Comparative study of the clinical characteristics and epidemiological trend of 244 COVID-19 infected children with or without GI symptoms

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Gastrointestinal (GI) symptoms1 2 and positive stool severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) detection3 have been reported in COVID-19 infected patients. However, these studies mainly focused on the adult population, and it is still not known whether children with COVID-19 have similar GI involvement.

We here report the clinical characteristics of 244 consecutive COVID-19 positive children from Wuhan, during the period 21 January to 20 March 2020. All were confirmed to have SARS-CoV-2 by reverse transcription-polymerase chain reaction (RT-PCR) on nasopharyngeal swabs. We specifically compared the differences between patients with and without GI symptoms (having at least one of the following: diarrhoea; nausea and vomiting; abdominal pain; and decreased feeding). In our cohort, 34 of 244 (13.9%) presented with GI symptoms on admission. These patients were much younger (14 vs 86 months; $p<0.05$), and more than half were under 3 years old.

For the clinical and laboratory parameters, patients with GI symptoms were more likely to have fever on admission (70.6% vs 35.7%, p<0.05) (table 1). No other significant differences were found between the two groups, including respiratory symptoms, the duration of RT-PCR positivity for COVID-19 and CT of the thorax.

Table 1: Epidemiological and clinical characteristics of COVID-19 children with or without GI symptoms

	GI symptoms (n=34)	Non-GI symptoms (n=210)	P value
Age (months)			
Median (IQR)	14 (3–93)	86 (28–139)	0.01*
Age group distribution (n (%))			0.02*
0–1 month	2 (5.9)	9 (4.3)	
1 month-12 months	14 (41.2)	30 (14.3)	
1–3 years old	4 (11.8)	23 (11.0)	
3–6 years old	3 (8.8)	24 (11.4)	
6–10 years old	5 (14.7)	61 (29.1)	
10–18 years old	6 (17.6)	63 (30.0)	
Sex (male) (n (%))	19 (55.9)	131 (62.4)	0.47
Birth weight (kg)	3.3 (2.9–3.7)	3.3 (3.0–3.6)	0.90
Clinical diagnostic classification (n (%))			0.47
Asymptomatic	0 (0)	51 (24.3)	<0.01*
Acute upper respiratory infection	7 (20.6)	43 (20.4)	
Mild pneumonia	25 (73.5)	107 (51.0)	
Severe pneumonia	0 (0)	7 (3.3)	
Critical pneumonia	2 (5.9)	2 (1.0)	
Contact history with infected family member	28 (79.4)	180 (85.7)	0.62
Symptoms (n (%))			
Fever	24 (70.6)	75 (35.7)	<0.01*
Vomit	23 (67.7)	–	
Diarrhoea	15 (44.1)	–	
Abdominal pain	4 (11.8)	–	
Decreased feeding	8 (23.5)	–	
Stool SARS-CoV-2 RT-PCR results (105 patients tested) (n (%))			
Positive	7/17 (41.2)	32/88 (36.4)	0.70

*denotes statistical significance.

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

One result of interest was the high positivity rate of stool SARS-CoV-2 RT-PCR for 105 patients tested, even in patients without any GI symptoms (7/17 (37.1%)) and those completely asymptomatic (6/18 (33.3%)). Using multivariate analysis, age and presence of fever were the only significant predictive factors for GI symptoms on admission.

When we plotted the whole cohort against admission dates (median admission date: 18th February), we found that more GI patients were admitted in the early period (26 vs 7; p<0.001). Conversely, patients admitted after 18 February were mostly asymptomatic (47 vs 4; p<0.001) (figure 1).

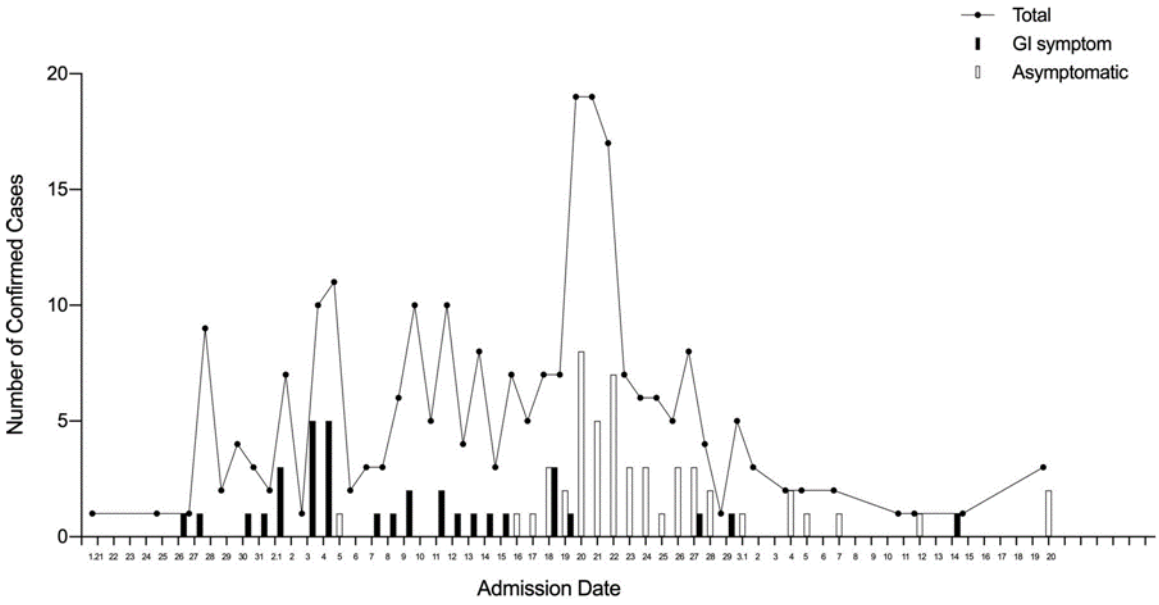

Figure 1: A graph showing the total number of paediatric patients (line), the number of patients admitted with GI symptoms (solid bar) and the number of patients admitted without GI symptoms (blank bar) infected with COVID-19 between 21st January to 20th March 2020.

A percentage of 13.9 of our cohort presented with GI symptoms (11.6% in adults, 30% in one small paediatric study).1 2 4 5 We also found that infants (younger than 2 years old) were more likely to present with GI symptoms than older children. The reason for this difference is not yet clear. Although our results support the findings by Jin et al1 that GI symptoms were associated with fever, the presence of fever in children did not correlate with disease severity.

Previous reports suggested that the presence of GI symptoms in patients with COVID-19 meant the faecal–oral route could be a possible route of transmission.5–7 We did not find any difference in faecal nucleic acid RT-PCR between children with or without GI symptoms. In fact, a high proportion of asymptomatic children were also found to have positive RT-PCR in stool. Our findings would therefore suggest RT-PCR detection of the virus was not due to gut infection but coming instead from the respiratory tract from swallowed sputum. Although detection of viral RNA without additional virological evidence does not necessarily imply infection and faecal–oral spread, live SARS-CoV-2 detected on electron microscopy in stool samples8 and elevated concentrations of SARS-CoV-2 detected in patients' toilet areas9 in recent reports mean that faecal–oral transmission remains a possibility. Contact precaution should be exercised in dealing with the excreta of patients with COVID-19, whether they have GI symptoms or not.

In contrast to adult series,10 11 our study showed a downward trend of children presenting with GI symptoms over time. Furthermore, most of the children were infected via family contact (85.2%) rather than community acquired. As the epidemic progressed in Wuhan, more diagnostic tests done

led to earlier disease detection through contact screening. This observation could be useful for public health planning in countries still experiencing the early stage of the pandemic. An increase in asymptomatic infections also means the public should remain on guard at all times.

References

1. Jin X, Lian J-S, Hu J-H, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut 2020;69:1002–9.doi:10.1136/gutjnl-2020-320926pmid:http://www.ncbi.nlm.nih.gov/pubmed/32213556
2. Lin L, Jiang X, Zhang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut 2020;69:997–1001.doi:10.1136/gutjnl-2020-
3. Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology 2020;158:1831–3.
4. Zhou Z, Zhao N, Shu Y, et al. Effect of gastrointestinal symptoms on patients infected with coronavirus disease 2019. Gastroenterology 2020;5085:30362–0.doi:10.1053/j.gastro.2020.03.020pmid:http://www.ncbi.nlm.nih.gov/pubmed/32199880
5. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. Nat Med 2020;26:502–5 https://doi.org/doi:10.1038/s41591-020-0817-4pmid:http://www.ncbi.nlm.nih.gov/pubmed/32284613
6. Chen Y, Chen L, Deng Q, et al. The presence of SARS-CoV-2 RNA in the feces of COVID-19 patients. J Med Virol 2020. doi:doi:10.1002/jmv.25825. [Epub ahead of print: 03 Apr 2020].pmid:http://www.ncbi.nlm.nih.gov/pubmed/32243607
7. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. Lancet Gastroenterol Hepatol 2020;5:434–5.doi:10.1016/S2468-1253(20)30083-2pmid:http://www.ncbi.nlm.nih.gov/pubmed/32199469
8. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020. doi:doi:10.1001/jama.2020.3786. [Epub ahead of print: 11 Mar 2020].pmid:http://www.ncbi.nlm.nih.gov/pubmed/32159775
9. Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. Nature 2020. doi:doi:10.1038/s41586-020-2271-3. [Epub ahead of print: 27 Apr 2020].pmid:http://www.ncbi.nlm.nih.gov/pubmed/32340022
10. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.doi:10.1016/S0140-6736(20)30183-5pmid:http://www.ncbi.nlm.nih.gov/pubmed/31986264
11. Luo S, Zhang X, Xu H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). Clin Gastroenterol Hepatol 2020;3565:30401–8.

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