

## GI symptoms as early signs of COVID-19 in hospitalised Italian patients

In their recent publication in *Gut*, Lin *et al* report 11% of patients infected with SARS-CoV-2 (COVID-19) to present at admission with GI symptoms<sup>1</sup>; early observations reported that COVID-19 could present with GI symptoms in 3% of patients.<sup>2,3</sup> Diarrhoea, nausea, vomiting and/or abdominal pain or discomfort have been described at disease onset or even before respiratory symptoms.<sup>4–7</sup>

We investigated all consecutive individuals suspected to harbour COVID-19 and admitted at the General Hospital of Crema between 21 February and 13 March 2020 to assess prevalence and features of GI symptoms in COVID-19 patients and their correlation with medical history, disease course and outcome.

All suspected individuals admitted to the hospital underwent a standardised work-up. Based on clinical, laboratory and radiological findings, patients were discharged to quarantine or hospitalised. Demographic data, date of onset and type of symptoms at admission, including GI symptoms (as either nausea, or vomiting or diarrhoea or abdominal pain), and hospitalisation data were recorded. Primary outcomes were: need of continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV), intensive care unit (ICU) admission and death.

Among 411 consecutive COVID-19 patients (with positive RT-PCR), 42 (10.2%, 15 females and 27 males, mean age  $68.2 \pm 14.2$ ) reported GI symptoms including nausea (18, 4.3%), vomiting (16, 3.8%), diarrhoea (15, 3.6%) or abdominal pain (5, 1.2%). GI symptoms had a mean onset of  $4.9 \pm 4.4$  days (range 1–20) before admission. Absence of cough was reported in 35/42 (83%) patients with GI symptoms compared with 225/369 (61%) patients without GI symptoms ( $p=0.004$ ), with 15% vs 13% of them, respectively, having negative chest imaging. The frequency of fever was similar ( $p=0.7$ ) in the two groups. In 5 of 411 patients (1.2%), GI symptoms were neither associated with fever nor cough. GI symptoms did not show any significant

correlation with syncope ( $p=0.3$ ), use of ACE inhibitors ( $p=0.1$ ), presence of comorbidities ( $p=0.3$ ) or use of multiple drugs ( $p=0.7$ ). Of the 42 patients presenting with GI symptoms, 9 (21.4%) required CPAP/NIV, 1 (2.3%) was admitted to ICU and 4 (9.5%) died. Table 1 shows correlation of GI symptoms with outcomes as either CPAP/NIV or ICU admission or death.

Our finding of 10% of patients confirms that the prevalence of GI symptoms at onset is not negligible.<sup>1,4</sup>

GI symptoms can herald COVID-19 as they presented on average 4.9 days before admission, with a very wide range with up to 20 days before admission. Our data confirm the importance of including GI symptoms among the spectrum of COVID-19 features, to allow early diagnosis and appropriate treatments even in patients without respiratory symptoms. This could be of particular importance considering the rapid human-to-human transmission among close contacts, which could be related to GI viral infection and potential oral-faecal transmission, possibly persisting even after viral clearance from the respiratory tract.<sup>5,6,8-10</sup> In our cohort, GI symptoms did not correlate with fever, syncope, use of ACE inhibitors or multiple drugs, comorbidities. Conversely, we found a strong correlation with the absence of cough: we suggest that, as rate of lung involvement was similar in the two groups, patients with GI involvement might have a more silent lung involvement. Even if a possibly more benign disease course in patients with GI symptoms could be suggested by the trend of ICU admissions and deaths, which was lower compared with patients without GI symptoms at onset, the difference proved non-significant.

GI manifestations of COVID-19 are early, and possibly isolated, signs of the disease. Patient management and isolation policies should be accordingly tailored.

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**Table 1** Correlation of GI symptoms with CPAP/NIV, ICU admission or death

	GI symptoms	Non-GI symptoms	P value
CPAP/NIV, n (%)	9 (21.4)	103 (27.9)	0.37
ICU, n (%)	1 (2.4)	27 (7.3)	0.23
Death, n (%)	4 (9.5)	68 (18.4)	0.15

CPAP, continuous positive airway pressure; ICU, intensive care unit; NIV, non-invasive ventilation.

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## REFERENCES

- Lin L, Jiang X, Zhang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. *Gut* 2020;69:997–1001.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.
- 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.
- Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential Fecal-Oral transmission. *Gastroenterology* 2020;158:1518–9.
- Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020;158:1831–3.
- Gao QY, Chen YX, Fang JY. 2019 novel coronavirus infection and gastrointestinal tract. *J Dig Dis* 2020;21:125–6.
- Zhang W, Du R-H, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect* 2020;9:386–9.
- Zhang H, Kang Z, Gong H, et al. Digestive system is a potential route of COVID-19: an analysis of single-cell coexpression pattern of key proteins in viral entry process. *Gut* 2020;69:1010–8.
- Ng SC, Tilg H. COVID-19 and the gastrointestinal tract: more than meets the eye. *Gut* 2020;69:973–4.