergent infectious disease caused by the Severe Acute Respiratory Coronavirus 2 (SARS-CoV-2), is a current global health emergency1. The confirmation of presumptive cases is often instigated by the presence of fever and respiratory symptoms2, although other manifestations such as gastrointestinal signs and symptoms with acute diarrhea are common3,4. A gastrointestinal presentation, without respiratory symptoms, poses important challenges, as diarrhea is one of the main causes of emergency consultations in pediatric services, but COVID-19 presentation is not distinguishable from other causes of diarrhea. Moreover, although the investigations of secondary cases among contacts of confirmed COVID-19 cases is an important strategy for control, this is rarely conducted for contacts of individuals who primarily present with a complaint of diarrhea.

We report a child with SARS-CoV-2 who attended an outpatient clinic in Aracaju, Northeast-Brazil with gastrointestinal symptoms and no respiratory problems and the subsequent screening of his close family members.

**Case report**

The index case

A 2-year and 9-months-old boy with diarrhea presented the 3rd May 2020 to a private clinic. The parent indicated the child had had two days of bloody diarrhea, with 6-8 stool episodes per day and no vomiting or significant fever. The child was managed as an ambulatory patient with the number and characteristics of feces turned normal one or two times per day. On examination two days from symptoms initiation (5th May) the child was afebrile and complained of sore throat and moderate abdominal pain. A swab of the naso/oropharynx collected the 7th May (two days after) was positive (cycle threshold [Ct] of 36), but the fecal sample was negative. Immunoglobulin (Ig) M and IgG antibodies tested 12 days after symptom onset were negative. Leukocyte count on day 12 was 8300/mm3, with lymphocytes count of 5644/mm3 (68%). C-Reactive Protein (CRP) and interleukin-6 (IL-6) on day 12 were within normal values. Further IgG and IgM assays on May 21st and 25th were negative (Table 1).

Investigation of contacts:

The mother was a 41 years-old healthy woman who had been in isolation since March 17th. A naso/oropharyngeal swab the 7th May was Real-Time Reverse-Transcription Polymerase Chain Reaction (RT-qPCR) negative, but her IgG test the 15th May was positive and her IgM was negative. Her leukocyte count was normal, her CRP was 16.0 mg/L and IL-6 was normal (Table 1).

The father was 56 years-old, asymptomatic and employed by the oil drilling industry. He had regular contact with people outside the household until the 20th April, his last working day, and sporadic contacts afterwards when purchasing essential supplies at the local shop. He indicated he wore home-made masks and alcohol-based hand-sanitizers when shopping. A naso/oropharyngeal swab the 7th May was negative. IgG and IgM were tested the 15th May and were 0.5 AU/mL (negative) and 16.4 AU/mL (positive), respectively. His leukocyte count and CRP were normal, but his IL-6 was just above the normal range (Table 1). He did not develop symptoms on follow up.

A 16 years-old asymptomatic sister residing in the same household who had no contacts outside her home since April the 20th, when she had visited her grandmother and relatives. Her naso/oropharyngeal swab (11th May) and IgG (15th May) were negative but her IgM (15th May) was positive. Her leukocyte count, CRP and IL-6 were normal (Table 1).

A further 41-year-old asymptomatic aunt who had visited the household the 28th April, had not been in contact with the child since his symptoms started. Her RT-qPCR (15th May), IgG, IgM, leukocyte count, CRP and IL-6 were normal (Table 1).

A 45 years-old asymptomatic uncle, who was unable to maintain social isolation due to work commitments had a positive naso/oropharyngeal RT-PCR the 15th May, but his IgM and IgG taken the same day were negative. His leukocyte count, CRP and IL-6 were normal (Table 1).

Lastly, a 19 years-old female cousin who had maintained social isolation since March the 17th and with contact with her parents and relatives studied here. On May the 9th and 10th she had attended an Emergency service because of two days of abdominal pain and diarrhea. On May the 15th her naso/oropharyngeal swab was negative, and her IgM and IgG collected 21 days after symptom onset were negative. Her leukocyte count, CRP and IL-6 were normal (Table 1). All relatives were followed until May 26th, 23 days after the child symptoms onset.

This is a case report comprising a child with a chief complaint of diarrhea and the clinical history of his six contact family members during the 20 days prior to the child symptoms onset.

The index case's parents and sister live with him in the same house and, therefore, have daily contact. While the uncle, aunt and cousin had contact with the child three times per week, having two hours each meeting. Uncles’ and cousin’ contact was disrupted when the child's symptoms began and diagnosis was defined (Table 1).

Demographic information, medical history, clinical presentation and laboratory findings were collected following standard protocols. Laboratory results included blood tests, CRP, IgM and IgG antibodies and leucocyte profile.

RNA for RT-qPCR assays were extracted from naso/oropharyngeal swabs and stool samples using the BioGene DNA/RNA Extractor Kit (Bioclin, Minas Gerais, Brazil). The RT-PCR was conducted using the BIOMOL OneStep/COVID-19 (BioManguinhos, Oswaldo Cruz Foundation, Brazil), on 7500 Applied Biosystems thermocycler.

Immunoassays for serum IgM and IgG antibodies against SARS-CoV-2 were conducted using a qualitative fluorescent immunoassay (IchromaTM COVID-19, Boditech Med Inc, Republic of Korea).

Serum IL-6 was measured using an enzyme-linked immunosorbent assay (ELISA) (eBioscience, San Diego CA, USA). A standard curve was generated for each set of samples following the manufacturer's instructions.

**Discussion**

The diagnosis of COVID-19 without fever or respiratory symptoms requires a high degree of clinical suspicion or epidemiological links. We report here a child with COVID-19 whose main presentation was of gastrointestinal symptoms without respiratory symptoms. We also describe the clinical findings, molecular and serological assays of the family members with whom he had been in contact up to 20 days before symptom onset. Although all contacts were asymptomatic, the molecular and serological assays demonstrated several relatives had current or past SARS-CoV-2 infections.

Children with SARS-CoV-2 are more likely to have asymptomatic or mild symptoms than adults5. Half of children may have gastrointestinal symptoms in the absence of respiratory symptoms4. Angiotensin-converting enzyme 2 (ACE2) receptors are highly expressed in the small intestine, which may lead to intestinal inflammation and diarrhea6. In this case, SARS-CoV-2 RNA was detected in samples from the respiratory tract, even though the main presentation was a gastrointestinal complaint.

RNA SARS-CoV-2 can be detected in fecal samples and its shedding may be present in feces for a longer time than in the respiratory tract7. However, in this child the stool sample was negative, but the two respiratory samples were positive. The infection's source of the child was unknown, but it could have originated from any of the three family members with SARS-CoV-2 antibodies. The child's father and sister had positive IgG, while the mother had positive IgM. One family member had positive RT-qPCR. As five of out six relatives were asymptomatic, it is possible that asymptomatic transmission had played a role in transmission, which is considered to represent and attributable fraction of 50%-80% of incident infections8.

Our index case did not have detectable antibodies even after 23 days from symptom onset. Non-seroconversion has been reported for SARS-CoV-2, SARS-CoV and Middle East respiratory syndrome (MERS)9.

In summary, this study showed the importance of clinical manifestations other than respiratory for the suspicion and diagnosis of COVID-19 in children with mild gastrointestinal symptoms. We demonstrated how contact tracking can document the spread of infection within a family nucleus. Based on the identification of positive cases of COVID-19, it is necessary to either investigate potentially transmitting contacts or indicate their self-isolation.

References

1. World Health Organization (WHO). IHR Emergency Committee on Novel Coronavirus (2019-nCoV). 2020. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-statement-on-ihr-emergency-committee-on-novel-coronavirus-(2019-ncov).

2. Chavez S, Long B, Koyfman A, Liang SY. Coronavirus Disease (COVID-19): A primer for emergency physicians. Am. J. Emerg. Med. 2020;20:1-10.

3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected

with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.

4. Tian Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and

the possibility of faecal transmission. Aliment. Pharmacol. Ther. 2020;51:843–51.

5. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 Infection in Children. N. Engl. J. Med. 2020;382:1663–5.

6. Liang W, Feng Z, Rao S, Xiao C, Xue X, Lin Z, et al. Diarrhoea may be underestimated: a missing link in 2019 novel coronavirus. Gut 2020;69:1141–3.

7. Santos VS, Gurgel RQ, Cuevas LE, Martins-Filho PR. Prolonged fecal shedding of SARS-CoV-2 in pediatric patients. A quantitative evidence synthesis. J. Pediatr. Gastroenterol. Nutr. 2020.

8. Li R, Pei S, Chen B, Song Y, Zhang T, Yang W, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Science 2020;493:489–93.

9. Dijkman R, Jebbink MF, El Idrissi NB, Pyrc K, Müller MA, Kuijpers TW, et al. Human coronavirus NL63 and 229E seroconversion in children. J. Clin. Microbiol. 2008;46:2368–73.

**CONFLICT OF INTEREST**

The authors have no conflict of interest to declare.