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COMMENTARY

Diarrhea: An underestimated symptom in Coronavirus disease 2019



Summary In a retrospective study in the *Nord Franche-Comté* hospital conducted between March 1st and March 17th 2020, and compared to the review of Li et al., diarrhea was a main symptom in patients with COVID-19. Out of the 114 patients, 55 (48%) had diarrhea; it was the fifth most common symptom. In the group of patients with diarrhea, the median age was 56 years (± 18) and 32 (58%) were female. Only 2 patients (3.6%) had a past history of inflammatory bowel disease. Fifty-six percent of patients ($n=30/54$) were hospitalised. Diarrhea appeared 4.5 days (± 1.8) after the onset of the first other symptoms in COVID-19. Of the 55 patients with diarrhea, 29 (52.7%) had at least one simultaneous gastrointestinal (GI) symptom other than diarrhea. Twenty-five patients (45.5%) had nausea, 19 patients (34.5%) had abdominal pain and 9 (16.3%) had vomiting. Myalgia, sore throat, sneezing and the other GI symptoms were statistically more frequent in the group with diarrhea than in the group without diarrhea ($P < 0.05$).

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Editorial

We conducted a retrospective study in the *Nord Franche-Comté* Hospital since a major French cluster of COVID-19 began on March 1st 2020 in Mulhouse city (less than 30 miles from our hospital). Between March 1st and March 17th 2020, we reported the data about 114 patients infected with COVID-19. For each patient, the diagnosis was confirmed by real-time RT-PCR on respiratory samples [1]. Out of the 114 patients, 55 (48%) had diarrhea. In our study, the main symptoms (> 50% of cases) were fatigue (107 [94%]), cough (92 [81%]), fever ($> 38^\circ\text{C}$) for 90 patients [79%] and pain syndrome (78 [68%]). Diarrhea was the fifth most common symptom followed by anosmia. In the group of patients with diarrhea, the median age was 56 years (± 18) and 32 (58%) were female. Only 2 patients (3.6%) had a past history of inflammatory bowel disease. Fifty-six percent of patients ($n=30/54$) were hospitalised. Diarrhea appeared 4.5 days (± 1.8) after the onset of the first other symptoms in COVID-19. Of the 55 patients with diarrhea, 29 (52.7%) had at least one simultaneous gastrointestinal (GI) symptom other than diarrhea. Twenty-five patients (45.5%) had nausea, 19

patients (34.5%) had abdominal pain and 9 (16.3%) had vomiting. The symptoms, which were statistically more frequent in the group with diarrhea than in the group without diarrhea, were: myalgia (44 vs. 36, $P=0.05$), sore throat (21 vs. 11, $P=0.027$), sneezing (22 vs. 10, $P=0.006$) and the other GI symptoms: nausea (25 vs. 12, $P=0.008$), abdominal pain (19 vs. 7, $P=0.004$) and vomiting (9 vs. 2, $P=0.028$). It is important to note that patients with diarrhea were less admitted in intensive care unit (ICU) for severe acute respiratory distress syndrome (4 vs. 8, $P=0.027$).

We strongly agree with Le et al [2], that SARS-CoV-2 invades the intestine. Patients with COVID-19 may develop GI symptoms [3], especially in cases with pre-existing digestive diseases [4]. It is known that the entry of SARS-CoV into human host cells is mediated mainly by a cellular receptor angiotensin-converting enzyme 2 (ACE2), which is expressed in human airway epithelia, lung parenchyma, but also in small intestine cells, which explains these clinical features [5].

In other parts, we found different results than Li et al. have about the occurrence of diarrhea. Diarrhea was present in half of our patients; compared to the review of Li et al.,

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diarrhea was clearly more often noticed in our study. A study with a prospective methodology confirmed our data. Lechien et al. described an occurrence of diarrhea in 51% of cases in 417 mild-to-moderate COVID-19 patients [6]. We can argue that their population was only ambulatory cases with mild or moderate COVID-19 and possibly the occurrence of diarrhea in hospitalised patients is different. However, more than half of our patients were hospitalised, and we have the same result. Our main point is that diarrhea is probably more prevalent than 5.8% in cases of COVID-19. We have few assumptions to explain the differences between Asia studies in comparison to these results. Firstly, the theoretical possibility of mutation of SARS-CoV-2 viral genome can be associated with a clinical impact, but not described until now. On the other hand, the affinity of SARS-CoV-2 for the ACE2 can be specific to an ethnic group and explain a variability of clinical expression between different ethnic groups. Finally, most of the studies in the review of Li et al. had a retrospective methodology. Our study was also retrospective, and data was collected from the medical files of patients; however, we have a strong and accurate description of functional symptoms due to our national guidelines, which recommended a home follow-up for patients who were not hospitalised [7]. Practically, patients, who were not hospitalised or patients who were discharged, were called 7 days (\pm 7 days) after the first symptoms and every week until their recoveries to follow their clinical evolution.

Another systematic review and meta-analysis showed that median fecal viral load (VL) was higher in patients with diarrhea than the VL in patients without diarrhea (5.1 log copies/mL vs. 3.9 log copies/mL; $P=0.06$) [8]. The same authors showed that Virus RNA was detected in stool samples from 48% patients—even in stool collected after respiratory samples tested negative [8], which concludes that stool samples are highly contagious in patients with COVID-19—even during patient recovery.

In this epidemic context, the diagnosis of COVID-19 should be considered for patients with GI symptoms. This will help to prevent the transmission of the virus in hospital settings, especially to health care workers and to not delay the management of patients with GI presentation. Diarrhea is the main GI symptom and seems to be present in half of patients with COVID-19. This data needs to be spread in the medical community and needs to be confirmed by other studies.

Contribution

SZ, TK and JNKO collected the epidemiological and clinical data and processed statistical data. SZ and TK drafted the manuscript. LT, PYR and VG revised the final manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

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